

Original Investigation

Association of Psoriasis With the Risk for Type 2 Diabetes Mellitus and Obesity

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← Editorial

IMPORTANCE Psoriasis has been shown to be associated with overweight and type 2 diabetes mellitus. The genetic association is unclear.

OBJECTIVE To examine the association among psoriasis, type 2 diabetes mellitus, and body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) in twins.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional, population-based twin study included 34 781 Danish twins, 20 to 71 years of age. Data from a questionnaire on psoriasis was validated against hospital discharge diagnoses of psoriasis and compared with hospital discharge diagnoses of type 2 diabetes mellitus and self-reported BMI. Data were collected in the spring of 2002. Data were analyzed from January 1 to October 31, 2014.

MAIN OUTCOMES AND MEASURES Crude and adjusted odds ratios (ORs) were calculated for psoriasis in relation to type 2 diabetes mellitus, increasing BMI, and obesity in the whole population of twins and in 449 psoriasis-discordant twins. Variance component analysis was used to measure genetic and nongenetic effects on the associations.

RESULTS Among the 34 781 questionnaire respondents, 33 588 with complete data were included in the study (15 443 men [46.0%]; 18 145 women [54.0%]; mean [SD] age, 44.5 [7.6] years). After multivariable adjustment, a significant association was found between psoriasis and type 2 diabetes mellitus (odds ratio [OR], 1.53; 95% CI, 1.03-2.27; $P = .04$) and between psoriasis and increasing BMI (OR, 1.81; 95% CI, 1.28-2.55; $P = .001$ in individuals with a BMI > 35.0). Among psoriasis-discordant twin pairs, the association between psoriasis and obesity was diluted in monozygotic twins (OR, 1.43; 95% CI, 0.50-4.07; $P = .50$) relative to dizygotic twins (OR, 2.13; 95% CI, 1.03-4.39; $P = .04$). Variance decomposition showed that additive genetic factors accounted for 68% (95% CI, 60%-75%) of the variance in the susceptibility to psoriasis, for 73% (95% CI, 58%-83%) of the variance in susceptibility to type 2 diabetes mellitus, and for 74% (95% CI, 72%-76%) of the variance in BMI. The genetic correlation between psoriasis and type 2 diabetes mellitus was 0.13 (−0.06 to 0.31; $P = .17$); between psoriasis and BMI, 0.12 (0.08 to 0.19; $P < .001$). The environmental correlation between psoriasis and type 2 diabetes mellitus was 0.10 (−0.71 to 0.17; $P = .63$); between psoriasis and BMI, −0.05 (−0.14 to 0.04; $P = .44$).

CONCLUSIONS AND RELEVANCE This study determines the contribution of genetic and environmental factors to the interaction between obesity, type 2 diabetes mellitus, and psoriasis. Psoriasis, type 2 diabetes mellitus, and obesity are also strongly associated in adults after taking key confounding factors, such as sex, age, and smoking, into account. Results indicate a common genetic etiology for psoriasis and obesity.

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Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by uncontrolled proliferation of keratinocytes, activated dendritic cells, release of proinflammatory cytokines, and recruitment of T cells to the skin.^{1,2} The disease affects approximately 2% to 3% of white individuals and is found worldwide in all populations.^{3,4} The metabolic syndrome is characterized by abdominal obesity, insulin resistance, dyslipidemia, and elevated blood pressure.⁵ Similar to psoriasis, systemic inflammation occurs in patients with metabolic syndrome, and levels of a number of inflammatory markers, such as tumor necrosis factor, are elevated in both diseases.⁶⁻⁸

Psoriasis has been associated with components of the metabolic syndrome, particularly obesity and type 2 diabetes mellitus. These comorbidities are important to recognize because they can lead to increased mortality, especially mortality due to cardiovascular disease.⁹⁻¹⁴ Herron et al¹⁵ and Cohen et al¹⁶ found that obesity is about twice as prevalent in patients with psoriasis compared with the general population. Cohen et al¹⁶ found that this prevalence was also the case for type 2 diabetes mellitus.

