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Gender differences in the association between life history of body silhouettes and asthma incidence: Results from the SAPALDIA cohort study

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ABSTRACT

Background: The association of obesity and asthma has been described in children and adults. However, whether a different life course of weight in men and women may explain gender differences in asthma incidence, has not been addressed.

Objectives: Using data from the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults, we investigated the role of overweight/obesity as measured by body silhouettes at different life stages in men and women for asthma incidence.

Methods: Our analysis included 5417 subjects who were asthma free at age 8, followed up to 2011, and had complete covariate information. The main predictor of interest was self-reported body silhouettes at age 8, menarche, 30, 45, menopause, and 60, and additionally changes in body silhouette number across these different time points. Asthma incidence was defined as newly reported doctor-diagnosed asthma after the body silhouette time point. Asthma incidence and its association with body silhouettes was analysed using sex stratified logistic regression, adjusting for age, atopy, urbanity, smoking, parental asthma, education and study area.

Results: Men at age 60 had an increased risk of asthma incidence per unit increase in body silhouette number (OR 1.93, 95% CI 1.13–3.30). This association was stronger in women at age 60 (OR 2.78, 95% CI 1.49–5.18) and observed also at menopause (OR 1.35, 95% CI 1.03–1.78), as well as per unit change in body silhouette number between age 45 – menopause (OR 1.74, 95% CI 1.15–2.63).

Conclusion: In this longitudinal study, the risk of incident asthma increased in men and women with a larger body silhouette in late adulthood. In women, this risk appeared present between age 45 and menopause. At age 60, both men and women were at higher risk of asthma incidence per unit increase in body silhouette, the risk being more pronounced in women. The age-related increase of obesity may underlie gender differences in asthma incidence at higher ages.

1. Introduction

The incidence of asthma almost doubles in those who are obese [1]. Although studies have shown a steady dose-response relationship between incident asthma and increasing BMI, only few have evaluated the interaction of sex and overweight/obesity on incident asthma [2–7]. Among those studies, many demonstrate the effect to be stronger in women than in men [7–12], however, the difference in point estimates between men and women is usually small, and other studies have shown conflicting results [6,13–15].

Furthermore, to the best of our knowledge, no study has addressed the association of life history of body weight and asthma in women and men even though the course of overweight across life is known to differ between men and women. This is well documented for the Swiss population by the Swiss Health Survey [16], with a male preponderance of overweight between the ages 20–50 years. In Europe, differences in

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Table 1
Main characteristics at baseline comparing those excluded from study population with those included, by sex.

Study population (N = 5417)*					Excluded (N = 4234)**				P-Value***	
	Male		Female		Male		Female		Male	Female
	N	%	N	%	N	%	N	%		
OVERALL	2614	48.3	803	51.7	2131	50.3	2103	49.6	0.98	
Age									< 0.01	< 0.01
≤30	591	22.6	551	19.7	451	21.2	402	19.1		
30–40	1029	39.4	1173	41.9	745	35.0	783	37.2		
45–60	994	38.0	1079	38.5	935	43.9	918	43.7		
Smoking status age 30–45									< 0.01	< 0.01
Never-smoker	1018	39.1	1512	54.2	545	28.0	929	47.4		
Former-smoker	760	29.2	631	22.6	549	28.2	406	20.7		
Current-smoker	825	31.7	648	23.2	852	43.7	626	31.9		
Smoking status age 45–60									< 0.01	< 0.01
Never-smoker	867	38.5	1375	54.7	370	27.5	708	50.0		
Former-smoker	898	39.8	682	27.1	498	37.0	343	24.2		
Current-smoker	489	21.7	456	18.2	478	35.5	364	25.7		
Smoking status age 60									< 0.01	0.03
Never-smoker	504	38.4	892	62.1	151	28.7	365	60.1		
Former-smoker	622	47.4	378	26.3	233	44.2	146	24.1		
Current-smoker	187	14.2	167	11.6	143	27.1	96	15.8		
Atopy	931	35.6	875	31.2	697	40.8	465	31.2	< 0.01	1.00
Parental asthma	221	8.5	326	11.6	219	10.3	231	11.0	0.03	0.50
Early-life respiratory infection	155	5.9	244	8.7	155	7.3	186	8.9	0.07	0.88
Education									< 0.01	< 0.01
Low	95	3.6	263	9.4	17	6.0	39	10.1		
Intermediate	1553	59.4	2004	71.5	156	55.3	267	69.0		
High	966	37.0	536	19.1	109	38.7	81	20.9		
Urban	1262	48.3	1360	48.5	1238	58.1	1239	58.9	< 0.01	< 0.01

* Study population: asthma free at age 8, participated in S3 and had complete covariate information.
** Excluded: having asthma ≤ age 8 or having missing covariate information.
***p-value: comparing distribution of characteristics within men and women separately. Using *t*-test for variable sex and age, and Fisher exact test for variables smoking, parental asthma, early-life respiratory infection, education, and atopy.

overweight and obesity across countries are larger in men (ranging between 51% and 69%) than in women (37.0% and 50.7%) [17]. There is a more rapid increase of overweight and obesity in the early adult years in men as compared to women, the assumption being that active boys become inactive adults without change to their eating behaviour [18]. Post-menopausal women, however, have twice the levels of visceral fat compared to pre-menopausal women ([19] see Table 1) and are at a higher risk of cardiovascular disease.

