APPENDIX S1

Study population

The Trøndelag Health Study (HUNT) is an ongoing population-based study, which has collected data in four surveys (1,2). We used data from HUNT4, carried out in 2017-2019 (1). All inhabitants in the Nord-Trøndelag region aged 20 years or older were invited and 56 042 (54.0%) participated. Participation included extensive questionnaires regarding lifestyle and medical history, non-fasting blood samples and clinical examinations. Participants with missing information regarding psoriasis status were excluded (n = 2669) and the population studied included 53 373 individuals. As some participants had missing information on outcomes, the number of individuals included in each analysis varies. A total of 16 434 individuals were genotyped for rs4406273, of which 931 had psoriasis. For models including genetic information, we excluded non-European and related individuals, leaving a population of 901 individuals with psoriasis for analysis.

Classification of psoriasis

Psoriasis was defined as an affirmative response to the following cluster question in HUNT4: "Have you ever had any of the following diseases?" "Psoriasis". Participants answering no to this question were defined as individuals without psoriasis. The psoriasis question has been validated in the third wave of HUNT (HUNT3) conducted between 2006 and 2008, with a positive predictive value of 78% (3).

Classification of comorbidities

The aforementioned cluster question also included myocardial infarction, angina, cardiac failure, atrial fibrillation, apoplexia, asthma, chronic obstructive pulmonary disorder (COPD), diabetes, hypothyroidism, hyperthyroidism, migraine, renal disease and gout. A positive response to either disease was classified as having that disease. In addition, biochemical measurements were used when available. Diabetes was defined as an affirmative answer and/or HbA1c $\geq$ 48 mmol/mol. Correspondingly, kidney disease was defined by an affirmative answer and/or an estimated glomerular filtration rate (eGFR) of $\leq$60 mL/min/1.73 m^2.

Clinical examination and laboratory measurements

All clinical examinations were performed by specially trained staff. Blood pressure was measured using Dinamap 845XT based on oscillometry. The average value of the second and third measurement was used. Height and weight were measured with the participants wearing light clothes and no shoes. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared (kg/m^2). Body composition of all participants was assessed using bioelectrical impedance analysis, on an *InBody 770*-instrument (Cerritos, CA, USA). Body composition parameters reported in kilograms (total body fat, skeletal muscle mass, soft lean mass and fat free mass) were reported as a percentage of total body weight. Analyses

of non-fasting blood samples were carried out using Architect cSystems ci8200 (Abbott Diagnostics, Longford Ireland).

Genotyping

Genotyping was performed using a custom Illumina HumanCoreExome array (UM HUNT Biobank v.2.0) (4). Ancestry was predicted using principal components of ancestry projected onto the 1000 Genomes Project. Ancestry principal components were generated, and eigen-values were estimated (Fig. S1a). The single nucleotide polymorphism (SNP) rs4406273 was used as a proxy-SNP for *HLA-C*06:02* status, which has shown excellent performance (Matthews correlation coefficient 0.965-1.000) (5). Individuals with psoriasis were classified as either *HLA-C*06:02*-positive (one or two copies of the rs4406273-A allele) or *HLA-C*06:02*-negative (no copies).

Statistical analysis

All descriptive cardiometabolic risk factors, including body composition parameters, are reported standardized for age applying Stata's analytic weights option, where observations are weighted inversely proportional to the variance of the observation. Means and 95% confidence intervals (95% CI) were reported for continuous variables and counts and percentages were reported for categorical variables. A generalized linear model was applied to estimate prevalence ratios (PR) for the different outcomes in the psoriatic and non-psoriatic groups. In cases where the model did not converge, we calculated differences in proportion based on predicted mean probabilities from a logistic regression model using Stata's adjrr command. To adjust for potential confounding in the models, covariates were chosen based on *a priori* knowledge on disease mechanisms. Two models were constructed; one adjusting for age, sex and BMI and another, fully adjusted model, also adjusting for smoking status, education and alcohol consumption. Subsequently, a sub-analysis was performed among psoriatic individuals, using *HLA-C*06:02* status as the exposure and self-reported disease as outcome. The model was adjusted for potential mediators and confounders; age, sex, BMI, smoking status, disease duration and cryptic population structure by four principal components. Precision was assessed by 95% CI. All statistical analyses were conducted using Stata MP v.17.0 (StataCorp, College Station, TX, USA).

Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics in Central Norway (REK Reference number: 27420), and the Norwegian Data Protection Authority. All HUNT participants gave written informed consent.

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