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The association of asthma with BMI and menarche in the 1958 British Birth Cohort

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Abstract

Background: Obesity and early menarche have been associated with asthma. In this report, we assess the association of asthma with BMI and with changes in BMI from childhood to early adulthood. In addition, we determine if, in girls, any observed association of asthma with menarche can be explained by BMI. *Methods*: In a large national birth cohort, the associations of asthma at age 7, 11, 16 and 33 years with BMI, and of, asthma at age 33 years with changes in BMI from age 7 to age 33 years was assessed using logistic and mixed effects models as appropriate. Associations of asthma with age of menarche in girls were similarly assessed with and without adjustment for BMI. *Results*: Information on asthma, BMI, onset of menarche and confounders at all assessments was available for 1968 girls and 2223 boys. Obesity was relatively uncommon (<2%) in childhood. Overweight (BMI 25+) girls had more asthma. Girls with early menarche were more likely to be overweight. At age 11 years, asthma was associated with early menarche (OR = 1.70, 95% CI 1.17–2.47, after adjustment for BMI OR = 1.60, 95% CI 1.10–2.34). Across all ages, asthma was significantly associated with BMI (OR = 1.50, 95% CI 1.18–1.90) but not with early menarche (OR = 1.24, 95% CI 0.95–1.63). *Conclusion*: Asthma is more common in overweight girls. Early menarche is more common in overweight girls but this does not explain its association with asthma at age 11 years. Early menarche is not a risk factor for asthma at age 33 years in this cohort.

Keywords

1958 British Birth Cohort, asthma, body mass index, menarche, wheezing

History

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Introduction

Several studies have reported cross-sectional associations of asthma with obesity and these observations are supported by longitudinal studies in which obesity was shown to precede the development of asthma [1].

Obesity in girls has been proposed as a possible explanation or effect modifier of gender differences in asthma [2–4]. Boys have more asthma in childhood than girls [5,6] but during adolescence girls have a higher prevalence of asthma and are less likely to have asthma that remits [7,8]. This ''gender switch'' may be explained by hormonal differences in boys and girls and is supported by observations that early menarche is associated with asthma [9,10]. However early menarche is more common in those who are obese [3].

In this report, we use longitudinal data from a large British birth cohort in which relevant information was collected during childhood and early adulthood to describe cross-sectional and longitudinal associations of asthma with BMI, and with changes in BMI from childhood to early adult life. The associations of asthma with menarche were assessed in girls and any observed associations were examined to see if they were explained or modified by BMI.

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Methods

Study design and study population

Data are from the UK National Child Development Study, a birth cohort of all children born in 1 week in 1958. Information was collected at age 7, 11, 16 and 33 years. From the 18 559 children recruited at birth, information on asthma and BMI was available for 13 363, 12 215, 9471 and 10 977 subjects at 7, 11, 16 and 33 years, respectively. Information on onset of menarche was available for 4524 girls and 1968 girls (2223 boys) had complete information on the presence of asthma, BMI and relevant confounders at all follow-ups (see Flowchart 1).

Definitions

Outcomes

Asthma was considered both as lifetime prevalence and as current asthma (symptoms in the 12 months prior to interview).

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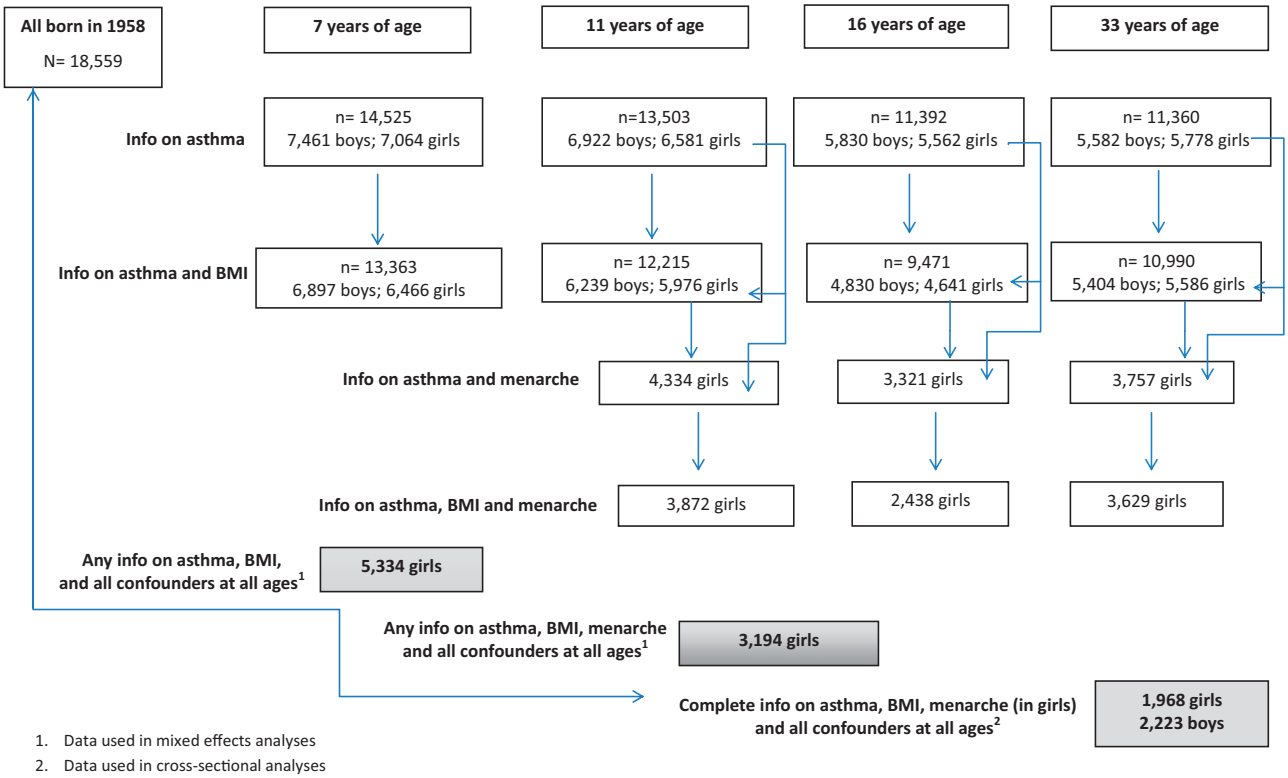

