



## EXTENDED REPORT

# Obesity and risk of incident psoriatic arthritis in US women

Wenqing Li,<sup>1</sup> Jiali Han,<sup>1,2,3</sup> Abrar A Qureshi<sup>1,2</sup>

► Additional supplementary tables are published online only. To view the files please visit the journal online (<http://ard.bmj.com/content/early/recent>)

<sup>1</sup>Department of Dermatology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA

<sup>2</sup>Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA

<sup>3</sup>Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA

## Correspondence to

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

Accepted 8 April 2012

## ABSTRACT

**Objectives** Both overall and central obesity have been associated with the risk of psoriasis in a prospective study. Data on the association between obesity and psoriatic arthritis (PsA) have been sparse and no evidence on obesity measures and the risk of incident PsA is available now. This study aimed to evaluate the association between obesity and the risk of incident PsA in a large cohort of women.

**Methods** 89 049 participants were included from the Nurses Health Study II over a 14-year period (1991–2005). Information on body mass index (BMI), weight change and measures of central obesity (waist circumference, hip circumference and waist–hip ratio) was collected during the follow-up. The incidence of clinician-diagnosed PsA was ascertained and confirmed by supplementary questionnaires.

**Results** 146 incident PsA cases were identified during 1 231 693 person-years of follow-up. Among all participants, BMI was monotonically associated with an increased risk of incident PsA. Compared with BMI less than 25.0, the RR was 1.83 for BMI 25.0–29.9 (95% CI 1.15 to 2.89), 3.12 for BMI 30.0–34.9 (95% CI 1.90 to 5.11) and 6.46 for BMI over 35.0 (95% CI 4.11 to 10.16). There was a graded positive association between weight change from age 18 years, measures of central obesity and risk of PsA (*p* for trend <0.001). The analysis among participants developing psoriasis during follow-up revealed a similar association (*p* for trend <0.01), indicating an increased risk of PsA associated with obesity among patients with psoriasis.

**Conclusion** This study provides further evidence linking obesity with the risk of incident PsA among US women.

Psoriatic arthritis (PsA) is a well-recognised comorbidity of psoriasis and an inflammatory musculoskeletal condition occurring in 0.25% of the US population.<sup>1,2</sup> Previous reports indicate that PsA leads to impaired quality of life due to joint damage and deformity, as well as an increased mortality.<sup>1</sup> Despite this major impact, there is little understanding of PsA risk factors, which limits prevention and early detection efforts.

A link between obesity and psoriasis and arthritis has been reported. Increased adiposity and weight gain have been associated with the risk of psoriasis in a prospective study.<sup>3</sup> Obesity is a significant risk factor for osteoarthritis at sites throughout the body, especially the knee.<sup>4,5</sup> The reports on obesity and rheumatoid arthritis (RA) have been conflicting, and one study only observed an increased risk of anti-cyclic citrullinated peptide-negative RA associated

with obesity.<sup>6–8</sup> Data on obesity and PsA are sparse and no prospective studies are available.<sup>9,10</sup> One study observed a higher body mass index (BMI) and waist–hip ratio (WHR) between PsA and healthy controls.<sup>9</sup> The other reported BMI at age 18 years as a risk factor for PsA compared with individuals with psoriasis.<sup>10</sup> The study did not indicate current BMI as a risk factor. No data on BMI, central obesity, weight change and the risk of PsA in a prospective design are available, although we have reported an association between visceral obesity and weight change correlated with psoriasis.<sup>3</sup> Given the differential cutaneous phenotypes between psoriasis and PsA, as well as the conflicting evidence on obesity and arthritis, the association between adiposity measurements and the risk of PsA deserves further examination in a prospective setting.

In this study, we prospectively investigated the association between BMI (BMI updated biennially during the follow-up, and BMI at age 18 years), weight change, waist circumference, hip circumference, WHR and the incidence of PsA both among all participants and among women with psoriasis from the Nurses' Health Study II (NHS II).

## METHODS

### Study cohort

NHS II is an ongoing longitudinal cohort of women established in 1989 when 116 430 female nurses aged 25–42 years responded to a mailed questionnaire enquiring about their medical history and lifestyle practices. Biennially, updated information on lifestyle factors and medical history was collected by mailed questionnaires. The follow-up rate exceeds 90%.

