Modifiable lifestyle and environmental factors associated with onset of psoriatic arthritis in patients with psoriasis: A systematic review and meta-analysis of observational studies

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Background: Psoriatic arthritis (PsA) is a progressive joint disease associated with psoriasis.

Objectives: To investigate the association of modifiable lifestyle and environmental factors with PsA risk among people with psoriasis.

Methods: We conducted a systematic search of PubMed, Embase, and Cochrane Library through May 2, 2020, for observational studies reporting lifestyle or environmental factors for PsA onset in patients with psoriasis. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were combined using a random-effects model.

Results: We included 16 studies comprising 322,967 individuals. Obesity and being overweight were associated with an increased PsA risk in patients with psoriasis (OR, 1.75 [95% CI, 1.42-2.16] and OR, 1.50 [95% CI, 1.08-2.09], respectively), with an increase of approximately 6% for each kg/m^2 rise in body mass index (OR, 1.06; 95% CI, 1.03-1.10). The presence of PsA was associated with a history of physical trauma (OR, 1.33; 95% CI, 1.16-1.54) or fracture (OR, 1.46; 95% CI, 1.22-1.74). No significant associations were observed regarding alcohol consumption (OR, 0.99; 95% CI, 0.88-1.13), smoking (OR, 0.89; 95% CI, 0.75-1.06), female hormonal exposure (OR, 1.45; 95% CI, 0.95-2.20), and psychologically traumatic events.

Limitations: Inherent limitations in the included observational studies.

Conclusions: Several lifestyle and environmental factors are associated with PsA onset among patients with psoriasis. These findings indicate that such risk may be modified with lifestyle changes or avoidance of physical trauma in people with psoriasis. (J Am Acad Dermatol 2021;84:701-11.)

Key words: environmental factors; lifestyle factors; meta-analysis; psoriatic arthritis; psoriasis.

Psoriatic arthritis (PsA) is a progressive and destructive inflammatory arthritis associated with psoriasis that occurs in approximately one third of patients with psoriasis.[1] The appearance of PsA not only causes pain, swelling, and joint stiffness but substantially increases the risk of comorbidities (eg, diabetes), impairs quality of life, and leads to considerable health care expenditure as well.[2-4] Currently, phenotypic, molecular, and cellular events underlying the transition to PsA remain elusive, which is commonly thought to involve both heredity and the environment.[5,6] The majority of patients develop PsA an average of 7 years after psoriasis onset.[7] As a result, determining the

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modifiable factors associated with the transition to PsA among patients with psoriasis may provide a unique opportunity for early prevention and deepen our understanding of the etiology of PsA as well.

In the past decades, the roles of many modifiable lifestyle and environmental factors have been proposed.[8-14] However, some of the conclusions remain limited and contradictory, confusing our knowledge on this topic. For example, smoking is correlated with a greater risk of PsA and psoriasis in the general population.[11,15] but it was found to be irrelevantly,[8,9,14] positively,[12] or even inversely[10,11,13] associated with developing PsA in patients with psoriasis according to previous reports. To date, to our knowledge, no comprehensive meta-analysis on modifiable lifestyle and environmental factors for the onset of PsA in patients with psoriasis has been conducted. To fill the gap, we performed this systematic review and meta-analysis of observational studies to identify lifestyle and environmental factors associated with developing PsA among patients with psoriasis.

CAPSULE SUMMARY

- We found significant increases in the risk of developing psoriatic arthritis in patients with psoriasis with obesity or physical trauma but not based on alcohol intake, smoking status, and psychologically traumatic events.
- These findings indicate that such risks may be modified with lifestyle changes or the avoidance of physical trauma in people with psoriasis.

MATERIALS AND METHODS

This article was carried out and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[16]

LITERATURE SEARCH AND INCLUSION CRITERIA

A search of all relevant literature using the electronic databases PubMed, Embase, and the Cochrane Library was performed without language restrictions from database inception through May 2, 2020. Studies were identified by combining 3 search themes: psoriatic arthritis; psoriasis; and study design, which combined the terms "case-control" and "cohort." The detailed search strategy is provided in the Supplemental Materials (available via Mendeley at https://doi.org/10.17632/xzwvcfjbbw.2). In addition, we also hand searched reference lists of the included studies and the conference proceedings for the American College of Rheumatology and European League Against Rheumatism (2014-2019) for additional reports.

Articles were eligible if they met the following inclusion criteria: (1) retrospective or prospective cohort or case-control studies, (2) reporting at least 1 lifestyle or environmental factors for PsA in psoriasis, (3) presenting odd ratios (ORs) (or relative risks or hazard ratios) with 95% confidence intervals (CIs) or the data necessary to calculate them. We excluded studies assessing the risk of PsA in the general population or only investigating other irrelevant risk factors (eg, genetic factors, skin phenotype, or comorbidities) instead of lifestyle factors and trauma. Publications without original data, such as reviews and comments, were excluded. When studies used overlapping cohorts from the same institution addressing equivalent risk factors, the study with the largest cohort was included in the analysis. The potential eligible non-English studies were translated in the aid of translation software or language scholars if necessary. Two investigators (WX and HH) independently evaluate the eligibility, and any discrepancies throughout were resolved by a third investigator (ZZ).