Given the gendered life-course pattern of asthma [20,21], and the differential course of overweight across life between men and women [16–18], it would be beneficial to investigate the life-course of overweight/obesity and asthma incidence in men and women. Romieu et al. (2003) found that an increase in body silhouette between menarche and adulthood relates to the incidence of asthma in later life in women from the French E3N cohort study [22]. A high BMI was significantly associated with the risk of asthma incidence, as was a change in body silhouette over time [22]. However, no such study exists in a general population sample including men and women in order to investigate the role of overweight/obesity at different life stages for asthma incidence.

Making use of the on-going Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA), now covering 20-years of longitudinal observation of a general population sample aged 18–60 years in 1991, we investigated the association of body silhouettes and asthma incidence in men and women, taking into account the history of body silhouettes at different life stages as well as changes in body silhouettes over time.

2. Methods

2.1. Study design and population

The SAPALDIA study (see appendix) was initiated in 1991 in eight geographically diverse areas in Switzerland. A total of 9651 persons (51% female) aged 18–60 years participated in the baseline study (SAPALDIA 1 (S1)) after having been recruited through random population sampling. Re-assessments took place In 2002/2003 (SAPALDIA2 (S2), n = 8047) and in 2010/2011 (SAPALDIA 3 (S3), n = 6088). In S3 participants were asked to assess their body silhouettes retrospectively from age 8 to current age (see Fig. 1a and b). The protocol and participation rates have been described in further detail elsewhere [23,24]. This analysis includes 5417 subjects who were asthma free at age 8, participated in S3 and had complete covariate information (see figure S1 in online supplement). Ethical approval was obtained from the Swiss Academy of Medical Sciences, the regional ethics committees, and written informed consent was obtained from all participants.

2.2. Definition of asthma and asthma incidence

Doctor-diagnosed asthma was defined as a positive answer to the questions ‘Have you ever had asthma?’ and ‘Was this confirmed by a doctor?’ Asthma incidence was defined as reported asthma having been diagnosed by a doctor after age 8. We additionally distinguished different incidence periods defined by the ages for which body silhouettes were assessed, i.e. age 8, menarche, age 30, age 45, menopause, and age 60. Asthma incidence was defined at these six different time points so that new-onset of asthma occurring after the age of reported body silhouettes could be investigated. In our statistical analysis, when investigating reported body silhouette at age 8, our outcome was new-onset of asthma occurring after age 8. When investigating change in

