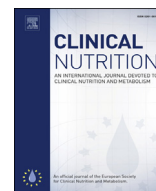




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Original article

Obesity increases the prevalence and the incidence of asthma and worsens asthma severity

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SUMMARY

Background & aims: We aimed to explore the association between obesity and asthma prevalence, incidence and severity.**Methods:** The study included 32,644 adults, 52.6% female, from a representative sample of the 4th Portuguese National Health Survey. The following asthma definitions were used: ever asthma (ever medical doctor asthma diagnosis), current asthma (asthma within the last 12 months), current persistent asthma (required asthma medication within the last 12 months), current severe asthma (attending an emergency department because of asthma within the last 12 months), and incident asthma (asthma diagnosis within the last 12 months). Body mass index was calculated based on self-reported weight and height and categorised according to WHO classification. Logistic regression models adjusted for confounders were performed.**Results:** Prevalence of ever asthma was 5.3%, current asthma 3.5%, current persistent asthma 3.0%, current severe asthma 1.4%, and incident asthma 0.2%. Prevalence of obesity was 16%, overweight 37.6%, normal weight 44.6% and underweight 0.2%. Being overweight, obesity class I and II, and obesity class III were associated with an OR (95% CI) with ever asthma 1.22 (1.21–1.24), 1.39 (1.36–1.41), 3.24 (3.08–3.40) respectively; current asthma 1.16 (1.14–1.18), 1.86 (1.82–1.90), 4.73 (4.49–4.98) respectively; current persistent asthma 1.08 (1.06–1.10), 2.06 (2.01–2.10), 5.24 (4.96–5.53), and current severe asthma 1.36 (1.32–1.40), 1.50 (1.45–1.55) and 3.70 (3.46–3.95), respectively. Considering the incidence of asthma, obesity more than quadrupled the odds (OR = 4.46, 95% CI 4.30, 4.62).**Conclusion:** Obesity is associated in a dose dependent way with an increase of prevalent and incident asthma, and it seems to increase the odds of a more persistent and severe asthma phenotype independently of socio-demographic determinants, physical activity, and dietary patterns. Our results provide rational for future lifestyle intervention studies for weight reduction in the obesity–asthma phenotype.

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1. Introduction

Asthma and obesity are both complex and multifactorial chronic health conditions, wherein host and environmental factors play a

determinant role, and represent a serious economic and social burden in health care systems and patient's quality of life [1,2]. Although there have been advances in the knowledge, management and treatment, asthma prevalence is rising globally and disease control remains difficult [3]. Furthermore, the lack of a precise and consensual definition of asthma hinders a reliable comparison of reported prevalence from different countries. Currently, global prevalence seems to range between 1 and 16%, with western Europe showing a decrease and low income regions, where

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prevalence was previous low, currently on the rise [2,4,5]. Meanwhile, National Health and Nutrition Examination Survey (NHANES) data has indicated that almost one in three asthma patients were obese and that the prevalence of obesity between subjects with current asthma has increased from 21.3% (NHANES I) to 32.8% (NHANES III) [6]. Recently, an EAACI meta-analysis showed that weight gain per se, almost double the odds of incident asthma [7].

The description of a putative link between the high prevalence of asthma and obesity must increase efforts to better understand the so far unclear mechanisms underlying the association between these two epidemics [1,8]. The literature describes some plausible leads such as mechanical factors, inflammatory conditions and stress triggers [9,10]. Indeed, obesity is known to be associated with chronic low-grade systemic inflammation, mediated by increased levels of the pro-inflammatory leptin and plasminogen activator inhibitor and decreased levels of the protective anti-inflammatory adiponectin [11]. Nonetheless, and providing support to the mechanical hypothesis linking obesity and asthma, we have previously reported a negative association between BMI and exhaled nitric oxide in overweight and obese asthmatics [12].

Moreover, evidence suggests that obesity increases, not only, the risk of asthma, but also, the severity of respiratory symptoms by decreasing lung function and increasing airway hyperreactivity (AHR), albeit contributing towards a more difficult-to-control asthma phenotype [2,13,14]. Severe asthma is considered an heterogeneous disease in which a variety of clinical, physiological and inflammatory markers determine distinct clinical phenotypes [15]. It is also worth referring that a meta-analysis showed that being overweight or obese increases the odds of incident asthma in a dose-dependent way [16]. Therefore, it is important to consider, within the clinical management of the obesity–asthma phenotype, the effect of weight reduction in obese patients. Several studies have demonstrated that weight reduction does improve lung function, symptoms, morbidity, and overall health status [17,18], with further reports of the reduction of asthma exacerbations with better control and quality of life [7,19–21]. Nevertheless, data from the previous National Health Survey (1998–99) indicated that obesity was not related with the prevalence of asthma [22], which suggests that further research on the epidemiology of obesity and asthma and on the feasibility of weight reduction recommendations should also consider other clinical outcomes and socio-economic determinants [23], including lifestyle factors such as dietary intake and physical activity.