DATA EXTRACTION AND OUTCOME ASSESSMENT

Data extraction of eligible studies was conducted by 2 independent review authors (WX and HH) using piloted data extraction sheets: author, publication year, country, study design, data source, setting, study period, diagnosis of psoriasis and PsA, demographic and clinical features, risk factors of interest, effect size data for risk of development of PsA, and adjustment factors (eg, age and sex). The methodologic quality of each study was rated by the Newcastle-Ottawa scale, and a maximum of 9 points was assigned to each study.[17]

DATA SYNTHESIS AND ANALYSIS

Extracted data for meta-analysis was performed with Stata statistical software, version 13.0 (StataCorp, College Station, TX). Pooled ORs with 95% CIs were calculated as an effect measure using the random-effects models. If available, we extracted the risk estimates that were adjusted for the most variables. When no raw data were available, relative risks and hazard ratios were taken as good estimates of ORs, in line with previous reports.[18-20] Sensitivity analyses were performed to assess the robustness of estimates. Funnel plots were produced to help detect potential publication bias.

Abbreviations used:

BMI: body mass index
CI: confidence interval
IL: interleukin
OR: odds ratio
PsA: psoriatic arthritis

RESULTS

Study selection and characteristics

An overview of the study selection process is shown in Supplemental Figure 1 (available via Mendeley at https://doi.org/10.17632/xzwvcfjbbw.2). Of 4528 citations, we identified 16 articles that met predefined criteria.[8-14,21-29] Characteristics of the selected articles and each group are presented in Supplemental Table I (available via Mendeley at https://doi.org/10.17632/xzwvcfjbbw.2). In total, 16 citations based on 10 data sets were published between 2002 and 2020. Of these, 6 studies were originated from United Kingdom,[9,13,14,25,27,28] 4 from the United States,[8,12,21,24] 4 from Canada,[10,11,23,26] and 1 each from Singapore[22] and Japan[29] (Supplemental Table I). Psoriasis was diagnosed according to interviews in 6 studies,[10,11,21-23,26] read codes in 5 studies,[13,14,25,27,28] medical records in 2 studies,[8,9] self-reported with physician diagnosis in 2 studies,[12,24] and clinically or histopathologically diagnosed in 1 study.[29] PsA diagnosis was according to Classification Criteria for PsA in 5 studies[10,11,23,26,29]; read codes in 5 studies[13,14,25,27,28]; and 2 each for medical records,[8,9] interview,[21,22] and questionnaire.[12,24] In the 7 case-control studies,[8-11,22,29] 1677 case patients and 1719 control individuals were included, and in the 9 cohort studies,[12-14,21,24-28] 8933 cases were identified from among 320,035 participants, with a mean follow-up of 4.1 to 7.0 years.

Smoking

The association between smoking and PsA development in patients with psoriasis was assessed by 9 articles with a median quality score of 8 (range, 5-9)[8,9,11-14,22,23,26] (Table I). Of these, 322,012 participants with psoriasis were included. The summary ORs were 0.89 (95% CI, 0.75-1.06; I^2 = 59.3%) for ever smokers in 9 studies, 0.89 (95% CI, 0.74-1.08; I^2 = 0%) for current smokers in 6 studies, and 0.98 (95% CI, 0.83-1.16; I^2 = 51.5%) for past smokers in 5 studies (Fig 1). Subgroup analysis by study design found that pooled ORs of ever smokers were 0.67 (95% CI, 0.54-0.85; I^2 = 0%) in the selected case-control studies[8,9,11,23,29] and 1.05 (95% CI, 0.85-1.28; I^2 = 68.4%) in the cohort studies (Supplemental Fig 2; available via Mendeley at https://doi.org/10.17632/xzwvcfjbbw.2),[12-14,26] indicating significant differences in smoking status between the case-control group and the cohort group. We investigated the influence of a single study on the risk estimates by jackknife sensitivity analysis (Supplemental Table II; available via Mendeley at https://doi.org/10.17632/xzwvcfjbbw.2). Pooled ORs were generally robust, but a borderline significance was observed after excluding the study conducted by Li et al[12] (pooled OR, 0.84; 95% CI, 0.74-0.97). No evident publication bias was obtained through Egger and Begg tests (Supplemental Table III; available via Mendeley at https://doi.org/10.17632/xzwvcfjbbw.2).

