

Risk of asthma in adult twins with type 2 diabetes and increased body mass index

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Abstract

Aim: To examine the relationship between asthma, type 2 diabetes and increased body mass index (BMI) in adult twins.

Methods: We performed record linkage between questionnaire-defined asthma and BMI, and hospital discharge diagnoses of type 2 diabetes in 34 782 Danish twins, 20–71 years of age.

Results: The risk of asthma was increased in subjects with type 2 diabetes relative to nondiabetic subjects both in men (13.5% vs 7.5%), $P = 0.001$ and in women (16.6% vs 9.6%), $P = 0.001$. The result remained significant after adjustment for age, BMI, smoking, symptoms of chronic bronchitis, marital status and zygosity, men: OR = 1.70 (1.07–2.70), $P = 0.026$; women: OR = 1.88 (1.24–2.85), $P = 0.003$. In this analysis, BMI remained a highly significant predictor for asthma independently of diabetes status in women, $P < 0.000$ but not in men, $P = 0.336$. Significant positive genetic correlations were found between asthma and type 2 diabetes, 0.20 (0.01–0.40), $P = 0.047$; between asthma and BMI in women, 0.15 (0.07–0.22), $P < 0.000$; and between BMI and type 2 diabetes, 0.40 (0.29–0.43), $P < 0.000$.

Conclusions: Asthma, type 2 diabetes and increased BMI are strongly associated in adults, particularly in women. These results suggest a common aetiology for asthma and metabolic syndrome.

Previous studies have found a positive association between asthma and increased body weight (1). Notably, a systematic review of prospective studies found that overweight and obesity are risk factors for asthma both in men and in women with an increased risk of about a factor two in obese relative to normal weight individuals (2).

While the relationship between obesity and asthma has been frequently studied, the association between asthma and other components of metabolic syndrome, such as manifest or subclinical type 2 diabetes, has been less well described. Cross-sectionally, Husemoen et al. (3) found that insulin resistance was associated with aeroallergen sensitization and allergic asthma but not nonallergic asthma in Danish adults. Moreover, an Australian study found signs of insulin resistance in 43% of allergic asthmatic children, 6–17 years of age (4). Longitudinally, Thuesen et al. (5) showed that insulin resistance increased the risk of incident wheezing and asthma-like symptoms in adults. A recent study showed that patients hospitalized with type 2 diabetes had an increased

frequency of asthma (6), whereas a large population-based study of Korean older adults showed that patients with type 2 diabetes report excess respiratory symptoms compared with nondiabetic subjects (7). On the contrary, observations from the Nurses' Health Study did not support an association between type 2 diabetes and asthma (8). These observations point to metabolic abnormalities in patients with asthma. Still, little is known about the relationship between asthma and type 2 diabetes at the population level.

Twin studies offer valuable insight into the origins of multifactorial disease. Notably, the twin design can be used to explore a possible common aetiology of associated diseases (9). We are unaware of any systematic analysis of the relationship between type 2 diabetes, body mass index (BMI) and atopic diseases in twins, and therefore, we aimed to examine the relationship between type 2 diabetes, BMI and atopic diseases, particularly asthma, in a population of twins. Specifically, we examined: (i) the direction and strength of the association between type 2 diabetes, BMI and asthma at

the population level; (ii) whether in twin pairs discordant for type 2 diabetes or BMI, the diabetic or heavier twin had a differential risk of asthma compared with his or her nondiabetic or lighter co-twin; (iii) whether the association between type 2 diabetes, BMI and asthma was confounded by genetic and environmental factors.

Methods

Population and definition of diseases

The studied population comprised twins born between 1931 and 1982 who were registered in the Danish Twin Registry (10). The ascertainment of the study population has been described in detail previously (11). In brief, the twins responded to a multidisciplinary questionnaire concerning health and lifestyle in 2002. In total, 34 782 twin individuals answered the questionnaire (response rate 75%). A history of asthma was defined as an affirmative response to the question 'Do you have, or have you ever had, asthma'. Twin zygosity was determined using four questions of similarity and mistaken identity, which assign zygosity correctly in more than 96% of the cases (12). Questionnaire responses were also used to identify rhinoconjunctivitis, atopic dermatitis, chronic bronchitis, height and weight, marital status and smoking history. BMI was calculated as the weight in kg divided by the square of height in metres (kg/m^2).