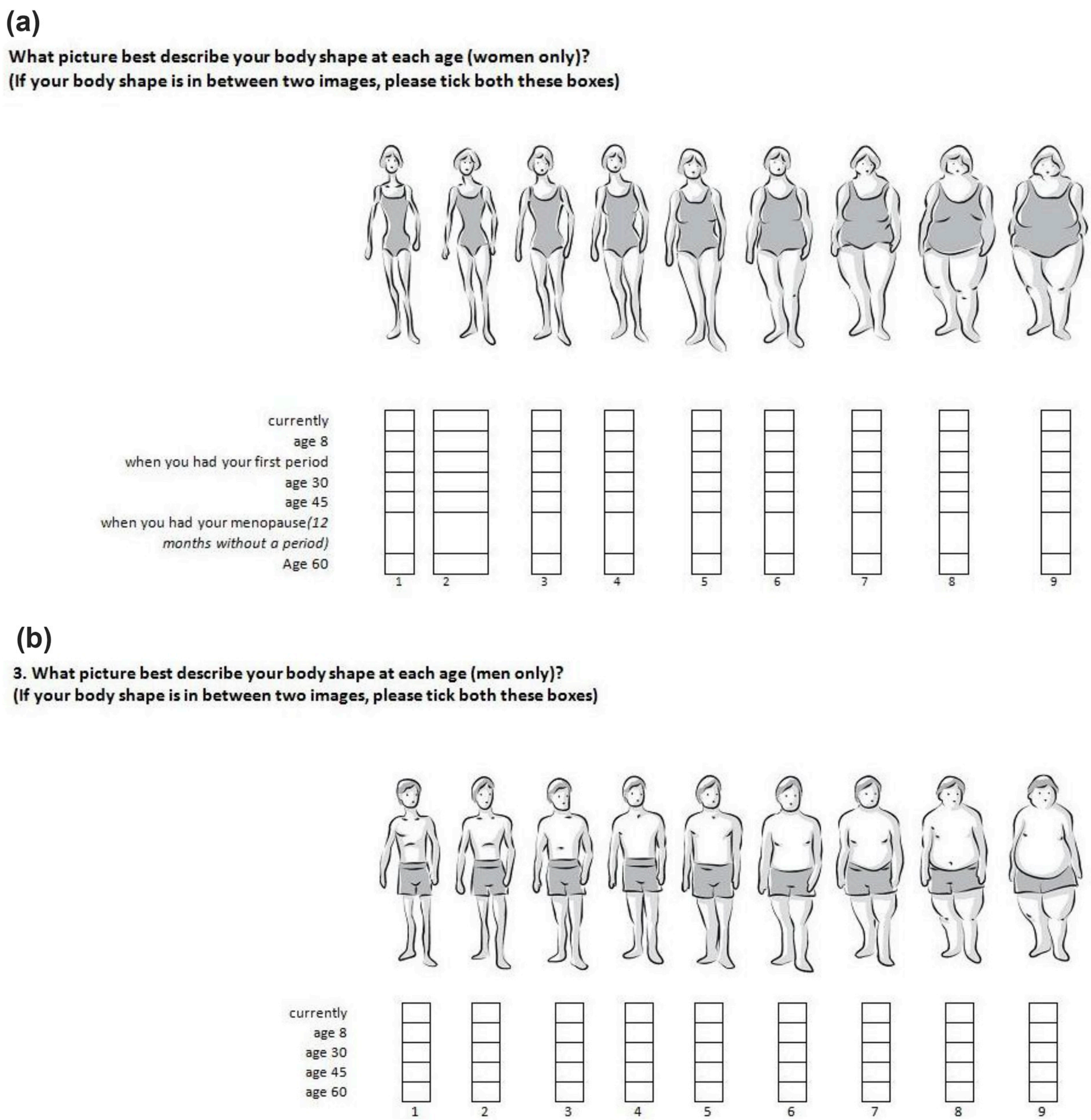

Fig. 1. a: Questionnaire body silhouettes women.
b: Questionnaire body silhouette men.

body silhouette from age period 8–30, then our outcome was asthma occurring after age 30 and so on.

2.3. Body silhouettes

The main predictor of interest was self-report of body silhouette number at specific ages, and additionally, the number of body silhouette changes in men and women over time. Participants were asked to report their body silhouette at age 8, menarche, age 30, age 45, menopause, and age 60 (see Fig. 1a and b). The body silhouette images are based on those created by Stunkard et al. (1983) and range from 1 (very lean) to 9 (very obese) [25]. If participants were unsure of their exact body silhouette, they could select two adjacent body silhouettes. For our analysis, we reported body silhouette as a continuous variable, using the average of the two selected body silhouettes when participants selected two silhouettes. Based on findings by Bulik et al. (2001) [26] we categorized participants who chose a body silhouette of 6 or more as being overweight and used this dichotomous variable in our sensitivity analysis.

Additionally, in order to assess the association between change in body silhouettes over time and asthma incidence, we created the following variables indicating the changes in silhouette score in men between ages 8–30, 30–45, 45–60, and in women between ages 8-menarche, menarche-30, 30–45, 45-menpause, menopause-60 in. For the descriptive table (Table 2), we grouped the number of changes into a score of the following four categories ≤0, 0, 1, 2 + following the example of Romeieu et al. (2003) [22]. For our statistical analysis, the number of changes in body silhouettes was used as a continuous variable.

2.4. Further covariates

Smoking status was categorized as never-smoker, former-smoker and current-smoker at S1, S2 and S3. Additionally, we created a

Table 2
Changes in body silhouette score at different age periods stratified by sex.

Men									Women								
Age	Number of changes[a]								Age	Number of changes[a]							
	≤0		0		1		2+			≤0		0		1		2+	
	n	%	n	%	n	%	n	%		n	%	n	%	n	%	n	%
	–	–	–	–	–	–	–	–	8 - menarche	116	5.2	1019	45.9	816	36.7	270	12.2
	–	–	–	–	–	–	–	–	Menarche – 30	294	13.4	746	33.9	862	39.2	296	13.5
8–30	135	6.1	311	14.1	728	33.1	1026	46.6	8–30	212	9.6	443	20.0	750	33.9	807	36.5
30–45	62	3.3	647	34.3	827	43.9	349	18.5	30–45	91	4.8	875	46.4	724	38.4	196	10.4
	–	–	–	–	–	–	–	–	45 – menopause	82	5.7	767	53.4	489	34.0	99	6.9
	–	–	–	–	–	–	–	–	Menopause - 60	69	7.5	473	51.1	316	34.1	68	7.3
45–60	63	6.0	277	26.5	455	43.6	249	23.9	45–60	63	6.3	316	31.8	409	41.2	205	20.6

[a] Number of changes in body silhouette from one age to the next.

smoking status variable indicating the smoking status of subjects corresponding to the time period of the reported body silhouettes, namely smoking status at ages 30–45, 45–60 and at age 60.

Baseline age was categorized into 3 groups roughly 15 years apart (< 30, 31–45, 46–60) for the descriptive table (Table 1). For the models, baseline age was used as a continuous variable (age in years). Atopy was defined as a positive response to the skin prick test or Phadiatop test (Phadia, Uppsala, Sweden) at baseline. A positive skin prick test was indicated by an adjusted mean wheal diameter of ≥3 mm to at least one of eight common allergens (grass, birch and Parietaria pollen, house dust mite, cat and dog epithelia and the moulds Alternaria and Cladosporium) [24,27]. The Phadiatop test, an *in vitro* allergy screening test, detects the presence of specific serum IgE against 11 common aero-allergens (*Cladosporium*, *Dermatophagoides* pteronyssinus., *Dermatophagoides farinae*, cat, dog, horse, birch, timothy grass [*Phleum pratense*], mugwort [*Artemisia*], olive, *Parietaria judaica* [spreading pellitory]. The percentage binding of the phadiatop was determined and results classified as positive or negative based on a cut-off of 0.35 kU/L [24,27,28]. Allergically sensitized subjects with doctor-diagnosed asthma were considered as having allergic asthma.

