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Psoriasis, psoriatic arthritis and increased risk of incident Crohn's disease in US women

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Abstract

Objective—Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), shares clinical and immunological features with psoriasis. Genome-wide association studies have found common susceptibility genes. However, epidemiologic data evaluating the association between psoriasis, psoriatic arthritis and risk of IBD are sparse. We aimed to evaluate the association between psoriasis, psoriatic arthritis and incident CD and UC among women in the USA.

Methods—174 476 women were enrolled in the Nurses' Health Study (NHS) (1996–2008) and NHS II (1991–2007). Lifetime history of physician-diagnosed psoriasis and psoriatic arthritis was confirmed by supplementary questionnaires. Information on CD and UC was obtained by self-reported questionnaires and confirmed by medical record review.

Results—We documented 188 incident cases of CD and 240 incident cases of UC during follow-up. Psoriasis was associated with a significantly increased risk of subsequent CD with a multivariate-adjusted relative risk (RR) of 4.00 (95% CI 1.72 to 9.27) for NHS and 3.76 (1.82 to 7.74) for NHS II. By contrast, we did not observe a significant increase in risk of UC associated with psoriasis. In a pooled analysis of both cohorts, women with psoriasis experienced a significantly increased risk of CD (RR, 3.86, 95% CI 2.23 to 6.67), but not UC (RR, 1.17, 95% CI

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Competing interests AAQ serves as a consultant for Abbott, Centocor, Novartis and the Centres for Disease Control and Prevention. ATC has served as a consultant for Bayer HealthCare, Millennium Pharmaceuticals, and Pfizer Inc. The other authors state no conflict of interest.

Patient consent Obtained.

Ethics approval This study was approved by institutional review board of Brigham and Women's Hospital (IRB Protocol Title: Psoriasis in large cohort studies, IRB Protocol Number: 2006P001156).

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0.41 to 3.36). The risk of CD was especially pronounced among psoriatics with concomitant psoriatic arthritis (RR, 6.43, 95% CI 2.04 to 20.32).

Conclusions—Psoriasis with concomitant psoriatic arthritis is associated with an increased risk of incident CD.

INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC), the two predominant types of inflammatory bowel disease (IBD), are chronic relapsing inflammatory disorders of the gastrointestinal tract.^{1–3} The prevalence has increased to 50–200/100 000 persons for CD, and 120–200/100 000 persons for UC in the western countries.^{4, 5} The aetiology of IBD necessitates an interaction between genetic factors and environmental precipitants, with disease hypothesised to rise in genetically susceptible individuals as a consequence of a dysregulated inflammatory response to intestinal microbes.^{1, 2} The interleukin-23 (IL23)-T helper (Th)17 pathway mediates microbial defence and intestinal inflammation. Multiple genes regulating this pathway, including *IL12B* and *IL23R*, have been associated with both CD and UC.^{6–8} Similarly, both genetic and environmental factors have been implicated in the development of psoriasis and psoriatic arthritis (PsA),^{9–11} an autoimmune disorder involving skin and joints also mediated by Th1 and Th17/IL23 pathways.^{12, 13} Prior genome-wide association studies have identified a number of genes associated with psoriasis and PsA, with *IL12B* and *IL23R* demonstrating a consistent associations.⁹ Previous reports have suggested common genetic associations between psoriasis, CD and UC,^{14–16} further indicating a possible overlap in pathogenic mechanisms.

Although patients with established CD and UC may have extraintestinal manifestations,^{17–20} including psoriasis, the risk of subsequent IBD among cases with established psoriasis is less clear. In a small study, the prevalence of microscopic inflammation in macroscopically normal colonic mucosa was higher among patients with psoriasis and PsA without bowel symptoms than patients without psoriasis.²¹ Prior studies examining the association between psoriasis and risk of CD or UC have been conflicting^{20, 22–24} and have been limited by their cross-sectional or retrospective design, which obscures the temporal relationship between psoriasis and onset of IBD. In addition, few have evaluated psoriasis with concomitant PsA. We therefore sought to examine the association between psoriasis, PsA and risk of incident CD and UC in two large ongoing prospective studies of US women, the Nurses' Health Study (NHS) and NHS II. With more than 30 years of biennially updated data on lifestyle and medical diagnoses, these cohorts provided us with a unique opportunity to prospectively examine the association between psoriasis and subsequent risk of UC and CD, while simultaneously adjusting for other risk factors.