Flowchart 1. Cohort information available at each follow-up and data used in analyses.

Lifetime prevalence of asthma at age 7 years was based on parent reported ''asthma attacks ever'' or ''bronchitis with wheeze ever'' and at ages 11 and 16 years as parentally reported ''attacks of asthma or wheezy bronchitis ever''. At age 33 years, participants reported if they ''ever had asthma''.

Current asthma was said to exist if at ages 11 and 16 years parents reported ''attacks of asthma or wheezy bronchitis in the last year'' and at age 33 years as self-reported ''asthma ever'' plus ''wheezing or whistling in the chest in the last year''.

Main predictors

Age of onset of menarche was reported by the participant's mother at the age 16-year follow-up, and was considered in the following groups: (1) early (<12 years), (2) normal (12–13 years – reference group), (3) middle (14–15 years) and (4) late (at age 16 years or not started by age 16 years).

Height and weight were measured at each follow-up. BMI was calculated as kg/m^2 and considered as underweight (<18.5), reference (18.5 < 25), overweight and obese (25+). Childhood BMI for age 7, 11 and 16 years, was grouped according to Cole's international cut offs stratified by sex [11,12].

Statistical analysis

In the first instance, analyses were conducted only on participants who had complete information on the presence of asthma and BMI at all follow-ups, plus relevant available confounders (birth weight (<2 kg, 2–2.49 kg, 2.5–2.9 kg, 3–3.49 kg (reference), 3.5–4 kg, 4+ kg), father's social class (Register General Classification based on occupation), parental history of asthma (yes, no), birth order (1st, 2nd, 3rd, 4th, 5+), regular smoking at age 33 years (yes, no)). In females the sample was further restricted to those who had information on age of menarche.

The cross-sectional associations of reporting ever having asthma with BMI in childhood, adolescence and early adult life and in each sex were examined in univariate and multivariate logistic regression models, and differences in males and females examined with the inclusion of an interaction term. The association of current asthma at age 33 years with BMI in childhood and adolescence, and with changes in BMI from age 7 to age 33 years was examined in a similar way.

The cross-sectional association of ever asthma at age 7, 11, 16 years and of current asthma at age 33 years with menarche was assessed in multivariate logistic regression models (with and without adjustment for BMI). The effect modification of BMI on menarche at each age was assessed with an interaction term and it was further explored in analyses stratified by changes in BMI from age 7 to age 33 years.

In the second approach, we performed multilevel effects logistic regression [13] (xtlogit command in STATA) to estimate the association of current asthma with BMI and menarche in girls who had taken part in the survey at least once between the ages of 7 and 33 years (but not necessarily at all the follow-ups) adjusting for the same confounders as in the logistic regression model described above. The effect modification of the association of BMI with menarche in relation to asthma was tested by inclusion of an interaction term.

All analyses were performed using STATA 12 (Stata Corporation, College Station, TX).

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Results

Table 1 shows the prevalence of reported asthma and asthma like symptoms and the distribution of BMI at each age in those with complete information at all ages. Boys had more asthma/wheezy bronchitis than girls at age 7 (19.8% versus 17.3%, $p = 0.04$) at age 11 (14.0% versus 9.9%, $p < 0.0001$) at age 16 years (14.5% versus 9.2%, $p < 0.0001$). By age 33 years, the prevalence of ever asthma and asthma with current wheeze was higher in females than in males (6.3% versus 4.9%, $p = 0.04$). Girls were more overweight than boys during childhood (10.0% versus 7.5%, $p = 0.01$ at age 7 years, 10.5% versus 7.2%, $p < 0.0001$, at age 11 years and 11.2% versus 7.4%, $p < 0.0001$ at age 16 years, $p < 0.0001$), but not at age 33 years, when more men than women were classified as overweight or obese (49.5% versus 36.2%, $p < 0.0001$). The prevalence of obesity (BMI>30 kg/m^2) was about 1.0% in boys and 1.8% in girls at all ages during childhood (difference between boys and girls at ages 7, 11 and 16 years $p \leq 0.005$). At age 33 years, 9.3% men and 11.3% women were obese ($p < 0.0001$).