Education was categorized into primary education (low), secondary or middle school education (intermediate), or having a technical or university degree (high). For the descriptive tables and models, education at baseline was used. Parental asthma was defined as a positive answer to the question 'did one or both of your parents ever have asthma?' The eight study areas participating in the SAPALDIA project (Geneva, Basel, Lugano, Aarau, Wald, Payerne, Davos, and Montana) were chosen to represent the variety of environmental conditions found in Switzerland concerning geography, climate, degree of urbanization and air pollution [24]. Urbanity was defined as residing in the following study areas: Basel, Lugano, Aarau or Geneva. All of these covariates were selected based on literature findings for an association with asthma.

2.5. Statistical analysis

Asthma incidence and its association with selected body silhouettes and the number of changes in body silhouette over time was analysed using logistic regression adjusting for age (S1), atopy (S1), smoking (S1-S3), parental asthma (S1), education (S1) and study area (S1) as described above. Models were stratified by sex and run separately for the given body silhouette time points (including, for women, menarche and menopause) with asthma incidence occurring after that given time point. Analyses were additionally stratified by atopy.

We conducted several sensitivity analyses. Firstly, in order to address potential bias in loss to follow up, inverse probability weighting was considered. Secondly, we ran our model using our dichotomous overweight variable, comparing those who were overweight (body silhouette ≥6) to those who were not (body silhouette < 6). Thirdly, we ran our analysis additionally adjusting for physical activity since studies have shown physical activity may be a protective factor against new asthma development [29] and obesity [30]. Physical activity was categorized into a binary variable comparing those reporting 150 min/week of moderate physical activity or 60 min/week of vigorous physical activity (sufficiently active) those who were reporting less than this (insufficiently active). Finally, we ran our analysis additionally adjusting for occupational exposures defined as a positive answer to at least one of the items in the question 'At your working place, are you currently exposed to dust, gas/smoke/aerosols/fumes/vapours?'

All analyses were conducted using Stata V.12 (StataCorp LP, College Station, TX, USA).

3. Results

3.1. Study population

Our study population consisted of 5417 subjects who were asthma free at age 8, participated in S3 and had complete covariate information (see figure S1). The characteristics of our study population, and of those excluded from our analyses, are presented in Table 1. Those excluded from our study population were more likely to be men, older, and smokers. Excluded men were also more likely to be atopic, report parental asthma, low education and early respiratory infections. However, when conducting inverse probability weighting for non-participation, results remained largely unchanged (data not shown).

In our study population, men were more likely to be atopic than women, more likely to be former or current smokers at all ages, and more likely to have a higher educational level, whereas women tended to report more parental asthma than men.

3.2. Body silhouettes

The reported body silhouettes in men and women at different ages are shown in Fig. 2a and b. Overall, higher proportions of lower body silhouettes were reported at younger than older ages. Irrespective of age of body silhouette, we observed considerable gender differences in the distributions of body silhouette. As for the number of changes in body silhouettes over the time, these are presented by sex in Table 2. More men than women reported an increase of body silhouette of 1 or more at all ages than did women.

3.3. Asthma incidence

New-onset of asthma occurring after each body silhouette time point is presented in table S1. New-onset of asthma was persistently higher among women than among men, particularly up to age 30.

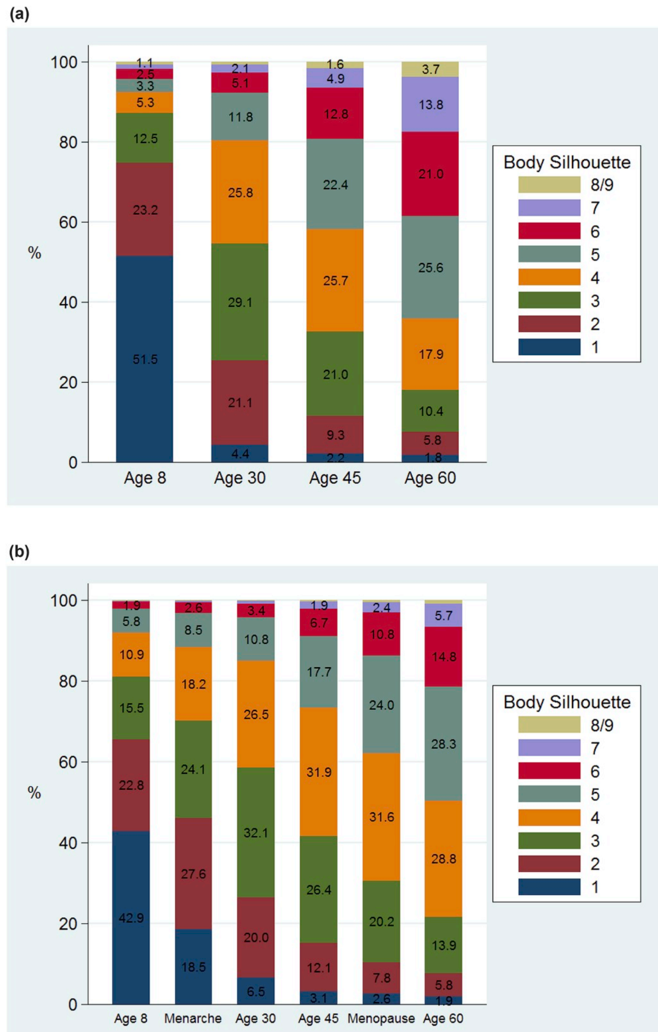

Fig. 2. a: Selected body silhouette* in men.
b: Selected Body Silhouette* in Women. * Body silhouette image ranging from 1 (very lean) to 9 (very obese).