### Assessment of main exposure

In 1989, participants responded to questions on their height, weight and weight at the age of 18 years. Weight was further recorded biennially thereafter. BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m<sup>2</sup>). Weight change since age 18 years was obtained by deducting the weight at age 18 years from the current weight. We asked participants to measure waist (measured at the umbilicus) and hip circumference (measured at the largest circumference) to the nearest quarter of an inch in 1993. The validation of self-reported anthropometric measurements was evaluated among 140 NHS participants. The Pearson correlation coefficient between self-report and the average of the two technician

measurements was 0.98 for weight, 0.91 for waist circumference and 0.87 for hip circumference.<sup>11</sup>

### Assessment of main outcome (PsA)

In 2005, we asked participants about physician-diagnosed psoriasis and the diagnosis date. Of the 97 476 responders, 2529 reported ever being diagnosed with psoriasis; of these, 1151 self-reported psoriasis patients diagnosis occurred after 1991. Psoriasis self-reports were confirmed by using the psoriasis screening tool, which has 99% sensitivity and 94% specificity.<sup>12</sup> This questionnaire was mailed to 1886 participants who self-reported psoriasis and responded to the 2007 main questionnaire. A diagnosis was validated if adhering to the scoring algorithms based on multiple a priori hypotheses. One thousand six hundred and thirty-seven (87%) responded and 1511 (92%) were confirmed.

We confirmed the diagnosis of PsA by using the psoriatic arthritis screening and evaluation (PASE) questionnaire, which includes both symptom and function scales.<sup>13 14</sup> A total score of 47 or greater has been shown to identify PsA with high accuracy.<sup>13 14</sup> We observed a positive association between PASE score and the 28-joint disease activity score (E. Soriano, personal communication, 2012). PASE also has good test–retest precision and is sensitive to change to therapy.<sup>13</sup> Furthermore, PASE can distinguish between the symptoms of PsA and osteoarthritis.<sup>14</sup>

### Assessment of covariates

Biennially from 1989, the smoking status and intensity among current smokers was assessed. Data on alcohol intake were available every 4 years from 1991. Physical activity was asked in 1991, 1997, 2001 and 2005, and a good validity and reproducibility was found.<sup>15</sup> Depressive symptoms were assessed with the mental health index 5 in 1993, 1997 and 2001, which has been shown to be valid for major depression.<sup>16</sup> Participants reported regular antidepressant medication use biennially from 1993. Menopausal status and postmenopausal hormone use, personal history of cancer, diabetes, cardiovascular disease, hypertension and hypercholesterolaemia were collected biennially.

### Statistical analysis

Two sets of analyses were performed to evaluate the risk of PsA associated with obesity among all participants, as well as among those with psoriasis. For all the main analyses, of the 97 476 responders, we excluded participants who did not respond to the psoriasis question in 2005 (N=58), prevalent psoriasis or PsA in 1991 (N=1376), those unable to pass the confirmation of self-reports (N=97) or without response to the psoriasis screening tool or PASE questionnaire (N=467), PsA with missing diagnosis date (N=2), and participants with BMI less than 10 or missing (N=6334). For the analysis among total participants, we excluded incident individuals with psoriasis without musculoskeletal phenotypes in the previous follow-up period (N=93); therefore 89 049 participants remained. For the analysis among individuals with psoriasis, we excluded participants who did not develop psoriasis (N=88 586), 556 with confirmed psoriasis remained. Because we excluded self-reported psoriasis cases that were not validated in the main analysis, we also performed a sensitivity analysis by using all self-reports.

We calculated person-years from the return date of the 1991 questionnaire to the psoriasis diagnosis date, or the end of follow-up (June 2005), whichever came first. Information on BMI was categorised as less than 25.0, 25.0–29.9, 30.0–34.9, or 35.0 or greater, and updated during the follow-up. The cutoffs were

consistent with the classification of WHO on overweight, obesity class I and obesity class II. Given the distribution of subjects, BMI at age 18 years was classified as less than 21.0, 21.0–22.9, 23.0–24.9, 25.0–29.9, or 30.0 or greater. Weight change was classified as four categories (loss or increase of <20.0, 20.0–49.9, 50.0–99.9, or ≥100.0 lbs). We analysed waist circumference, hip circumference and WHR in tertiles. Cox proportional hazards analysis stratified by age and follow-up interval was performed to calculate the age and multivariate-adjusted RR and 95% CI. Multivariate models were adjusted for age (continuous), smoking (never, past, current with 1–14, 15–24, or ≥25 cigarettes/day), vigorous physical activity (metabolic equivalent hours/week, in quintiles) and alcohol intake (0, <4.9, 5.0–9.9, 10–14.9, 15–29.9, or ≥30.0 g/day). Linear trend tests were conducted by using the median in different categories. To evaluate the change of association, we performed association analyses between obesity and the risk of PsA by including cases with PASE scores less than the first, second, third and fourth quartile, respectively.

