EDITOR'S CHOICE

EXTENDED REPORT

Smoking and risk of incident psoriatic arthritis in US women

Wenqing Li,[1] Jiali Han,[1,2,3] Abrar A Qureshi[1,2]

► Additional data (supplementary tables) are published online only. To view these files please visit the journal online (http://ard.bmj.com/content/71/6.toc).

[1]Department of Dermatology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA [2]Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA [3]Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA

Correspondence to
Abrar A Qureshi, Department of Dermatology, Harvard Medical School, Brigham and Women's Hospital, 45 Francis Street, 221L, Boston, MA 02115, USA; aqureshi@bics.bwh.harvard.edu.

Received 6 July 2011
Accepted 10 September 2011
Published Online First 8 November 2011

ABSTRACT

Objectives Psoriatic arthritis (PsA) is an inflammatory arthritis that is associated with psoriasis. Previous studies have found an association between smoking and psoriasis, but the association with PsA is unclear. The authors aimed to evaluate the association between smoking and the risk of incident PsA in a large cohort of women.

Methods 94 874 participants were included from the Nurses' Health Study II over a 14-year period (1991–2005). Information on smoking was collected biennially during follow-up. The incidence of clinician-diagnosed PsA was ascertained and confirmed by self-reported questionnaires.

Results During 1 303 970 person-years' follow-up, the authors identified 157 incident PsA cases. Among total participants, smoking was associated with an elevated risk of incident PsA. Compared with never smokers, the RR was 1.54 for past smokers (95% CI 1.06 to 2.24) and 3.13 for current smokers (95% CI 2.08 to 4.71). With increasing smoking duration or pack-years, the risk of PsA increased monotonically (p for trend <0.0001). The increase in risk was particularly significant for PsA cases with more severe phenotypes. Secondary analysis among participants developing psoriasis during the follow-up replicated the association, demonstrating an increased risk of PsA among psoriasis cases. The risk was significant for those with higher cumulative measures of smoking or PsA cases with more severe phenotypes.

Conclusion In this study smoking was found to be associated with a risk of PsA and cumulative measures of smoking were also associated with a higher risk of PsA among women.

Psoriatic arthritis (PsA) is an inflammatory joint condition affecting an estimated 520 000 individuals in the US population.[1] As a pleomorphic clinical entity, PsA occurs in 6–42% of psoriasis cases and the onset of joint symptoms does not usually occur until 8–10 years' duration of psoriasis skin lesions.[1 2]

A delayed diagnosis and treatment of PsA may lead to an erosive arthropathy and impair quality of life.[1] PsA can augment the risk of incident diabetes and cardiovascular disease beyond the effect of psoriasis (unpublished data). Evidence is conflicting on the severity of skin phenotypes between psoriasis and PsA.[1 3–5] Therefore, prevention and early detection is warranted by understanding the risk factors for PsA.

The unfavourable cutaneous and joint effects of smoking have been suggested from past association studies.[6 7] However, only sparse evidence regarding the association between smoking and PsA has been reported.[8–12] To the best of our knowledge, no prospective data on smoking and PsA have been reported thus far.

In this study, we investigated the association between smoking status, duration, intensity and incidence of PsA in 94 874 participants from the Nurses' Health Study II (NHS II).

METHODS
Study cohort
NHS II is an ongoing longitudinal cohort of women that was established in 1989 when 116 430 female nurses aged 25–42 years returned a baseline questionnaire on their medical history and lifestyle practices. Biennially, cohort members receive a questionnaire enquiring about diseases and health-related factors. The follow-up rate exceeds 90%.

Assessment of main exposure
In 1989, participants responded to a question on the lifetime history of smoking 20 packs (one pack equals 20 cigarettes) of cigarettes or more and if they were a past smoker, how many years had passed since quitting (<1 or ≥1 year). The questionnaire enquired about the quantities of smoking at different ages (<15, 15–19, 20–24, 25–29, 30–35 and 36–42 years) in six categories (1–4, 5–14, 15–24, 25–34, 35–44 and ≥45). Biennially, participants reported their smoking status. These questionnaires also enquired about the quantity of smoking in current smokers by the number of cigarettes per day in the above-mentioned six categories.