Table 2 shows the cross-sectional association of asthma with BMI at age 7, 11, 16 and 33 years in those with complete information. At each age, overweight/obese females were more likely to have asthma compared to normal weight females, but this only reached conventional levels of statistical significance at ages 11 and 16 years. This pattern was not seen in boys where the tendency was for underweight boys to have more asthma. The association of asthma with BMI was different in males and females at ages 11 and 16 years (p for interaction <0.05). At age 33 years (when obesity was more common), there was no association of asthma with being overweight or being obese in men or in women (in women OR 1.39 95% CI 0.81–2.38; in men OR 1.19 95% CI 0.61–2.32; p for interaction >0.05).

Table 3 shows the association of current asthma at age 33 years with BMI at age 7, 11 and 16 years, respectively, and with changes in BMI from age 7 to age 33 years. Overall males and females who were *underweight* in childhood tended to report more asthma at age 33 years, although this only reached conventional levels of statistical significance in males for BMI at age 11 years. The association of current asthma at age 33 years with being overweight in childhood was less clear, but both males and females who were overweight at age 7 years tended to have more asthma, although these results did not reach conventional significance. None of the associations were substantially altered by further adjustment for BMI at age 33 years.

Some children changed their obesity status as they aged but the patterns of association with asthma were difficult to interpret. For example, girls (but not boys) who changed from being obese in childhood to normal BMI at age 33 years, were more likely to report asthma than those who had remained normal weight throughout.

The majority of girls reached menarche between 12 and 15 years. Among 1968 girls with complete information at all surveys, 16.0% had menarche by age 12 years (early menarche), 59.6% at ages 12 or 13 years (normal menarche), 22.5% at ages 14 or 15 years (middle menarche) and 1.9% had menarche at or after age 16 years (late menarche). Figure 1 shows the relation of menarche with BMI at age 7, 11 and 16 years in these girls. Compared to girls with menarche at 13–15 years, girls with early menarche were more likely to be overweight at each age, and girls with late menarche were more likely to be underweight reflecting that BMI and age of onset of menarche are highly correlated (all p for difference in proportions <0.0001 for data shown in Figure 1a–c).

Table 4 shows the association of asthma with menarche in girls who had health outcome, BMI and confounder information at each follow-up. Girls with an early menarche had more asthma at all ages, the association reaching statistical significance only at age 11 years (OR = 1.69, 95% CI 1.17–2.46). These associations were little altered by further

Table 1. Prevalence of asthmatic phenotypes and BMI by gender, at 7, 11, 16 and 33 years of age in those with information at all ages.

	Age at follow-up							
	7 years		11 years		16 years		33 years	
Asthmatic outcomes	Boys $n = 2223$	Girls $n = 1968$	Boys $n = 2223$	Girls $n = 1968$	Boys $n = 2223$	Girls $n = 1968$	Men $n = 2223$	Women $n = 1968$
Lifetime prevalence (%(*N*)) as reported at follow-up								
Ever attacks of asthma or bronchitis with wheezing (age 7 years)	19.8 (440)	17.3 (340)	14.0 (312)	9.9 (195)	14.5 (322)	9.2 (181)	n/a	n/a
Ever attacks of asthma or wheezy bronchitis (age 11 and 16 years)								
Ever asthma (age 33 years)	n/a	n/a	n/a	n/a	n/a	n/a	8.3 (185)	9.5 (188)
Prevalence of current asthma (%(*N*)) as reported at follow-up								
Attack of asthma or wheezy bronchitis in the last year (age 11 and 16 years)	n/a	n/a	4.4 (99)	3.5 (68)	3.5 (77)	2.5 (49)	n/a	n/a
Ever asthma and wheezing in the chest in the last 12 months (age 33 years)	n/a	n/a	n/a	n/a	n/a	n/a	4.9 (108)	6.3 (125)
BMI (% (*N*))								
Underweight[a]	9.8 (218)	10.2 (200)	12.4 (276)	14.2 (279)	11.8 (263)	10.2 (200)	1.0 (23)	4.2 (83)
Normal	82.7 (1838)	79.9 (1572)	80.3 (1786)	75.4 (1483)	80.8 (1796)	78.6 (1547)	49.5 (1100)	59.5 (1172)
Overweight/obese[b]	7.5 (167)	10.0 (196)	7.2 (161)	10.5 (206)	7.4 (164)	11.2 (221)	49.5 (1100)	36.2 (713)

[a]<18.5 kg/m^2 for adults. For children as per Cole international sex-specific cut-offs defined to pass through BMI of 18.5 kg/m^2 at age 18 years.
[b]25+ kg/m^2 for adults. For children as per Cole international sex-specific cut-offs defined to pass through BMI of 25 kg/m^2 at age 18 years.