METHODS

Study population

The NHS is a prospective cohort study in which 121 701 US nurses aged 30–55 years were enrolled in 1976 after they completed a mailed questionnaire inquiring about their medical history and lifestyle factors. The NHS II was established in 1989 when 116 430 US female nurses aged 25–42 years returned a similar questionnaire. In both cohorts, questionnaires have been administered biennially to update information. A response rate exceeding 90% has been achieved in each follow-up cycle. The study was approved by the institutional review board of Brigham and Women's Hospital. Participants' completion and return of the questionnaire was considered informed consent.

Assessment of main exposure (psoriasis)

In 2008, we queried NHS participants about physician-diagnosed psoriasis and the diagnosis date (1997 or before, 1998–2001, 2002–2005, 2006–2007 or 2008). In 2005, NHS II participants were asked about physician-diagnosed psoriasis and the diagnosis date (before 1991, 1991–1994, 1995–1998, 1999–2002 or 2003–2005). We confirmed self-reported psoriasis by using the Psoriasis Screening Tool (PST).²⁵ This self-administered questionnaire inquired about being diagnosed with psoriasis and phenotypes of psoriasis. We developed scoring algorithms to assign a diagnosis of psoriasis depending on the response to the PST. We have completed three phases of validation. In each phase of validation in NHS and the third phase in NHS II, we also asked about the involved body surface area defined by using the palm (ie, the subject's flat hand and thumb together, fingers not included),^{26, 27} in the following categories: none/very little, 1–2, 3–4, 5–10, 11–20 or >20 palm areas. A validation study showed the PST questionnaire is 99% sensitive and 94% specific for psoriasis.²⁵ With a response rate of 87%, we successfully confirmed 92% of self-reported psoriasis in NHS II.

We confirmed the diagnosis of PsA by using the PsA Screening and Evaluation (PASE) questionnaire, which includes both symptom and function scales.^{28, 29} A total score of 47 has been shown to identify PsA with high accuracy.^{28, 29} We observed a positive association between PASE score and 28-joint Disease Activity Score (personal communication, E. Soriano, 2012). PASE also has good test–retest precision and is sensitive to change to therapy. Furthermore, PASE can distinguish between symptoms of PsA and osteoarthritis. A new version of PASE was applied to NHS participants where we had a question on ever being diagnosed with PsA by a rheumatologist and the diagnosis age.

Assessment of main outcome (CD and UC)

We have previously detailed our methods for confirming cases of CD and UC.³⁰ Briefly, since 1976 (NHS) and 1989 (NHS II), participants have reported diagnoses of UC or CD through an open-ended response on biennial surveys. In NHS, we have also specifically queried participants about diagnoses of UC since 1982 and CD since 1992. In NHS II, we have specifically queried participants about diagnoses of both UC and CD since 1993. When a diagnosis was reported biennially, a supplementary questionnaire and related medical records were requested and reviewed by two gastroenterologists blinded to exposure. We excluded participants who denied the diagnosis on the supplementary questionnaire or permission to review their records. From the medical records, we extracted data on diagnostic tests, histopathology, anatomic location of disease and disease behaviour. Using standardised criteria, UC diagnosis was based on a typical clinical presentation >4 weeks and endoscopic or surgical pathological specimen consistent with UC (eg, evidence of chronicity). CD diagnosis was based on a typical clinical history for >4 weeks and endoscopy or radiologic evaluation demonstrating small bowel findings, or surgical findings consistent with CD combined with pathology suggesting transmural inflammation or granuloma contributed to a diagnosis of CD. Disagreements were resolved through consensus. Among women from whom we received adequate medical records, the case confirmation rate for IBD was 78% in NHS and 74% in NHS II.³⁰

