

LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



LSHTM Research Online

Langan, SM; Seminara, NM; Shin, DB; Troxel, AB; Kimmel, SE; Mehta, NN; Margolis, DJ; Gelfand, JM; (2012) Prevalence of Metabolic Syndrome in Patients with Psoriasis: A Population-Based Study in the United Kingdom. *The Journal of investigative dermatology*, 132 (3 Pt 1). pp. 556-62. ISSN 0022-202X DOI: <https://doi.org/10.1038/jid.2011.365>

Downloaded from: <http://researchonline.lshtm.ac.uk/20433/>

DOI: <https://doi.org/10.1038/jid.2011.365>

**Usage Guidelines:**

Please refer to usage guidelines at <https://researchonline.lshtm.ac.uk/policies.html> or alternatively contact [researchonline@lshtm.ac.uk](mailto:researchonline@lshtm.ac.uk).

Available under license: <http://creativecommons.org/licenses/by-nc-nd/2.5/>

<https://researchonline.lshtm.ac.uk>



Published in final edited form as:

*J Invest Dermatol.* 2012 March ; 132(3): 556–562. doi:10.1038/jid.2011.365.

## Prevalence of metabolic syndrome in patients with psoriasis: A population-based study in the United Kingdom

**Sinéad M. Langan, MRCP, PhD<sup>1,2</sup>, Nicole M. Seminara, MA<sup>2</sup>, Daniel B. Shin, MA<sup>2</sup>, Andrea B. Troxel, ScD<sup>3,5</sup>, Stephen E. Kimmel, MD, MSCE<sup>4</sup>, Nehal N. Mehta, MD, MSCE<sup>3,4</sup>, David J. Margolis, MD, PhD<sup>2,3</sup>, and Joel M. Gelfand, MD, MSCE<sup>2,3</sup>**

<sup>1</sup>Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London, UK

<sup>2</sup>Department of Dermatology, University of Pennsylvania, Philadelphia, PA, USA

<sup>3</sup>Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, PA, USA

<sup>4</sup>Department of Medicine, University of Pennsylvania, Philadelphia, PA, USA

<sup>5</sup>Department of Biostatistics and Epidemiology, University of Pennsylvania, Philadelphia, PA, USA

### Abstract

Increasing epidemiological evidence suggests independent associations between psoriasis and cardiovascular and metabolic disease. Our objective was to test the hypothesis that directly-assessed psoriasis severity relates to the prevalence of metabolic syndrome and its components.

Population-based, cross-sectional study using computerized medical records from The Health Improvement Network Study population included individuals aged 45-65 years with psoriasis and practice-matched controls. Psoriasis diagnosis and extent were determined using provider-based questionnaires. Metabolic syndrome was defined using National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III criteria.

44,715 individuals were included: 4,065 with psoriasis and 40,650 controls. 2,044 participants had mild psoriasis ( $\leq 2\%$  body surface area (BSA)), 1,377 had moderate (3-10% BSA), and 475 had severe psoriasis ( $> 10\%$  BSA). Psoriasis was associated with metabolic syndrome, adjusted odds ratio (OR) 1.41 (95% CI 1.31-1.51), varying in a “dose-response” manner, from mild (adj. OR 1.22, 95% CI 1.11-1.35) to severe psoriasis (adj. OR 1.98, 95% CI 1.62-2.43).

Psoriasis is associated with metabolic syndrome and the association increases with increasing disease severity. Furthermore, associations with obesity, hypertriglyceridemia and hyperglycemia increase with increasing disease severity independent of other metabolic syndrome components.

---

Correspondence to: Dr Sinéad Langan, Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK. sinead.langan@lshtm.ac.uk, Tel: +44 2079272680; Fax: +44 2075806897.

Conflict of Interest: JMG has received grants from Amgen, Pfizer, Novartis, and Abbott, and is a consultant for Amgen, Celgene, Pfizer, Novartis, and Centocor; DJM is on separate data safety monitoring boards for Abbott and Astellas that might have an interest in the submitted work in the previous 3 years; none of the other authors have any conflict of interest to declare.

Contributors: JMG, DM, NM, ABT, SK were involved in the conception of the research question, planning the study and applying for funding. DBS extracted the data from the THIN database and assisted with data management and guidance on the use of THIN. Further data management was carried out by SL and NMS. SL, NMS, ABT and JMG were involved in analysis of the data. SL and JMG drafted the manuscript which was reviewed by all authors. SL is the guarantor. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

These findings suggest that screening for metabolic disease should be considered for psoriasis, especially when extensive.