Alcohol consumption

Our meta-analysis of alcohol consumption included 8 studies involving 166,224 patients with psoriasis with a median quality score of 8 (range, 5-9)[8,9,11,14,22,26,27,29] (Table I). Fig 2 summarizes the pooled results for studies, showing no significant association between alcohol consumption and PsA development in patients with psoriasis, with no evidence of heterogeneity (pooled OR, 0.99; 95% CI, 0.88-1.13; I^2 = 0%). Further jackknife sensitivity analysis suggested that the pooled OR was robust and was not influenced excessively by omitting any single study, with a range from 0.97 (95% CI, 0.84-1.11) to 1.01 (95% CI, 0.84-1.44) (Supplemental Table II). Two studies additionally analyzed the association between different degrees of alcohol consumption (social and daily drinking compared with nondrinking) and PsA risk, yielding similar results (pooled OR, 0.92 [95% CI, 0.70-1.22] and OR, 1.16; [95% CI, 0.49-2.78], respectively) (Fig 2, *B* and *C*).[11,26] Additionally, in the study by Green et al,[14] the ORs and 95% CIs of developing PsA in patients with psoriasis were 1.57 (95% CI, 1.16-2.11) and 0.94 (95% CI, 0.56-1.58), respectively, for moderate and heavy drinkers compared with nondrinkers. Finally, Egger and Begg tests indicated no obvious publication bias (Supplemental Table III).

Body mass index

A total of 8 studies comprising 240,546 participants with psoriasis investigated the risk of PsA onset with regard to body mass index (BMI).[14,21,23-27,29] The median quality score of the 8 studies was 8, ranging from 7 to 8 (Table I). In pooled analysis, obesity (BMI $\geq$ 30 kg/m^2)[14,23-27] and overweight (25 kg/m^2 $\leq$ BMI $<$ 30 kg/m^2)[14,25-27] were associated with increased risk for developing PsA in patients with psoriasis (pooled OR, 1.75 [95% CI, 1.42-2.16] and pooled OR, 1.50 [95% CI, 1.08-2.09], respectively) (Fig 3). Sensitivity analysis confirmed that the pooled OR was robust and nonskewed by a

Table I. Summary of combinable risk factors in included studies

Reference	Year	Country	Design	PsA/control or cohort size	Risk factors, effect size (95% CI)							Adjustment	Quality score
					Smoking	Alcohol use	BMI	Physical trauma	Fractures	Anxiety/depression	Other risk factors		
Thumboo et al[8]	2002	United States	Case-control	60/120	Ever: 0.55 (0.24-1.25)	0.77 (0.32-1.89)	—	1.58 (0.73-3.41)	1.50 (0.58-3.91)	0.93 (0.36-2.36)	Female hormone exposure: 2.90 (0.68-12.3) College education: 0.95 (0.41-2.20) Pregnancy ever: 0.19 (0.04-0.95)	Age, sex, psoriasis duration, alcohol consumption, severity of psoriasis	8
Pattison et al[9]	2008	United Kingdom	Case-control	98/163	Ever: 0.68 (0.39-1.17)	0.57 (0.27-1.20)	—	1.10 (0.65 1.86)	1.00 (0.34-2.96)	0.67 (0.27-1.70)	Female hormone exposure: 1.39 (0.71-2.70) Traffic accident: 1.15 (0.41-3.03) Death in family: 1.10 (0.60-2.00) Job change: 1.72 (0.85-3.50) Move: 2.29 (1.21-4.40) Pregnancy ever: 1.06 (0.44-2.55) Treated for fertility: 0.17 (0.04-0.79)	Age, sex	7
Soltani-Arabshahi et al[21]	2010	United States	Cohort	250/943	—	—	BMI (continuous): 1.06 (1.02-1.10)	—	—	—	—	Age, sex, family history, age at psoriasis onset, psoriasis severity	7
Tey et al[22]	2011	Singapore	Case-control	134/266	Current: 0.81 (0.50-1.32)	0.88 (0.46-1.66)	—	—	—	—	—	None	5
Eder et al[10]	2011	Canada	Case-control	159/159	Ever: 0.47 (0.29-0.77) Current: 0.54 (0.31-0.96) Past: 0.52 (0.31-0.88)	—	—	1.97 (0.99-3.96)	1.20 (0.54-2.51)	0.80 (0.39-1.45)	Female hormone exposure: 1.33 (0.74-2.39) Traffic accident: 1.10 (0.32-3.74) Death in family: 1.10 (0.63-1.79) Job change: 1.2 (0.73-2.07) Move: 1.10 (0.67-1.82) College education: 1.18 (0.66-3.35) Treated for fertility: 0.90 (0.26-2.98)	Age, sex, education level, alcohol, duration, severity of psoriasis	9
Bhole et al[23]	2012	Canada	Case-control	644/448	Ever: 0.61 (0.40-0.94)	—	Obesity: 1.61 (1.10-2.37)	—	—	—	—	Age, sex, smoking, duration, PASI score, medication use	8
Eder et al[11]	2012	Canada	Case-control	728/404	Ever: 0.67 (0.48-0.96) Current: 0.57 (0.41-0.81) Past: 0.81 (0.56-1.12)	Social: 0.94 (0.68-1.28) Daily: 1.65 (0.99-2.76)	—	—	—	—	—	Age, sex, education level, alcohol, duration, severity of psoriasis	9