As a sensitivity analysis, level of depressive symptoms (mental health index 5 scores, 86–100, 76–85, 53–75 or 0–52) or antidepressant medication use (never, past or current), postmenopausal hormone use (premenopausal, never or ever users), personal history of chronic diseases (yes or no, including cancer, diabetes, cardiovascular disease, hypertension and hypercholesterolaemia) were concomitantly adjusted for. Another sensitivity analysis was performed in a case–control design to include all PsA and confirmed individuals with psoriasis before and after 1991. Analyses were carried out by using SAS software (version 9.2). All p values were two-tailed with the significance level set at p<0.05. The study was approved by the institutional review board of Partners Health Care System. The participants' return of a completed questionnaire was accepted as informed consent to the present study.

### RESULTS

Participants with higher BMI were more likely to be older and tended to have less alcohol intake and less physical activity. We observed an increase in weight at age 18 years, weight gain, waist and hip circumference and WHR, with increasing categories of BMI in 1991 (table 1).

We documented 146 incident PsA cases during 1231 693 person-years of follow-up. The risk of PsA was monotonically elevated with increasing BMI (p for trend <0.0001). Compared with BMI less than 25.0, the risk of BMI 25.0–29.9, 30.0–34.9 and 35.0 or greater increased to 1.83 (95% CI 1.15 to 2.89), 3.12 (95% CI 1.90 to 5.11) and 6.46 (95% CI 4.11 to 10.16), respectively (table 2). There was a trend towards an increased risk of PsA by weight change since the age of 18 years and the RR of PsA by weight gain of 10 lb was 1.17 (95% CI 1.12 to 1.22). The positively graded association persisted when analysing the central adiposity measures (p for trend <0.001). When one measure of central obesity (waist circumference, hip circumference, or WHR) was included in the model with BMI, its association remained significant except for WHR after adjusting for BMI (p for trend=0.064) (table 2 and supplementary tables S1 and S2, available online only).

We repeated all the analyses by excluding participants without developing psoriasis to examine the risk of PsA among individuals with psoriasis (table 3). Participants with BMI of 35.0 or greater were 2.98 times more likely to develop PsA (95% CI 1.86 to 4.78, p for trend <0.0001). Similarly, the risk of PsA among confirmed psoriasis was monotonically elevated with weight change (p for trend <0.0001) and measures of central obesity (p for trend all <0.01). We also evaluated the effect estimates

**Table 1** Characteristics of study participants by body mass index in 1991, Nurses' Health Study II\*

	Body mass index			
	<25.0	25.0–29.9	30.0–34.9	≥35.0
n	58 947	18 225	7 144	4 733
Age,† mean (SD), years	35.9 (4.6)	36.6 (4.7)	37.0 (4.6)	37.3 (4.4)
Current smokers (yes, %)	11.3	12.1	11.4	10.9
Alcohol intake, g/day, mean (SD)	3.5 (6.3)	2.8 (6.0)	2.0 (5.0)	1.6 (4.7)
Vigorous physical activity, metabolic equivalent hours/week, mean (SD)	15.3 (24.3)	11.6 (19.2)	9.4 (16.1)	7.5 (14.2)
Height, inches, mean (SD)	64.9 (2.5)	64.8 (2.7)	64.7 (2.7)	64.7 (3.0)
Weight at age 18 years, lb, mean (SD)	120.7 (15.4)	133.0 (20.5)	143.8 (25.3)	161.8 (33.3)
Weight change from age 18 years, lb, mean (SD)	9.3 (13.4)	28.8 (18.4)	47.9 (23.1)	75.9 (33.9)
Waist circumference, inches, mean (SD)	28.8 (3.1)	33.5 (3.9)	37.9 (4.5)	42.8 (5.7)
Hip circumference, inches, mean (SD)	37.5 (2.6)	41.7 (3.3)	45.6 (3.9)	51.0 (5.4)
Waist–hip ratio, mean (SD)	0.77 (0.07)	0.81 (0.08)	0.83 (0.08)	0.84 (0.09)
Mental health index ≤52 (yes, %)‡	12.2	14.1	15.9	17.4
Antidepressant use (yes, %)‡	9.6	11.5	13.5	17.1
Postmenopausal (yes, %)	3.1	3.5	4.1	5.6
Personal history of chronic diseases (yes, %)				
Diabetes	0.3	0.5	1.4	2.6
Cancer	1.5	1.2	1.1	0.9
Cardiovascular disease	0.4	0.4	0.7	0.9
Hypertension	1.6	4.0	8.0	14.7
Hypercholesterolaemia	7.3	11.7	16.3	16.9

\*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.