## Introduction

The metabolic syndrome is a clustering of cardiovascular risk factors, specifically obesity, hypertension, dyslipidemia and insulin resistance (Eckel *et al.*, 2005), which has been associated with increased risk of cardiovascular disease (CVD) beyond traditional risk factors (Mente *et al.*, 2010). The prevalence of metabolic syndrome is increasing in the United States (US) (Ford *et al.*, 2002) and Europe in part paralleling the rising prevalence of obesity worldwide (Mente *et al.*, 2010; Mokdad *et al.*, 2003). Systemic inflammation is associated with metabolic syndrome, with T helper cell type 1 (Th-1) pro-inflammatory cytokines such as tumor necrosis factor  $\alpha$  and non-specific measures of inflammation such as C reactive protein levels being elevated compared to those without the metabolic syndrome (Lakka *et al.*, 2002). However, there is a limited understanding of the relationship between chronic inflammatory diseases and the prevalence of metabolic syndrome.

Psoriasis is the most common Th-1 inflammatory disease, affecting more than 125 million people worldwide (National Psoriasis Foundation). The severity of psoriasis in the general population is variable, with most patients having mild disease (Kurd and Gelfand, 2009) defined as involving  $\leq 2\%$  body surface area. Epidemiological evidence suggests that psoriasis is associated with an increased frequency of cardiovascular risk factors and adverse cardiovascular outcomes including myocardial infarction (Gelfand *et al.*, 2006), stroke (Gelfand *et al.*, 2009) and cardiovascular death (Mehta *et al.*, 2009). Psoriasis, especially if severe, may be a risk factor for atherosclerotic CVD, beyond traditional risk factors (Gelfand *et al.*, 2009; Gelfand *et al.*, 2006; Mehta *et al.*, 2009). Moreover, patients with severe psoriasis die approximately 5 years younger than patients without psoriasis, with cardiovascular death being the most common cause of excess mortality in these patients (Abuabara *et al.*, 2010). Mechanistic studies of the metabolic syndrome (Shah *et al.*, 2009) and insulin resistance (Mehta *et al.*, 2010) suggest that chronic Th-1 inflammation that characterizes psoriasis, metabolic syndrome, diabetes and CVD may in part explain the association of these phenotypically distinct diseases.

A number of small, epidemiological studies have reported associations between psoriasis and metabolic syndrome (Al-Mutairi *et al.*, 2010; Azfar and Gelfand, 2008; Gisondi and Girolomoni, 2009; Mebazaa *et al.*, 2010), however, population-based data in which severity of psoriasis is objectively determined and individual components of metabolic syndrome are directly measured are lacking (Augustin *et al.*, 2010). Our objective therefore was to examine whether there is an association between psoriasis and the metabolic syndrome in a broadly representative population of patients. We also investigate whether the degree of association varies by extent of skin involvement with psoriasis.

## Results

Table 1 describes the demographics of the study population. At the end of the survey collection period 4,634 of 4,900 provider-based surveys were completed giving a response rate of 95%. Our cohort included 4,065 people with confirmed psoriasis and 40650 matched controls. The mean age of psoriasis patients was 1.2 years older than controls ( $p < 0.001$ ) and 51% of psoriasis patients were male compared to 48% of controls ( $p < 0.001$ ). 2,044 (53%) participants had mild psoriasis ( $\leq 2\%$  body surface area (BSA)), 1,377 (35%) had moderate disease (3-10% BSA), and 475 (12%) had severe psoriasis ( $> 10\%$  BSA). Information on body mass index, blood pressure, HDL, glucose and triglycerides was available for 41,249

(92%), 44,019 (98%), 25234 (56%), 26,144 (64%) and 25,067 (56%) of patients, respectively (Table 2). The availability of these variables was similar in patients with and without psoriasis.

Metabolic syndrome was identified in 34% of participants with psoriasis compared to 26% of controls, odds ratio (OR) 1.50 (95% confidence interval (CI) 1.40-1.61). This association persisted after adjusting for age, gender and follow up, adjusted (adj.) OR 1.41 (95% CI 1.31-1.51). Adjusting for smoking and social class did not change study findings and these were not retained in the final model. Psoriasis severity affected the degree of association, with metabolic syndrome seen in 32% with mild disease (adj. OR 1.22, 95% CI 1.11-1.35), 36% with moderate disease (adj. OR 1.56, 95% CI 1.38-1.76) and 40% of those with severe psoriasis (adj. OR 1.98, 95% CI 1.62-2.43). Modest but statistically significant interactions were detected between psoriasis and age and between psoriasis and sex whereby the odds ratio of metabolic syndrome and psoriasis was slightly higher in younger age groups and in women (data not shown).

Studying the components of metabolic syndrome, the following factors were more common in psoriasis patients than in controls: obesity in 38% vs. 31% (OR 1.38, 95% CI 1.29-1.48), raised triglycerides in 36% vs. 28% (OR 1.49, 95% CI 1.39-1.60), diagnosed hypertension in 31% vs. 28% (OR 1.20, 95% CI 1.11-1.29) and raised glucose in 22% vs. 16% (OR 1.44, 95% CI 1.33-1.56) (Table 2).