Therefore, this study aims to explore the association between obesity and asthma in a large representative adult population, adjusting for socio-economic and lifestyle confounders, namely physical activity and dietary patterns. The hypothesis was that obesity would be associated with asthma prevalence and incidence, according to a gradient of severity in both conditions.

2. Materials and methods

2.1. Participants and study design

Data from the 4th Portuguese National Health Survey, carried out by the National Institute of Health and National Institute of Statistics (NIS), between 2005 and 2006, was analysed. The methodology of the NHS has been previously described [24,25]. In summary, the sampling frame was made based on census data and participants were selected from households during that period, using a multi-stage random probability design (hospitals, prisons, military houses and community care institutions were excluded). A representative sample of 41,193 participants from all ages was included, according to the 7 main Portuguese territorial units

(NUTS II), namely North, Centre, Lisbon, Alentejo, and Algarve, and Madeira and Azores archipelagos. The primary sampling unit (PSU) was the housing unit and sampling was based on the population and housing census. Two levels were defined within each NUTS II: the parish (corresponding to townships); and geographically defined units of 240 lodgings (within the parish). The PSUs were then randomly selected within each territorial unit, and subjects living in the sampling unit were surveyed. Interviews were conducted in the households by trained staff interviewers, and the questionnaire included information on social and demographic characteristics, health, and chronic diseases including asthma. The survey response rate reported by NIS, defined as the percentage of households who responded, was 76% [24,25]. For the purposes of this study, a representative sub-sample of adult participants NHS surveyed was analysed (32,644 participants).

2.2. Asthma

The following asthma definitions were used: ever asthma (ever had a medical doctor asthma diagnosis), current asthma (asthma within the last 12 months), current persistent asthma (required asthma medication within the last 12 months), current severe asthma (attending an emergency department because of asthma within the last 12 months), and incident asthma (asthma diagnosis within the last 12 months).

2.3. Body mass index

Body mass index (weight/height²) was calculated based on self-reported weight (kilograms) and height (meters), and categorised according to the World Health Organization Classification [26], in underweight (<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), obesity class I (30.0–34.9 kg/m²), class II (35.0–39.9 kg/m²) and class III (≥40.0 kg/m²). For the descriptive and logistic regression analyses for asthma prevalence definitions we have merged obesity classes I (prevalence of 12.7%) and II (prevalence of 2.5%), due to the low prevalence of the later. Obesity class III was analysed separately in order to better address the increase of asthma severity according the clinical severity of obesity as well. Considering the low incidence of asthma (0.2%), the logistic regression models for incident asthma could not be performed with the four categories. Therefore, and for the purposes of this specific analysis, BMI was categorised in obesity vs. non-obesity with an agreed cut off of BMI ≥ 30.0 kg/m².

2.4. Socio-demographic, physical activity and dietary patterns

Age, gender, education, family income, smoking, physical activity level, and dietary patterns were also addressed by NHS, and analysed as potential confounders.

The physical activity level was classified as Low, Moderate and High based on questions from the short version of the International Physical Activity Questionnaire (IPAQ) [27] included in the NHS. The short 7 days self-administered version is a 7-item questionnaire that provides information about frequency and duration of 4 domains: sedentary activity, time spent walking and moderate- and vigorous-intensity PA. Physical activity within domains was estimated by weighting the reported frequency (events per week) by duration (minutes per event) and by a MET level assigned to each activity (Walking = 3.3; Moderate-intensity PA = 4.0; and Vigorous-intensity PA = 8.0). A combined total physical activity was computed as the sum of the activity domains scores (Total PA = Walking + Moderate-intensity PA + Vigorous-intensity PA) and reported as categorical score.

Table 1

Characteristics of participants according to asthma prevalence.