Diabetes diagnoses were obtained from the Danish National Patient Registry. This registry records all hospitalizations in Denmark since 1977. Based on the eighth and the tenth revisions of the International Statistical Classification of Diseases and Related Health Problems, subjects with at least one of the following discharge diagnoses were considered type 2 diabetic cases: diabetes mellitus, insulino independente (dia25000 through dia25009) and diabetes mellitus non-ex insulino dependens (E11.0 through E11.9). To prevent mix-up of type 1 and type 2 diabetic cases, subjects with both a type 1 and a type 2 diabetes diagnosis were categorized as type 2 diabetic. Typically, these cases were first given a type 2 diabetes diagnosis and after some years, a type 1 diabetes diagnosis. A total of 17 subjects with a diagnosis of diabetes could not be classified (unspecified diabetes). We also were able to detect the presence of diabetes (but not which sub-type) based on responses to the questionnaire, and we used this information to validate the hospital discharge diagnoses, which constituted our primary diagnostic criterion.

Statistical analysis

The risk of asthma 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 risk of asthma in twin pairs discordant for type 2 diabetes or BMI, respectively (13). The matching was performed with the diabetic or the heavier twin in each pair being the case and the nondiabetic or lighter twin being the control. Risk estimates were given as odds

ratios (ORs) with 95% confidence intervals (CIs). Dizygotic (DZ) same-sex and DZ opposite-sex twin pairs were pooled in the analysis and sex was included as covariate.

Subsequently, data were analysed with latent factor models. These assume that the 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 includes variance because of measurement error (9). The expected covariance for monozygotic (MZ) twins is $A + C$, while for DZ twins it is $0.5 \times A + C$. The significance of the contribution of the individual parameters 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). An exception to this was type 2 diabetes in men for which we initially fitted a model including dominance genetic effects (*D*) (9) because of a much higher similarity in MZ than DZ twins for this trait in men. Because the most parsimonious model for all traits included only components *A* and *E*, bivariate analyses based on the AE model were conducted between type 2 diabetes, BMI and asthma to obtain estimates of the correlation between genetic and environmental effects for these diseases (9). Data were analysed with the statistical packages spss 16.0 (SPSS Inc., Chicago, IL, USA) and Mx (14).

Results

Descriptive analysis of the cohort

The sample contained significantly more women than men (54% vs 46%), $P < 0.000$. More women than men had a history of asthma (7.6% vs 9.7%), whereas more men than women had type 2 diabetes (1.5% vs 1.2%) and were obese (8.7% vs 7.6%) (Table 1). The mean BMI was 23.7 kg/m^2 in women and 25.4 in men. The prevalence of type 2 diabetes increased with age and with increasing level of BMI from 0.7% in individuals with a BMI < 25 –9.1% in subjects with a BMI ≥ 35 . Likewise, the prevalence of obesity within subjects with type 2 diabetes was significantly higher than in nondiabetic subjects (32.4% vs 7.8%).

The prevalence of asthma and type 2 diabetes and the mean BMI was not significantly different in broken twin pairs compared with pairs where both twins answered the questionnaire. The prevalence of asthma was not significantly different in MZ and DZ twins, whereas we observed a slightly higher prevalence of type 2 diabetes and mean BMI in DZ twins compared with MZ twins.

The risk of asthma was increased in subjects with type 2 diabetes relative to nondiabetic subjects both in men (13.5% vs 7.5%) and in women (16.6% vs 9.6%), and also, the risk of asthma increased linearly according to increasing level of BMI (Table 2). In multivariable analysis after adjusting for age, BMI, smoking, symptoms of chronic bronchitis, marital status and zygosity, type 2 diabetes remained a statistically

Table 1 Descriptive characteristics of 34 782 Danish twin subjects, 20–71 years of age