‡Mental health index and antidepressant use in 1993.

by concomitantly adjusting for BMI and one measure of central obesity, BMI and WHR remained significant when cross-adjusting (table 3 and supplementary tables S1 and S2, available online only). The effect values of BMI remained similar across analyses adjusting for measures of central obesity.

We compared the association between obesity and PsA with severity scores less than the first (49), second (53), third (58) and fourth (75) quartile both among the total participants and among individuals with psoriasis. We observed an elevation of RR when including PsA with the higher PASE scores (data not shown).

Stratified analysis by smoking or physical activity did not find any material differences. We performed secondary analyses by adjusting for the level of depressive symptomatology or anti-depressive medication use, postmenopausal hormone use and personal history of chronic diseases and no material change of the results was observed. Sensitivity analysis was carried out to examine the association between obesity and PsA among all self-reported individuals with psoriasis (data not shown). A case-control analysis was conducted to incorporate the information of prevalent cases (supplementary tables S3 and S4, available online only) and the association remains robust.

## DISCUSSION

We prospectively evaluated the association between measures of adiposity and the risk of incident PsA in a well-established cohort of women. Our results indicated a markedly accumulated risk of PsA, correlated with BMI, weight change since early adulthood, waist and hip circumference and WHR, both among total participants and among women with psoriasis. These associations existed in a dose-dependent fashion, highlighting the effect of adiposity in the development of PsA.

The cutaneous and musculoskeletal effects of adiposity have received great interest recently. Obesity was demonstrated as an independent risk factor for psoriasis in our prospective study.<sup>3</sup>

A cross-sectional study also pointed to the link particularly among those with severe psoriasis.<sup>17</sup> However, there is still a lack of agreement on the severity of skin phenotypes between psoriasis and PsA.<sup>18 19</sup> The adverse effect of obesity on the risk of osteoarthritis has been published.<sup>4 5</sup> Although obesity was found to be associated with an increased risk of RA, several recent studies did not support this association, as reviewed by Stavropoulos-Kalinoglou *et al.*<sup>6</sup> Interestingly, RA patients with high BMI have lower mortality than thinner patients.<sup>20</sup> Given the marked differences between PsA and other types of arthritis, addressing the role of obesity in PsA development was needed. Moreover, in this study, we were able to evaluate the correlation between obesity and PsA both among the total participants and among those with psoriasis.

In general, there are sparse data on the association between obesity and PsA. Tam *et al*<sup>9</sup> observed a higher current BMI and WHR among PsA compared with healthy controls, but failed to find a significant difference for waist circumference. Soltani-Arabshahi *et al*<sup>10</sup> suggested that BMI in early adulthood increased the risk of PsA, but they did not observe an association between current BMI or other measures of obesity and PsA. In addition, the study design left uncertainty regarding the temporal relationship and did not allow for causal inference. In our prospective analysis, BMI conveys a significantly increased risk of PsA in a dose-dependent manner. In contrary to a report on RA,<sup>20</sup> the association was stronger in our study, when including more severe PsA, as defined by higher PASE scores. Weight gain from early adulthood and measures of central obesity also monotonically increased the risk. The effect was robust among never and ever smokers, those with more or less physical activity, comprehensively demonstrating the independent role of high adiposity in the development of PsA.

Obesity at age 18 years appears to be the only measure that became null when we performed the analyses among psoriasis cases, which did not replicate the observation among total

**Table 2** Age and multivariate-adjusted RR for the association of adiposity measurements with risk of psoriatic arthritis among all participants\*