Based on information obtained biennially, smoking duration was obtained by deducting the age at smoking onset from the current age for current smokers, or from the age of cessation for past smokers. The pack-years were evaluated as the number of packs per day multiplied by the number of years of smoking.

We have the detailed information on smoking biennially for 115 770 participants from 1989, including smoking status, intensity, duration, etc. There was no marked difference in the main characteristics between those with complete and those with missing information on smoking.

Assessment of main outcome (PsA)
In 2005, NHS II participants responded to a question on clinician-diagnosed psoriasis and the diagnosis date (before 1991, 1991–4, 1995–8, 1999–2002 or 2003–5). Of the 97 476 responders, 2529 women reported psoriasis; 1151 cases occurred since 1991.

Table 1 Age-standardised baseline characteristics of study participants by smoking status, NHS II*

	Smoking status		
	Never	Past	Current
Age,† mean (SD), years	35.8 (4.7)	37.0 (4.5)	36.6 (4.6)
Body mass index, kg/m², mean (SD)	24.6 (5.3)	24.6 (5.2)	24.5 (5.1)
Alcohol intake, g/day, mean (SD)	2.4 (4.9)	4.3 (6.7)	5.2 (9.0)
Vigorous physical activity, metabolic equivalent h/week, mean (SD)	13.3 (21.9)	15.2 (24.8)	12.9 (22.2)
Postmenopausal (yes, %)	3.2	3.0	4.5
Personal history of chronic diseases (yes, %)			
Diabetes	0.6	0.5	0.4
Cancer	1.2	1.7	1.5
Cardiovascular disease	0.4	0.4	0.5
Hypertension	3.4	3.1	3.0
Hypercholesterolaemia	9.0	8.8	10.1

*Characteristics of participants at the beginning of follow-up (return date of the 1991 questionnaire). Values are means (SD) or percentages and are standardised to the age distribution of the study population.
†Values are not age-adjusted.
NHS II, Nurses' Health Study II.

Table 2 Age and multivariate-adjusted RR for the association of smoking status with the risk of PsA among all participants*

	Cases	Person-years	Age-adjusted RR (95% CI)	Multivariate-adjusted RR† (95% CI)
Reference: never smokers	76	865 189	1.00	1.00
Smoking status				
Past smokers	46	309 749	1.55 (1.07 to 2.23)	1.54 (1.06 to 2.24)
Current smokers	35	129 032	3.08 (2.06 to 4.61)	3.12 (2.07 to 4.69)
1–14 cigarettes/day	12	62 479	2.19 (1.19 to 4.02)	2.34 (1.27 to 4.33)
≥15 cigarettes/day	23	66 553	3.92 (2.45 to 6.27)	3.77 (2.35 to 6.06)
p for trend			<0.0001	<0.0001
Duration, years				
<25	55	366 471	1.68 (1.19 to 2.38)	1.70 (1.19 to 2.42)
≥25	26	72 310	3.20 (2.02 to 5.07)	3.12 (1.96 to 4.97)
p for trend			<0.0001	<0.0001
Pack-years				
<20	44	342 974	1.43 (0.99 to 2.08)	1.48 (1.02 to 2.16)
20–44	34	91 129	3.67 (2.42 to 5.56)	3.33 (2.19 to 5.06)
≥45	3	4678	4.53 (1.41 to 14.56)	3.91 (1.21 to 12.59)
p for trend			<0.0001	<0.0001

*Psoriasis cases with only skin phenotypes were excluded during the follow-up.
†Adjusted for age (continuous variable), body mass index (<18.5, 18.5–24.9, 25–29.9, 30–34.9 or ≥35 kg/m²), alcohol drinking (no, <4.9, 5.0–9.9, 10–14.9, 15–29.9 or ≥30.0 g/day), vigorous physical activity (metabolic equivalent h/week, in quintiles).
PsA, psoriatic arthritis.

We confirmed self-reported psoriasis by using the psoriasis screening tool (PST) questionnaire, which enquired about the type of clinicians making the diagnosis and the phenotypes.[13] We developed scoring algorithms based on multiple a priori hypotheses to assign a diagnosis according to the response. The PST reached 99% sensitivity and 94% specificity for psoriasis screening.[13] This questionnaire was mailed to 1886 participants who self-reported psoriasis and responded to the 2007 main questionnaire; 1637 (87%) responded and 1511 (92%) were confirmed.