In the fully adjusted model to understand which components of the metabolic syndrome were associated with psoriasis after adjusting for other elements of metabolic syndrome and age, gender and duration of follow up, the strongest association between a component of the metabolic syndrome and psoriasis was with obesity, adj. OR 1.25 (95% CI 1.16-1.34). The association with obesity demonstrated a dose-response with a 14% increase in obesity with mild psoriasis, adj. OR 1.14 (95% CI 1.03-1.27), 34% increase in obesity with moderate psoriasis, adj. OR 1.34 (95% CI 1.18-1.53), increasing to a 66% increased odds of being obese in those with severe psoriasis, adj. OR 1.66 (95% CI 1.33-2.07) (Table 3). Hypertriglyceridemia and hyperglycemia showed similar dose-response relationships with severity of psoriasis. There was a 20% increased odds of having raised triglycerides in individuals with psoriasis overall independent of obesity, adj. OR 1.20 (95% CI 1.10-1.31). This association also demonstrated an increase from mild psoriasis where the odds of raised triglycerides was 10% (adj. OR 1.10, 95% CI 0.98-1.25) to a 46% increase in those with severe psoriasis, adj. OR 1.46 (95% CI 1.13-1.88). Raised glucose was also associated with psoriasis independent of obesity, with a 16% increased odds of raised glucose overall, adj. OR 1.16 (95% CI 1.06-1.27) with the association strongest in the group with the most extensive disease (Table 3).

Sensitivity analysis using revised ATP III, International Diabetes Federation (IDF) criteria or limiting lab values to the first or most recent observation and excluding individuals on psoriasis treatments known to impact components of metabolic syndrome, e.g. ciclosporin or acitretin did not significantly change study conclusions (data not shown).

## Discussion

Psoriasis is associated with the metabolic syndrome in a “dose-response” fashion, with a 22% increase in the odds of metabolic syndrome in mild psoriasis, 56% increase in moderate disease, and a 98% increase in those with severe psoriasis. In a fully adjusted model looking at associations between factors comprising the metabolic syndrome and psoriasis after adjusting for other components, independent associations were seen between psoriasis and

obesity (25% increased odds), raised triglycerides (20% increased odds) and raised serum glucose (16% increased odds in a “dose-response fashion” from mild to severe psoriasis.

Strengths of this investigation are that it is a large population-based study with a population broadly representative of the UK population aged 45-65 years, which minimizes selection bias and increases the external validity (i.e., generalizability) of the findings. The “dose response” association detected provides compelling evidence for an association between psoriasis and metabolic syndrome. Study findings were based on laboratory values and objectively measured disease extent which allowed observation of novel findings. Observational study designs are associated with a number of limitations. These include the cross-sectional nature of this study which does not allow us to determine which developed first, psoriasis or the metabolic syndrome. Secondly, we cannot be certain that psoriasis caused the metabolic syndrome; factors including diet, physical inactivity, alcohol or genetic predisposition which have not been evaluated in this study may be acting as confounding or effect modifying factors in this relationship (Davidovici *et al.*, 2010) leading to the possibility of residual confounding. In terms of information bias, two aspects of this study make this an unlikely explanation for the findings: firstly, laboratory and clinical values were recorded at similar rates in psoriasis patients and controls as part of routine medical care by general practitioners unaware of the hypothesis under study, and secondly, the persistence of the study findings in the sensitivity analysis restricting to the first laboratory or clinical value per person. Disease severity was determined by asking the GPs to rate the extent of skin involvement with psoriasis into simple discreet categories

“Disease severity was determined by asking the GPs to rate the extent of skin involvement with psoriasis into simple discreet categories. While previous studies have suggested that UK GPs are reasonably accurate in terms of diagnosing psoriasis (Basarab, et al) direct data on the accuracy of GP assessment of extent of skin involvement with psoriasis is not, to our knowledge, available. We have previously demonstrated “construct validity” of this approach in that patients rated by GPs as having higher BSA categories are more likely to require frequent visits for psoriasis and require systemic therapy specific for psoriasis or phototherapy (Seminara *et al.*, 2010). Moreover, we used the same categories used in epidemiological studies conducted by NHANES and NPF in which patients are asked to rate their degree of skin involvement with psoriasis suggesting that this approach is acceptable (ie. “face” validity). (Dommasch *et al.*, 2009; Krueger *et al.*, 2001; Seminara *et al.*, 2010). Moreover, these data represent “real world” data where extent of psoriasis has been assessed by hundreds of GPs around the UK and resulted in discrimination of the prevalence of metabolic disorders based upon these clinical assessments, demonstrating the usefulness of this approach. Nevertheless, our findings are subject to a form of error (i.e. misclassification of extent of skin involvement) which would be expected to be non-differential and thus bias towards the null. General practitioners were asked to assess the body surface area of involvement the patient typically demonstrates; this measure may not be stable over time, although a previous large cohort study demonstrated that despite various therapeutic interventions, the severity of psoriasis for individuals did not generally change over time. (Nijsten *et al.*, 2007)