Statistical analysis

We set the baseline at 1996 for NHS and 1991 for NHS II, because data regarding the exact diagnosis year of psoriasis was available since then. Of 79 314 responders to both the 1976 and 2008 questionnaire in the NHS, we excluded self-reported CD or UC cases occurring before 1996 (n=934) or missing psoriasis diagnosis year (n=169), leaving 78 211 women in the analysis. In NHS II, of 97 476 responders to both 1989 and 2005 questionnaires, we

excluded self-reported CD or UC cases occurring before 1991 (n=1155), or missing psoriasis diagnosis year (n=56), leaving 96 265 in the analysis.

We ensured that the exposure (psoriasis) occurred before the outcome (CD or UC). Person-years of follow-up were calculated from the return date of 1996 (NHS) or 1991 (NHS II) questionnaire to the date of diagnosis of CD or UC, or the end of follow-up (June 1, 2008 for NHS and 1 June 2007 for NHS II), whichever came first. We used time-dependent Cox proportional hazards models stratified by age to estimate the relative risks (RRs) and 95% CI. Multivariate analysis was performed by adjusting for age (continuous), body mass index (BMI) (<18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9 or ≥35.0 kg/m²), smoking (never, past, current 1–14, 15–24 or ≥25/d), alcohol intake (no, <4.9, 5.0–14.9 or ≥15.0 g/d), physical activity (<3, 3.0–8.9, 9.0–17.9, 18.0–26.9 or ≥27.0 metabolic equivalent hours/week), use of postmenopausal hormone, oral contraceptive, aspirin and non-aspirin non-steroidal anti-inflammatory drugs (never, past or current). In sensitivity analyses, we further adjusted for personal history of chronic diseases (yes or no), including type 2 diabetes, coronary artery disease, cancer, hypertension and hypercholesterolemia. All the covariates were updated during follow-up. For analysis of the association between age at psoriasis diagnosis or length of time with psoriasis and risk of CD or UC in NHS II, we excluded psoriasis occurring before 1991 since we did not have information on the exact year of diagnosis for them.

For the combined analysis of the two 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). Analyses were conducted by using the SAS (V.9.2; SAS Institute Inc, Cary, North Carolina, USA) and all p values were 2-tailed.

RESULTS

There were a total of 174 476 participants in our analysis, including 78 211 from the NHS and 96 265 from the NHS II. 2752 reported psoriasis at baseline (1402 in NHS and 1350 in NHS II). An additional 512 women in NHS and 1122 women in NHS II reported psoriasis over follow-up through 2005. The baseline characteristics are shown in table 1. Women with psoriasis tended to be older, had a higher BMI, consumed more alcohol and were less physically active. Psoriatics were also more likely to be current smokers, and users of postmenopausal hormone, oral contraceptive and non-steroidal anti-inflammatory drugs.

In NHS, we confirmed 72 cases of CD and 74 cases of UC from 1996 to 2008. In NHS II, we confirmed 116 cases of CD and 166 cases of UC from 1991 to 2007. Psoriatics had an elevated risk of developing CD with multivariate-adjusted RRs (95% CI) of 4.05 (1.75 to 9.38) in NHS and 3.76 (1.82 to 7.74) in NHS II. In a pooled analysis, psoriasis was associated with a RR of 3.86 (95% CI 2.23 to 6.67). By contrast, we did not observe a significantly increased risk of UC associated with psoriasis in either NHS or NHS II (table 2).

Consistent with our results among self-reported psoriatics, we observed that women with confirmed psoriasis had a higher risk of CD in the pooled analysis (RR=5.20, 95% CI 2.81 to 9.62). The association between confirmed psoriasis and CD remained significant after excluding women with moderate-to-severe psoriasis (RR=4.89, 95% CI: 1.78 to 13.49) in NHS (table 3).