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Table 2. Prevalence and odds ratios of association of asthmatic phenotypes with respect to BMI at age 7, 11, 16 and 33 years, stratified by gender (cross-sectional) in those with complete information at all ages.

	Boys ($n = 2223$)		Girls ($n = 1968$)		All ($n = 4184$)
Asthmatic phenotypes	Prevalence %	Adjusted OR[a] (95% CI)	Prevalence %	Adjusted OR[a] (95% CI)	Sex–BMI interaction boys versus girls[b]
Ever asthma at age 7 years					
Underweight	20.2	1.02 (0.72–1.46)	15.5	0.84 (0.56–1.27)	$p = 0.3$
Normal	19.6	1	17.0	1	
Overweight and obese	21.6	1.16 (0.78–1.71)	20.9	1.30 (0.89–1.88)	
		p for trend*** $= 0.7$		p for trend $= 0.1$	
Ever asthma at age 11 years					
Underweight	18.1	1.43 (1.02–2.01)	8.6	0.88 (0.56–1.39)	$p = 0.003$
Normal	13.5	1	9.4	1	
Overweight and obese	12.4	0.92 (0.57–1.51)	15.0	1.65 (1.08–2.52)	
		p for trend $= 0.06$		p for trend $= 0.03$	
Ever asthma at age 16 years					
Underweight	16.7	1.23 (0.86–1.76)	8.0	0.89 (0.52–1.53)	$p = 0.02$
Normal BMI	14.4	1	8.7	1	
Overweight and obese	12.2	0.86 (0.53–1.41)	13.6	1.63 (1.06–2.50)	
		p for trend $= 0.2$		p for trend $= 0.04$	
Current asthma at age 33 years					
Underweight	13.0	3.35 (0.94–11.9)	3.6	0.61 (0.19–2.00)	$p = 0.2$
Normal	4.8	1	6.0	1	
Overweight and obese	4.7	0.97 (0.65–1.45)	7.3	1.16 (0.80–1.69)	
		p for trend $= 0.5$		p for trend $= 0.2$	
Overweight	4.5	0.92 (0.60–1.41)	6.7	1.06 (0.69–1.64)	
Obese	5.8	1.19 (0.61–2.32)	8.5	1.39 (0.81–2.38)	

[a]Adjusted for birth weight, father's social class, parental history of asthma and birth order (plus smoking status at age 33 years only).
[b]Interaction tested between gender and trend for BMI (<18.5, 18.5 < 25, 25+) adjusted as above.
***p values for test of linear trend adjusted as above.

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Table 3. The odds ratios of current asthma at age 33 years with respect to BMI at ages 7, 11 and 16 years, stratified by gender (in those with complete information at all ages).

	Current asthma at age 33 years			
	Boys ($n = 2223$)		Girls ($n = 1968$)	
	Prevalence %	Adjusted OR[a] (95% CI)	Prevalence %	Adjusted OR[a] (95% CI)
BMI at age 7 years				
Underweight	6.0	1.34 (0.72–2.47)	8.0	1.35 (0.77–2.38)
Normal	4.5	1	5.8	1
Overweight and obese	7.2	1.77 (0.94–3.35)	9.2	1.63 (0.95–2.79)
BMI at age 11 years				
Underweight	8.0	1.84 (1.11–3.05)	8.2	1.44 (0.89–2.33)
Normal	4.5	1	5.9	1
Overweight and obese	3.7	0.89 (0.38–2.06)	6.8	1.15 (0.64–2.07)
BMI at age 16 years				
Underweight	6.8	1.47 (0.86–2.52)	7.5	1.25 (0.71–2.22)
Normal BMI	4.7	1	6.3	1
Overweight and obese	3.7	0.82 (0.35–1.92)	5.9	0.91 (0.50–1.66)
Changes in BMI from age 7 to age 33 years				
Normal at 7 and at 33[b]	4.6	1	5.2	1
Normal at 7–Overweight and obese at 33[c]	4.2	0.9 (0.60–1.42)	6.9	1.28 (0.82–1.99)
Overweight and obese at 7–Normal at 33[d]	5.0	1.15 (0.26–5.00)	15.5	3.55 (1.62–7.80)
Overweight and obese at 7 and at 33[e]	7.9	1.99 (0.96–4.13)	6.8	1.25 (0.59–2.62)

[a]Adjusted for father's social class, birth-weight, parental history of asthma, birth order, smoking at age 33 years only, in girls with complete information at all ages.
[b]Thin/normal (BMI < 18.5 kg/m^2) at age 7 years who remained thin/normal at age 33 years.
[c]Thin/normal (BMI < 18.5 kg/m^2) at age 7 years who become overweight/obese (BMI 25+ kg/m^2) at age 33 years.
[d]Overweight/obese (BMI 25+ kg/m^2) at age 7 years who become thin/normal (BMI<18.5 kg/m^2) at age 33 years.
[e]Overweight/obese (BMI 25+ kg/m^2) at age 7 years who remained overweight/obese at age 33 years (too few participants in this category for analysis.