	Total n = 32,644				Ever asthma			Current asthma			Current persistent asthma			Current severe asthma			Incident asthma		
					Yes = 5.3%	No = 95.7%	p	Yes = 3.5%	No = 96.5%	p	Yes = 3.0%	No = 97%	p	Yes = 1.4%	No = 98.6%	p	Yes = 0.2%	No = 99.8%	p
Gender (%)																			
Female	52.4	60.1	51.9	<0.001	61.3	52.1	<0.001	62.0	52.1	<0.001	65.4	52.2	<0.001	46.0	52.4	<0.001	54.0	47.6	
Male	47.6	39.9	48.1		38.7	47.9		38.0	47.9		34.6	47.8		54.0	47.6				
Age (%)																			
20–39 y	37.8	33.2	38.0	<0.001	25.7	38.2	<0.001	25.3	38.2	<0.001	28.7	37.9	<0.001	30.8	37.8	<0.001			
40–64 y	40.5	37.9	40.7		42.1	40.5		39.4	40.6		34.9	40.6		49.4	40.5				
65–84 y	19.8	26.5	19.4		29.0	19.4		31.7	19.4		31.0	19.6		19.8	19.8				
≥85 y	1.9	2.4	1.9		3.2	1.9		3.6	1.9		5.4	1.9		0.0	1.9				
Education (%)																			
None	12.7	17.0	12.4	<0.001	21.1	12.4	<0.001	20.8	12.4	<0.001	23.2	12.5	<0.001	17.5	12.7	<0.001			
1st cycle	34.1	34.2	34.1		39.3	33.9		38.8	33.9		39.5	34.0		43.3	34.1				
2nd and 3rd cycles	27.8	21.8	28.1		16.1	28.2		16.3	28.1		19.2	27.9		12.6	27.8				
High school	12.2	10.3	12.3		8.9	12.4		7.7	12.4		9.6	12.3		8.9	12.2				
College	13.1	16.5	12.9		14.6	13.1		16.4	13.0		8.5	13.2		17.8	12.7				
Family income (%)																			
≤500€/month	23.7	29.0	23.4	<0.001	32.8	23.4	<0.001	31.5	23.5	<0.001	33.9	23.6	<0.001	28.9	23.7	<0.001			
501–1200€/month	44.1	40.1	44.3		39.6	44.3		41.4	44.2		40.8	44.1		47.3	44.1				
1201€–2000€/month	20.0	17.1	20.1		14.2	20.2		16.0	20.1		15.5	20.0		0.0	20.0				
>2000€/month	12.2	13.9	12.1		13.4	12.1		11.1	12.2		9.8	12.2		23.9	12.2				
Proxy reporting information (%)	29.8	24.5	30.0	<0.001	22.0	30.0	<0.001	22.7	30.0	<0.001	21.5	29.9	<0.001	6.9	29.8	<0.001			
Smoking (%)																			
No smoker	61.7	63.2	61.6	<0.001	63.4	61.7	<0.001	65.3	61.6	<0.001	63.2	61.7	<0.001	67.8	61.7	<0.001			
Current smoker	21.4	17.7	21.6		14.8	21.6		12.8	21.7		18.8	21.4		11.7	21.4				
Past smoker	16.8	19.1	16.7		21.7	16.7		21.9	16.7		18.0	16.8		20.5	16.8				
Level physical activity (%)																			
Low	39.0	52.5	38.2	<0.001	56.2	38.3	<0.001	55.9	38.4	<0.001	64.4	38.5	<0.001	28.3	39.0	<0.001			
Moderate	46.1	37.4	46.6		31.2	46.7		30.7	46.6		27.3	46.5		0.0	46.2				
High	14.9	10.0	15.2		12.6	15.0		13.4	15.0		8.3	15.0		71.7	14.9				
Dietary patterns, mean (SD)																			
“Dairy and fruit” DP	−0.05 (0.66)	−0.30 (0.66)	−0.47 (0.66)	<0.001	−0.06 (0.65)	−0.04 (0.66)	<0.001	−0.03 (0.63)	−0.05 (0.66)	<0.001	−0.11 (0.64)	−0.04 (0.66)	<0.001	−0.7 (0.57)	−0.05 (0.66)	<0.001			
“Soup and starchy foods” DP	−0.03 (0.56)	−0.09 (0.57)	−0.02 (0.56)	<0.001	−0.05 (0.58)	−0.03 (0.56)	<0.001	−0.06 (0.55)	−0.03 (0.56)	<0.001	−0.11 (0.59)	−0.03 (0.56)	<0.001	0.18 (0.52)	−0.03 (0.56)	<0.001			
“High fat, sugar and salt” DP	0.17 (0.63)	0.20 (0.68)	0.17 (0.63)	<0.001	0.16 (0.68)	0.17 (0.63)	<0.001	0.14 (0.66)	0.17 (0.63)	<0.001	0.21 (0.71)	0.17 (0.63)	<0.001	0.06 (0.43)	0.17 (0.63)	<0.001			
“Fish, fruit and vegetables” DP	−0.01 (0.58)	−0.04 (0.60)	0.01 (0.58)	<0.001	−0.03 (0.61)	0.01 (0.58)	<0.001	−0.03 (0.58)	0.01 (0.58)	<0.001	−0.10 (0.64)	0.01 (0.58)	<0.001	0.17 (0.44)	0.01 (0.58)	<0.001			
“Sugary and fatty foods” DP	0.02 (0.50)	0.00 (0.50)	0.02 (0.50)	<0.001	0.00 (0.50)	0.02 (0.50)	<0.001	0.01 (0.50)	0.20 (0.50)	<0.001	0.01 (0.48)	0.02 (0.50)	<0.001	−0.08 (0.37)	0.01 (0.50)	<0.001			
BMI classes (%)																			
Underweight/normal weight	46.4	44.3	46.6	<0.001	40.1	46.7	<0.001	42.1	46.6	<0.001	45.1	46.5	<0.001	34.2	46.5	<0.001			
Overweight	37.6	33.6	37.8		33.7	37.7		32.4	37.7		30.2	37.7		19.8	37.6				
Obesity classes I and II	15.2	20.2	15.0		22.9	15.0		23.0	15.0		22.6	15.1		34.4	15.2				
Obesity class III	0.8	1.9	0.7		3.2	0.7		2.5	0.7		2.1	0.7		11.7	0.7				