	Males <i>n</i> = 15 846	Females <i>n</i> = 18 936	Total <i>n</i> = 34 782	<i>P</i> -value
<i>Asthma</i>				
All	1192 (7.6)	1812 (9.7)	3004 (8.7)	0.000
20–30 years of age	260 (9.0)	416 (11.1)	676 (10.2)	
31–40 years of age	293 (8.7)	429 (9.6)	722 (9.2)	
41–50 years of age	240 (7.0)	360 (9.5)	600 (8.3)	
51–60 years of age	195 (5.4)	354 (8.6)	549 (7.1)	
61–71 years of age	204 (8.7)	253 (9.9)	457 (9.3)	
Atopic dermatitis	583 (3.7)	1493 (8.0)	2076 (6.1)	0.000
Rhinoconjunctivitis	3051 (19.6)	4244 (22.9)	7295 (21.4)	0.000
<i>BMI</i>				
<25	7857 (51.2)	12 793 (71.1)	20 650 (61.9)	0.000
25–29	6145 (40.1)	3845 (21.4)	9990 (30.0)	
30–34	1127 (7.3)	1004 (5.6)	2131 (6.4)	
35+	213 (1.4)	362 (2.0)	575 (1.7)	
<i>Mean BMI</i>				
All	25.4 (3.5)	23.7 (4.3)	24.5 (4.0)	0.000
20–30 years of age	23.8 (3.4)	22.4 (3.7)	23.0 (3.6)	
31–40 years of age	25.1 (3.3)	23.5 (4.3)	24.2 (4.0)	
41–50 years of age	25.5 (3.4)	23.8 (4.2)	24.6 (3.9)	
51–60 years of age	26.1 (3.5)	24.4 (4.3)	25.2 (4.0)	
61–71 years of age	26.2 (3.5)	24.8 (4.7)	25.5 (4.2)	
<i>Obesity</i>				
Within type 2 diabetes	1340 (8.7)	1366 (7.6)	2706 (8.1)	0.000
Within nontype 2 diabetes	67 (29.9)	73 (35.1)	140 (32.4)	0.250
	1268 (8.4)	1291 (7.3)	2559 (7.8)	0.000
<i>Type 2 diabetes</i>				
All	235 (1.5)	224 (1.2)	459 (1.3)	0.014
20–30 years of age	3 (0.1)	7 (0.2)	10 (0.1)	
31–40 years of age	20 (0.6)	19 (0.4)	39 (0.5)	
41–50 years of age	45 (1.3)	43 (1.1)	88 (1.2)	
51–60 years of age	56 (1.5)	80 (1.9)	136 (1.7)	
61–71 years of age	111 (4.6)	75 (2.9)	186 (3.7)	
<i>Within BMI</i>				
<25	67 (0.9)	73 (0.6)	140 (0.7)	0.016
25–29	90 (1.5)	62 (1.6)	152 (1.5)	0.557
30–34	46 (4.1)	42 (4.2)	88 (4.1)	0.923
35+	21 (9.9)	31 (8.6)	52 (9.1)	0.615

Numbers in brackets are percentages; SD for BMI, calculated from available data.

BMI, body mass index.

significant risk factor for asthma in men, OR = 1.70 (1.07–2.70), $P = 0.026$, and in women, OR = 1.88 (1.24–2.85), $P = 0.003$, whereas BMI remained a significant predictor for asthma independently of diabetes status in women, $P < 0.000$, but not in men, $P = 0.336$. A test for interaction between BMI and type 2 diabetes on the risk of asthma was not significant in either sex.

We also examined the relationship between self-reported atopic dermatitis and symptoms of rhinoconjunctivitis, and BMI and type 2 diabetes. The prevalence of atopic dermatitis was lower in subjects with type 2 diabetes compared with nondiabetic subjects (3.2% vs 6.1%), $P = 0.009$, but this relationship did not remain statistically significant after adjusting for confounders.

Analysis of discordant twin pairs

The sex-adjusted risk of asthma in a total of 241 twin pairs discordant for type 2 diabetes was higher in the diabetic twin relative to the nondiabetic co-twin (11.9% vs 11.3%), OR = 1.07 (0.54–2.14), $P = 0.844$. Zygosity-specific risk estimates were not obtainable for MZ twins, but among DZ twins the sex-adjusted risk of asthma was further increased in the type 2 diabetic twin relative to the nondiabetic co-twin, (13.4% vs 12.1%), OR = 1.23 (0.60–2.52), $P = 0.571$, suggesting an attenuation of the effect sizes for these associations in MZ twins.