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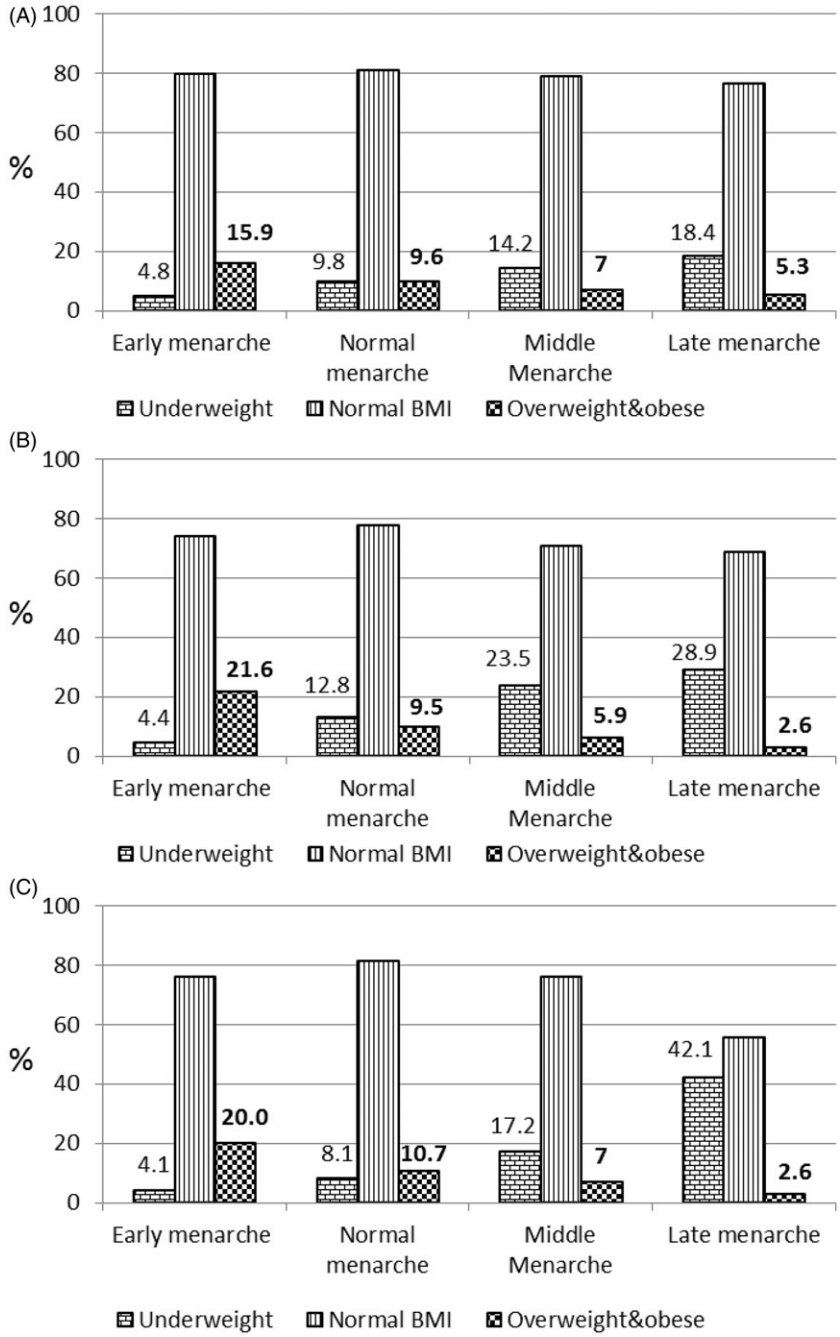

Figure 1. Distribution of BMI at each age by onset of menarche. (a) Onset of menarche and BMI at age 7 years. (b) Onset of menarche and BMI at age 11 years. (c) Onset of menarche and BMI at age 16 years.

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adjustment for BMI and were similar in girls with low and high BMI ($p > 0.05$ in all tests for BMI–menarche interactions).

To explore this further, we looked at the associations of current asthma at age 33 years with menarche in those girls who had maintained normal BMI from age 7 to age 33 years, and in those girls who had changed their BMI over the same period (Table 5). Asthma was more common in those with early menarche in all change of BMI groups except those who were obese though (all $p > 0.05$).

Finally, the mixed effects logistic regression (Table 6) confirmed that being overweight or obese was associated with more asthma in girls (OR = 1.51, 95% CI 1.19–1.91) independent of early menarche (OR after adjustment for menarche 1.50, 95% CI 1.18–1.90). In this analysis, non-significant positive associations of asthma with early menarche were observed (OR = 1.28, 95% CI 0.64–2.57). No significant BMI–menarche interaction was found (p for interaction = 0.8).