3.4. Determinants of asthma incidence

When adjusting for relevant confounders, the risk of new-onset of asthma associated with a 1 unit increase in body silhouette for men and women is presented for men and women separately in Table 3. In men and women, the association became statistically significant at age 60 (men OR 1.93, 95% CI 1.13–3.30), (women OR 2.78, 95% CI 1.49–5.18) and additionally, in women after menopause (OR 1.35, 95% CI 1.03–1.78).

Women also had an increased risk of asthma incidence per 1 unit change in body silhouette between the age 45-menopause (OR 1.74, 95% CI 1.15–2.63) (Table 4). In women, the risk of new-onset of asthma with each unit of increasing body silhouette from menopause to age 60 was borderline significant (OR 1.97, 95% CI 1.00–3.90). We saw no association between change in body silhouette and asthma incidence in men.

3.5. Sensitivity analysis

When stratifying by atopic status, there was a tendency, albeit low statistical power, for a stronger body silhouette-asthma onset association after age 60 in non-atopic men (OR 2.34, 95% CI 1.09–5.05) and non-atopic women (OR 4.14, 95% CI 1.39–12.38) (Table 3). In women the OR for incident asthma after menarche was stronger in atopic women with each unit of increase in body silhouette at menarche (OR 1.19, 95% CI 1.02–1.38) (Table 3) whereas it was stronger in non-atopic women when looking at changes in body silhouette from menarche – age 30 (OR 1.25, 95% CI 1.01–1.55).

When running our analysis with our dichotomous body silhouette variable comparing those with a body silhouette of ≥6 to those with a body silhouette of < 6, the ORs increased in all age groups for both body silhouettes at a specific age (Table 3) and also increase in body silhouette changes over time (Table 4).

We ran our analysis additionally adjusting for physical activity (table S2 and S3 online supplement). The results did not significantly change. However, the OR for men with a higher body silhouette at age 60 became slightly larger (OR 1.83, 95% CI 1.09–3.07), as did the OR for incident asthma after age 60 in women (OR 2.69, 95% CI 1.44–5.02) (table S2 online supplement). When additionally adjusting for physical activity when looking at the association between change of body silhouettes and incident asthma, the association with 1 unit increase in body silhouette score in women between age 45 and menopause became significant (OR 1.67, 95% CI 1.09–2.58) (table S3 online supplement).

When additionally adjusting for occupational exposure, the association of body silhouette at different ages with asthma incidence did not change (table S4 online supplement). Results also did not change when looking at change in body silhouette number across different age periods and its association with incident asthma (table S5 online supplement).

4. Discussion

4.1. Main findings

A larger body silhouette later in life, but not at young ages, increases the risk of incident asthma in men, and even more so in women. In men, each unit increase in body silhouette at age 60 doubled the likelihood for asthma after age 60. The likelihood for incident asthma in women was 1.5 as likely for the body silhouette at menopause and 3 times as likely for age 60. Change in body silhouette number over time was only significantly associated with the likelihood of incident asthma in women between age 45- menopause, with an almost twofold increase in likelihood. Despite low numbers, atopic status seemed to be a modifying effect in women at menarche and menopause. The results point to an important effect of weight on asthma at older ages and particularly in postmenopausal women.

4.2. Comparison with other studies

Very few studies have evaluated the interaction of sex and overweight/obesity on newly acquired asthma, which is important given the sex effect observed in previous studies on obesity and asthma [14,31]. Brumpton et al. (2013) prospectively explored the association of BMI and waist circumference on asthma incidence in a Norwegian study population aged 19–65 years old [5]. They found that BMI-derived general overweight and obesity was a risk factor for incident asthma for males and females, and, in addition, that waist circumference derived abdominal obesity was a risk factor for incident asthma only in females. Egan et al. (2014) have also used measures in addition to BMI to assess the risk for asthma incidence but in a slightly younger Norwegian study population (12–30 years old) [6]. They found that baseline general overweight and abdominal obesity were significantly associated with an increased risk of newly acquired asthma, however when stratified by sex, this association remained significant only in men [6]. This is in contrast to previous findings which found BMI to be associated with incident asthma in adolescent and young females, but not in males [2,31]. This effect, however, has been inconsistent among children, possibly due to the differences in body fat accumulation and distribution around timing of puberty, particularly among females. Egan et al.

Table 3
Association of body silhouettes at different ages and reproductive time points with new-onset of asthma, stratified by sex, atopic status & overweight.