Several factors might explain the association between psoriasis and the metabolic syndrome, notably genetics, environmental exposures such as tobacco smoking, alcohol consumption, psychological stress, and physical activity, and shared immunoinflammatory pathways. These various factors may act in concert to explain the co-occurrence of psoriasis and the metabolic syndrome.

Twin studies offer valuable insight into the origins of multifactorial diseases. The twin design can be used to explore a possible common etiology of associated diseases.¹⁷ The aim of this study was to investigate the association between psoriasis, type 2 diabetes mellitus, and obesity (body mass index [BMI] [calculated as the weight in kilograms divided by the height in meters squared]) in a population of Danish twins. Specifically, we examined (1) the association between psoriasis, type 2 diabetes mellitus, and obesity at the population level; (2) whether twin pairs discordant for psoriasis had a differential BMI and risk for type 2 diabetes mellitus and obesity; and (3) to what extent the association between the 3 diseases was explained by genetic and environmental factors.

Methods

Study Population and Definition of Diseases

The studied sample consisted of twins born from January 1, 1931, to December 31, 1982, who were registered in the national Danish Twin Registry.¹⁸ The first part of this cohort included twins born from 1931 to December 31, 1952. This cohort was identified and enrolled in the Danish twin registry in 1996, and corresponded to 69% of all twin pairs born in Denmark during these years. The second part of the cohort included twins born from January 1, 1953, to December 31, 1982. This cohort was identified and enrolled in the Danish Twin Registry in 1991 and corresponded to 74% of all twin pairs born in Denmark from 1953 to December 31, 1967, and 97% of all twin pairs born in Denmark from January 1, 1968, through 1982. Zygosity was estab-

Key Points

Question What is the association between psoriasis, type 2 diabetes mellitus, and obesity?

Findings This population-based twin study found that psoriasis is strongly associated with type 2 diabetes, body mass index, and obesity. A genetic correlation was found especially between psoriasis and obesity.

Meaning These results indicate that the association between psoriasis and obesity is partly the result of a common genetic cause.

lished using 4 questions of similarity and mistaken identity, which have a frequency of misclassification of less than 5%.¹⁹ According to Danish law, purely registry-based and questionnaire studies do not require further evaluation by the Scientific Ethics Committee, and informed consent is not needed.

In 2002, the twins participated in a multidisciplinary questionnaire study concerning health and lifestyle in which a history of psoriasis was recorded. A history of psoriasis was defined as an affirmative response to the question “Has a doctor ever told you that you have, or have had, psoriasis?”

Diagnoses of psoriasis were also obtained from the Danish National Patient Registry, where all hospitalizations in Denmark since 1977 and all hospital outpatient visits since 1994 are recorded. Based on the *International Classification of Diseases, Eighth Revision (ICD-8)*, and the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)*, individuals with the following discharge diagnoses recorded before 2010 were considered to have psoriasis: *ICD-8* diagnosis codes 68693.4, 69609.10, 69609.19, and 69609.99 and *ICD-10* diagnosis codes L40.0 to L40.9. The questionnaire data were cross-linked with the discharge diagnoses of psoriasis to validate the questionnaire responses, which constituted our primary diagnostic criterion.

Questionnaire responses were also used to identify height, weight, and smoking history. Obesity was defined as a BMI of 30.0 or greater. The response rate to the questionnaire was 75%, resulting in 34 781 participants, among whom 33 588 (96.6%) had complete data on psoriasis and were included in this study. Diagnoses of type 2 diabetes mellitus were obtained from the Danish National Patient Registry; individuals with at least 1 of the following discharge diagnoses before 2003 were considered to have type 2 diabetes mellitus: *ICD-8* codes 25000 to 25009 and *ICD-10* codes E11.0 to E11.9. Seventeen subjects with a diagnosis of diabetes mellitus could not be classified (unspecified diabetes mellitus) and were omitted. Data were collected during the spring of 2002.