We specifically examined psoriasis with concomitant PsA and subsequent risk of CD (table 4). Compared with those without psoriasis, an increased risk of CD was observed among

those with psoriasis only (RR=3.49; 95% CI 1.89 to 6.44) and psoriasis with concomitant PsA (RR=6.54; 95% CI 2.07 to 20.65).

We evaluated the association between psoriasis and risk of incident CD according to subgroups defined by age at diagnosis (<40 or ≥40 years) or duration of disease (<10 or ≥10 years). We observed a particularly high risk of CD among psoriatics diagnosed <40 years of age or lasting ≥10 years. We considered the possibility that psoriasis was associated with the onset of preclinical manifestations of IBD before a formal diagnosis of CD or UC. However, repeating our analyses after excluding CD or UC cases occurring within 2 years of psoriasis diagnosis did not appreciably change our findings. To exclude the possibility, antitumor necrosis factor- α (anti-TNF- α) antibody therapy may have influenced our results, we conducted analyses limiting follow-up through 2004 and observed similar results. Additionally adjusting for other chronic diseases did not materially change our risk estimates.

DISCUSSION

An increased incidence of psoriasis among patients with established IBD has been described, with psoriasis widely considered an extraintestinal manifestation of IBD,^{17, 18} and also a known complication of anti-TNF- α therapy for IBD.^{23, 31} By contrast, it was unclear whether individuals with established psoriasis and PsA have an increased risk of subsequently developing CD or UC. In this study, we observed that women with psoriasis, particularly with concomitant PsA, had a significantly increased risk of developing CD. We excluded the likelihood that our observations were affected by anti-TNF- α therapy. To our knowledge, this is the first prospective study providing evidence of an association between psoriasis, PsA and subsequent risk of incident CD.

Prior studies support our observed association. In a small study of 15 patients with psoriasis and PsA without bowel symptoms or macroscopic evidence of colitis, all had evidence of microscopic changes on colonic biopsies, with nine exhibiting signs of inflammation (neutrophilic infiltration).²¹ A few case-control studies have investigated the association between psoriasis and IBD with inconsistent results.^{22–24} Two studies have reported an increased risk of IBD among patients with psoriasis, with the magnitude of the association higher for CD compared with UC.^{22, 23} However, another study by Tsai *et al*²⁴ did not observe an increased risk of IBD associated with psoriasis. As these studies were retrospective or cross-sectional by design, it is difficult to infer the timing of the diagnosis of psoriasis relative to IBD. Moreover, these studies relied on discharge coding rather than physician-adjudication to identify cases of CD or UC, which may not reflect true diagnoses. Few studies have evaluated the risk of IBD specifically among psoriasis cases with concomitant PsA.

Our findings are biologically plausible. Both psoriasis and CD are well-recognised autoimmune disorders, for which Th17 cells have been implicated as playing a crucial role in sustaining chronic inflammation.^{13, 32} IL-23 stimulates survival and proliferation of Th17 cells and induces the secretion of a characteristic set of cytokines, thus serving as a key cytokine regulator in autoimmune inflammatory diseases.^{8, 12} Genes implicated in the IL-23 pathway have been commonly associated with both psoriasis and CD.^{6, 9} Other overlapping genetic regions have also been uncovered, including the 6P21 locus which encompasses *IBD3*, associated with CD, and *PSORS1* associated with psoriasis.³³ In addition, anti-TNF- α antibodies, such as infliximab and adalimumab, are effective therapeutic approaches for the treatment of CD,^{34, 35} as well as moderate-to-severe psoriasis.³⁶ Psoriasis, PsA and CD also share some common environmental risk factors. Smoking has been associated with increased risk of psoriasis and CD,^{37, 38} despite controversial evidence on PsA.^{10, 39} Obesity

may induce a proinflammatory state and has been correlated with a risk of psoriasis, PsA and CD.^{11, 40}

In our study, we did not observe an increased risk of incident UC associated with psoriasis. This is consistent with two previous studies that suggested higher-effect estimates for the association between psoriasis and CD.^{22, 23} Although CD and UC share some clinical manifestations, genetic susceptibility loci and immune pathways, they have distinct features which may partly explain the difference in their association with psoriasis and PsA. For example, in contrast with CD, current smoking has not been associated with an increased risk of UC.³⁸ Despite previous reports on the varied cytokine profiles between CD and UC,^{1, 2} this remains controversial, and further study is warranted to elucidate the mechanisms underlying the observed differential effects on CD and UC.^{8, 41}