Discussion

In this large birth cohort, asthma was more common in girls who were overweight compared to those who were not, but this pattern was not seen so clearly in boys. There was no strong evidence in either sex that being overweight during childhood was independently associated with asthma at age 33 years. From the age of 7 years to early adult life, girls with early menarche have more asthma than those who have menarche at ages 12–15 years but in this population this difference only reached conventional levels of significance at age 11 years, and, at age 11 years was not fully explained by

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Table 4. Odds ratios of asthma at age 11, 16 and 33 years with respect to age at onset of menarche.

Onset of menarche	Ever asthma at age 7 years		Ever asthma at age 11 years		Ever asthma at age 16 years		Current asthma at age 33 years	
	Adjusted OR[a] (95% CI)	BMI-adjusted OR[b] (95% CI)	Adjusted OR[a] (95% CI)	BMI-adjusted OR[b] (95% CI)	Adjusted OR[a] (95% CI)	BMI-adjusted OR[b] (95% CI)	Adjusted OR[a] (95% CI)	BMI-adjusted OR[b] (95% CI)
Early (<12 years)	1.14 (0.83–1.58)	1.12 (0.81–1.55)	1.70 (1.17–2.47)	1.60 (1.10–2.34)	1.29 (0.86–1.92)	1.22 (0.82–1.83)	1.36 (0.84–2.19)	1.32 (0.81–2.14)
Baseline (12–13 years)	1	1	1	1	1	1	1	1
Middle (14–15 years)	0.98 (0.73–1.31)	0.99 (0.74–1.33)	0.94 (0.64–1.39)	0.97 (0.66–1.43)	0.71 (0.47–1.09)	0.74 (0.48–1.13)	1.00 (0.63–1.58)	1.02 (0.64–1.61)
Late (16+)	1.16 (0.50–2.68)	1.19 (0.51–2.76)	0.89 (0.27–2.94)	0.93 (0.28–3.10)	1.80 (0.73–4.44)	1.95 (0.78–4.92)	0.95 (0.22–4.05)	1.00 (0.23–4.29)

[a]Adjusted for father's social class, birth-weight, parental history of asthma, birth order, smoking at age 33 years only, in girls with complete information at all ages.
[b]Adjusted for all of the above and BMI.

associations of asthma with BMI (or by BMI modifying the effect of early menarche on asthma).

Our report shows the sex differences in asthma prevalence (more asthma in boys than girls in childhood and the reverse in early adult life). This is in line with reports from many studies [14,15] and from other analyses on this cohort [16]. As in other studies, the association of asthma with obesity is more apparent in females than in males. Unlike other studies, we have been able to examine relationships of obesity in childhood with asthma in early adult life. We were unable to show clear and significant associations in either sex. However, the strength of the associations of obesity at age 7 years with asthma at age 33 years (1.77 in boys and 1.63 in girls) lends some support to the hypothesis that being overweight in childhood may be associated with asthma in adult life. Furthermore, our data provide some evidence that this risk may remain even if overweight girls have normal BMI as adults.

Prevalence of childhood obesity in this cohort was low compared to current levels in UK [17] and BMI in childhood is a poor predictor of BMI by the age of 33 years in this cohort [18] and other national cohorts [19].

Our more novel finding is that there is a possible independent association of early menarche with asthma at age 11 years, which may still be present in young adults (although all associations at these older ages were below conventional levels of significance). None of the associations were modified by adult BMI or by change in BMI from childhood to adulthood. There have been three previous longitudinal studies in which early menarche was found to be associated with incident [9] and persistent asthma in adolescent females [20] and with incident asthma in women up to the age of 28 years [21]. These studies included fewer than 1200 girls. In the ECRHS, which included about 3500 women aged 27–57 years [10], prevalent asthma (BHR, symptoms and higher asthma score) was more common in those who reported earlier age of menarche. Two further studies suggest there is an interaction of menarche with BMI for current symptoms [22] and disease severity [2] both showing that BMI is more strongly associated with adverse health effects in those who have early menarche. Our report and these other reports (except that by Mascali et al.) defined early menarche as onset at or before 12 years of age. However, none of these studies described the longitudinal association of early menarche on asthma at different ages from adolescence to early adulthood.

The mechanisms explaining the association of asthma with BMI are not understood. Fatter people have higher levels of leptin which is thought to have pro-allergic, pro-inflammatory effects. There are isolated reports that link leptin level with the presence of asthma but it is difficult to identify the separate associations of fatness and leptin with disease, because the two are so highly correlated [23]. The underlying biological reasons for the relationship of early menarche with asthma are unknown and the determinants of early menarche itself are complex. They include genetic, environmental, hormonal and social factors. Higher BMI, shorter height, high level of serum estradiol, insulin, estrogens, androgens and FSH are associated with early menarche [24–27]. A few studies have suggested that this association might be due to

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Table 5. Odds ratios of current asthma at age 33 years with respect to age at menarche stratified by change in BMI from 7 to 33 years of age.