The diagnosis of PsA was confirmed by using the psoriatic arthritis screening and evaluation (PASE) questionnaire, which includes a symptom scale with seven items and a function scale with eight items.[14] Details of the instrument design and pilot studies have been described previously.[14 15] For each item, participants chose one of five categories relating to agreement (strongly agree to strongly disagree). A total score of 47 or greater has been shown in our pilot study to identify PsA with a high sensitivity and specificity.[14 15] PASE scores were positively associated with the 28-joint disease activity score (unpublished data). PASE has good test–retest reliability and is sensitive to change with an individual's response to therapy.[15] Furthermore, it can distinguish between symptoms of PsA and osteoarthritis.[14]

Statistical analysis

We performed two sets of association analyses. One was analysed among the total participants. The other set was performed by only including individuals with psoriasis to evaluate the risk of PsA associated with smoking among those with psoriasis. We excluded self-reported psoriasis cases that were not validated for the main analysis. Simultaneously, we performed a sensitivity analysis by using all self-reports. Of the 97 476 responders, for both the two sets, we excluded participants with the psoriasis item passing through (N=58), PsA or psoriasis that occurred before 1991 (N=1376), self-reported psoriasis cases who were not confirmed (N=97) or did not respond to the PST or PASE questionnaire (N=467), PsA cases with a lack of diagnosis date (N=2), and participants with missing information on smoking (N=506). For the first set, we excluded incident psoriatics without joint phenotypes in the first follow-up period (N=96); therefore 94 874 participants remained. For the second set, we

Table 3 Age and multivariate-adjusted RR for the association between smoking and the risk of PsA with different severity scores*

	Person-years	Scores 47–57	Multivariate-adjusted RR† (95% CI)	Scores ≥57	Multivariate-adjusted RR† (95% CI)
Reference: never smokers	865 189	54	1.00	22	1.00
Smoking status					
Past smokers	309 749	35	1.61 (1.04 to 2.48)	11	1.34 (0.64 to 2.79)
Current smokers	129 032	19	2.30 (1.35 to 3.91)	16	5.34 (2.78 to 10.28)
1–14 cigarettes/day	62 479	7	1.88 (0.85 to 4.16)	5	3.62 (1.36 to 9.65)
≥15 cigarettes/day	66 553	12	2.64 (1.40 to 4.98)	11	6.81 (3.27 to 14.16)
p for trend			0.002		<0.0001
Duration, years					
<25	366 471	42	1.80 (1.19 to 2.72)	13	1.43 (0.71 to 2.86)
≥25	72 310	12	1.80 (0.95 to 3.43)	14	7.89 (3.81 to 16.35)
p for trend			0.002		<0.0001
Pack-years					
<20	342 974	33	1.54 (0.99 to 2.40)	11	1.32 (0.64 to 2.75)
≥20	95 807	21	2.47 (1.47 to 4.17)	16	6.05 (3.08 to 11.89)
p for trend			0.001		<0.0001

*Psoriasis cases with only skin phenotypes were excluded during the follow-up. PsA cases were classified into two groups by the cutoff of scores at 57, picked to include those with the top third of the scores into one category.
†Adjusted for age (continuous variable), body mass index (<18.5, 18.5–24.9, 25–29.9, 30–34.9 or ≥35 kg/m^2), alcohol drinking (no, <4.9, 5.0–9.9, 10–14.9, 15–29.9 or ≥30.0 g/day), vigorous physical activity (metabolic equivalent h/week, in quintiles).
PsA, psoriatic arthritis.

Table 4 Age and multivariate-adjusted RR for the association between smoking and the risk of PsA among participants with psoriasis

	Cases	Person-years	Age-adjusted RR (95% CI)	Multivariate-adjusted RR* (95% CI)
Reference: never smokers	76	2356	1.00	1.00
Smoking status				
Past smokers	46	1191	1.17 (0.77 to 1.78)	1.39 (0.89 to 2.16)
Current smokers	35	805	1.56 (0.98 to 2.47)	1.62 (1.00 to 2.63)
1–14 cigarettes/day	12	328	1.12 (0.55 to 2.29)	1.22 (0.58 to 2.56)
≥15 cigarettes/day	23	477	1.91 (1.11 to 3.27)	1.93 (1.09 to 3.40)
p for trend			0.004	0.006
Duration, years				
<25	55	1680	1.18 (0.81 to 1.74)	1.35 (0.90 to 2.04)
≥25	26	316	1.85 (1.08 to 3.17)	1.90 (1.09 to 3.33)
p for trend			0.024	0.012
Pack-years				
<20	44	1453	1.08 (0.71 to 1.63)	1.22 (0.79 to 1.89)
≥20	37	543	1.87 (1.17 to 3.01)	2.02 (1.24 to 3.29)
p for trend			0.084	0.082