The same pattern was also observed among twin pairs discordant for BMI, in that the twin with the highest BMI

Table 2 Predictors of asthma in Danish twin subjects, 20–71 years of age

	Asthma (%)		Crude OR (95% CI)	P-value	Adjusted OR (95% CI)*	P-value
	Among affected	Among unaffected				
Males						
Type 2 diabetes	31/230 (13.5)	1160/15 448 (7.5)	1.92 (1.31–2.82)	0.001	1.70 (1.07–2.70)	0.026
BMI						
<25	577/7814 (7.4)		1.00	0.023	1.00	0.336
25–29	454/6105 (7.4)		1.01 (0.89–1.15)	0.907	1.08 (0.94–1.25)	0.269
30–34	91/1111 (8.2)		1.12 (0.89–1.41)	0.339	1.15 (0.89–1.48)	0.301
35+	27/210 (12.9)		1.85 (1.23–2.80)	0.003	1.43 (0.87–2.35)	0.155
Age (per 10 years)	43.6 (14.4)	45.1 (13.6)	0.93 (0.89–0.97)	0.000	0.87 (0.82–0.92)	0.000
Smoking	683/9056 (7.5)	472/6274 (7.5)	1.00 (0.89–1.13)	0.965	0.96 (0.83–1.10)	0.520
Chronic bronchitis	232/1035 (22.4)	865/14 125 (6.1)	4.43 (3.77–5.21)	0.000	4.76 (3.98–5.69)	0.000
Zygosity						
MZ	304/3947 (7.7)		1.00		1.00	
DZ	845/11 236 (7.5)		0.98 (0.85–1.12)	0.711	0.97 (0.84–1.13)	0.724
Married	811/11 232 (7.2)	381/3357 (8.5)	0.83 (0.73–0.95)	0.005	0.96 (0.83–1.12)	0.605
Females						
Type 2 diabetes	36/217 (16.6)	1776/18 489 (9.6)	1.87 (1.31–2.69)	0.001	1.88 (1.24–2.85)	0.003
BMI						
<25	1104/12 699 (8.7)		1.00	0.000	1.00	0.000
25–29	418/3812 (11.0)		1.29 (1.15–1.46)	0.000	1.37 (1.20–1.57)	0.000
30–34	135/998 (13.5)		1.64 (1.36–1.99)	0.000	1.54 (1.23–1.93)	0.000
35+	63/358 (17.6)		2.24 (1.70–2.97)	0.000	1.88 (1.37–2.59)	0.000
Age (per 10 years)	43.2 (14.0)	44.1 (13.6)	0.95 (0.92–0.99)	0.009	0.90 (0.86–0.94)	0.000
Smoking	1059/9994 (10.6)	701/8147 (8.6)	1.26 (1.14–1.39)	0.000	1.10 (0.97–1.23)	0.127
Chronic bronchitis	414/1233 (33.6)	1170/16 552 (7.1)	6.65 (5.82–7.59)	0.000	6.43 (5.56–7.43)	0.000
Zygosity						
MZ	454/4978 (9.1)		1.00		1.00	
DZ	1316/13 260 (9.9)		1.10 (0.98–1.23)	0.102	1.08 (0.95–1.23)	0.246
Married	1230/13 311 (9.2)	582/5398 (10.8)	0.84 (0.76–0.94)	0.001	0.92 (0.82–1.04)	0.199

BMI, body mass index; DZ, dizygotic.

*Odds ratios are multivariately adjusted. Interaction term between BMI and type 2 diabetes removed ($P = 0.087$ for men, $P = 0.509$ for women). Percentages calculated from available data.

had the highest risk of asthma among all twin pairs (8.7% vs 8.2%), sex-adjusted OR = 1.13 (1.01–1.26), $P = 0.027$ and among DZ twin pairs (9.1% vs 8.0%), OR = 1.23 (1.08–1.39), $P = 0.002$ but not among MZ twin pairs (8.0% vs 8.5%), OR = 0.89 (0.71–1.11), $P = 0.291$. In DZ twin pairs, the risk of asthma was further increased in the heavier twin relative to the lighter twin with increasing BMI difference between the two twins in the pair; risk when discordance $> 5 \text{ kg/m}^2$, (10.5% vs 8.8%), OR = 1.34 (0.94–1.92), $P = 0.111$; when discordance $> 10 \text{ kg/m}^2$, (18.1% vs 9.1%), OR = 2.22 (1.05–4.69), $P = 0.038$; when discordance $> 15 \text{ kg/m}^2$, (25.5% vs 12.8%), OR = 2.64 (0.80–8.75), $P = 0.112$ and when discordance $> 20 \text{ kg/m}^2$, (28.6% vs 14.3%), OR = 2.74 (0.27–28.14), $P = 0.397$, whereas this effect was not seen among MZ

twin pairs, indicating genetic confounding between asthma and BMI.