Li et al[24]	2012	United States	Cohort	146/556	—	—	BMI of 25-29.9 kg/m^2: 1.81 (1.12-2.93) BMI of 30-34.9 kg/m^2: 1.90 (1.13-3.18) BMI of ≥35 kg/m^2: 2.98 (1.86-4.78)	—	—	—	—	Age, smoking, alcohol drinking, physical activity	8
Li et al[12]	2012	United States	Cohort	157/581	Current: 1.62 (1.00-2.63) Past: 1.39 (0.89-2.16)	—	—	—	—	—	—	Age, BMI, alcohol, physical activity	8
Love et al[25]	2012	United Kingdom	Cohort	976/75,395	—	—	BMI of 25-29.9 kg/m^2: 1.09 (0.93-1.28) BMI of 30-34.9 kg/m^2: 1.22 (1.02-1.47) BMI of ≥35 kg/m^2: 1.48 (1.20-1.81)	—	—	—	—	Age, sex, smoking, alcohol, trauma	8
Eder et al[26]	2016	Canada	Cohort	60/464	Current: 1.10 (0.52-2.32) Past: 1.30 (0.71-2.39)	Social: 0.87 (0.49-1.55) Daily: 0.66 (0.24-1.82)	Overweight: 1.65 (0.79-3.44) Obesity: 2.02 (0.97-4.24)	1.39 (0.40-4.85)	—	0.92 (0.35-2.34)	—	Age, sex, psoriasis duration	8
Lewinson et al[27]	2017	United Kingdom	Cohort	1466/71,981	—	1.01 (0.85 1.20)	Obesity: 1.61 (1.40-1.86)	—	—	—	—	Age, sex, obesity, smoking, alcohol, psoriasis severity, etc	8
Thorarensen et al[28]	2017	United Kingdom	Cohort	1010/67,616	—	—	—	1.32 1.13 1.54	1.49 (1.22-1.74)	—	—	Age, sex, entry date, BMI, smoking, alcohol, duration, etc	8
Tsuruta et al[29]	2017	Japan	Case-control	55/276	Ever: 0.93 (0.49-1.76)	0.96 (0.49-1.87)	BMI (continuous): 1.07 (1.00-1.16)	—	—	—	—	Age, sex, BMI, family history, commodities, nail lesion, BSA	8
Nguyen et al[13]	2018	United Kingdom	Cohort	7057/220,644	Current: 0.88 (0.83-0.94) Past: 1.03 (0.95-1.12)	—	—	—	—	—	—	Age, sex, BMI, alcohol, trauma	8
Green et al[14]	2020	United Kingdom	Prospective cohort	1490/88,780	Current: 0.94 (0.76-1.16) Past: 0.83 (0.69-1.02)	Ever: 1.06 (0.69-1.62) Moderate: 1.57 (1.16-2.11) Heavy: 0.94 (0.56-1.58)	BMI of 25-29.9 kg/m^2: 1.76 (1.41-2.19) BMI of 30-34.9 kg/m^2: 2.04 (1.60-2.60) BMI of ≥35 kg/m^2: 2.42 (1.85-3.16)	—	—	—	—	Age, sex, duration, BMI, smoking, alcohol. trauma, diabetes, psoriasis severity	8

BMI, Body mass index; *BSA*, body surface area; *CI*, confidence interval; *PASI*, Psoriasis Area and Severity Index.