Adjusted for age (continuous variable), body mass index (<18.5, 18.5–24.9, 259–29.9, 30–34.9 or ≥35 kg/m^2), alcohol drinking (no, <4.9, 5.0–9.9, 10–14.9, 15–29.9 or ≥30.0 g/day), vigorous physical activity (metabolic equivalent h/week, in quintiles).
PsA, psoriatic arthritis.

excluded participants who did not develop psoriasis (N=94 389); 581 with confirmed psoriasis remained.

Person-years of follow-up were calculated by deducting the return date of the 1991 questionnaire from the date of PsA diagnosis, or June 2005, whichever came first.

Information on smoking was updated during the follow-up. Smoking status was categorised as never, past and current. The quantities of current smokers were classified to 1–14 or 15 or more cigarettes per day. Other variables included smoking duration (<25 or ≥25 years) and pack-years (<20, 20–44 or ≥45 pack-years).

Stratified by age and follow-up interval, we performed Cox proportional hazards analysis to calculate the age and multivariate-adjusted RR and 95% CI for the association between smoking and incident PsA. Multivariate-adjusted analysis was performed after adjusting for age (continuous variable), body mass index (<18.5, 18.5–24.9, 25–29.9, 30–34.9 or ≥35 kg/m^2), vigorous physical activity (metabolic equivalent h/week, in quintiles) and alcohol intake (0, <4.9, 5.0–9.9, 10–14.9, 15–29.9 or ≥30.0 g/day). As a sensitivity analysis, postmenopausal hormone use (premenopausal, never, or ever users), personal history of cancer, diabetes, cardiovascular disease, hypertension and hypercholesterolaemia (yes or no) were concomitantly adjusted for. For multicategorical measures of smoking, trend tests were carried out by using the median in different categories. All analyses were updated because the variables are all time varying.

We performed a sensitivity analysis in a case–control design to include all PsA and confirmed psoriasis cases before and after 1991.

We performed association analyses between smoking and the risk of PsA with different severity scores (47–57 or ≥57). We set the cutoff value as 57 because approximately a third of the PsA cases in our study had a score higher than 57.

Statistical analysis system software (SAS, version 9.2) was used to conduct statistical analyses. All tests were two-tailed, and the significance level was set at p<0.05.

Table 5 Age and multivariate-adjusted RR for the association between smoking and the risk of PsA with different severity scores among participants with psoriasis*

	Person-years	Scores 47–57	Multivariate-adjusted RR† (95% CI)	Scores ≥57	Multivariate-adjusted RR† (95% CI)
Reference: never smokers	2356	54	1.00	22	1.00
Smoking status					
Past smokers	1191	35	1.35 (0.78 to 2.35)	11	1.21 (0.51 to 2.87)
Current smokers	805	19	1.27 (0.68 to 2.39)	16	2.72 (1.15 to 6.42)
1–14 cigarettes/day	328	7	0.93 (0.35 to 2.47)	5	1.95 (0.57 to 6.69)
≥15 cigarettes/day	477	12	1.55 (0.73 to 3.28)	11	3.48 (1.24 to 9.77)
p for trend			0.146		0.017
Duration, years					
<25	1680	42	1.32 (0.80 to 2.19)	13	1.15 (0.50 to 2.62)
≥25	316	12	1.30 (0.61 to 2.79)	14	4.29 (1.65 to 11.18)
p for trend			0.259		0.005
Pack-years					
<20	1453	33	1.19 (0.69 to 2.03)	11	0.94 (0.38 to 2.30)
≥20	543	21	1.61 (0.85 to 3.06)	16	3.86 (1.62 to 9.19)
p for trend			0.592		0.030

*PsA cases were classified into two groups by the cutoff of scores at 57, picked to include those with the top third of the scores into one category.
†Adjusted for age (continuous variable), body mass index (<18.5, 18.5–24.9, 25–29.9, 30–34.9 or ≥35 kg/m^2), alcohol drinking (no, <4.9, 5.0–9.9, 10–14.9, 15–29.9 or ≥30.0 g/day), vigorous physical activity (metabolic equivalent h/week, in quintiles).
PsA, psoriatic arthritis.