Variance components analysis

Variance decomposition showed that additive genetic factors accounted for 62% of the variance in the susceptibility to asthma, 74% for type 2 diabetes and 73% for BMI, whereas shared environment did not significantly influence the disease susceptibility (Table 3). The influence of genetic factors was not significantly different in men and women for these traits. Significant genetic correlations were found between asthma and type 2 diabetes, 0.20 (0.01–0.40), $P = 0.047$; between asthma and BMI in women, 0.15 (0.07–0.22), $P < 0.000$ and between BMI and type 2 diabetes, 0.40 (0.29–0.43),

Table 3 Variance components analysis of asthma, type 2 diabetes and body mass index (BMI) in Danish twins, 20–71 years of age

Model	Variance components*			Fit statistics		
	A	C/D	E	$\Delta-2 \log Q$	Δdf	P-value
<i>Asthma</i>						
Males						
ACE	0.63 (0.31–0.76)	0.05 (0.00–0.32)	0.32 (0.24–0.43)			
AE	0.68 (0.59–0.76)	–	0.32 (0.24–0.41)	0.116	1	0.733
Females						
ACE	0.43 (0.16–0.64)	0.12 (0.00–0.33)	0.45 (0.36–0.55)			
AE	0.57 (0.49–0.65)	–	0.43 (0.35–0.51)	1.156	1	0.282
All						
ACE	0.50 (0.29–0.64)	0.10 (0.00–0.27)	0.40 (0.38–0.47)			
AE	0.62 (0.56–0.68)	–	0.38 (0.38–0.44)	1.405	1	0.236
<i>Type 2 diabetes</i>						
Males						
ADE	0.00 (0.00–0.76)	0.64 (0.00–0.83)	0.36 (0.17–0.64)			
DE	–	0.64 (0.36–0.83)	0.36 (0.17–0.64)	0.00	1	1.00
AE	0.60 (0.31–0.80)	–	0.40 (0.20–0.69)	1.714	1	0.190
Females						
ACE	0.46 (0.00–0.86)	0.24 (0.00–0.67)	0.30 (0.13–0.57)			
AE	0.73 (0.51–0.88)	–	0.27 (0.12–0.49)	0.751	1	0.386
CE	–	0.56 (0.37–0.71)	0.44 (0.29–0.63)	1.835	1	0.175
All						
ACE	0.66 (0.22–0.84)	0.07 (0.00–0.38)	0.27 (0.16–0.44)			
AE	0.74 (0.60–0.84)	–	0.26 (0.15–0.40)	0.200	1	0.655
<i>BMI</i>						
Males						
ACE	0.67 (0.61–0.76)	0.06 (0.00–0.17)	0.27 (0.23–0.31)			
AE	0.74 (0.70–0.77)	–	0.26 (0.23–0.30)	1.128	1	0.288
Females						
ACE	0.74 (0.61–0.79)	0.02 (0.00–0.13)	0.24 (0.21–0.28)			
AE	0.76 (0.72–0.79)	–	0.24 (0.21–0.27)	0.117	1	0.733
All						
ACE	0.71 (0.69–0.75)	0.02 (0.00–0.10)	0.27 (0.26–0.29)			
AE	0.73 (0.71–0.74)	–	0.27 (0.24–0.29)	0.189	1	0.664

Preferred model showed in bold print. AE model preferred over DE model for male type 2 diabetes because of biological plausibility. $\Delta-2 \log Q$, difference in model fit (log-likelihood) between saturated model and nested model; Δdf , difference in degrees of freedom between saturated model and nested model.

*Standardized parameter estimates (95% confidence intervals) of additive genetic factors (A), shared environmental factors (C), nonshared genetic factors (D) and nonshared environmental factors (E) adjusted for age and sex when males and females are combined.

$P < 0.000$. Environmental correlations between the traits were not statistically significant (Table 4).