Data presented as proportions (%), and mean (SD). Sample weighted for all variables (pond 1); DP: dietary patterns. Qui-square test; p-value <0.05.

Three categories or levels of physical activity were calculated. High PA (category 3) was defined by any one of the following 2 criteria: vigorous-intensity activity on ≥ 3 days and accumulating at least 1500 MET-minutes/week; or 7 days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 3000 MET-minutes/week. Moderate PA (category 2) was defined by any one of the following 3 criteria: ≥ 3 days of vigorous activity of at least 20 min per day; or ≥ 5 days of moderate-intensity activity or walking ≥ 30 min per day; or ≥ 5 of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 600 MET-min/week. Low PA level was defined for those individuals who do not meet the criteria for categories 2 or 3, and were considered low or inactive.

Dietary patterns were identified by Latent Variable Models [28,29], based on dietary intake list of 20 usual foods and beverages consumed at meals (milk, cheese and yogurt; vegetable soup; bread and cereal products; meat; fish; potatoes, rice and pasta; pulses; vegetables; fruit; and pastry, chocolates or sweet desserts), and snacks (fruit; bread or sandwiches; milk, cheese and yogurt; juices; soft drinks; pastry, chocolates or sweet desserts; other candies; salty snacks; chips; and alcoholic beverages). The dietary patterns assessment data of the NHS was previously detailed and described [30].

In summary, Latent Models can be divided into two frameworks: latent trait models (LTM), which assume that the latent variables are metrical (factors), and latent class models (LCM) that consider latent variables as categorical (clusters). Latent trait model is a Binary Data Factor Analysis that considers one or more factors. LTM assume that the dietary intake of each individual is explained by one or more factors, usually called 'latent variables'. Interpretation of the model is done considering the standardised factor loadings, which expresses the correlation coefficient between the latent variable and an underlying continuous variable obtained from each food item. Coefficient correlations (r) > 0.350 and < -0.350 were considered for selecting food items. Geomin rotation was applied to simplify the standardised factor loadings matrix, and the following criteria to determine the number of latent variables in the model was considered: the model with lowest value in the Bayesian information criteria, the global goodness of fit of the considered latent models assessed through the likelihood ratio test, via parametric bootstrapping (100 samples) and the residuals inspection.

2.5. Statistical analysis

Descriptive analysis, including mean (standard deviation) and proportions, was performed to characterise the sample, and conducted with sampling weights. Student's *t*-tests, ANOVA, and chi-squared tests were performed to determine the association

between obesity, asthma, and confounder variables. Unconditional logistic regression models were performed to analyse whether BMI classes were associated with asthma prevalence and control; and whether obesity is associated with the incidence of asthma. Age, gender, education, family income, proxy reporting information, smoking, physical activity and dietary patterns were analysed as confounders.