Most cases of PsA do not occur until 8–10 years after the onset of psoriasis skin phenotypes,⁴² and type 1 psoriasis, which typically occurs before age 40 years, has a more severe phenotype than type 2 psoriasis.⁴³ We observed a particularly high risk of CD among psoriatics with PsA, longer duration of psoriasis, and earlier onset of psoriasis. Such manifestations may reflect greater ongoing inflammation, which could be associated with an increased susceptibility to CD. Alternatively, they may share a greater number of genetic loci or pathogenic mechanisms with CD than milder psoriatics or psoriatics without joint phenotypes.

Our study has several strengths. First, our study design permitted a clearer delineation of the temporal association between psoriasis, PsA and the development of CD and UC. This minimised the likelihood that our observed associations were due to extraintestinal manifestations or complications of anti-TNF- α therapy among patients with established IBD. Moreover, our study avoids the potential recall and selection biases of case-control studies that collect data after diagnosis of CD or UC. Second, we confirmed all cases of CD and UC through medical record review, an advantage over studies that rely on self-report or discharge codes, which may not accurately reflect true diagnoses. Third, the availability of detailed and validated information on covariates allowed us to control for a number of potential confounders that may have influenced these associations.

We acknowledge some limitations. First, we did not have information on therapy, including anti-TNF- α treatment typically. However, reports of anti-TNF therapy inducing CD among psoriasis and PsA patients have been sparse. Moreover, in agreement with previous reports,^{26, 27} most cases (87.5% in NHS and 89.0% in NHS II) reported mild psoriasis (2 palm area's body involvement), and the observed association with incident CD persisted even after excluding moderate-to-severe psoriatics for which anti-TNF therapy would be a more common therapeutic approach. Moreover, we observed a significant association between psoriasis with risk of CD in analyses limited to follow-up through 2004, a time period within which anti-TNF therapy was not approved by the Food and Drug Administration for treatment of psoriasis. Anti-TNF- α therapy could also theoretically increase risk of CD indirectly by increasing body weight. However, we comprehensively adjusted for BMI and did not see a differential effect among women with low BMI. Second, mis-classification of PsA cases could have been caused by the PASE questionnaire. One recent report indicated a lower sensitivity of PASE, raising the concern about possible mis-ascertained PsA cases.⁴⁴ Because PASE picks up individuals with active disease who are potentially more likely to have inflamed joints and increased systemic inflammation, it probably underestimates the number of cases particularly in NHS II, thereby leading to a conserved estimation of the research effect. A full rheumatologic assessment might have yielded higher numbers with PsA. Third, we cannot rule out the possibility of residual confounding by additional unmeasured or imperfectly measured confounders. Fourth,

because our study was conducted among female health professionals, our results require further confirmation in other populations. Last, some have suggested psoriasis may be associated with a state of symptomatic bowel inflammation (eg, 'psoriatic colitis') that is, distinct from CD or UC.⁴⁵ However, two gastroenterologists blinded to the exposure independently confirmed diagnoses of CD using widely used criteria. Thus, if a separate disorder of mucosal inflammation is associated with psoriasis and PsA, our results suggest its clinical and pathological manifestations are quite similar to that of CD.

In conclusion, our prospective study demonstrates that women with psoriasis and PsA are at a significantly elevated risk of CD, providing evidence that these diseases may have common underlying pathogenic mechanisms. Moreover, we did not observe a significantly increased risk of UC associated with psoriasis, suggesting that psoriasis may share fewer overlapping pathways with UC compared with CD. Further understanding of the mechanisms that mediate the diseases could eventually lead to elucidation of new targets for interventions that may modulate their incidence or their activity.