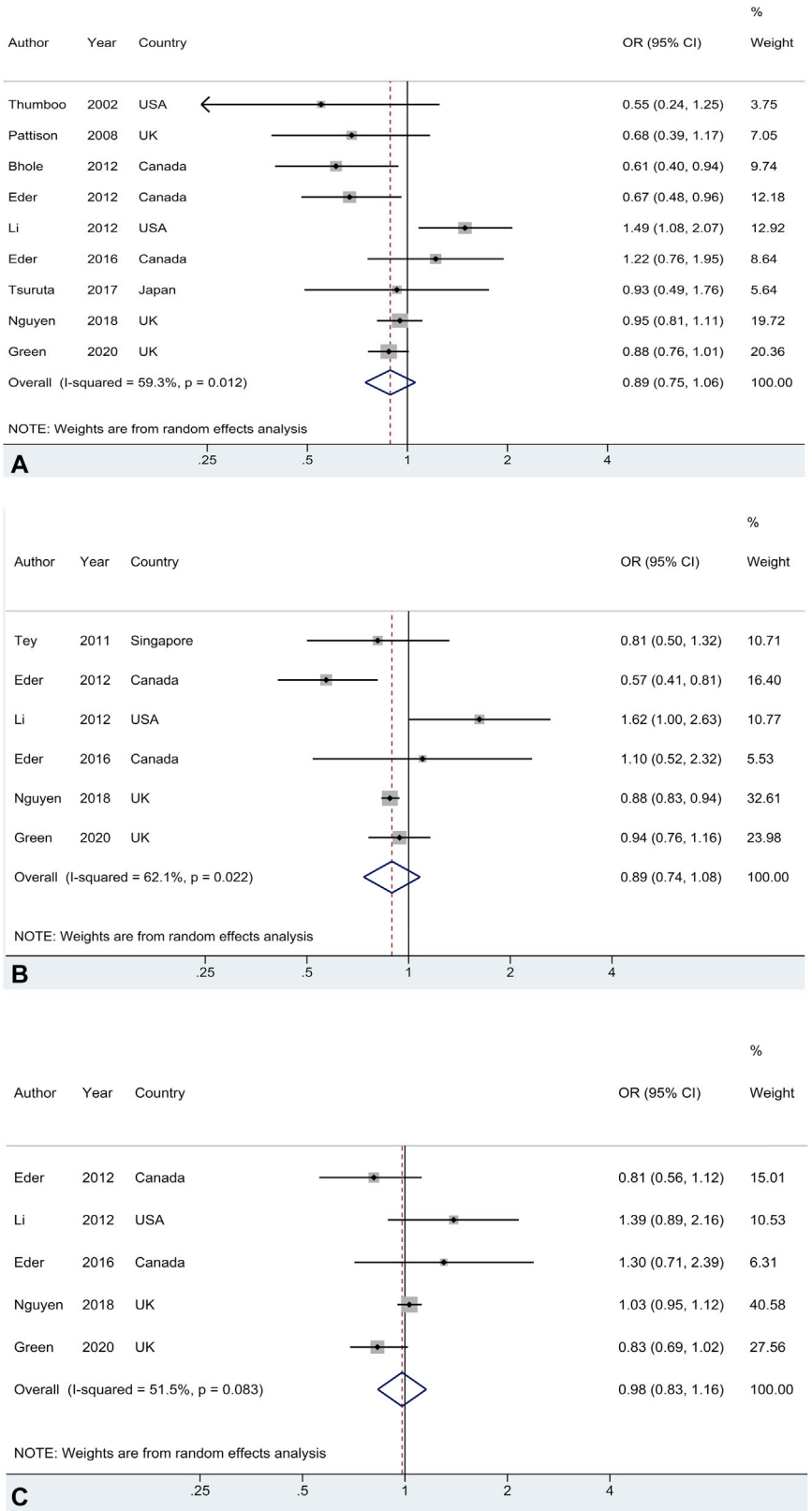

Fig 1. Forest plots of the odds ratios for the risk of developing psoriatic arthritis in patients with psoriasis: (**A**) ever smoker versus lifetime nonsmoker, (**B**) current smoker versus lifetime nonsmoker, and (**C**) past smoker versus lifetime nonsmoker. *CI*, Confidence interval; *OR*, odds ratio.