A 0.05 level of significance and 95% CI were considered. Data analysis was performed using the statistical package SPSS®, version 18.0 (SPSS Inc., Chicago, IL, USA).

3. Results

The final analysis included 32,644 adults (≥ 20 years-old), and 52.6% were female. Table 1 summarises the characteristics regarding socio-demographic, physical activity and dietary patterns of the participants according to asthma prevalence. Considering dietary patterns analysis, the goodness-of-fit test suggests that the 5-factor LTM was the best solution. Factor 1 ("dairy and fruit" DP) was positively correlated with milk and dairy products ($r = 0.575$) at meals and snacks, fruit ($r = 0.484$) at snacks, and negatively correlated with alcoholic beverages ($r = -0.405$) at snacks. Factor 2 ("soup and starchy foods" DP) was positively correlated with vegetable soup ($r = 0.526$), bread ($r = 0.443$) and pulses ($r = 0.432$) at meals. Factor 3 ("high fat, sugar and salt" DP) was positively correlated with pastry, chocolate and sweet desserts ($r = 0.370$), other candies ($r = 0.630$), salty snacks ($r = 0.711$), chips ($r = 0.918$), fruit juices ($r = 0.568$), soft drinks ($r = 0.648$), and alcoholic beverages ($r = 0.392$) at snacks. Factor 4 ("fish, fruit and vegetables" DP) was positively correlated with fish ($r = 0.443$), vegetables ($r = 0.538$) and fruit ($r = 0.448$) at meals. Factor 5 ("sugary and fatty foods" DP) was positively correlated with, pastry, chocolate and sweet desserts at meals ($r = 0.464$) and snacks ($r = 0.395$).

Prevalence of ever asthma was 5.3%, current asthma 3.5%, current persistent asthma 3.0%, current severe asthma 1.4%, and incident asthma 0.2%. Prevalence of underweight was 2.0%, normal weight 44.6%, overweight 37.6% and obesity was 16.0% (obesity class I 12.7%, class II 2.5% and class III 0.8%).

Table 2 summarises the association between BMI classes and asthma prevalence adjusted for confounders, including physical activity. Overweight, obesity class I and II, and obesity class III were associated with ever asthma (respectively OR = 1.18, 95% CI 1.16, 1.20; OR = 1.32, 95% CI 1.30, 1.35; OR = 2.85, 95% CI 2.72, 3.00), with current asthma (OR = 1.13, 95% CI 1.11, 1.16; OR = 1.78, 95% CI 1.75, 1.82; OR = 4.75, 95% CI 4.52, 4.99), and with current severe asthma (OR = 1.25, 95% CI 1.22, 1.28; OR = 1.33, 95% CI 1.29, 1.38; OR = 3.05, 95% CI 2.86, 3.24). Obesity class I and II (OR = 1.79, 95% CI 1.75, 1.83) and obesity class III (OR = 4.14, 95% CI 4.19, 4.64) were associated

Table 2
Association between BMI classes and asthma prevalence considering physical activity.

	Ever asthma		Current asthma		Current persistent asthma		Current severe asthma		Incident asthma	
	aOR (95% CI) ^a	p-trend	aOR (95% CI) ^a	p-trend	aOR (95% CI) ^a	p-trend	aOR (95% CI) ^a	p-trend	aOR (95% CI) ^b	p-trend
Overweight (25.0–29.9 kg/m ²)	1.18 (1.16; 1.20)	<0.001	1.13 (1.11; 1.16)	<0.001	0.98 (0.96; 1.00)	<0.001	1.25 (1.22; 1.28)	<0.001		
Obesity class I and II (30.0–39.9 kg/m ²)	1.32 (1.30; 1.35)		1.78 (1.75; 1.82)		1.79 (1.75; 1.83)		1.33 (1.29; 1.38)		4.09 (3.95; 4.23)	<0.001
Obesity class III (≥ 40.0 kg/m ²)	2.85 (2.72; 3.00)		4.75 (4.52; 4.99)		4.41 (4.19; 4.64)		3.05 (2.86; 3.24)			

aOR: adjusted Odds Ratio; p-value < 0.05.

^a Unconditional logistic regression models with sampling weight, adjusted for gender, age, education, family income, proxy reporting information, smoking, and physical activity level.

^b Unconditional logistic regression between obesity (≥ 30.0 kg/m²) and incident asthma with sampling weight, adjusted for gender, age, education, family income, proxy reporting information and smoking.