Statistical Analysis

Data were analyzed from January 1 to October 31, 2014. The risk for psoriasis was calculated with logistic regression analysis for unpaired data, whereas a 1:1 matched conditional logistic regression analysis (co-twin control analysis) was used to calculate the association of BMI, obesity, and type 2 diabetes mellitus with psoriasis in twin pairs discordant for psoriasis, with adjustment for smoking.²⁰ The matching was performed with

the affected twin (ie, the twin with psoriasis) in each pair identified as the case and the unaffected twin as the control. The size of the intrapair difference of the examined variables in a twin pair discordant for psoriasis is a measure of the correlation between the variables and psoriasis. Larger intrapair differences for the variables resulted in larger correlations. Risk estimates were given as odds ratios (ORs) with 95% CIs. Only monozygotic (MZ) and dizygotic (DZ) same-sex twin pairs were used in the analysis; consequently, the matching of the twins in the co-twin control design adjusts indirectly for sex, age, and childhood environment²¹ that would otherwise confound the association between psoriasis and the examined risk factors.

In the co-twin control design, if the association between psoriasis and the examined risk factor is mediated purely via genetics, we would not expect to find any intrapair difference or an increased OR within discordant MZ twin pairs, who share all their genes, whereas we would expect to find an increased risk among discordant DZ twin pairs, who on average only share half of their genetic variants. In contrast, if the association between psoriasis and the examined risk factor is mediated via environmental effects (external and internal), then the intrapair difference will be greater among MZ compared with DZ twin pairs, and we would expect to find an increased OR among discordant MZ twin pairs compared with discordant DZ twin pairs. Finally, if a direct (causal) effect of the examined risk factor on the risk for psoriasis exists, or if the association is owing to genetic and environmental factors, then we would expect to find intrapair differences and increased ORs alike between discordant MZ and DZ twin pairs.²⁰

Finally, we analyzed data with variance component analysis. According to the classic twin method described by Neale and Cardon,²² variance in susceptibility to a disease can be partitioned into additive genetic effects (loci contributing additively to trait variance [A]); shared environmental effects (environmental factors that increase the resemblance between members of the same family [C]); and nonshared environmental effects (influences unique to the individual [E]). The E component also contains variance owing to measurement error.¹⁷ The expected covariance for MZ twin pairs is $A + C$, whereas for DZ twin pairs it is $0.5 \times (A + C)$. The significance of the contribution of the individual variables to the trait variance was determined by a likelihood ratio test for the difference between the full ACE model and subsequently fitted nested models (AE and CE models). The most parsimonious model for all traits included only components A and E, and therefore, bivariate analyses based on the AE model were conducted between psoriasis, type 2 diabetes mellitus, and BMI to obtain estimates of the correlation between genetic and environmental effects for these diseases.¹⁷ Data were analyzed with the statistical packages SPSS (version 16.0; SPSS Inc) and Mx (<http://www.vcu.edu/mx/>).

Results

Descriptive Analysis of the Cohort

Among the 34 781 questionnaire respondents, 33 588 with complete data were included in the study (15 443 men [46.0%]; 18 145 women [54.0%]). The prevalence of psoriasis in the total

twin sample was 4.2%, with no significant difference between men and women (630 [4.1%] and 771 [4.2%], respectively; $P = .44$). The mean (SD) age of the population was 44.5 (7.6) years. The prevalence of type 2 diabetes mellitus was 1.4% (235 women and 224 men). The mean BMI for the total cohort was 24.5; most individuals had a BMI of less than 25.0 (62.1%), whereas the fraction of participants with a BMI ranging from 25.0 to 29.0 was 29.9%. Individuals with a BMI ranging from 30.0 to 34.0 constituted only 6.3% of the population, whereas individuals with a BMI of 35.0 or greater accounted for 1.7%.

Association Between Psoriasis, Type 2 Diabetes Mellitus, and BMI in the Whole Cohort

Among 459 individuals with type 2 diabetes mellitus, the prevalence of psoriasis was 7.6% ($n = 31$) compared with only 4.1% ($n = 1370$) among individuals without type 2 diabetes mellitus (OR, 1.90; 95% CI, 1.31-2.76; $P = .001$). The association remained significant after adjusting for sex, age, smoking, and BMI (OR, 1.53; 95% CI, 1.03-2.27; $P = .04$) (Table 1).