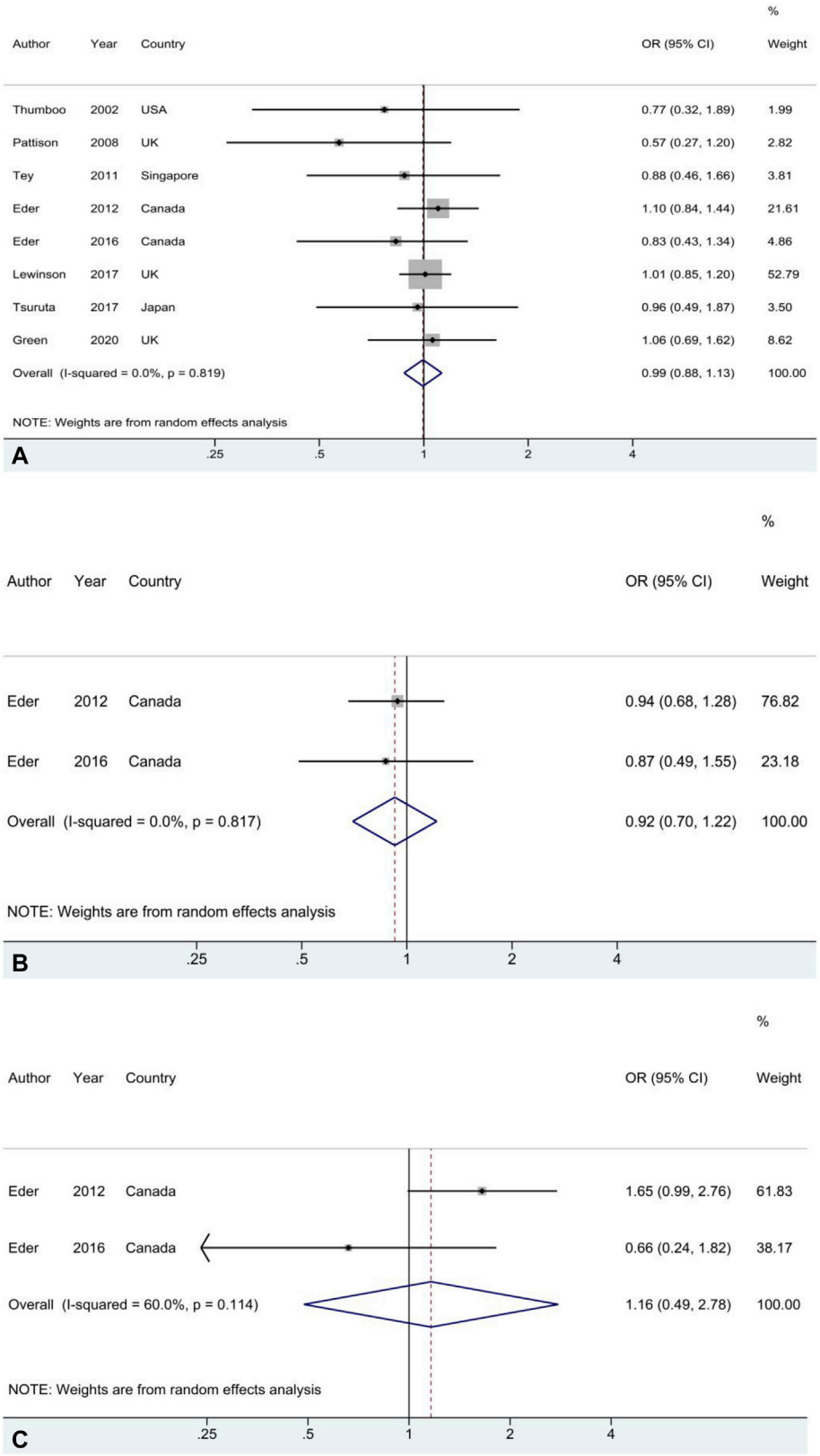

Fig 2. Forest plots of the odds ratios for the risk of developing psoriatic arthritis in patients with psoriasis: (**A**) drinker versus nondrinker, (**B**) social drinker versus nondrinker, and (**C**) daily drinker versus nondrinker. *CI*, Confidence interval; *OR*, odds ratio.

single dominant study (Supplemental Table II). The results from the Egger and Begg tests suggested no proof of publication bias (Supplemental Table III). Furthermore, a dose effect between increased BMI and the risk of PsA development in patients with psoriasis was recorded compared with BMI of less than 25 kg/m^2 (pooled OR, 1.50 [95% CI, 1.08-2.09] for BMI of 25-29.9 kg/m^2; OR, 1.64 [95% CI, 1.11-2.43] for BMI of 30-34.9 kg/m^2; and OR, 2.13 [95% CI, 1.39-3.24] for BMI of ≥35 kg/m^2)[14,25-27] (Fig 3). Additionally, a summary of 2 further studies showed a 6% increased PsA risk for each unit increment in BMI (pooled OR, 1.06; 95% CI, 1.03-1.10)[21,29] (Supplemental Fig 3; available via Mendeley at https://doi.org/10.17632/xzwvcfjbbw.2).

Physical trauma and psychological traumatic events

There were 5 studies involving 69,690 participants about physical trauma, with a median quality score of 8 (range, 7-9).[8-10,26,28] In the primary analysis, the presence of PsA was significantly associated with a history of any cause of trauma (pooled OR, 1.33; 95% CI, 1.16-1.54)[8-10,26,28] or fracture (pooled OR, 1.46; 95% CI, 1.22-1.74),[8-10,28] with no evidence of heterogeneity (Fig 4). Regarding road traffic accidents, no significant association was detected based on 2 studies (pooled OR, 1.13; 95% CI, 0.53-2.45) (Fig 4).[9,10] In addition, only 1 study reporting the association between trauma leading to medical care and the risk of PsA onset found a strong relationship (OR, 2.53; 95% CI, 1.10-6.00).[9] The combined OR of any cause of trauma and fracture was consistent without apparent fluctuation according to the results of sensitivity analysis (Supplemental Table II). Based on the results from the Egger and Begg tests, no evidence for publication bias was detected (Supplemental Table III).

There was a trend toward increased risk of progression to PsA regarding psychological traumatic events, but it failed to reach significance. The summary ORs were 1.11 (95% CI, 0.85-1.47) for depression/anxiety,[8-10,26] 1.10 (95% CI, 0.74-1.63) for death in the family,[8,10] 1.36 (95% CI, 0.90-2.07) for changing job,[8,10] and 1.51 (95% CI, 0.75-3.15) for moving house[8,10] (Fig 4).

Other factors

For the rest of combinable factors, no significant associations were observed (pooled OR, 1.06 [95% CI, 0.59-1.90] for college education[8,10]; pooled OR, 1.46 [95% CI, 0.95-2.20] for female hormone exposure[8-10]; pooled OR, 0.51 [95% CI, 0.10-2.70] for pregnancy ever[8,9]; pooled OR, 0.41 [95% CI, 0.08-2.11] for treatment for fertility[9,10]) (Fig 4). In addition, another 18 factors were included only in the systematic review because the assessment was performed in only 1 study (Supplemental Table IV; available via Mendeley at https://doi.org/10.17632/xzwvcfjbbw.2).