Models	OR Body Silhouette Men[a]		OR Body Silhouette Women[a]	
	N	OR (95% CI)	N	OR (95% CI)
Age 8[e]				
Overall model[b]	2208	1.01 (0.90–1.13)	2245	1.04 (0.94–1.14)
Dichotomous overweight model[c]	2208	1.31 (0.62–2.77)	2245	1.50 (0.65–3.49)
Stratified atopic model[d]	781	1.03 (0.90–1.18)	703	1.10 (0.96–1.26)
Stratified non-atopic model[d]	1427	0.95 (0.76–1.20)	1542	0.98 (0.85–1.13)
Menarche[f]				
Overall model[b]	–	–	2191	1.05 (0.94–1.16)
Dichotomous overweight model[c]	–	–	2191	1.25 (0.58–2.69)
Stratified atopic model[d]	–	–	684	**1.19** (1.02–1.38)
Stratified non-atopic model[d]	–	–	1507	0.93 (0.79–1.08)
Age 30[g]				
Overall model[b]	2136	1.13 (0.96–1.33)	2125	1.12 (0.98–1.29)
Dichotomous overweight model[c]	2136	1.70 (0.82–3.57)	2125	1.52 (0.71–3.27)
Stratified atopic model[d]	711	1.22 (0.99–1.52)	622	1.21 (0.97–1.51)
Stratified non-atopic model[d]	1425	0.98 (0.75–1.28)	1503	1.06 (0.88–1.27)
Age 45[h]				
Overall model[b]	1776	1.12 (0.90–1.39)	1752	1.12 (0.90–1.39)
Dichotomous overweight model[c]	613	**4.66** (1.06–20.45)	1752	2.20 (0.95–5.13)
Stratified atopic model[d]	541	1.11 (0.80–1.53)	440	1.17 (0.82–1.69)
Stratified non-atopic model[d]	1235	1.12 (0.81–1.53)	1265	1.09 (0.82–1.43)
Menopause[i]				
Overall model[b]	-	-	1136	**1.35** (1.03–1.78)
Dichotomous overweight model[c]	-	-	1136	2.22 (0.96–5.15)
Stratified atopic model[d]	-	-	275	1.48 (0.92–2.38)
Stratified non-atopic model[d]	-	-	700	1.23 (0.85–1.76)
Age 60[j]				
Overall model[b]	613	**1.93** (1.13–3.30)	877	**2.78** (1.49–5.18)
Dichotomous overweight model[c]	613	**4.66** (1.06–20.46)	877	**6.17** (1.68–22.69)
Stratified atopic model[ll]	130	1.40 (0.58–3.41)	124	3.27 (0.88–12.21)
Stratified non-atopic model[ll]	312	**2.34** (1.09–5.05)	274	**4.14** (1.39–12.38)

Data are presented as odds ratios (OR) representing the increased likelihood per 1 unit increase in body silhouette number at given age or reproductive time point, and 95% confidence intervals (CI). Bold indicates significance at p ≤ 0.05.

[a] Body silhouettes men and women: selected body silhouette [1–9] (see figure S1a and S1b).

[b] Overall model: logistic regression stratified by sex, adjusting for body silhouette as a continuous variable, age, atopy, urbanity, smoking at the corresponding interval of the body silhouette, parental asthma, education and study area.

[c] Dichotomous overweight model: overall model but using body silhouette as a dichotomous variable comparing those reporting a body silhouette ≥6 (overweight) to those reporting body silhouette < 6 (not overweight).

[d] Atopic/non-atopic model: overall model stratified by atopic status at baseline.

[e] Age 8: overall model using body silhouette reported at age 8 and its association with asthma occurring after 8 years age.

[f] Menarche: overall model investigating body silhouette reported at menarche and its association with asthma occurring after menarche.

[g] Age 30: overall model investigating body silhouette reported at age 30 and its association with asthma occurring after age 30.

[h] Age 45: overall model investigating body silhouette reported at age 45 and its association with asthma occurring after age 45.

[i] Menopause: overall model investigating body silhouette reported at menopause and its association with asthma occurring after menopause.

[j] Age 60: overall model investigating body silhouette reported at age 60 and its association with asthma occurring after age 60.

(2014) could not adjust for duration and intensity of physical activity, nor could they differentiate between atopic and non-atopic asthma [6]. However, Beckett et al. (2001) found that gain in BMI is associated with new asthma diagnosis in young female adults even when adjusting for changes in physical activity [9].

In order to assess the life history of body weight, the use of body silhouette images [25,32] offers a practical method when asking elderly subjects to recall the distant past and childhood build [33–37] or when measured and self-reported BMI are not available [38]. The use of body silhouettes has been validated [36,37,39] and used in studies assessing incident diabetes [40] and asthma incidence in women [22]. Romieu et al. (2003) found a higher BMI to be significantly associated with the

Table 4
Association of change in body silhouette across different age periods with new-onset of asthma, stratified by sex, atopic status & overweight.