This study significantly advances the existing literature looking at psoriasis and the metabolic syndrome as this is the first population-based study to use objective measures of psoriasis severity, direct measurement of the components of metabolic syndrome and standard criteria for diagnosis of metabolic syndrome. Of special interest is the clear “dose response” relationship between psoriasis severity and the metabolic syndrome. No previous study has to our knowledge shown a directional increase in the association with raised triglycerides and increasing psoriasis severity independent of the effects of obesity. The consistency with other study findings (Al-Mutairi *et al.*, 2010; Augustin *et al.*, 2010;

Gisondi and Girolomoni, 2009; Love *et al.*, 2010; Mebazaa *et al.*, 2010), presence of a “dose response” relationship, strong associations and biological plausibility support some causality, but further mechanistic and longitudinal studies are required (Rothman and Greenland, 2005).

A possible biologic mechanism which may account for this association is that the proinflammatory state associated with psoriasis acts as a central driving force for development of the metabolic syndrome. In psoriasis patients, Th1 inflammatory cytokines e.g. TNF- $\alpha$ , IL-1 and IL-6, are increased in skin and blood (Azfar and Gelfand, 2008). These inflammatory mediators may have a range of effects on insulin signalling, lipid metabolism and adipogenesis. Additionally, inflammation-induced insulin resistance may lead to development of a systemic insulin resistant state (Mehta *et al.*, 2010) Further mechanistic studies will be needed to test this hypothesis.

Study findings demonstrate a strong association between psoriasis and the metabolic syndrome, with increasing psoriasis severity being associated with increasing odds of metabolic syndrome. Increased odds of raised triglycerides and serum glucose were seen in individuals with psoriasis independent of the effects of obesity. The results of this study firmly establish that metabolic syndrome is an important comorbidity with psoriasis and that vigilance and enhanced screening may be important in psoriasis patients, particularly those with severe disease. Examining the components of metabolic syndrome associated with psoriasis, weight reduction is clearly a key step to prevent CVD; however our findings also show that screening for the other components of metabolic syndrome, particularly hypertriglyceridemia and raised glucose as these tests are more likely to be abnormal in patients with psoriasis independent of traditional risk factors (such as obesity). Small increases in the individual components of metabolic syndrome have led to an 8% absolute increase in the prevalence of metabolic syndrome overall and a 14% increase in those with severe psoriasis. Further prospective studies are required to determine the directionality of the association between psoriasis and metabolic syndrome and to study other unexplored confounders including diet, physical activity, alcohol and genetic factors which may be important residual confounders in this relationship.

## Materials and methods

### Study design

We conducted a cross-sectional study utilizing The Health Improvement Network (THIN).

### Study population

THIN is a computerised longitudinal general practice database with demographic data similar to the general United Kingdom (UK) population. THIN has anonymised medical record data on 3.4 million “active” patients followed for a cumulative 50 million person years and is broadly representative of the UK population. The THIN database contains demographic details, diagnoses, laboratory results, and prescriptions recorded by general practitioners (GPs), the gatekeepers for medical care in the UK. The version of THIN we used contained data from 413 general practices that use the “In Practice Vision” software. A number of studies have confirmed that THIN data are highly accurate making it ideal for use in epidemiological research (Lewis *et al.*, 2007; Seminara *et al.*, 2010). The cohort was identified from individuals aged 45 to 64 years with at least one psoriasis Read code (using a previously validated coding algorithm (Seminara *et al.*, 2010)) in the two years before the survey. Patients were required to be registered with a general practice contributing actively to Additional Information Services (AIS). AIS practices have an agreement to respond to questionnaires; 55% (n=228) of THIN practices were AIS active at the time of sampling.

4,900 eligible patients with psoriasis diagnostic codes were randomly sampled, and questionnaires were sent to their general practitioners through AIS to verify the presence of psoriasis and extent of disease. Up to 10 controls aged 45 to 64 years were randomly matched to each psoriasis patient based on practice; similar to cases, controls needed to be alive and actively registered with at least one general practitioner visit within 2 years at the time of sampling

## Outcomes

Patients were defined as having psoriasis if their diagnosis was confirmed by a questionnaire completed by their general practitioner. The questionnaire also determined the severity of psoriasis, namely mild psoriasis (<2% body surface area), moderate psoriasis (3-10% body surface area) and severe psoriasis (>10% body surface area). This approach has been previously well accepted (Feldman, 2004). Cardiovascular risk factors, specifically body mass index (BMI) calculated using standard formulation (overweight was defined as BMI  $\geq 25$  kg/m<sup>2</sup> and <30 kg/m<sup>2</sup>, obese was defined as  $\geq 30$  kg/m<sup>2</sup>), hypertension, hyperlipidaemia, smoking and diabetes mellitus, were identified by the presence of diagnostic Read codes and additional recording and laboratory values in the Additional Health Details portion of the database.