Discussion

This study showed that the risk of asthma is almost doubled in subjects with type 2 diabetes compared with nondiabetic

individuals. This effect was seen both in men and in women and was independent of known confounding factors such as age, smoking, chronic bronchitis and BMI. In women, increasing BMI was an independent risk factor for asthma after adjustment for confounders. Our results further indicated that genetic factors for asthma and type 2 diabetes are positively correlated, and also, as previously has been

Table 4 Genetic correlations (below diagonal) and environmental correlations (above diagonal) between asthma, type 2 diabetes and body mass index (BMI) in Danish twins, 20–71 years of age

Disease	Asthma	Type 2 diabetes	BMI
<i>Males</i>			
Asthma	1	−0.37 (−0.87 to 0.13)	−0.03 (−0.12 to 0.14)
Type 2 diabetes	0.26 (−0.05 to 0.53)	1	0.03 (−0.14 to 0.39)
BMI	−0.01 (−0.11 to 0.09)	0.22 (0.02–0.44)*	1
<i>Females</i>			
Asthma	1	−0.13 (−0.32 to 0.06)	0.04 (−0.11 to 0.18)
Type 2 diabetes	0.01 (−0.17 to 0.36)	1	0.08 (−0.21 to 0.35)
BMI	0.15 (0.07–0.22)***	0.44 (0.28–0.62)***	1
<i>All</i>			
Asthma	1	−0.13 (−0.49 to 0.24)	0.01 (−0.06 to 0.08)
Type 2 diabetes	0.20 (0.01–0.40)*	1	0.05 (−0.04 to 0.14)
BMI	0.09 (0.03–0.15)**	0.40 (0.29–0.43)***	1

Adjusted for age and sex when males and females are combined.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

reported that asthma and BMI to some extent share genetic variance (15), particularly in women (16). We also confirmed that BMI and type 2 diabetes share genetic risk factors to a certain degree (17). Our observations corroborate and add to previous findings, which suggest a common aetiology for metabolic syndrome and asthma in adults (18).

We recognize that a significant proportion of adults with type 2 diabetes may be undiagnosed in our population, particularly because we used hospital-based registries as the source of validation. Notably, we found a relatively low prevalence of type 2 diabetes (0.1% among the ages 20–30 years rising to 3.7% among the ages 61–71 years). However, we were able to also assess the presence of self-reported diabetes by the questionnaire and cross-linked these data with the hospital discharge diagnoses to estimate the magnitude of underdiagnosis of type 2 diabetes. Among subjects without a hospital discharge diagnosis of type 2 diabetes, a total of 299 subjects (0.9%) reported a history of diabetes in the questionnaire. We were not able to decide whether these were type 1 or type 2 diabetic cases but the major part are likely to be type 2 diabetic and therefore confirm the presence of underdiagnosis. Conversely, among subjects with a hospital discharge diagnosis of type 2 diabetes, a total of 56 subjects (12.4%) did not report such history in the questionnaire, whereas a total of 26 individuals (5.8%) reported a past history of diabetes in the questionnaire. Of these, 61.5% were women, which could indicate confounding because of gestational diabetes. We would have increased our capture rate if we had used a more detailed registration of type 2 diabetic cases. Notably, compared with a study that estimated the prevalence of type 2 diabetes based on information about all redemptions of subsidized and prescribed drugs in one Danish county (19), we found significantly lower rates of type 2 diabetes in our population. Particularly, the prevalence of type 2 diabetes based on drug prescription rates was around 2% among subjects aged 40–64 years and around 4% among subjects aged 65 years or older (19). It is likely that our population of type 2 diabetes constitute individuals with

severe disease and possibly also diabetic complications as these are possibly more likely to appear in hospital databases. Furthermore, we cannot rule out that type 2 diabetes is more likely to be diagnosed among patients hospitalized with asthma thereby favouring our conclusion (6).

The asthma diagnosis was based on questionnaire responses and therefore also included a significant number of both false-positive and false-negative cases. Notably, we verified the asthma diagnosis in an earlier clinical study of a subpopulation of the age group 20–49 years and discovered a misclassification rate of 12% (20). In older adults, the presence of chronic obstructive pulmonary disease could have induced misclassification of asthma. We tried to correct for this bias by adjusting for smoking history and symptoms of chronic bronchitis, and therefore, the observed association between asthma and type 2 diabetes is independent of these factors. In spite of limitations in the diagnostic method for the studied diseases, we obtained heritability estimates that are comparable to earlier findings (15, 17).

The strength of the present study is the combined information from two independent data resources, namely questionnaire responses, as well as hospital discharge diagnoses. Participants were thus unaware of the purpose of the study, which improved the internal validity. Furthermore, our cohort included a large number of individuals, which increased the precision of our findings.

We conclude that asthma, type 2 diabetes and increased BMI are strongly associated in adults, particularly in women. The association is independent of other known risk factors such as age, smoking and chronic bronchitis. We found that asthma shares genetic risk factors with type 2 diabetes and BMI suggesting a common aetiology for asthma and metabolic syndrome.

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