Models	OR Change Body Silhouette Men[a]		OR Change Body Silhouette Women[e]	
	N	OR (95% CI)	N	OR (95% CI)
Age 8-menarche[d]				
Overall model[b]	–	–	2156	0.98 (0.83–1.14)
Stratified atopic model[c]	–	–	675	1.08 (0.87–1.35)
Stratified non-atopic model[c]	–	–	1481	0.87 (0.69–1.10)
Menarche- age 30[ll]				
Overall model[b]	–	–	2066	1.15 (0.98–1.34)
Stratified atopic model[c]	–	–	616	1.02 (0.81–1.30)
Stratified non-atopic model[c]	–	–	1450	**1.25** (1.01–1.55)
Age 8 - age 30[e]				
Overall model[b]	2081	1.02 (0.87–1.21)	–	–
Stratified atopic model[c]	697	1.06 (0.85–1.32)	–	–
Stratified non-atopic model[c]	1384	0.98 (0.76–1.26)	–	–
Age 30 - age 45[f]				
Overall model[b]	1757	1.18 (0.87–1.59)	1722	0.92 (0.66–1.30)
Stratified atopic model[c]	535	1.01 (0.64–1.57)	432	0.70 (0.37–1.34)
Stratified non-atopic model[c]	1222	1.34 (0.90–1.99)	1243	1.06 (0.69–1.61)
Age 45 - menopause[g]				
Overall model[b]	-	–	1086	**1.74** (1.15–2.63)
Stratified atopic model[c]	-	-	266	1.64 (0.82–3.29)
Stratified non-atopic model[c]	-	-	658	**1.83** (1.07–3.12)
Age 45 - age 60[h]				
Overall model[b]	498	1.38 (0.69–2.75)	–	-
Stratified atopic model[c]	101	0.48 (0.17–1.35)	-	-
Stratified non-atopic model[c]	218	2.07 (0.88–4.87)	-	-
Menopause – age 60[i]	-	-		
Overall model[b]	-	-	527	1.97 (1.00–3.90)
Stratified atopic model[c]	-	-	52	329.9 (0.33–334797.9)
Stratified non-atopic model[c]	-	-	192	1.37 (0.51–3.71)

Data are presented as odds ratios (OR) representing the increased likelihood per 1 unit change in silhouette number across the given age period, and 95% confidence intervals (CI).
[a] Change body silhouettes men and women: change in selected body silhouette score [1–9] (see figure S1a and S1b).
[b] Overall model: logistic regression stratified by sex, adjusting for change in body silhouette as a continuous variable, age, atopy, urbanity, smoking at the corresponding interval of the body silhouette, parental asthma, education and study area.
[c] Atopic/non-atopic model: overall model stratified by atopic status at baseline.
[d] Age 8-menarche: overall model using changes in body silhouette score between age 8 and menarche as a continuous variable and asthma incidence occurring after menarche.
[e] Age 8 - age 30: overall model using changes in body silhouette score between age 8 and age 30 as a continuous variable and asthma incidence occurring after age 30.
[f] Age 30 - age 45: overall model using number changes in body silhouette score between age 30 and age 45 as a continuous variable and asthma incidence occurring after age 45.
[g] Age 45 - menopause: overall model using changes in body silhouette score between age 45 and menopause as a continuous variable and asthma incidence occurring after menopause.
[h] Age 45 - age 60: overall model using changes in body silhouette score between age 45 and age 60 as a continuous variable and asthma incidence occurring after age 60.
[i] Menopause – age 60: overall model using changes in body silhouette score between menopause and age 60 as a continuous variable and asthma incidence occurring after age 60.

risk of asthma incidence, and also, that an increase in body silhouette between menarche and adulthood related to the incidence of asthma in later life [22]. Women who gained two or more silhouette points (approximately ≥ 10 kg) after menarche had a 66% increased risk of asthma when compared with women who did not change silhouette, after adjustment for relevant confounders (multivariate RR = 1.66, 95% CI 1.18, 2.23, test for trend: $p < 0.001$). Similarly, an 89% increased risk of asthma was observed for women who gained two or more silhouettes after the age of 20 years (multivariate RR = 1.89, 95% CI 1.37, 2.60, test for trend: $p < 0.001$). When they restricted the analysis to women who had a BMI of 20–24 ("normal") at menarche or around 20 years of age, results remained similar, suggesting that estimates were not driven by women with high BMIs who gained additional weight [22]. The observed association between an increase in body silhouette after menarche and adult onset of asthma in this study somewhat contradicts our findings. In our study, body silhouette at menopause and later was a significant predictor for asthma incidence in women. A change of body silhouette as of age 45 was only borderline significant in our study. But when stratifying by atopy, atopic women with a larger body silhouette at menarche were more likely than other women at the same age to newly develop asthma after menarche (OR 1.19, 95% CI 1.02–1.38). Perhaps this partly accounts for the highest asthma incidence seen in young atopic women in the study by Hansen et al. (2015) [20].

To the best of our knowledge, no study has addressed the association of life history of body silhouettes and asthma in men, even though the life course of overweight is known to differ between men and women [16], as is the fat distribution [41]. In our previous study, women were twice as likely as men to newly develop asthma [20]. This association was modified by age and atopy: the highest risk of incident asthma being in young atopic women. Gender differences were most pronounced in non-atopic subjects and decreased with increasing age [20]. In our current study, atopic women at menarche with a larger body silhouette number were at increased risk for incident asthma, which could potentially explain the high incidence of asthma in young atopic women which we observed previously. At age 60, both men and women were at higher risk of asthma incidence per unit increase in body silhouette, the risk being more pronounced in women. These findings are consistent with and support the life course pattern of incident asthma we observed previously ([20] see Fig. 2a and b). The associations of larger body silhouettes with asthma incidence in our current study may help explain gender differences in asthma incidence.