The participants' completion and return of the self-administered questionnaires was accepted as informed consent for the present study.

RESULTS

The age-adjusted baseline characteristics of the participants by smoking status are reported in table 1. Alcohol intake tended to increase from the never smokers to the current smokers.

During 1 303 970 person-years of follow-up, 157 were identified as PsA. Compared with never smokers, we observed an increased risk of incident PsA among past (multivariate-adjusted RR 1.54, 95% CI 1.06 to 2.24) or current smokers (RR 3.12, 95% CI 2.07 to 4.69). The risk of PsA was monotonically associated with increasing smoking quantities among current smokers (p for trend <0.0001; table 2). There was a graded association between duration or pack-years of smoking and the risk of PsA (p for trend <0.0001). The RR was 1.70 for duration less than 25 years and 3.12 for 25 years or over; 1.48 for less than 20 pack-years, 3.33 for 20–44 pack-years and 3.91 for 45 or more pack-years.

We evaluated the association between smoking and PsA with different severity scores. The association appears much stronger for PsA with scores of 57 or greater (table 3).

We repeated the analyses after excluding all participants without developing psoriasis to evaluate the risk of PsA among psoriasis cases. As is shown in table 4, the risk of PsA among confirmed psoriasis was monotonically elevated with smoking intensity and duration, but only significantly increased among current smokers with 15 or more cigarettes per day (RR 1.93, 95% CI 1.09 to 3.40), those with duration of 25 years or more (RR 1.90, 95% CI 1.09 to 3.33), or 20 or more pack-years (RR 2.02, 95% CI 1.24 to 3.29). We also evaluated the association by using all self-reported individuals with psoriasis and observed similar results (see supplementary table S1, available online only).

Among individuals with psoriasis, the risk of PsA with more severe phenotypes (PASE score ≥57) was remarkably elevated with the increasing smoking intensity or duration (p for trend <0.05; table 5). However, we did not observe a significant association for PsA with PASE scores of 47–57.

Secondary analyses were performed to adjust for postmenopausal hormone use and personal history of chronic diseases. The association was only slightly attenuated. Secondary analyses were also performed by excluding baseline chronic diseases, and no material change was observed (data not shown). We conducted a case–control analysis to include all psoriasis and PsA cases before and after 1991 and the association remains robust (see supplementary tables S2 and 3, available online only).

DISCUSSION

In this study, we observed that smokers were at an independently increased risk of developing PsA. The risk was positively correlated with smoking intensity and duration.

PsA is a chronic inflammatory arthritis associated with psoriasis.[1][2] It has been postulated that smoking may play a role in the development of psoriasis through a variety of mechanisms, which may also be similar in PsA. Smoking induces oxidative stress and reduces antioxidant levels, leading to an imbalance of oxidants and antioxidants.[16][17] More importantly, smoking can adversely alter the immunological and inflammatory processes, which could play important roles in the development of PsA.[18][19]

The association between smoking and psoriasis has been evaluated previously.[6] Smoking is an established risk factor for rheumatoid arthritis.[7] These data suggest a possible role of smoking in the development of PsA. However, the direct evidence regarding the association between smoking and PsA is sparse.[8–12] Duffin et al[8] reported that smoking may modulate the effect of interleukin-13 polymorphisms on risk of PsA. Several case–control studies including both women and men and psoriasis with different severities did not demonstrate an increased risk of PsA associated with smoking. Two did not point to a link between smoking and PsA in individuals with psoriasis.[9][10] One indicated smoking as a protective for PsA.[11] Another study showed that smoking may delay the onset of PsA in individuals with psoriasis.[12] Given the study design, those results may have been affected by selection and information bias. Moreover, those studies are limited by study design such that they cannot determine the temporal association between smoking and later PsA onset. They did not adjust for the main confounders. They also failed to indicate a dose–response relationship to validate their reports. Our longitudinal data provide evidence regarding the association between updated smoking status, intensity, duration and the risk of PsA. Given the temporal sequence, our results indicate that smoking is a risk factor for the development of PsA.