	Cases	Person-years	Age-adjusted RR (95% CI)	Multivariate-adjusted RR† (95% CI)
Updated BMI (kg/m <sup>2</sup> )	146	1 231 693		
<25.0	40	703 190	1.00	1.00
25.0–29.9	35	297 149	1.88 (1.19 to 2.96)	1.83 (1.15 to 2.89)
30.0–34.9	28	133 146	3.22 (1.98 to 5.26)	3.12 (1.90 to 5.11)
≥35.0	43	98 208	6.60 (4.26 to 10.23)	6.46 (4.11 to 10.16)
p for trend			<0.0001	<0.0001
BMI at age 18 years (kg/m <sup>2</sup> )	145	1 222 076		
<21.0	67	701 559	1.00 (0.64 to 1.58)	1.04 (0.66 to 1.64)
21.0–22.9	26	272 700	1.00	1.00
23.0–24.9	24	125 453	2.01 (1.15 to 3.50)	1.93 (1.11 to 3.37)
25.0–29.9	17	93 857	1.88 (1.02 to 3.46)	1.74 (0.94 to 3.21)
≥30.0	11	28 508	4.07 (2.01 to 8.24)	3.55 (1.75 to 7.23)
p for trend			<0.0001	<0.0001
Weight change from age 18 years (lb)	145	1 222 076		
Loss or increase of <20.0	32	563 364	1.00	1.00
Increase of 20.0–49.9	45	435 087	1.68 (1.06 to 2.65)	1.72 (1.09 to 2.72)
Increase of 50.0–99.9	50	191 981	3.88 (2.46 to 6.13)	3.67 (2.31 to 5.84)
Increase of ≥100.0	18	31 645	8.09 (4.48 to 14.64)	7.00 (3.78 to 12.96)
p for trend			<0.0001	<0.0001
Waist circumference (inches)	72	599 200		
Tertile 1, <28.0	7	168 183	1.00	1.00
Tertile 2, 28.0–31.9	17	227 235	1.72 (0.71 to 4.16)	1.65 (0.68 to 4.00)
Tertile 3, ≥32.0	48	203 782	5.05 (2.28 to 11.20)	4.82 (2.15 to 10.83)
p for trend			<0.0001	<0.0001
Hip circumference (inches)	70	597 544		
Tertile 1, <38.0	13	233 613	1.00	1.00
Tertile 2, 38.0–40.9	13	187 362	1.18 (0.55 to 2.56)	1.25 (0.58 to 2.72)
Tertile 3, ≥41.0	44	176 569	4.02 (2.16 to 7.51)	4.32 (2.27 to 8.24)
p for trend			<0.0001	<0.0001
Waist–hip ratio	70	596 835		
Tertile 1, <0.744	12	199 028	1.00	1.00
Tertile 2, 0.744–0.800	20	207 096	1.58 (0.77 to 3.23)	1.49 (0.73 to 3.06)
Tertile 3, >0.800	38	190 712	3.12 (1.63 to 5.98)	2.84 (1.48 to 5.48)
p for trend			0.0002	0.0006

\*Psoriasis cases with only skin phenotypes were excluded during the follow-up.

†Adjusted for age (continuous variable), smoking (never, past, current with 1–14, 15–24, or ≥25 cigarettes/day), 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 hours/week, in quintile), and height (inches, for the analysis of waist circumference, hip circumference and waist–hip ratio), and weight at 18 years (for the analysis of weight change from 18 years).  
BMI, body mass index.

participants and of a previous report.<sup>10</sup> On the other hand, weight gain from age 18 years was robustly associated with the risk of PsA with a beyond 10% elevated risk per 10 lb weight increase. Weight change rather than weight at early adulthood may serve as a major relevant factor.

Anthropometric measures of abdominal obesity have been proposed as substantial indicators of health risk.<sup>21–23</sup> Our analysis showed similar trends in the risk of PsA associated with waist circumference, hip circumference and WHR. Cross-adjustment of BMI and measures of central obesity reached similar effect values of BMI, even some of which did not fulfil statistical significance possibly due to the increased standard error by co-linearity. Central obesity measures were greatly attenuated but still had a residual effect on the risk of PsA even after adjusting for BMI. Stratified analysis by BMI indicated especially for the non-obese participants (BMI <30 kg/m<sup>2</sup>) central obesity was significantly associated with the risk of PsA.