Table 3

Association between BMI classes and asthma prevalence considering physical activity and dietary patterns.

	Ever asthma		Current asthma		Current persistent asthma		Current severe asthma		Incident asthma	
	aOR (95% CI) ^a	p-trend	aOR (95% CI) ^a	p-trend	aOR (95% CI) ^a	p-trend	aOR (95% CI) ^a	p-trend	aOR (95% CI) ^b	p-trend
Overweight (25.0–29.9 kg/m ²)	1.22 (1.21; 1.24)	<0.001	1.16 (1.14; 1.18)	<0.001	1.08 (1.06; 1.10)	<0.001	1.36 (1.32; 1.40)	<0.001		
Obesity class I and II (30.0–39.9 kg/m ²)	1.39 (1.36; 1.41)		1.86 (1.82; 1.90)		2.06 (2.01; 2.10)		1.50 (1.45; 1.55)		4.46 (4.30; 4.62)	<0.001
Obesity class III (≥40.0 kg/m ²)	3.24 (3.08; 3.40)		4.73 (4.49; 4.98)		5.24 (4.96; 5.53)		3.70 (3.46; 3.95)			

aOR: adjusted Odds Ratio; p-value < 0.05.

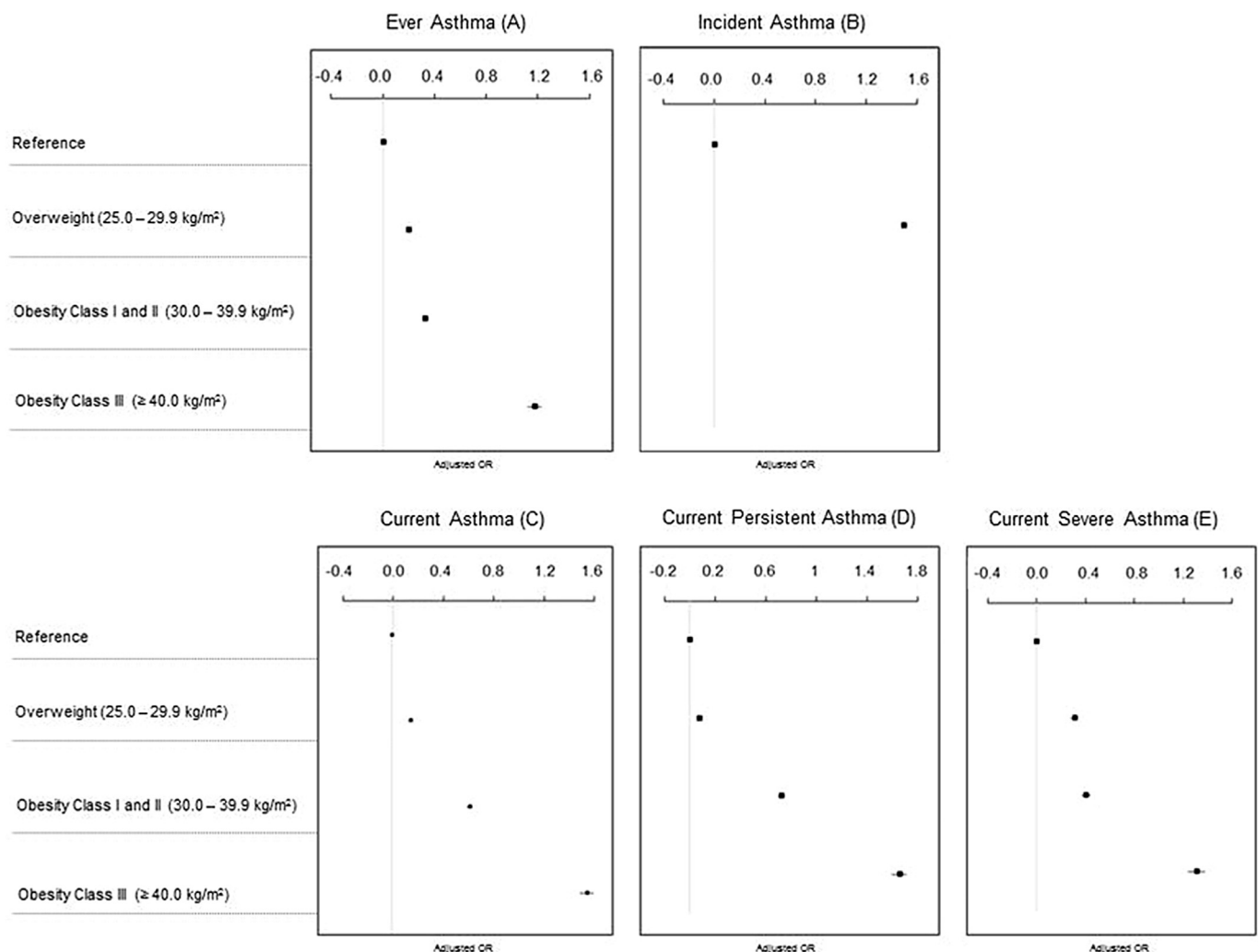
^a Unconditional logistic regression models with sampling weight, adjusted for gender, age, education, family income, proxy reporting information, smoking, physical activity level, and dietary patterns.^b Unconditional logistic regression between obesity (≥30.0 kg/m²) and incident asthma with sampling weight, adjusted for gender, age, education, family income, proxy reporting information, smoking, and dietary patterns.