Previous studies showed that smoking impacts the occurrence or severity of psoriasis in a dose-dependent fashion.[6][20] In the

present study, we observed a gradually elevated risk of developing PsA corresponding with the increasing quantities of current smokers, smoking duration and pack-years. Furthermore, according to the distribution, we categorised the PsA cases and found that the effect of smoking appeared stronger for those with higher PsA severity scores.

Our study is the first cohort study on the association between smoking and the development of PsA. We evaluated multiple measures of smoking associated with the risk of PsA. We performed secondary analyses by excluding or adjusting for psoriasis comorbidities for their possible association with smoking. We compared the effect of smoking on the risk of PsA among total participants as well as only among individuals with psoriasis. These analyses observed a consistently increased risk of PsA associated with smoking, which supported the robustness of the association.

In our study, physician-diagnosed psoriasis was collected in 2005; therefore survival bias may exist because we cannot obtain information for individuals with psoriasis who died. However, this is a younger female cohort of health professionals. We found that the mean age of responders to the psoriasis question was even a little higher than non-responders; therefore, it is less likely that our results were greatly distorted. We did not ask the question on PsA in the main questionnaire and ascertained the diagnosis by using the PASE questionnaire among self-reported individuals with psoriasis. Case ascertainment could be a concern due to misclassification. However, the psoriasis self-reports have reached a confirmation rate of 92%.[13] Pilot studies indicated that PASE was a valid and reliable tool to screen for PsA, especially active PsA among individuals with psoriasis.[14 15] As our pilot study on PST and PASE showed high accuracy, we expect an overall high validity of confirmation among registered nurses. The prevalence of PsA among confirmed psoriasis cases from 1991 is 21.2%, which fell within the intervals of previous reports. There could be concerns about possible misclassification with other musculoskeletal conditions, such as fibromyalgia and osteoarthritis. However, PASE can distinguish between symptoms of PsA and osteoarthritis.[14] In addition, evidence showed an inverse or no association between smoking and the risk of osteoarthritis.[21 22] There is little concern about fibromyalgia because this occurs less commonly in psoriasis and the studies on smoking and fibromyalgia still seem conflicting.[23 24]

Our study has other limitations. Most of the participants are Caucasian women younger than 60 years, which limits the generalisation to men or other ethnic groups. The generalisation to older women should be made with caution considering there could be a different proportion of type 1 and type 2 psoriasis,[25] although little is known about these two types. All the PsA cases had concomitant psoriasis. PsA can also affect individuals with limited or no skin manifestations, although accounting for a quite small proportion,[5 26] further work is warranted on the role of smoking in such cases. Moreover, this is an observational study. We cannot rule out the possibility of residual confounding by unmeasured or imperfectly measured confounders.

In conclusion, our study suggests that smoking was associated with an increased risk of developing PsA in a dose-dependent fashion in women, with a significantly elevated risk among heavy smokers or those with higher cumulative measures of smoking. The mechanisms underlying the association remain to be elucidated and further work is warranted to uncover the molecular or biological pathways linking exposure to cigarette smoke and the development of PsA. Our study has implications for public health, adding PsA to the long list of diseases that may be prevented by smoking cessation.