	Adjusted ORs[a]			
Onset of menarche	N7–N33[b] ($N = 2730$)	N7–O33[c] ($N = 1297$)	O7–N33[d] ($N = 182$)	O7–O33[e] ($N = 315$)
Early (<12 years)	1.31 (0.69–2.52)	1.54 (0.79–3.00)	1.25 (0.20–7.98)	0.34 (0.05–2.20)
Baseline (12–13 years)	1	1	1	1
Middle (14–15 years)	1.26 (0.77–2.05)	1.54 (0.76–3.14)	1.43 (0.19–10.50)	0.46 (0.05–4.67)
Late (16+)	0.97 (0.22–4.15)	2.80 (0.31–25.57)	~	~

[a]Adjusted for father's social class, birth-weight, parental history of asthma, birth order, smoking at age 33 years only, in girls with complete information at all ages.
[b]Thin/normal (BMI < 18.5 kg/m^2) at age 7 years who remained thin/normal at age 33 years.
[c]Thin/normal (BMI < 18.5 kg/m^2) at age 7 years who become overweight/obese (BMI 25+ kg/m^2) at age 33 years.
[d]Overweight/obese (BMI 25 + kg/m^2) at age 7 years who become thin/normal (BMI < 18.5 kg/m^2) at age 33 years.
[e]Overweight/obese (BMI 25 + kg/m^2) at age 7 years who remained overweight/obese at age 33 years.
~Too few participants in this category for analysis.

Table 6. Odds ratios of current asthma at each age with respect to BMI and menarche in females with any information from 7 to 33 years of age (results from mixed effects analyses).

	Average effects on asthma across ages 7–33 years Adjusted OR[a]
Overweight BMI versus normal (all girls, $n = 5334$)	1.56 (1.30–1.88)
Overweight BMI versus normal (girls with age at menarche $n = 3194$)	1.51 (1.19–1.91)
+adjustment for menarche[b]	1.50 (1.18–1.90)
Early menarche versus normal menarche	1.27 (0.97–1.65)
+adjustment for BMI[c]	1.24 (0.95–1.63)
Late menarche versus normal menarche	1.23 (0.62–2.42)
+adjustment for BMI[c]	1.28 (0.64–2.57)

[a]Adjusted for father's social class, birth-weight, parental history of asthma, birth order, smoking at age 33 years only, in girls with any information at any ages.
[b]Adjusted for all of the above and menarche.
[c]Adjusted for all of the above and BMI.

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complex inflammatory processes in the lung triggered by increase in estrogen levels or insulin resistance [10,28] but a clear pathway is still to be established.

Our first analyses focussed on children with complete information on asthma and all relevant confounders at all ages, so that we could see associations during the entire life course in the same group of participants at each age. However, this approach only uses some of the wealth of data available in this cohort. Therefore, we also used mixed effects modelling which allows exploration of these associations within the entire sample while accounting for variation within and between subjects. This latter approach clearly shows that BMI, is independently associated with asthma, and that there is only a weak positive non-significant association with early menarche. The association of asthma with late menarche was similar in magnitude to the association with early menarche (although both failed to reach statistical significance). This may reflect confounding by factors that affect puberty (co-morbidities, poor nutrition, paediatric chronic treatment with steroids) but as the group of children with late menarche is relatively small (n = 100) these data should be interpreted cautiously.

Our analysis is based on repeated measurements of asthma and BMI made on a population based birth cohort. This cohort is one of the few large cohorts that have reached adulthood. Unfortunately, the questions used for ascertainment of disease in childhood differ slightly at each survey reflecting labelling of disease at the time, in particular the use of the word ''bronchitis''. However, the symptoms are likely to reflect the presence of asthma and asthma-like illness. Age of onset of menarche was reported by the participant's mother when the participant was aged 16 years which may have produced some random error. We do not have any information to verify this further. Measures of height and weight were made at clinical examination and were not self-reported. Response to the survey was high up to the age of 16 years, but fell during the period when the cohort entered the work force. An overview of non-response in the cohort showed the cohort tends to under-represent those whose fathers had low social class but in many aspects remains largely representative of those initially recruited [29]. Interviews with cohort members who have missed some follow-ups but taken part in others suggests that failure to respond to some follow-ups is related life event such as marriage, divorce house moves rather than health related events [30]. Complex response biases have to be present in order to identify false associations within a cohort, even in the presence of an overall low response rate.

In conclusion, we have shown that asthma is more common in girls who are overweight. Early menarche is more common in girls who are overweight and in this cohort early menarche is associated with asthma at age 11 years, independently of BMI. In older age groups, early menarche was not significantly associated with asthma. Ongoing birth cohorts, which are likely to have a higher prevalence of obesity, earlier menarche, and a more consistent definition of asthma throughout the period of follow-up should assess these relationships as their participants approach puberty, using more precise measures of obesity and hormonal status.

Authors' contributions

D.J. conceived the study, acquired the data and revised the final manuscript for submission. L.G. carried out the statistical analyses and drafted the manuscript. B.K. and R.N. provided advice and supervision for the statistical analyses. M.M. suggested additional analyses and revised the manuscript. All authors read and approved the final manuscript.

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Declaration of interest

None of the authors have competing interests.