The mean BMI among individuals with psoriasis was significantly higher than among individuals without psoriasis (25.0 vs 24.4; $P < .001$). Also, the risk for obesity (BMI > 30.0) was significantly increased in individuals with psoriasis compared with individuals without psoriasis (10.8% vs 7.9%; $P < .001$). The prevalence of psoriasis increased significantly with increasing BMI, so that individuals with a BMI of at least 35.0 had an almost 2-fold risk for psoriasis compared with normal-weight individuals before (OR, 1.91; 95% CI, 1.36-2.67) and after (OR, 1.81; 95% CI, 1.28-2.55) adjustment for confounders (Table 1).

Association Between Psoriasis, Type 2 Diabetes Mellitus, and BMI in Discordant Twin Pairs

In total 720 twin pairs were discordant for psoriasis, including 179 MZ pairs, 270 DZ same-sex pairs, 257 DZ opposite-sex pairs, and 14 pairs with unknown zygosity. The DZ opposite-sex pairs and pairs with unknown zygosity were omitted from the analyses, leaving a total of 449 twin pairs discordant for a lifetime history of psoriasis.

The twins with psoriasis had a higher mean BMI than the co-twins without psoriasis (25.1 vs 24.7) and were more likely to be obese (11.6% vs 8.1%) (Table 2). The risk for obesity was increased almost 2-fold in the twin with psoriasis compared with the co-twin without psoriasis after adjustment for confounders (OR, 1.92; 95% CI, 1.06-3.46; $P = .03$). The risk was the highest among DZ twin pairs (OR, 2.13; 95% CI, 1.03-4.39; $P = .04$) compared with MZ twin pairs (OR, 1.43; 95% CI, 0.50-4.07; $P = .50$) (Table 3). In contrast, the prevalence of type 2 diabetes mellitus was the same in the twins with psoriasis compared with the co-twins without psoriasis (6 [1.3%] vs 6 [1.3%]). Only 12 twin pairs were discordant for psoriasis and had type 2 diabetes mellitus.

Variance Component Analysis

The probability that one twin was affected with psoriasis given that the co-twin was affected (the probandwise concordance) was 33% among MZ twins and 17% among DZ twins. Variance decomposition showed that additive genetic factors ac-

Table 1. Predictors of Self-reported Psoriasis in Danish Twins^a

Characteristic	No. (%) of Participants With Psoriasis	Crude OR (95% CI)	P Value	Adjusted OR (95% CI) ^b	P Value
Sex					
Men	630 (4.1)	1 [Reference]		1 [Reference]	NA
Women	771 (4.2)	1.04 (0.94-1.16)	.44	1.14 (1.01-1.27)	.03
Age group, y					
20-49	780 (3.8)	1 [Reference]		1 [Reference]	NA
50-71	621 (4.8)	1.29 (1.16-1.43)	<.001	1.14 (1.02-1.28)	.03
Smoking^c					
Never	397 (2.8)	1 [Reference]		1 [Reference]	NA
Ever	961 (5.2)	1.90 (1.69-2.14)	<.001	1.85 (1.64-2.09)	<.001
Type 2 diabetes mellitus					
Yes	31 (7.6)	1.90 (1.31-2.76)	.001	1.53 (1.03-2.27)	.04
No	1370 (4.1)	1 [Reference]		1 [Reference]	NA
BMI^d					
<25.0	762 (3.8)	1 [Reference]		1 [Reference]	NA
25.0-29.0	436 (4.5)	1.20 (1.06-1.35)	.003	1.17 (1.03-1.33)	.01
30.0-34.0	107 (5.2)	1.40 (1.13-1.72)	.002	1.33 (1.08-1.65)	.009
≥35.0	38 (7.0)	1.91 (1.36-2.67)	<.001	1.81 (1.28-2.55)	.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NA, not applicable; OR, odds ratio.

^a Includes 1401 participants with psoriasis.

^b Indicates multivariably adjusted.