REFERENCES

1. **Gelfand JM**, Gladman DD, Mease PJ, *et al.* Epidemiology of psoriatic arthritis in the population of the United States. *J Am Acad Dermatol* 2005;**53**:573.
2. **Nograles KE**, Brasington RD, Bowcock AM. New insights into the pathogenesis and genetics of psoriatic arthritis. *Nat Clin Pract Rheumatol* 2009;**5**:83–91.
3. **Elkayam O**, Ophir J, Yaron M, *et al.* Psoriatic arthritis: interrelationships between skin and joint manifestations related to onset, course and distribution. *Clin Rheumatol* 2000;**19**:301–5.
4. **Gisondi P**, Tinazzi I, Del Giglio M, *et al.* The diagnostic and therapeutic challenge of early psoriatic arthritis. *Dermatology (Basel)* 2010;**221**:6–14.
5. **Pitzalis C**. Skin and joint disease in psoriatic arthritis: what is the link? *Br J Rheumatol* 1998;**37**:480–3.
6. **Setty AR**, Curhan G, Choi HK. Smoking and the risk of psoriasis in women: Nurses' Health Study II. *Am J Med* 2007;**120**:953–9.
7. **Sugiyama D**, Nishimura K, Tamaki K, *et al.* Impact of smoking as a risk factor for developing rheumatoid arthritis: a meta-analysis of observational studies. *Ann Rheum Dis* 2010;**69**:70–81.
8. **Duffin KC**, Freeny IC, Schrodi SJ, *et al.* Association between IL13 polymorphisms and psoriatic arthritis is modified by smoking. *J Invest Dermatol* 2009;**129**:2777–83.
9. **Tey HL**, Ee HL, Tan AS, *et al.* Risk factors associated with having psoriatic arthritis in patients with cutaneous psoriasis. *J Dermatol* 2010;**37**:426–30.
10. **Pattison E**, Harrison BJ, Griffiths CE, *et al.* Environmental risk factors for the development of psoriatic arthritis: results from a case-control study. *Ann Rheum Dis* 2008;**67**:672–6.
11. **Eder L**, Law T, Chandran V, *et al.* Association between environmental factors and onset of psoriatic arthritis in patients with psoriasis. *Arthritis Care Res (Hoboken)* 2011;**63**:1091–7.
12. **Rakkhit T**, Wong B, Nelson TS, *et al.* Time to development of psoriatic arthritis decreases with smoking prior to psoriasis onset and increases with smoking after psoriasis onset. *J Invest Dermatol* 2007;**127**:1.
13. **Dominguez PL**, Assarpour A, Kuo H, *et al.* Development and pilot-testing of a psoriasis screening tool. *Br J Dermatol* 2009;**161**:778–84.
14. **Husni ME**, Meyer KH, Cohen DS, *et al.* The PASE questionnaire: pilot-testing a psoriatic arthritis screening and evaluation tool. *J Am Acad Dermatol* 2007;**57**:581–7.
15. **Dominguez PL**, Husni ME, Holt EW, *et al.* Validity, reliability, and sensitivity-to-change properties of the psoriatic arthritis screening and evaluation questionnaire. *Arch Dermatol Res* 2009;**301**:573–9.
16. **Attwa E**, Swelam E. Relationship between smoking-induced oxidative stress and the clinical severity of psoriasis. *J Eur Acad Dermatol Venereol* 2011;**25**:782–7.
17. **Vassalle C**, Maffei S, Ndreu R, *et al.* Age-related oxidative stress modulation by smoking habit and obesity. *Clin Biochem* 2009;**42**:739–41.
18. **Arnson Y**, Shoenfeld Y, Amital H. Effects of tobacco smoke on immunity, inflammation and autoimmunity. *J Autoimmun* 2010;**34**:J258–65.
19. **Sopori M**. Effects of cigarette smoke on the immune system. *Nat Rev Immunol* 2002;**2**:372–7.
20. **Fortes C**, Mastroeni S, Leffondré K, *et al.* Relationship between smoking and the clinical severity of psoriasis. *Arch Dermatol* 2005;**141**:1580–4.
21. **Hui M**, Doherty M, Zhang W. Does smoking protect against osteoarthritis? Meta-analysis of observational studies. *Ann Rheum Dis* 2011;**70**:1231–7.
22. **Mnatzaganian G**, Ryan P, Norman PE, *et al.* Smoking, body weight, physical exercise, and risk of lower limb total joint replacement in a population-based cohort of men. *Arthritis Rheum* 2011;**63**:2523–30.
23. **Mäkelä M**, Heliövaara M. Prevalence of primary fibromyalgia in the Finnish population. *BMJ* 1991;**303**:216–19.
24. **Yunus MB**, Arslan S, Aldag JC. Relationship between fibromyalgia features and smoking. *Scand J Rheumatol* 2002;**31**:301–5.
25. **Griffiths CE**, Barker JN. Pathogenesis and clinical features of psoriasis. *Lancet* 2007;**370**:263–71.
26. **Soltani-Arabshahi R**, Wong B, Feng BJ, *et al.* Obesity in early adulthood as a risk factor for psoriatic arthritis. *Arch Dermatol* 2010;**146**:721–6.