Inflammation may be the key mechanism underlying our findings. Obesity in psoriasis has been associated with both decreased plasma levels of adiponectin and enhanced systemic inflammation and oxidative stress.<sup>24–28</sup> Adiposity can augment

cytokine expression by the recruited inflammatory infiltrate, such as interleukin 6 and tumour necrosis factor  $\alpha$ , relevant to psoriasis pathophysiology.<sup>26–28</sup> The leptin and resistin overload may elicit the cutaneous pro-inflammatory changes in psoriasis.<sup>29</sup> Given that PsA is a well-recognised systemic inflammatory disorder, a fundamental pathological process that leads to PsA could be the chronic inflammatory state induced by adiposity.<sup>1, 2</sup> Alternatively, obesity and PsA may share some still unknown common cause. Despite a statistical association, it is early to jump to a conclusion about a causal link. Obesity may serve as a surrogate endpoint for other risk factors of PsA, although smoking or physical activity does not seem to modify the association. Another possible mechanism to explain this link is mental health disorders. Psoriasis has been associated with depression, which appears to be reciprocally correlated with obesity.<sup>30, 31</sup> We observed a higher percentage of participants with depression symptoms and antidepressant medication use among the obese. However, sensitivity analyses accounting for depression did not materially change the results in this study, indicating that the role of obesity is independent of depression.

**Table 3** Age and multivariate-adjusted RRs for the association of adiposity measurements with risk of psoriatic arthritis among participants with confirmed psoriasis

	Cases	Person-years	Age-adjusted RR (95% CI)	Multivariate-adjusted RR* (95% CI)
Updated BMI (kg/m <sup>2</sup> )	146	6838		
<25.0	40	3245	1.00	1.00
25.0–29.9	35	1533	1.80 (1.12 to 2.88)	1.81 (1.12 to 2.93)
30.0–34.9	28	1051	1.98 (1.19 to 3.28)	1.90 (1.13 to 3.18)
≥35.0	43	1009	2.97 (1.88 to 4.69)	2.98 (1.86 to 4.78)
p for trend			<0.0001	<0.0001
BMI at age 18 years (kg/m <sup>2</sup> )	145	6791		
<21.0	67	3265	1.23 (0.77 to 1.96)	1.28 (0.79 to 2.06)
21.0–22.9	26	1668	1.00	1.00
23.0–24.9	24	858	1.74 (0.98 to 3.09)	1.73 (0.96 to 3.13)
25.0–29.9	17	610	1.69 (0.89 to 3.20)	1.69 (0.88 to 3.26)
≥30.0	11	390	1.61 (0.76 to 3.42)	1.53 (0.71 to 3.29)
p for trend			0.10	0.20
Weight change from age 18 years (lb)	145	6791		
Loss or increase of <20.0	32	2669	1.00	1.00
Increase of 20.0–49.9	45	2285	1.36 (0.84 to 2.18)	1.34 (0.82 to 2.17)
Increase of 50.0–99.9	50	1513	2.31 (1.46 to 3.68)	2.42 (1.49 to 3.91)
Increase of ≥100.0	18	324	3.28 (1.76 to 6.11)	3.84 (1.93 to 7.63)
p for trend			<0.0001	<0.0001
Waist circumference (inches)	72	3272		
Tertile 1, <28.0	7	746	1.00	1.00
Tertile 2, 28.0–31.9	17	1045	1.67 (0.63 to 4.38)	1.46 (0.54 to 3.99)
Tertile 3, ≥32.0	48	1481	3.23 (1.36 to 7.69)	3.02 (1.21 to 7.56)
p for trend			0.002	0.004
Hip circumference (inches)	70	3245		
Tertile 1, <38.0	13	931	1.00	1.00
Tertile 2, 38.0–40.9	13	917	1.31 (0.56 to 3.05)	1.24 (0.51 to 3.00)
Tertile 3, ≥41.0	44	1397	2.35 (1.15 to 4.79)	2.59 (1.18 to 5.69)
p for trend			0.009	0.006
Waist–hip ratio	70	3245		
Tertile 1, <0.744	12	1008	1.00	1.00
Tertile 2, 0.744–0.800	20	996	1.43 (0.67 to 3.06)	1.41 (0.63 to 3.15)
Tertile 3, >0.800	38	1241	2.36 (1.18 to 4.74)	2.48 (1.20 to 5.15)
p for trend			0.009	0.008

\*Adjusted for age (continuous variable), smoking (never, past, current with 1–14, 15–24, or ≥25 cigarettes/day), 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 hours/week, in quintile), and height (inches, for the analysis of waist circumference, hip circumference and waist–hip ratio) and weight at 18 years (for the analysis of weight change from 18 years).  
BMI, body mass index.

To our knowledge, this is the first prospective study on this topic. We observed a compelling association by employing multiple markers of obesity to probe into the risk of PsA. Because the anthropometric measures may change over time, using updated BMI and weight change over time instead of only BMI at baseline allowed us to evaluate the harms of continuing gain in weight and also to evaluate the benefits of weight loss. Our study was reasonably powered. A variety of sensitivity analyses were applied and the results did not differ appreciably, arguing for the robustness of the observations.