DISCUSSION

Our meta-analysis identified that BMI had a dose-dependent increase in the risk of PsA development in patients with psoriasis, with a statistically significant 75% increased risk for obesity. In recent years, BMI has been reported as a potential risk factor for PsA in a dose-dependent manner among both patients with psoriasis and the general population.[12] Although the potential causal association between PsA and obesity was suggested, the underlining mechanisms are not completely understood.[30,31] A very plausible explanation for the association is a systemic and chronic low-grade inflammation status in obese individuals, representing an increase in inflammatory cytokines (tumor necrosis factor α, interleukin [IL] 1, IL-6, IL-8, IL-17, and IL-23, etc) and an alteration in adipokines (leptin and adiponectin), which may lead to PsA development in predisposed individuals.[32,33] On the other hand, the interaction between PsA and obesity can also be highlighted by biomechanical stress and joint microtraumas induced by increased body mass.[34] Together with other genetic, environmental, and immunologic factors, obesity may finally trigger the development of PsA in susceptible individuals with pre-existing psoriasis. Thus, according to best available data sets, obesity was associated with an increased incidence of PsA in patients with psoriasis, and weight control is a potential strategy worth considering among these patients, although more large, well-designed studies are needed to confirm these findings.

The findings of an association between smoking and risk of PsA among people with psoriasis are severely conflicting, largely because of study design, as shown in our study. One previous case-control study initially found a protective relationship between smoking and PsA in patients with psoriasis,[10] supported by a population-based cohort study based on The Health Improvement Network database.[27] However, the most recently updated research from The Health Improvement Network database showed that smoking status appears unrelated to significant alteration in PsA risk in patients with psoriasis.[13] More intriguingly, a remarkably elevated risk of developing PsA among individuals with psoriasis was confirmed in a large cohort of women from the Nurses' Health Study II.[12] The present study comprehensively showed that there was no association between smoking status (ever, current, past) and the risk of PsA among the psoriasis population.