Table S1. Age- and multivariate-adjusted RRs for the association between smoking and risk of PsA among participants with self-reported psoriasis

	Cases	Person-years	Age-adjusted RR (95% CI)	Multivariate-adjusted RR[*] (95% CI)
Reference: Never smokers	76	4,516	1.00	1.00
Smoking status				
Past smokers	46	2,081	1.25 (0.83-1.90)	1.41 (0.93-2.16)
Current smokers	35	1,423	1.66 (1.05-2.60)	1.71 (1.07-2.73)
Quantity, 1-14 cigarettes/day	12	550	1.32 (0.65-2.65)	1.33 (0.65-2.73)
Quantity, ≥15 cigarettes/day	23	873	1.89 (1.12-3.18)	1.98 (1.15-3.42)
P for trend			0.004	0.003
Duration				
Duration, <25 years	55	2,869	1.31 (0.89-1.92)	1.44 (0.97-2.14)
Duration, ≥25 years	26	636	1.73 (1.02-2.91)	1.78 (1.03-3.05)
P for trend			0.015	0.006
Pack-years				
Pack-years, <20	44	2,503	1.18 (0.78-1.79)	1.27 (0.83-1.93)
Pack-years, ≥20	37	1,001	1.87 (1.19-2.95)	2.08 (1.30-3.32)
P for trend			0.057	0.036

[*] Adjusted for age (continuous variable), body mass index (<18.5, 18.5-24.9, 25-29.9, 30-34.9 or ≥35 kg/m^2), alcohol drinking (no, <4.9, 5.0-9.9, 10-14.9, 15-29.9 or ≥30.0 g/d), vigorous physical activity (metabolic equivalent hours/wk, in quintile).

Table S2. Selected characteristics of all confirmed psoriasis and PsA cases before and after 1991

Characteristics	Psoriasis	PsA
	N=981	N=324
Age, year, mean (SD)	36.6 (4.7)	37.5 (4.5)
Psoriasis diagnosis age, year, mean (SD) [*]	45.9 (6.0)	45.3 (6.7)
Body mass index, kg/m^2, mean (SD)	25.1 (5.3)	28.9 (8.1)
Alcohol intake, g/d, mean (SD)	3.7 (7.2)	3.4 (10.6)
Vigorous physical activity, metabolic equivalent hours/wk, mean (SD)	11.6 (21.7)	11.2 (17.9)
Smoking pack-years, mean (SD)	5.5 (8.5)	7.5 (10.3)
Smoking duration, mean (SD)	6.9 (8.9)	8.4 (10.1)

[*] Only for psoriasis/PsA diagnosed after 1991. We do not have the diagnosis year of those before 1991.

Table S3. Age- and multivariate-adjusted RRs for the association between smoking and risk of PsA in a case-control analysis

	Controls (psoriasis) N=981	Cases (PsA) N=324	Age-adjusted RR (95% CI)	Multivariate-adjusted RR[*] (95% CI)
Reference: Never smokers	554	172	1.00	1.00
Smoking status				
Past smokers	272	81	0.91 (0.67-1.23)	0.95 (0.69-1.31)
Current smokers	155	71	1.41 (1.02-1.97)	1.49 (1.05-2.11)
Quantity, 1-14 cigarettes/day	62	25	1.25 (0.76-2.06)	1.37 (0.82-2.32)
Quantity, ≥15 cigarettes/day	93	46	1.52 (1.02-2.26)	1.56 (1.03-2.36)
P for trend			0.029	0.028
Duration				
Duration, <25 years	384	125	1.02 (0.78-1.33)	1.08 (0.82-1.44)
Duration, ≥25 years	43	27	1.69 (0.99-2.86)	1.67 (0.96-2.91)
P for trend			0.061	0.037
Pack-years				
Pack-years, <20	350	104	0.94 (0.71-1.24)	1.00 (0.74-1.34)
Pack-years, ≥20	77	48	1.78 (1.18-2.68)	1.81 (1.17-2.79)
P for trend			0.005	0.005

[*] Adjusted for age (continuous variable), body mass index (<18.5, 18.5-24.9, 25-29.9, 30-34.9 or ≥35 kg/m^2), alcohol drinking (no, <4.9, 5.0-9.9, 10-14.9, 15-29.9 or ≥30.0 g/d), vigorous physical activity (metabolic equivalent hours/wk, in quintile).