Our study also has retrospective characteristics and selection and information bias may be a concern. Survivorship bias would be a major concern on the selection of participants given that the psoriasis question was asked in 2005. However, a cohort of younger women ensures our results were less likely to be greatly distorted. The mean age of those who did not respond to the psoriasis question was even slightly younger compared with responders. Potential recall bias may be caused by retrospective enquiry of the main outcome. However, the healthcare-related professional background of our participants was reassuring and psoriasis self-reports have reached a confirmation rate of 92%.<sup>12</sup> Case ascertainment of

clinician-diagnosed PsA by PASE questionnaire among self-reported individuals with psoriasis could be another major concern, which may lead to misclassification bias. However, PASE was testified to be a valid and reliable screening tool for PsA, particularly active PsA among psoriasis cases in previous pilot studies.<sup>13 14</sup> The prevalence of PsA among individuals with confirmed psoriasis from 1991 is 21.2%, falling within the range of previous reports.<sup>1</sup> There may be concerns about possible misclassification with other musculoskeletal diseases. Previous studies reported an adverse effect of obesity on osteoarthritis and fibromyalgia.<sup>4 5 32</sup> However, PASE can distinguish the symptoms of PsA from osteoarthritis, albeit less of a concern in a younger cohort. Fibromyalgia seldom occurs in patients with psoriasis. It would be worth noting that central obesity was only asked once during the follow-up, while we had the opportunity to update BMI and weight change over time. However, a previous study has indicated the validity of the measurements.<sup>11</sup> PsA cases without concomitant psoriasis were excluded in our analysis. The effect of obesity on these cases, known as seronegative inflammatory arthritis or spondyloarthritis, needs to be clarified further. The participants were primarily younger and middle-aged female Caucasians.

Although the biological effects of adiposity should be similar and the homogeneity of study participants led to less confounding by socioeconomic status, the generalisability to other populations, particularly men, and other racial/ethnic minorities, may be made cautiously.

In conclusion, our large well-characterised cohort study provides evidence of a dose-dependent relationship between overall obesity, central adiposity and an increased risk of PsA in women. The effect of obesity on PsA goes beyond that on psoriasis skin phenotypes alone. In this issue, another paper on a similar topic by Love *et al*<sup>63</sup> was also published, which followed up a cohort of psoriasis patients by general practitioners in northern UK, providing further testifying evidence to our study. The implication of the observations may be substantial as obesity is a modifiable factor that is becoming increasingly prevalent. Further studies are warranted to elucidate the underlying mechanisms and clarify the causative association.

**Contributors** AAQ had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: AAQ, JH and WL. Acquisition of data: AAQ and JH. Analysis and interpretation of data: WL, AAQ and JH. Drafting of the manuscript: WL, AAQ and JH. Critical revision of the manuscript for important intellectual content: WL, AAQ and JH. Statistical analysis: WL. Obtained funding: AAQ. Administrative, technical, or material support: AAQ and JH. Study supervision: WL, AAQ and JH.

**Funding** The work is supported by the Department of Dermatology, Brigham and Women's Hospital, NHS II grant R01 CA50385.

**Competing interests** AAQ has received a grant from Amgen/Pfizer to evaluate 'Biomarkers in psoriasis and psoriatic arthritis'. AAQ also serves as a consultant for Abbott, Centocor, Novartis and the Centers for Disease Control and Prevention. The other authors state no conflict of interest.