Subjects were defined as having metabolic syndrome using the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III diagnostic criteria (Expert Panel on Detection, 2001). Using NCEP criteria, a person with metabolic syndrome fulfills 3 or more of the following criteria: central obesity (determined by a BMI  $\geq 30$  in THIN), hypertriglyceridaemia  $\geq 1.7$  mmol/l, low HDL cholesterol (in men <1.03 mmol/l and in women <1.29 mmol/l), high blood pressure  $\geq 130/85$  mmHg and high fasting glucose  $\geq 6.1$  mmol/l. Time-varying variables were dealt with by selecting the maximum laboratory value or clinical measurement and using the most recent value for body mass index. Measurement of conditions occurred from the patients start date (defined as the latest of the Vision software or computerisation in the practice and registration dates of the patient) while the end of the study was defined as earliest date of transfer out, death or end of the study period in February 2009.

## Study size

We calculated that a sample size of 4,900 would yield 4,190 patients which would be sufficient to detect increased relative risks of 1.14 for a BMI of 25 or greater, 1.37 for hypertension, 1.71 for hyperlipidaemia and 2.0 for diabetes mellitus with 80% power respectively assuming a two-sided test and a significance level of 0.05 and we were satisfied that such differences would be clinically meaningful.

## Statistical methods

Odds ratios (OR) and 95% confidence intervals (CI) for the association between psoriasis overall and by psoriasis extent were calculated using conditional logistic regression. Multiplicative interaction terms were fitted to assess effect modification by age and sex. Adjusted ORs were determined adjusting for confounders including age, sex and duration of follow up time in THIN. Other possible confounders which were explored included smoking and social class, measured using Townsend scores (Phillimore *et al.*, 1994). Further analyses were undertaken of the association between psoriasis and disease extent and the components of metabolic syndrome to ensure that findings were not explained by individual components such as obesity. Sensitivity analyses were undertaken using the revised NCEP ATP III definition (glucose cut point >5.6 mmol/l) and the International Diabetes Federation (IDF) definitions of metabolic syndrome (Zimmet *et al.*, 2005). Sensitivity analyses were also carried out using only the first and most recent laboratory value for each individual and in

patients who did not receive psoriasis treatments that may affect blood pressure and lipids (i.e. ciclosporin or acitretin). All analyses were carried out in Stata SE10 (Stata Corporation, College Station, TX, USA)

## Ethics

This study was approved by the University of Pennsylvania institutional review board and the Cambridgeshire Research Ethics Committee and was funded by the National Heart Lung and Blood Institute of the NIH.

## Role of the funding source

The sponsors had no role in the conduct or interpretation of the study. The corresponding and senior author had full access to all data in the study and had final responsibility for the decision to submit for publication.

## Acknowledgments

This study was supported by an R01 grant and a Graduate Research Supplement (NMS) grant from the National Heart, Lung, and Blood Institute of the NIH RO1HL089744 (JMG). The funders played no role in the design, analysis or interpretation of this research.

Dr Langan is funded by fellowships from the British Association of Dermatologists and the National Psoriasis Foundation. Ms Seminara is funded by a Graduate Research Supplement grant from the National Heart, Lung, and Blood Institute of the NIH RO1HL089744.

Dr. Mehta is funded by a grant from the National Psoriasis Foundation and from the National Heart, Lung, and Blood Institute of the NIH K23 HL097151

## References

- Abuabara K, Azfar RS, Shin DB, Neimann AL, Troxel AB, Gelfand JM. Cause-specific mortality in patients with severe psoriasis: a population-based cohort study in the U.K. *Br J Dermatol.* 2010; 163:586–92. [PubMed: 20633008]
- Al-Mutairi N, Al-Farag S, Al-Mutairi A, Al-Shiltawy M. Comorbidities associated with psoriasis: an experience from the Middle East. *J Dermatol.* 2010; 37:146–55. [PubMed: 20175849]
- Augustin M, Reich K, Glaeske G, Schaefer I, Radtke M. Co-morbidity and age-related prevalence of psoriasis: Analysis of health insurance data in Germany. *Acta Derm Venereol.* 2010; 90:147–51. [PubMed: 20169297]
- Azfar R, Gelfand J. Psoriasis and metabolic disease: epidemiology and pathophysiology. *Curr Opin Rheumatol.* 2008; 20:416–22. [PubMed: 18525354]
- Davidovici BB, Sattar N, Prinz JC, Jörg PC, Puig L, Emery P, et al. Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. *J Invest Dermatol.* 2010; 130:1785–96. [PubMed: 20445552]
- Dommasch E, Shin D, Troxel A, Margolis D, Gelfand J. Reliability, validity and responsiveness to change of the Patient Report of Extent of Psoriasis Involvement (PREPI) for measuring body surface area affected by psoriasis. *Br J Dermatol.* 2009
- Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet.* 2005; 365:1415–28. [PubMed: 15836891]
- Expert Panel on Detection Ea, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA.* 2001; 285:2486–97. [PubMed: 11368702]
- Feldman SR. A quantitative definition of severe psoriasis for use in clinical trials. *J Dermatolog Treat.* 2004; 15:27–9. [PubMed: 14754646]



- Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*. 2002; 287:356–9. [PubMed: 11790215]
- Gelfand J, Dommasch E, Shin D, Azfar R, Kurd S, Wang X, et al. The risk of stroke in patients with psoriasis. *J Invest Dermatol*. 2009; 129:2411–8. [PubMed: 19458634]
- Gelfand J, Neimann A, Shin D, Wang X, Margolis D, Troxel A. Risk of myocardial infarction in patients with psoriasis. *JAMA*. 2006; 296:1735–41. [PubMed: 17032986]
- Gisoni P, Girolomoni G. Psoriasis and atherothrombotic diseases: disease-specific and non-disease-specific risk factors. *Semin Thromb Hemost*. 2009; 35:313–24. [PubMed: 19452407]
- Krueger G, Koo J, Lebwohl M, Menter A, Stern RS, Rolstad T. The impact of psoriasis on quality of life: results of a 1998 National Psoriasis Foundation patient-membership survey. *Arch Dermatol*. 2001; 137:280–4. [PubMed: 11255325]
- Kurd SK, Gelfand JM. The prevalence of previously diagnosed and undiagnosed psoriasis in US adults: results from NHANES 2003-2004. *J Am Acad Dermatol*. 2009; 60:218–24. [PubMed: 19022533]
- Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA*. 2002; 288:2709–16. [PubMed: 12460094]
- Lewis J, Schinnar R, Bilker W, Wang X, Strom B. Validation studies of the health improvement network (THIN) database for pharmacoepidemiology research. *Pharmacoepidemiol Drug Saf*. 2007; 16:393–401. [PubMed: 17066486]
- Love TJ, Qureshi AA, Karlson EW, Gelfand JM, Choi HK. Prevalence of the Metabolic Syndrome in Psoriasis: Results From the National Health and Nutrition Examination Survey, 2003-2006. *Arch Dermatol*. 2010
- Mebazaa A, El Asmi M, Zidi W, Zayani Y, Cheikh Rouhou R, El Ounifi S, et al. Metabolic syndrome in Tunisian psoriatic patients: prevalence and determinants. *J Eur Acad Dermatol Venereol*. 2010
- Mehta N, Azfar R, Shin D, Neimann A, Troxel A, Gelfand J. Patients with severe psoriasis are at increased risk of cardiovascular mortality: cohort study using the General Practice Research Database. *Eur Heart J*. 2009
- Mehta NN, McGillicuddy FC, Anderson PD, Hinkle CC, Shah R, Pruscino L, et al. Experimental endotoxemia induces adipose inflammation and insulin resistance in humans. *Diabetes*. 2010; 59:172–81. [PubMed: 19794059]
- Mente A, Yusuf S, Islam S, McQueen MJ, Tanomsup S, Onen CL, et al. Metabolic syndrome and risk of acute myocardial infarction a case-control study of 26,903 subjects from 52 countries. *J Am Coll Cardiol*. 2010; 55:2390–8. [PubMed: 20488312]
- Mokdad AH, Ford ES, Bowman BA, Dietz WH, Vinicor F, Bales VS, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. *JAMA*. 2003; 289:76–9. [PubMed: 12503980]
- National Psoriasis Foundation. [Accessed 22 November 2010]  
<[http://www.psoriasis.org/netcommunity/learn\\_statistics](http://www.psoriasis.org/netcommunity/learn_statistics)>
- Nijsten T, Looman CW, Stern RS. Clinical severity of psoriasis in last 20 years of PUVA study. *Arch Dermatol*. 2007; 143:1113–21. [PubMed: 17875871]
- Phillimore P, Beattie A, Townsend P. Widening inequality of health in northern England, 1981-91. *BMJ*. 1994; 308:1125–8. [PubMed: 8173452]
- Rothman K, Greenland S. Causation and causal inference in epidemiology. *Am J Public Health*. 2005; 95 1:S144–50. [PubMed: 16030331]
- Seminara NM, Abuabara K, Shin DB, Langan SM, Kimmel SE, Margolis D, et al. Validity of The Health Improvement Network (THIN) for the study of psoriasis. *Br J Dermatol*. 2010
- Shah R, Lu Y, Hinkle CC, McGillicuddy FC, Kim R, Hannenhalli S, et al. Gene profiling of human adipose tissue during evoked inflammation in vivo. *Diabetes*. 2009; 58:2211–9. [PubMed: 19581417]
- Zimmet P, Magliano D, Matsuzawa Y, Alberti G, Shaw J. The metabolic syndrome: a global public health problem and a new definition. *J Atheroscler Thromb*. 2005; 12:295–300. [PubMed: 16394610]