References

1. Dixon AE, Holguin F, Sood A, et al. An official American Thoracic Society Workshop report: obesity and asthma. Proc Am Thorac Soc 2010;7:325–35.
2. Varraso R, Siroux V, Maccario J, et al. Asthma severity is associated with body mass index and early menarche in women. Am J Respir Crit Care Med 2005;171:334–9.
3. Dunger DB, Ahmed ML, Ong KK. Early and late weight gain and the timing of puberty. Mol Cell Endocrinol 2006;254–255:140–5.
4. Boyne MS, Thame M, Osmond C, et al. Growth, body composition, and the onset of puberty: longitudinal observations in Afro-Caribbean children. J Clin Endocrinol Metab 2010;95:3194–200.
5. Luyt DK, Burton PR, Simpson H. Epidemiological study of wheeze, doctor diagnosed asthma, and cough in preschool children in Leicestershire. BMJ 1993;306:1386–90.
6. Anderson HR, Bland JM, Patel S, Peckham C. The natural history of asthma in childhood. J Epidemiol Community Health 1986;40: 121–9.
7. Nicolai T, Pereszlenyiova-Bliznakova L, Illi S, et al. Longitudinal follow-up of the changing gender ratio in asthma from childhood to adulthood: role of delayed manifestation in girls. Pediatr Allergy Immunol 2003;14:280–3.
8. De Marco R, Locatelli F, Cerveri I, et al. Incidence and remission of asthma: a retrospective study on the natural history of asthma in Italy. J Allergy Clin Immunol 2002;110: 228–35.
9. Al-Sahab B, Hamadeh MJ, Ardern CI, Tamim H. Early menarche predicts incidence of asthma in early adulthood. Am J Epidemiol 2011;173:64–70.
10. Macsali F, Real FG, Plana E, et al. Early age of menarche, lung function and adult asthma. Am J Respir Crit Care Med 2011;183: 8–14.
11. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. BMJ 2007;335:194.
12. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000;320:1240–3.
13. Diggle PJ, Heagerty P, Liang KY, Zeger SL. Analysis of longitudinal data. Oxford: Oxford Univesity Press; 2002.
14. Nicolai T, Illi S, Tenborg J, et al. Puberty and prognosis of asthma and bronchial hyper-reactivity. Pediatr Allergy Immunol 2001;12: 142–8.
15. Becklake MR, Kauffmann F. Gender differences in airway behaviour over the human life span. Thorax 1999;54:1119–38.
16. Anderson HR, Pottier AC, Strachan DP. Asthma from birth to age 23: incidence and relation to prior and concurrent atopic disease. Thorax 1992;47:537–42.
17. Lobstein TJ, James WP, Cole TJ. Increasing levels of excess weight among children in England. Int J Obes Relat Metab Disord 2003; 27:1136–8.
18. Power C, Lake JK, Cole TJ. Body mass index and height from childhood to adulthood in the 1958 British born cohort. Am J Clin Nutr 1997;66:1094–101.
19. Shaheen SO, Sterne JA, Montgomery SM, Azima H. Birth weight, body mass index and asthma in young adults. Thorax 1999;54: 396–402.
20. Guerra S, Wright AL, Morgan WJ, et al. Persistence of asthma symptoms during adolescence: role of obesity and age at the onset of puberty. Am J Respir Crit Care Med 2004;170: 78–85.
21. Salam MT, Wenten M, Gilliland FD. Endogenous and exogenous sex steroid hormones and asthma and wheeze in young women. J Allergy Clin Immunol 2006; 117:1001–7.
22. Herrera-Trujillo M, Barraza-Villarreal A, Lazcano-Ponce E, et al. Current wheezing, puberty, and obesity among mexican adolescent females and young women. J Asthma 2005;42:705–9.
23. Sood A. Obesity, adipokines, and lung disease. J Appl Physiol 2010;108:744–53.
24. Grumbach MM. The neuroendocrinology of human puberty revisited. Horm Res 2002;57:2–14.
25. Karapanou O, Papadimitriou A. Determinants of menarche. Reprod Biol Endocrinol 2010;8:115.
26. Apter D, Reinila M, Vihko R. Some endocrine characteristics of early menarche, a risk factor for breast cancer, are preserved into adulthood. Int J Cancer 1989;44:783–7.
27. Vihko R, Apter D. Endocrine characteristics of adolescent menstrual cycles: impact of early menarche. J Steroid Biochem 1984;20:231–6.
28. Haggerty CL, Ness RB, Kelsey S, Waterer GW. The impact of estrogen and progesterone on asthma. Ann Allergy Asthma Immunol 2003;90:284–91.
29. Atherton K, Fuller E, Shepherd P, et al. Loss and representativeness in a biomedical survey at age 45 years: 1958 British birth cohort. J Epidemiol Community Health 2008;62:216–23.
30. Parsons S, Understanding participation: being part of the 1958 National Child Development Study from birth to age 50. *Working papers, London Centre for Longitudinal Studies Institute of Education*; 2010.

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