^c Forty-three participants were missing data.

^d Fifty-eight participants were missing data.

Table 2. Distribution of Risk Factors for Self-reported Psoriasis Among 449 Twin Pairs^a

Risk Factor	Twin Pairs			Monozygotic (n = 179)			Dizygotic (n = 270)		
	All (N = 449)	Affected	Unaffected	Affected	Unaffected	Difference	Affected	Unaffected	Difference
BMI, mean (SD)	25.1 (4.3)	25.1 (4.3)	24.7 (3.8)	25.2 (4.4)	25.0 (3.9)	0.2 (3.2)	25.0 (4.1)	24.4 (3.7)	0.6 (4.4)
Obesity, No. (%)	50 (11.1)	50 (11.1)	35 (7.8)	19 (10.6)	17 (9.5)	2 (1.1)	31 (11.5)	18 (6.7)	13 (4.8)
Type 2 diabetes mellitus, No. (%)	6 (1.3)	6 (1.3)	6 (1.3)	3 (1.7)	1 (0.6)	2 (1.1)	3 (1.1)	5 (1.9)	-2 (-0.8)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

^a Includes twin pairs discordant for a lifetime history of psoriasis (age range, 20-71 years).

counted for 68% (95% CI, 60%-75%) of the variance in the susceptibility to self-reported psoriasis and to 51% (95% CI, 15%-76%) of the variance in susceptibility to hospital-diagnosed psoriasis, whereas shared environment did not significantly influence the disease susceptibility for either definition of psoriasis. Genetic factors accounted for 73% (95% CI, 58%-83%) of the variance in susceptibility to type 2 diabetes mellitus and 74% (72%-76%) of the variance in BMI. The genetic correlation between psoriasis and type 2 diabetes mellitus was 0.13 (95% CI, -0.06 to 0.31; $P = .17$) and between psoriasis and BMI was 0.12 (95% CI, 0.08 to 0.19; $P < .001$), whereas environmental correlations were 0.10 (95% CI, -0.71 to 0.17; $P = .63$) and -0.05 (95% CI, -0.14 to 0.04; $P = .44$), respectively.

Validation of Self-reported Psoriasis

Data on self-reported psoriasis from the questionnaire was cross-linked with hospital-discharge diagnoses of psoriasis from the Danish National Patient Registry (Table 4). The prevalence of hospital-diagnosed psoriasis was 0.6% (196 participants). The sensitivity of the psoriasis question was 65.3% (95% CI, 58.3%-71.8%), whereas the specificity was 96.2% (95% CI, 96.1%-96.2%) against the hospital diagnosis. The corresponding positive predictive value was 9.1% (95% CI, 8.2%-10.0%), and the negative predictive value was 99.8% (95% CI, 99.7%-99.8%).

Data from the questionnaire had a misclassification rate of 3.8% (95% CI, 3.9%-4.1%) in reference to the hospital diagnosis. However, of the 68 participants with a hospital diagnosis of psoriasis and no self-reported psoriasis in the questionnaire, 40 (58.8%) received a diagnosis after 2002. Excluding these 40 participants increased the sensitivity to 82.1% (95% CI, 75.0%-87.5%). Use of a hospital diagnosis of psoriasis to estimate the association among psoriasis, type 2 diabetes mellitus, obesity, and BMI gave results similar to the associations observed when using self-reported data on psoriasis (Table 5).

Discussion

Psoriasis was significantly associated with type 2 diabetes mellitus and obesity in this nationwide study of Danish twins, even after adjustment for confounders. Furthermore, this study is the first, to our knowledge, to determine the contribution of genetic and environmental factors to the interaction between obesity, type 2 diabetes mellitus, and psoriasis.