## Abbreviations

<b>NCEP</b>	National Cholesterol Education Program
<b>ATP</b>	Adult Treatment Panel
<b>BSA</b>	body surface area
<b>OR</b>	odds ratio
<b>CI</b>	95% confidence interval
<b>CVD</b>	cardiovascular disease
<b>Th-1</b>	T helper cell type 1
<b>THIN</b>	The Health Improvement Network
<b>AIS</b>	Additional Information Services
<b>BMI</b>	body mass index

**Table 1**  
**Demographic details of cohort**

Characteristic	No Psoriasis (n, %)	Psoriasis (n, %)
<b>Overall</b>	40,650 (90.9)	4,065 (9.1)
<b>By psoriasis extent</b>		
≤2%	N/A	2044 (52.5)
3-10%	N/A	1377 (35.3)
>10%	N/A	475 (12.2)
<b>Gender</b>		
Men	19304 (47.5)	2081 (51.2)
Women	21346 (52.5)	1984 (48.8)
<b>Age group (years)</b>		
<50	13348 (32.8)	1082 (26.6)
50-54	10040 (24.7)	1000 (24.6)
55-59	9271 (22.8)	945 (23.3)
>60	7991 (19.7)	1038 (25.5)
	<b>Median (Interquartile range measurements) of maximum individual</b>	
Body mass index (kg/m <sup>2</sup> )	27.1 (23.7-31.2)	28.4 (24.9-32.9)
Systolic blood pressure (mmHg)	144 (130-162)	149 (135-168)
Diastolic blood pressure (mmHg)	90 (80-100)	90 (82-100)
Triglyceride level (mmol/l)	1.7 (1.1-2.5)	1.9 (1.2-2.8)
Cholesterol level (mmol/l)	5.8 (5.1-6.7)	6.0 (5.2-6.8)
High density lipoprotein (mmol/l)	1.5 (1.2-1.8)	1.4 (1.2-1.7)
Low density lipoprotein (mmol/l)	3.6 (2.9-4.3)	3.7 (3.0-4.3)
Glucose (mmol/l)	5.4 (4.9-6.4)	5.6 (4.9-6.6)
C reactive protein (mg/l)	5 (3-10)	7 (4-13)
Metabolic syndrome n (%)	10515 (25.9)	1389 (34.2)

**Table 2**

<b>Table 2a Factors associated with metabolic syndrome</b>			
<b>Factors associated with metabolic syndrome</b>	<b>No psoriasis (n, %)</b>	<b>Psoriasis (n, %)</b>	<b>OR (95% CI)</b>
Body mass index <25kg/m <sup>2</sup> *	10,744 (28.7)	827 (21.9)	1.0
Body mass index 25-<30kg/m <sup>2</sup> *	14,143 (37.7)	1401 (37.1)	1.30 (1.19-1.42)
Body mass index 30-<35kg/m <sup>2</sup> *	7678 (20.5)	887 (23.5)	1.52 (1.37-1.68)
Body mass index >35kg/m <sup>2</sup> *	4907 (13.1)	662 (17.5)	1.78 (1.59-1.98)
Triglycerides ≥ 1.7mmol/l**	11181 (27.5)	1453 (35.7)	1.49 (1.39-1.60)
Low HDL (<1.04mmol/l (men) and <1.29mmol/l (women))***	8180 (20.1)	1007 (24.7)	1.32 (1.22-1.43)
Raised BP (Systolic ≥130 or diastolic ≥85mmHg)****	24187 (59.5)	3571 (87.9)	1.36 (1.24-1.50)
Hypertension diagnosis	11204 (27.6)	1265 (31.1)	1.20 (1.11-12.9)
Type 2 diabetes mellitus	3445 (8.5)	454 (11.2)	1.36 (1.23-1.51)
High glucose measurement (>6.1mmol/l)*****	6644 (16.3)	884 (21.8)	1.44 (1.33-1.56)
*BMI measured in 41249; 3777 (93%) with psoriasis, 37,472 (92%) controls			
** Triglycerides measured in 25,067: 2545 (63%) with psoriasis, 22522 (55%) controls			
***HDL measured in 25,234: 2538 (62%) with psoriasis, 22696 (56%) of controls			
****BP measured in 44019: 4023 (99%) with psoriasis, 39996 (98%) of controls			
*****Glucose measured in 26144: 2599 (64%) with psoriasis, 26144 (64%) of controls			