Fig. 1. Association between body mass index classes and asthma prevalence considering physical activity and dietary patterns. *Unconditional logistic regression models between BMI classes and asthma prevalence (A), current asthma (C), current persistent asthma (D) and current severe asthma (E), with sampling weight, adjusted for gender, age, education, family income, proxy reporting information, smoking, physical activity level, and dietary patterns. Overweight (25.0–29.9 kg/m²), obesity class I (30.0–34.9 kg/m²) and II (35.0–39.9 kg/m²), and obesity class III (≥40.0 kg/m²). LN adjusted Odds Ratio; p < 0.05. *Unconditional logistic regression between obesity (≥30.0 kg/m²) and incident asthma (B) with sampling weight, adjusted for gender, age, education, family income, proxy reporting information, smoking, and dietary patterns; LN adjusted Odds Ratio; p < 0.05.

with current persistent asthma, and obesity (OR = 4.09, 95% CI 3.95, 4.23) more than quadrupled the odds of incident asthma.

Considering logistic regression models adjusted for confounders, including dietary patterns (Table 3 and Fig. 1), the observed associations still remain significant, with increased odds. Overweight, obesity class I and II, and obesity class III were

associated with ever asthma (respectively OR = 1.22, 95% CI 1.21, 1.24; OR = 1.39, 95% CI 1.36, 1.41; OR = 3.24, 95% CI 3.08, 3.40), with current asthma (OR = 1.16, 95% CI 1.14, 1.18; OR = 1.86, 95% CI 1.82, 1.90; OR = 4.73, 95% CI 4.49, 4.98), with current severe asthma (OR = 1.36, 95% CI 1.32, 1.40; OR = 1.50, 95% CI 1.45, 1.55; OR = 3.70, 95% CI 3.46, 3.95), and with current persistent asthma (OR = 1.08,

95% CI 1.06, 1.10; OR = 2.06, 95% CI 2.01, 2.10; OR = 5.24, 95% CI 4.96, 5.53). Obesity class III more than tripled the odds of having asthma and severe asthma, and more than quintuples the odds of having current persistent asthma. Considering the incidence, obesity more than quadrupled the odds of asthma (OR = 4.46, 95% CI 4.30, 4.62).

4. Discussion

In this study we observed that being overweight or obesity in the adult population was significantly associated with asthma prevalence and more than quadrupled the incidence of asthma, independently of the others socio-economic and lifestyle confounders, such as physical activity and dietary patterns. Additionally, the odds increase according to a gradient of obesity and asthma persistency and severity, with higher odds for obesity class III.

Our findings are supported by the fact that a large sample of adults of both genders from a representative nationwide observational cross-sectional study has been used, and that it also took in consideration physical activity and dietary patterns. The 4th Portuguese National Health Survey (NHS) allowed for the inclusion of important socio-economic and lifestyle confounders regarding obesity and asthma, such as age, gender, education, family income, BMI, smoking, proxy reporting information, physical activity level and dietary intake. For all these reasons, this is the first large scale survey on obesity and asthma adjusted for dietary patterns identified by Latent Trait Model analysis [28,29]. Even though, the previous NHS (1998–99) reported that obesity was not associated with asthma prevalence [22], methodological differences between both NHS editions are explained by the fact that dietary intake and physical activity variables were not available to include as confounders in the 3rd NHS (1998–99). Plus this discrepancy between the two editions and their reported results could point, as previously mentioned, towards an asthma–obesity phenotype, illustrating the trend between an increased asthma prevalence alongside an increase in obesity.