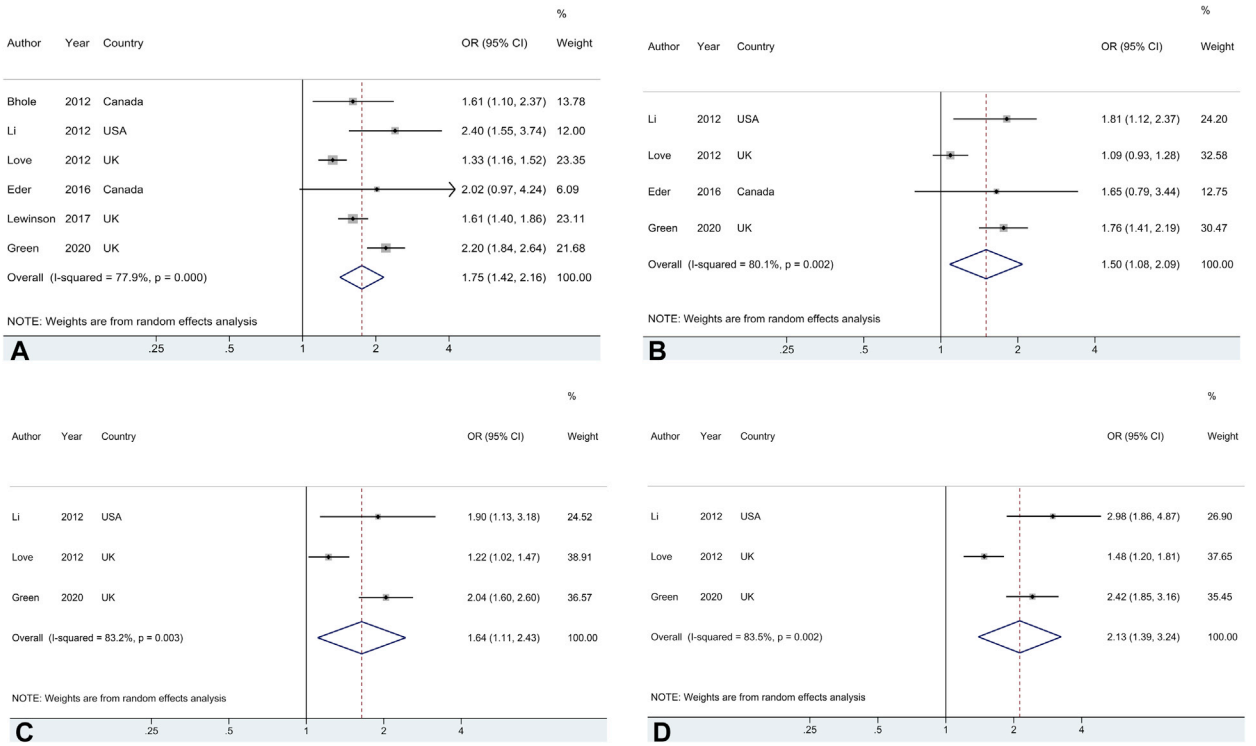

Fig 3. Forest plots of the odds ratios for the risk of developing psoriatic arthritis in psoriasis patients: (**A**) obesity (BMI ≥ 30 kg/m^2) versus BMI of less than 25 kg/m^2; (**B**) overweight (BMI of 25-29.9 kg/m^2) versus BMI of less than 25 kg/m^2; (**C**) BMI of 30 to 34.9 kg/m^2 versus BMI of less than 25 kg/m^2; and (**D**) BMI of 35 kg/m^2 or greater versus BMI of less than 25 kg/m^2. *BMI*, Body mass index; *CI*, confidence interval; *OR*, odds ratio.

Risk Factors	Study number	Odds ratio (95%CI)	I^2
Physical trauma			
Any physical trauma	5	1.33 (1.16-1.54)	0.0%
Fracture	4	1.46 (1.22-1.74)	0.0%
Road traffic accident	2	1.13 (0.53-2.45)	0.0%
Trauma leading to medical care	1	2.53 (1.10-6.00)	—
Psychological traumatic events			
Depression/anxiety	4	1.11 (0.85-1.47)	10.9%
Death in family	2	1.10 (0.74-1.63)	0.0%
Change job	2	1.36 (0.90-2.07)	0.0%
Moved home	2	1.51 (0.75-3.15)	67.7%
Other factors			
Female hormonal exposure	3	1.45 (0.95-2.20)	0.0%
College education	2	1.06 (0.59-1.90)	0.0%
Pregnancy ever	2	0.51 (0.10-2.70)	71.1%
Treated for fertility	2	0.41 (0.08-2.11)	65.2%

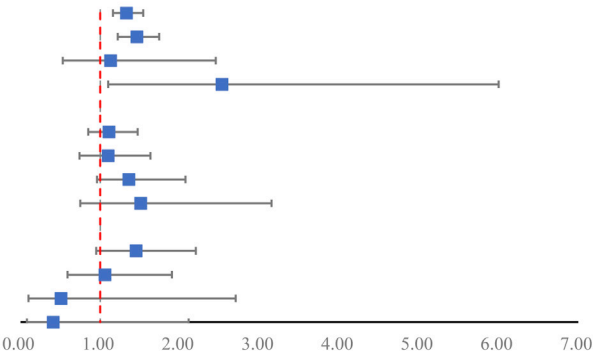

Fig 4. Forest plots of the odds ratios for the risk of developing psoriatic arthritis in patients with psoriasis for environmental factors. *CI*, Confidence interval.

On the contrary, smoking has been found to be associated with increased risk of psoriasis and PsA in the general population.[11,13] This phenomenon may indicate that the impact of smoking on the risk of PsA was mediated mainly through the effect of smoking on psoriasis.

A significantly increased risk of PsA in patients with psoriasis was observed to be associated with the presence of traumatic injury, especially for physical trauma (eg, fracture). The recent concept of a synovioentheseal complex may provide a scientific rationale for biomechanical trauma as an initiating event in the pathogenesis of PsA.[35,36] In contrast to other skeletal locations, the entheses bear higher biomechanical stress, which may trigger an inflammatory cytokine cascade by

monocyte and lymphocyte infiltration, resulting in an articular inflammatory response, subsequent adjacent synovitis, proliferation, and fibrous degeneration of synovial tissues.[36,37] The predisposed individuals with psoriasis exposed to physical trauma (second hit) may lead to the psoriasis transition to PsA and provide a biological basis for the increased risk of PsA with a history of physical trauma.

There were several limitations to our study. First, the interpretation of the evidence from observational studies requires caution, because these can generate more bias than randomized controlled trials (recall bias, selection bias, etc). Therefore, causal links of the risk estimates cannot be definitely determined. Second, although the quality of the included studies was generally high, not all studies made enough adjustment for potential confounders. We cannot fully unify the confounders either. Third, various diagnosis criteria of PsA were applied in the included studies, mostly by interview or read codes, rather than the Classification Criteria for PsA. This may lead to an underestimation or overestimation of the risk estimates attributable to lifestyle and environmental factors. Fourth, although the currently available databases were retrieved, there are insufficient data on several risk factors for PsA development in patients with psoriasis, which did not allow us to perform more detailed subgroup analyses.

In summary, this comprehensive systematic review and meta-analysis showed statistically significant increases in the risk of developing PsA in patients with obesity and physical trauma. Our results strengthen public health to promote awareness and endeavor to reduce the risk of transition to PsA in patients with psoriasis and furthermore to deepen our understanding of the etiology of PsA.

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