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Table 1

Baseline characteristics of the study population according to diagnosis of psoriasis: Nurses' Health Study and Nurses' Health Study II

	Psoriasis	
	No	Yes
Nurses' Health Study		
n	76809	1402
Age [*] , mean (SD), year	61.1 (6.9)	61.3 (6.7)
Body mass index, kg/m ² , mean (SD)	26.6 (5.1)	27.5 (5.6)
Current smoking (%)	11.4	14.7
Alcohol intake, g/d, mean (SD)	5.0 (8.8)	5.3 (10.0)
Physical activity, metabolic equivalent hours/week, mean (SD)	18.3 (22.5)	16.4 (19.0)
Postmenopausal hormone use (%)	61.7	63.1
Oral contraceptive use [†] (%)	52.0	53.3
Aspirin use (%)	47.2	48.6
Non-aspirin non-steroidal anti-inflammatory drugs use (%)	25.6	30.9
Nurses' Health Study II		
n	94912	1353
Age [*] , mean (SD), year	36.2 (4.7)	36.7 (4.6)
Body mass index, kg/m ² , mean (SD)	24.5 (5.2)	25.4 (5.8)
Current smoking (%)	13.4	16.6
Alcohol intake, g/d, mean (SD)	3.1 (6.1)	3.2 (5.6)
Physical activity, metabolic equivalent hours/week, mean (SD)	20.8 (26.7)	19.8 (27.3)
Postmenopausal hormone use (%)	2.6	3.2
Oral contraceptive use (%)	84.7	86.3
Aspirin use (%)	11.2	12.4
Non-aspirin non-steroidal anti-inflammatory drugs use (%)	18.3	21.0

* All values other than age are age-adjusted. Baseline characteristics are based on the 1996 questionnaire in NHS and 1991 in NHS II.

[†] Oral contraceptive use in 1976.

Table 2

The relative risk (RR) of incident Crohn's disease and ulcerative colitis according to a diagnosis of psoriasis

	Person-years	Cases	Age-adjusted RR (95% CI)	Multivariate-adjusted RR (95% CI)*
Nurse's Health Study				
Crohn's disease				
No psoriasis	911944	66	1.00	1.00
Psoriasis	19091	6	4.35 (1.88 to 10.04)	4.05 (1.75 to 9.38)
Ulcerative colitis				
No psoriasis	911939	71	1.00	1.00
Psoriasis	19093	3	1.98 (0.62 to 6.27)	1.90 (0.60 to 6.06)
Nurse's Health Study II				
Crohn's disease				
No psoriasis	1490002	108	1.00	1.00
Psoriasis	28529	8	4.12 (2.00 to 8.46)	3.76 (1.82 to 7.74)
Ulcerative colitis				
No psoriasis	1489944	164	1.00	1.00
Psoriasis	28535	2	0.67 (0.17 to 2.68)	0.63 (0.16 to 2.56)
Nurse's Health Study/Nurse's Health Study II				
Crohn's disease				
No psoriasis	2401946	174	1.00	1.00
Psoriasis	47620	14	4.21 (2.44 to 7.27)	3.86 (2.23 to 6.67)
Ulcerative colitis				
No psoriasis	2401883	235	1.00	1.00
Psoriasis	47628	5	1.23 (0.43 to 3.54)	1.17 (0.41 to 3.36)

* Adjusted for age, body mass index (<18.5, 18.5–24.9, 25–29.9, 30 kg/m²), smoking (never, past, current with 1–14, 15–24, 25 cigs/day), alcohol drinking (no, <4.9, 5.0–9.9 or 10.0 g/d), physical activity (<3, 3.0–8.9, 9.0–17.9, 18.0–26.9 or 27.0 metabolic equivalent hours/week), post menopausal hormone (premenopausal, never, past or current use), oral contraceptive (never, past or current use), aspirin (never, past or current use), and non-aspirin, non-steroidal anti-inflammatory drugs (never, past or current use).

NHS, Nurse's Health Study.