Our findings are in accordance with a meta-analysis of 42 observational studies²³ that estimated the risk for type 2 diabetes mellitus to be increased 1.76-fold in patients with psoriasis and psoriatic arthritis. Another meta-analysis²⁴ found a 1.42-

Table 3. Risk Factors for Self-reported Psoriasis Among 449 Twin Pairs^a

Risk Factor	Twin Pairs ^b					
	All (N = 449)		Monozygotic (n = 179)		Dizygotic (n = 270)	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Model 1 ^c						
BMI	1.52 (0.92-2.53)	.10	1.26 (0.48-3.34)	.69	1.64 (0.90-2.99)	.11
Type 2 diabetes mellitus	1.04 (0.54-2.03)	.90	1.72 (0.55-5.34)	.35	0.70 (0.28-1.75)	.45
Model 2 ^d						
Obesity	1.92 (1.06-3.46)	.03	1.43 (0.50-4.07)	.50	2.13 (1.03-4.39)	.04
Type 2 diabetes mellitus	1.01 (0.52-1.97)	.97	1.66 (0.53-5.19)	.38	0.70 (0.28-1.75)	.45

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); OR, odds ratio.

^a Includes twin pairs discordant for a lifetime history of psoriasis (age range, 20-71 years).

^b All ORs are adjusted for smoking.

^c Includes BMI as a continuous variable (OR for BMI is per 10-unit increase).

^d Includes BMI as a binary variable (obesity is BMI >30.0).

fold increased risk for type 2 diabetes mellitus among patients with psoriasis based on data from 22 critically evaluated observational studies. Less than half of the studies used in these 2 meta-analyses have adjusted for smoking or BMI. Confounding can therefore not be excluded as a potential explanation for the observed association. In a population-based study, Brauchli et al²⁵ adjusted for smoking status, BMI, hypertension, dyslipidemia, infections, and use of systemic corticosteroids and still found an increased risk for developing type 2 diabetes mellitus among patients with psoriasis (OR, 1.31). Furthermore, that study found an increasing risk for diabetes mellitus with increasing severity and duration of psoriasis.

We found that individuals with psoriasis had a significantly higher mean BMI than individuals without psoriasis. Furthermore, increasing BMI was found to increase the risk for psoriasis in a positive dose-dependent manner, which is in accordance with previous studies.^{12,25-28} Obesity was more common in the twin with psoriasis compared with the twin without psoriasis among psoriasis-discordant twin pairs, and with a dilution of the risk estimate in MZ compared with DZ twins, suggesting some degree of genetic confounding between psoriasis and obesity. This effect was independent of known confounding factors such as smoking and type 2 diabetes mellitus, and in addition, the matched co-twin control study design allowed inherent adjustment for other factors such as sex, age, and childhood environment, which would otherwise confound the association. In a case-control study, Cohen et al²⁷ found an OR of 1.3 for obesity among patients with psoriasis after adjusting for sex, age, ischemic heart disease, and components of the metabolic syndrome. Sommer et al²⁸ investigated adult patients hospitalized for psoriasis in a case-control study and found an OR for obesity of 2.3. The high OR might in part reflect that hospitalized patients with psoriasis are more prone to have severe psoriasis and therefore more likely to have other comorbidities.

The present study is cross-sectional; consequently directionality of the associations could not be determined. Psoriasis may predispose to a more sedentary lifestyle, leading to behaviors that predispose to obesity and type 2 diabetes mellitus, or these conditions could be causative of psoriasis. In the study by Herron et al,¹⁵ patients with psoriasis were asked to self-report

Table 4. Self-reported vs Hospital-Diagnosed Psoriasis in Danish Twins^a

Self-reported Psoriasis	Hospital-Diagnosed Psoriasis, No. of Participants		
	Yes	No	Total
Yes	128	1273	1401
No	68	32 119	32 187
Total	196	33 392	33 588

^a Includes 33 588 participants (age range, 20-71 years).

their weight and body images at 18 years of age and at the onset of psoriasis; these data were compared with the results of their examination at the time of enrollment, which indicated that overweight and obesity developed after the onset of psoriasis. The concentration of lipids, lipoproteins, and apolipoproteins has been found to be abnormal at the onset of psoriasis; furthermore, patients with psoriasis are enriched with common genetic variants that predispose to increased risk for dyslipidemia, supporting a genetic rather than an acquired cause of the association.^{29,30} Our results from the zygosity-specific analysis indicate that genetic factors, to some extent, are responsible for the association between psoriasis and obesity, and with a significant genetic correlation between the 2 disorders of 0.12.