<b>Table 2b. Factors including psoriasis extent associated with metabolic syndrome</b>					
<b>Factors associated with metabolic syndrome</b>	<b>No psoriasis (n, %)</b>	<b>Mild psoriasis (n, %) CI)</b>	<b>OR (95% CI)</b>	<b>Moderate psoriasis (n, %), OR (95% CI)</b>	<b>Severe psoriasis (n, %), OR (95% CI)</b>
Body mass index <25kg/m <sup>2</sup> *	10,744 (28.7)	472 (24.7), 1.0		247 (19.4), 1.0	72 (16.6), 1.0
Body mass index 25-<30kg/m <sup>2</sup> *	14,143 (37.7)	715 (35.0), 1.15 (1.02-1.30)		483 (35.1), 1.49 (1.27-1.74)	140 (32.2), 1.48 (1.11-1.96)
Body mass index 30-<35kg/m <sup>2</sup> *	7678 (20.5)	415 (21.7), 1.23 (1.07-1.41)		316 (24.8), 1.79 (1.51-2.12)	126 (29.0), 2.45(1.83-3.28)
Body mass index >35kg/m <sup>2</sup> *	4907 (13.1)	310 (16.2), 1.44 (1.24-1.67)		228 (17.9), 2.02 (1.68-2.43)	97 (22.3), 2.94 (2.17-4.01)
Triglycerides ≥ 1.7mmol/l**	11181 (27.5)	686 (33.6), 1.33 (1.21-1.46)		511 (37.1), 1.56 (1.39-1.74)	202 (42.5), 1.95 (1.62-2.34)
Low HDL (<1.04mmol/l (men) and <1.29mmol/l (women))***	8180 (20.1)	480 (23.5), 1.22 (1.10-1.35)		348 (25.3), 1.34 (1.19-1.52)	139 (29.3), 1.64 (1.35-2.00)
Raised BP (Systolic ≥130 or diastolic ≥85mmHg)****	24187 (59.5)	1306 (63.9), 1.20 (1.10-1.32)		907 (65.9), 1.31 (1.17-1.47)	329 (69.3), 1.53 (1.26-1.87)

**Table 2b. Factors including psoriasis extent associated with metabolic syndrome**

Factors associated with metabolic syndrome	No psoriasis (n, %)	Mild psoriasis (n, %), OR (95% CI)	Moderate psoriasis (n, %), OR (95% CI)	Severe psoriasis (n, %), OR (95% CI)
Hypertension diagnosis	11204 (27.6)	627 (30.7), 1.16 (1.06-1.28)	433 (31.5), 1.21 (1.07-1.35)	151 (31.8), 1.21 (0.98-1.49)
Type 2 diabetes mellitus	3445 (8.5)	220 (10.8), 1.28 (1.11-1.48)	150 (10.9), 1.30 (1.10-1.56)	58 (12.2), 1.50 (1.14-1.98)
High glucose measurement (>6.1mmol/l)*****	6644 (16.3)	429 (21.0), 1.36 (1.22-1.52)	291 (21.1), 1.37 (1.20-1.57)	129 (27.2), 1.91 (1.56-2.34)

**Table 3**  
**Association between psoriasis severity and the components of metabolic syndrome independent of other components**

Psoriasis extent	High blood pressure OR (CI)	Raised triglycerides OR (CI)	Low HDL OR (CI)	Hyperglycaemia OR (CI)	Obesity (BMI >30kg/m <sup>2</sup> ) OR (CI)
No psoriasis (n=40650)	1.0	1.0	1.0	1.0	1.0
Psoriasis overall n=4065	1.07 (0.96-1.19)	1.20 (1.10-1.31)	0.98 (0.89-1.08)	1.16 (1.06-1.27)	1.25 (1.16-1.34)
<b>By extent</b>					
Mild psoriasis (≤2%) n=2044	1.03 (0.89-1.20)	1.10 (0.98-1.25)	0.99 (0.87-1.13)	1.11 (0.97-1.26)	1.14 (1.03-1.27)
Moderate psoriasis (3-10%), n=1377	1.02 (0.85-1.24)	1.31 (1.13-1.51)	0.94 (0.80-1.11)	1.16 (0.99-1.35)	1.34 (1.18-1.53)
Severe psoriasis (>10%), n=475	1.32 (0.91-1.92)	1.46 (1.13-1.88)	1.05 (0.80-1.39)	1.31 (1.00-1.71)	1.66 (1.33-2.07)