4.3. Strengths and limitations

The Swiss Cohort on Lung and Heart Disease in Adults (SAPALDIA) offers the unique opportunity to investigate the role of body silhouettes from a life course perspective for men and women. In addition, with the extensive SAPALDIA data, a number of further factors can be taken into account, such as allergic and non-allergic asthma, as well as duration and intensity of physical activity. And finally, strength lies in SAPALDIA's large data base representing the general population of Switzerland across urban, rural and mountainous areas with different environmental exposure characteristics and building on standardised measurements and a health questionnaire which was developed along with the European Community Respiratory Health Survey (ECHRS) [24,42].

In studies prospectively investigating the association between obesity and asthma, reported sex-related differences are inconsistent [43]. It has been argued that BMI cannot distinguish between fat mass and muscle mass [44]. Most notably, BMI has limitations in predicting abdominal fat deposition, which is associated with reduced pulmonary function, metabolic syndrome and cardiovascular complications [45–47]. BMI may inadequately reflect fat distribution and may under- or overestimate obesity as wide variations in body fat distribution can occur within the same BMI percentile group [48]. BMI does not differentiate between fat and lean body mass, and for a given BMI, females generally have a higher proportion of body fat than males [49]. This is where the use of body silhouettes is important and beneficial. Abdominal obesity may better reflect metabolic differences in subcutaneous and visceral fat deposits known to influence systemic inflammation.

A possible limitation of this study is the remote recall and accuracy of self-reported body silhouettes and asthma prior to baseline. Worse recall of body silhouettes at younger ages may have biased associations with asthma onset during earlier years towards null. However, Must et al. (1993) found good correlations between body silhouettes and measured BMI for females, even when using adult silhouettes to represent their body sizes at age 10 and 15 years [34]. Troy et al. (1995) reported correlation of 0.66 between BMI at age 18 years and silhouettes compared with a correlation of 0.84 for actual and recalled BMI at 18 years [50] whereas Munoz et al. (1996) obtained correlations of 0.75 for BMI and silhouettes compared with 0.89 for actual and recalled BMI [33]. As for Koprowski et al. (2001) they found that recall of body shape at menarche was considered to be a less precise measure than asking about weight and height, but use of body silhouettes may offer a more practical method for obtaining information for the past [35]. And finally, Bulik et al. (2002) found that figural stimuli are effective in classifying individuals as obese or thin [26].

As the SAPALDIA study is prospective in nature, recall bias is unlikely. However, since participants were 18–60 at baseline, information on body silhouettes and asthma onset prior to this age, were collected retrospectively. This may have biased results at age 8 towards the null. We cannot dismiss that remote recall of self-reported asthma may have introduced some recall bias and possibly led to insignificant odds ratios at younger ages. However, previous studies have shown reported year of asthma onset to be realistically accurate [51] and that variation in reporting age at diagnosis to be low across categories of participant characteristics such as gender [52]. Furthermore, in our previous study, using additional asthma incidence definitions with stricter restriction criteria on inconsistencies in the reporting of first attack of asthma did not change results [20]. Future studies may need to prospectively assess body silhouettes and asthma incidence from childhood in order to better assess the association at younger ages.

5. Conclusion

According to this longitudinal study, body silhouettes matter most for asthma onset at older ages in men and women. Additionally, increasing in body silhouette number from age 45 - menopause significantly increases the risk of incident asthma in women. Despite low numbers, atopic status seems to be a modifying effect in women at menarche and menopause. The increasing prevalence of obesity may therefore lead to more asthma at higher ages in adults. Pooling data or having future studies with an even larger study population with an older age range may help to better understand the role of body silhouettes in gender differences in asthma, especially the potential modification by atopy.

Author contributions

Study conception and design: Sofie Hansen, Elisabeth Zemp, Dirk Keidel, Christian Schindler, Nicole Probst-Hensch.

Acquisition of data: SAPALDIA team (see appendix).

Analysis and interpretation of data: Sofie Hansen, Elisabeth Zemp, Ayoung Jeong, Dirk Keidel, Christian Schindler, Nicole Probst-Hensch.

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Conflicts of interest

The authors declare no conflict of interest.

Declarations of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yrmex.2019.100001.

Appendix

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(e), D Miedinger (o), M Pons (p), F Roche (c), T Rothe (p), P Schmid-Grendelmeyer (a), D Stolz (p), A Schmidt-Trucksäss (pa), J Schwartz (e), A Turk (p), A von Eckardstein (cc), E Zemp Stutz (e).

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(a) allergology, (c) cardiology, (cc) clinical chemistry, (e) epidemiology, (exp) exposure, (g) genetic and molecular biology, (m) meteorology, (n) nutrition, (o) occupational health, (p) pneumology, (pa) physical activity, (pd) pediatrics, (s) statistics.

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