Increased plasma levels of tumor necrosis factor, tumor necrosis factor receptors, and interleukin 6, which have important roles in the pathogenesis of psoriasis, have been found to be linked with obesity. The production is thought to occur in adipose tissue by macrophages and adipocytes.³¹⁻³³ The association between type 2 diabetes mellitus and psoriasis also might be owing to increased tumor necrosis factor production from psoriatic inflammation and low-grade obesity inflammation, because it contributes to insulin resistance.^{8,34,35}

The diagnosis of psoriasis, obesity, and information on BMI and smoking was primarily based on answers to a questionnaire with a resulting risk for false-positive and false-negative answers and recall bias. However, the diagnosis of self-reported psoriasis was validated against a hospital discharge diagnosis of psoriasis, which resulted in a misclassification rate of only 3.8%. Patients with hospital-diagnosed psoriasis probably represent severe cases of psoriasis or patients with other severe diseases that cause contact with the hospital. The low

Table 5. Risk Factors for Hospital-Diagnosed Psoriasis Among Danish Twins^a

	No. (%) of Participants With Psoriasis	Crude OR (95% CI)	P Value	Adjusted OR (95% CI) ^b	P Value
Model 1 ^c					
Type 2 diabetes mellitus					
Yes	7 (1.5)	3.85 (1.80-8.22)	<.001	1.48 (0.59-3.70)	.40
No	216 (0.4)	1 [Reference]	NA	1 [Reference]	NA
BMI					
<25.0	111 (0.5)	1 [Reference]	NA	1 [Reference]	NA
25.0-29.0	59 (0.6)	1.10 (0.80-1.51)	.56	1.17 (0.84-1.64)	.36
30.0-34.0	20 (0.9)	1.75 (1.09-2.83)	.02	1.80 (1.11-2.96)	.02
≥35.0	8 (1.4)	2.61 (1.27-5.38)	.009	2.20 (1.01-4.85)	.046
Model 2 ^d					
Type 2 diabetes mellitus					
Yes	7 (1.5)	3.85 (1.80-8.22)	<.001	1.52 (0.61-3.78)	.37
No	216 (0.4)	1 [Reference]	NA	1 [Reference]	NA
Obesity					
Yes	28 (1.0)	1.88 (1.26-2.80)	.002	1.79 (1.18-2.72)	.006
No	170 (0.6)	1 [Reference]	NA	1 [Reference]	NA

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NA, not applicable; OR, odds ratio.

^a Includes 196 participants with hospital-diagnosed psoriasis (age range, 20-71 years).

^b Indicates adjusted for sex, age, and smoking.

^c Includes BMI as an ordinal variable.

^d Includes BMI as binary variable (obesity is BMI >30.0).

positive predictive value is therefore misleading and does not reflect a true high rate of false discovery but rather that many patients with psoriasis have the disease without contact with the hospital. A study on the same cohort by Pedersen et al³⁶ confirmed the diagnosis of psoriasis in 89% to 100% of the twins.

The association between psoriasis and type 2 diabetes mellitus might be underestimated because of the relatively low prevalence (1.3%) of type 2 diabetes mellitus in our population. A significant proportion of type 2 diabetes mellitus in adults may be undiagnosed or unreported, especially because the prevalence only reflects those patients who have been in contact with the hospital. In comparison, a study by Støvring et al³⁷ estimated the prevalence of type 2 diabetes mellitus in Denmark, based on information about

all redemptions of subsidized and prescribed drugs, and found a prevalence rate of type 2 diabetes mellitus of approximately 2% among participants aged 40 to 64 years, and approximately 5% among participants 65 years or older.

Conclusions

Psoriasis, type 2 diabetes mellitus, and obesity are strongly associated in adults after taking key confounding factors, such as sex, age, and smoking, into account. Results indicate a common genetic etiology of psoriasis and obesity. Conducting future studies on specific genes and epigenetic factors that cause this association is relevant.

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