Evidence has been mounting suggesting that obesity does contribute to the risk of asthma with a more difficult-to-control phenotype [2,14]. Our results are in agreement with this and show that obesity increases prevalent asthma and seems to promote an asthma phenotype more persistent and severe, independently of socio-demographic and lifestyle determinants, such as physical activity and dietary patterns. It is also been showed in this study that obesity more than quadrupled the odds of incident asthma.

Several cross-sectional and case–control studies found that obesity was associated with asthma diagnosis, respiratory symptoms, poor lung function and increased airways hyperreactivity (AHR) [13] according to mechanical or inflammatory causes. Firstly, the increased abdominal and chest wall mass causes a decrease in the functional residual capacity and a reduction in lung and tidal volumes [31,32]. Moreover, gastroesophageal reflux disease (GERD) and hiatal hernia are common comorbidities of obesity. Although GERD is known to increase the risk of asthma, in large epidemiological surveys, adjustment for GERD did not substantially affect the relationship between obesity and asthma, suggesting that the increase risk of asthma in obese adult subjects is independent of GERD [8,9,33]. Secondly, obesity has been suggested as a pro-inflammatory state [11], hence an increase in BMI might influence a certain degree of airway inflammation, but the evidence available is scarce and somewhat conflicting [8,34]. In adults, BMI was inversely associated with exhaled NO in overweight and obese asthmatics [12], while in children no association was found [35–37], supporting the mechanical hypothesis [12]. In another instance, a case–control study has described a correlation between BMI and serum leptin levels in asthmatics and non-asthmatics, but likewise exhaled NO was not related with serum leptin levels in asthmatic patients [38]. Lastly,

and according to the mechanisms already referred and reported results, obesity has the potential of an even greater impact, because it may influence the asthma treatment response, particularly in those cases with an increased severity of illness [17]. Thus, clarifying the mechanisms underlying the epidemiology of obesity and asthma phenotypes will allow to improve and better design weight loss interventions in overweight populations to reduce asthma incidence; and with this strategies strive improve asthma control and quality of life of the asthmatic obese patient [7]. A randomised trial to compare effects of dietary restriction and exercise in obese asthmatic patients showed that a 5–10% weight reduction resulted in clinical improvements in asthma control (58%) and quality of life in 83% of patients. These clinical improvements were accompanied by a reduction in neutrophilic airway inflammation, suggesting that reducing of weight should be further explored in the clinical management of obese–asthma phenotype [20]. These results taken together suggest that nutritional intervention has a clinical impact in control and severity of asthma, namely dietary strategies based in the modification of dietary fat intake may be useful in reducing airway neutrophilia [20]. Also, physical activity has an important role in energy balance and adequate body weight maintenance, and may provide, as well an immunomodulation link between obesity and asthma [39–41].

The results described here are limited by the cross sectional nature of data not allowing to establish causal relationship. Another constraint might be the self-reported nature of asthma prevalence, incidence and control assessment; however this has been the usual approach in large-scale studies addressing asthma and allergic diseases prevalence [1,4]. In conjunction, weight and height were also addressed by self-report, even though this may be less of an issue in large scale surveys, as it is known that self-reporting can be significant associated with weight and height measurements in cohort surveys [42,43]. Likewise, and although BMI is not the gold standard to assess body composition, it is correlated with total body fat content and has been the most widely used measure to assess overweight or obesity, and to monitor changes in body weight [42,43]. Future research should consider more complex anthropometric measurements (e.g., waist-circumference, skinfold thickness, or bioelectrical impedance analysis) that assess total body mass distribution, including body fat mass measurements, although it is methodologically difficult to measure in such a large sample.

In summary, our study shows that obesity increases both prevalent and incident asthma and seems to change asthma phenotype towards a more persistent and severe disease independently of socio-demographic, physical activity and dietary patterns. Therefore, our results reinforce the importance of tackling the relationship between asthma and obesity, indicating that issues such excessive body weight should be considered and integrated in the clinical asthma management and that adequate body weight maintenance should be recommended as primary prevention to minimise the burden of asthma in the global health care systems. Our study also provides rationale for future studies exploring the feasibility of lifestyle interventions to reduce the severity of obesity–asthma phenotype. More studies are needed to better understand which nutritional intervention and dietary modifications will be able to optimise, not only the weight loss, but also, asthma related clinical outcomes i.e. treatment and control, ultimately, improving these patients' quality of life.

Conflict of interest

The authors declare no conflict of interest.

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