**Ethics approval** The institutional review board of Partners Health Care System approved this study.

**Patient consent** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

## REFERENCES

- 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.
- Nogales KE, Brasington RD, Bowcock AM. New insights into the pathogenesis and genetics of psoriatic arthritis. *Nat Clin Pract Rheumatol* 2009;**5**:83–91.
- Setty AR, Curhan G, Choi HK. Obesity, waist circumference, weight change, and the risk of psoriasis in women: Nurses' Health Study II. *Arch Intern Med* 2007;**167**:1670–5.
- Griffin TM, Huebner JL, Kraus VB, *et al*. Induction of osteoarthritis and metabolic inflammation by a very high-fat diet in mice: effects of short-term exercise. *Arthritis Rheum* 2012;**64**:443–53.
- Sowers MR, Karvonen-Gutierrez CA. The evolving role of obesity in knee osteoarthritis. *Curr Opin Rheumatol* 2010;**22**:533–7.
- Stavropoulos-Kalinoglou A, Metsios GS, Koutedakis Y, *et al*. Obesity in rheumatoid arthritis. *Rheumatology (Oxford)* 2011;**50**:450–62.
- 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.
- Pedersen M, Jacobsen S, Klarlund M, *et al*. Environmental risk factors differ between rheumatoid arthritis with and without auto-antibodies against cyclic citrullinated peptides. *Arthritis Res Ther* 2006;**8**:R133.
- Tam LS, Tomlinson B, Chu TT, *et al*. Cardiovascular risk profile of patients with psoriatic arthritis compared to controls—the role of inflammation. *Rheumatology (Oxford)* 2008;**47**:718–23.
- 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.
- Rimm EB, Stampfer MJ, Colditz GA, *et al*. Validity of self-reported waist and hip circumferences in men and women. *Epidemiology* 1990;**1**:466–73.
- Dominguez PL, Assarpour A, Kuo H, *et al*. Development and pilot-testing of a psoriasis screening tool. *Br J Dermatol* 2009;**161**:778–84.
- 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.
- 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.
- Wolf AM, Hunter DJ, Colditz GA, *et al*. Reproducibility and validity of a self-administered physical activity questionnaire. *Int J Epidemiol* 1994;**23**:991–9.
- Berwick DM, Murphy JM, Goldman PA, *et al*. Performance of a five-item mental health screening test. *Med Care* 1991;**29**:169–76.
- Neimann AL, Shin DB, Wang X, *et al*. Prevalence of cardiovascular risk factors in patients with psoriasis. *J Am Acad Dermatol* 2006;**55**:829–35.
- 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.
- Gisondi P, Tinazzi I, Del Giglio M, *et al*. The diagnostic and therapeutic challenge of early psoriatic arthritis. *Dermatology (Basel)* 2010;**221** (Suppl 1):6–14.
- Escalante A, Haas RW, del Rincón I. Paradoxical effect of body mass index on survival in rheumatoid arthritis: role of comorbidity and systemic inflammation. *Arch Intern Med* 2005;**165**:1624–9.
- Bigaard J, Thomsen BL, Tjønneland A, *et al*. Does waist circumference alone explain obesity-related health risk? *Am J Clin Nutr* 2004;**80**:790–1; author reply 791–2.
- Bray GA. Don't throw the baby out with the bath water. *Am J Clin Nutr* 2004;**79**:347–9.
- Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 2004;**79**:379–84.
- Gerdes S, Rostami-Yazdi M, Mrowietz U. Adipokines and psoriasis. *Exp Dermatol* 2011;**20**:81–7.
- Kaur S, Zilmer K, Kairane C, *et al*. Clear differences in adiponectin level and glutathione redox status revealed in obese and normal-weight patients with psoriasis. *Br J Dermatol* 2008;**159**:1364–7.
- Davidovici BB, Sattar N, Prinz JC, *et al*. Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. *J Invest Dermatol* 2010;**130**:1785–96.
- Hamminga EA, van der Lely AJ, Neumann HA, *et al*. Chronic inflammation in psoriasis and obesity: implications for therapy. *Med Hypotheses* 2006;**67**:768–73.
- Sterry W, Strober BE, Menter A. Obesity in psoriasis: the metabolic, clinical and therapeutic implications. Report of an interdisciplinary conference and review. *Br J Dermatol* 2007;**157**:649–55.
- Johnston A, Arnadottir S, Gudjonsson JE, *et al*. Obesity in psoriasis: leptin and resistin as mediators of cutaneous inflammation. *Br J Dermatol* 2008;**159**:342–50.
- Luppino FS, de Wit LM, Bouvy PF, *et al*. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry* 2010;**67**:220–9.
- Campolmi E, Zanieri F, Santosuosso U, *et al*. The importance of stressful family events in psoriatic patients: a retrospective study. *J Eur Acad Dermatol Venereol* [Epub ahead of print 29 Sep 2011]. doi: 10.1111/j.1468-3083.2011.04268.x.
- Ursini F, Naty S, Grembale RD. Fibromyalgia and obesity: the hidden link. *Rheumatol Int* 2011;**31**:1403–8.
- Love TJ, Zhu Y, Zhang Y, *et al*. Obesity and the risk of psoriatic arthritis: a population-based study. *Ann Rheum Dis* 2012;**71**:1273–7.