Table 3

The relative risk (RR) of incident Crohn's disease and ulcerative colitis according to confirmed diagnoses of psoriasis

Psoriasis	Person-years	Cases	Age-adjusted RR (95% CI)	Multivariate-adjusted RR (95% CI)*
Nurse's Health Study				
Crohn's disease				
No psoriasis	908686	65	1.00	1.00
Psoriasis	13047	5	5.38 (2.16 to 13.37)	4.98 (2.00 to 12.43)
Ulcerative colitis				
No psoriasis	908680	71	1.00	1.00
Psoriasis	13049	3	2.92 (0.92 to 9.27)	2.75 (0.86 to 8.75)
Nurse's Health Study II				
Crohn's disease				
No psoriasis	1490818	109	1.00	1.00
Psoriasis	12517	6	6.07 (2.65 to 13.88)	5.40 (2.35 to 12.39)
Ulcerative colitis				
No psoriasis	1490760	165	1.00	1.00
Psoriasis	12520	1	0.66 (0.09 to 4.69)	0.60 (0.08 to 4.32)
Nurse's Health Study/Nurse's Health Study II				
Crohn's disease				
No psoriasis	2399504	174	1.00	1.00
Psoriasis	25564	11	5.75 (3.11 to 10.60)	5.20 (2.81 to 9.62)
Ulcerative colitis				
No psoriasis	2399440	236	1.00	1.00
Psoriasis	25569	4	1.73 (0.43 to 6.97)	1.60 (0.39 to 6.65)

* Adjusted for age, body mass index (<18.5, 18.5–24.9, 25–29.9, ≥30 kg/m²), smoking (never, past, current with 1–14, 15–24, ≥25 cigs/day), alcohol drinking (no, <4.9, 5.0–9.9 or ≥10.0 g/d), physical activity (<3, 3.0–8.9, 9.0–17.9, 18.0–26.9 or ≥27.0 metabolic equivalent hours/week), post menopausal hormone (premenopausal, never, past or current use), oral contraceptive (never, past or current use), aspirin (never, past or current use), and non-aspirin, non-steroidal anti-inflammatory drugs (never, past or current use).

Table 4

The relative risk of Crohn's Disease by diagnosis of psoriasis with or without psoriatic arthritis

Psoriasis	Person-years	Cases	Age-adjusted RR	Multivariate-adjusted RR*
<i>Nurse's Health Study</i>				
Crohn's disease				
No psoriasis	911944	66	1.00	1.00
Psoriasis	17070	5	4.07 (1.64 to 10.09)	3.80 (1.53 to 9.48)
Psoriasis/psoriatic arthritis	2021	1	6.76 (0.94 to 48.80)	5.94 (0.82 to 43.15)
<i>Nurse's Health Study II</i>				
Crohn's disease				
No psoriasis	1490002	108	1.00	1.00
Psoriasis	24890	6	3.50 (1.54 to 7.98)	3.25 (1.43 to 7.43)
Psoriasis/psoriatic arthritis	3640	2	8.70 (2.14 to 35.32)	6.87 (1.67 to 28.17)
<i>Nurse's Health Study/Nurse's Health Study II</i>				
CD				
No psoriasis	2401946	174	1.00	1.00
Psoriasis	41960	11	3.74 (2.03 to 6.89)	3.49 (1.89 to 6.44)
Psoriasis/psoriatic arthritis	5661	3	7.99 (2.55 to 25.08)	6.54 (2.07 to 20.65)

* Adjusted for age, body mass index (<18.5, 18.5–24.9, 25–29.9, ≥30 kg/m²), smoking (never, past, current with 1–14, 15–24, ≥25 cigs/day), alcohol drinking (no, <4.9, 5.0–9.9 or ≥10.0 g/d), physical activity (<3, 3.0–8.9, 9.0–17.9, 18.0–26.9 or ≥27.0 metabolic equivalent hours/week), post menopausal hormone (premenopausal, never, past or current use), oral contraceptive (never, past or current use), aspirin (never, past or current use), and non-aspirin, non-steroidal anti-inflammatory drugs (never, past or current use).

CD, Crohn's Disease; RR, relative risk.