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Increasing body mass index from age 5 to 14 years predicts asthma among adolescents: evidence from a birth cohort study

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Abstract

Background: Obesity and asthma are common disorders, and the prevalence of both has increased in recent decades. It has been suggested that increases in the prevalence of obesity might in part explain the increase in asthma prevalence. This study aims to examine the prospective association between change in body mass index (BMI) z-score between ages 5 and 14 years and asthma symptoms at 14 years.
Methods: Data was taken from the Mater University Study of Pregnancy and its outcomes (MUSP), a birth cohort of 7223 mothers and children started in Brisbane (Australia) in 1981. BMI was measured at age 5 and 14 years. Asthma was assessed from maternal reports of symptoms at age 5 and 14 years. In this study analyses were conducted on 2911 participants who had information on BMI and asthma at both ages.
Results: BMI z-score at age 14 and the change in BMI z-score from age 5 to 14–years were positively associated with asthma symptoms at age 14 years, whereas BMI z-score at age 5 was not associated with asthma at age 14. Adjustment for a range of early-life exposures did not substantially alter these findings. The association between change in BMI z-score with asthma symptoms at 14 years appeared stronger for male subjects compared with female subjects but there was no statistical evidence for a sex difference (*P*=0.36).
Conclusions: Increase in BMI z-score between age 5 and 14 years is associated with increased risk of asthma symptoms in adolescence.
Keywords: asthma, body mass index, change in body mass index, early-life factors

Introduction

Asthma in childhood and adolescence is associated with considerable morbidity and reduced quality of life.[1] The prevalence of childhood asthma in Australia is one of the highest in the world[2] and has increased by twofolds over recent decades.[1, 3] A large number of studies have shown an association between obesity and asthma and there has been considerable debate about whether obesity leads to increased risk of asthma or vice versa. Although the association may be bi-directional, with, for example, reduced physical activity related to asthma symptoms leading to increased obesity, a number of prospective studies now support the hypothesis that obesity leads to an increased risk of asthma among both children and adults.[4, 5, 6, 7, 8, 9] Some of these studies suggest a stronger association in female subjects compared with male subjects,[10, 11, 12] but this sex difference is not consistently found and such subgroup analyses should always be treated with caution.

Very few studies have examined the association between change in body mass index (BMI) over time in childhood and the risk of developing asthma. One study found that for boys and girls, extremes of annual BMI growth rates increased the risk of asthma. In a second study female subjects, but not male subjects, who became overweight between the age of 6 and 11 years were seven times more likely to develop asthma at age 11 and 13 years than those whose weight gain remained normal during these ages.[6] The possibility that an increase in BMI, rather than, or in addition to, absolute BMI at one time point, has strong effects on future asthma risk is important in terms of developing preventive strategies. However, as the association of weight change in childhood has only been assessed in a small number of studies, further examinations of this association is warranted. Further, most of the previous studies of the association between obesity and asthma in childhood have been unable to take account of early life factors, such as maternal smoking during pregnancy, birth weight, breast feeding and family socioeconomic position, which are associated with both BMI and asthma, and might therefore explain any association between these two.

This study aims to examine the prospective association between change in BMI z-score between age 5 and 14 and asthma at age 14 years, whereas taking account of a number of early life factors that might explain any association.

Methods

Data source

The Mater University of Queensland Study of Pregnancy (MUSP) is a longitudinal study of women and their offspring born during 1981–1984 at one of the two major obstetric hospitals in Brisbane, Australia. In total, 7223 mothers agreed to participate, delivered a live singleton baby (52% male subjects) who was not adopted before leaving hospital and completed both initial phases of data collection; these mothers and their offspring form the MUSP prospective cohort, which has been described in detail elsewhere.[13]

Mothers and children have been followed up prospectively with maternal questionnaires being administered at first antenatal clinic visit, 3–5 days post-delivery, 6 months after birth, 5 and 14 years after birth. In addition, at age 5 and 14 detailed physical, cognitive and developmental examinations of the children were undertaken and at 14 years the children completed health, welfare and lifestyles questionnaires. At 14 years, mothers and children were invited to the Mater Hospital where they completed a self-administered questionnaire. MUSP research staff also undertook a physical assessment of the participants including the measurements of height and weight. Where participants were unable to attend the Mater Hospital for these assessments, they were offered a home visit where the same measurements were taken. Finally, in a small number of instances, respondents who lived too far away from the hospital were able to answer a postal questionnaire or responded to a researcher-administered survey via the telephone. Of the original 7223 participants, (BMI, weight in kg divided by height in meter square) and asthma symptoms were available on 3861 children at age 5, 3759 at 14 years and 2911 at both the 5 and 14 years follow-up assessments.

Measurements of outcome and exposure

Asthma symptoms were assessed at 5 and 14 years through maternal self-reports. At 5 years, mothers were asked: 'Has your child had any of these conditions or symptoms continuing longer than 3 months? ('Asthma attack', 'Wheezy bronchitis'). Mothers could select from the following prompts: 'No, not longer than 3 months' 'Yes, but it limited activities very little' or 'Yes, it limited activities a lot'. Because in clinical practice diagnostic terms such as wheezy bronchitis and asthma tended to be used interchangeably until the late 1980s (covering the early period of our study),[14] it is possible that mothers may have indicated that a child who would by today's standards be diagnosed with asthma had bronchitis. For this reason, in our analyses, symptoms of asthma (272 cases) and bronchitis (76 cases) were summed, so all those whose mothers indicated that they had either of these conditions (only 34 cases overlapped) were considered a case at age 5.

The mothers were asked two questions concerning asthma symptoms at the 14-year follow-up: Has your child had any of the following? (one option being 'Asthma') – response options Yes or No. Which best describes your child in the last 6 months? (one option being 'Asthma') – response option Yes or No. We used a positive response to both of these questions as our main outcome .[15] The mothers were also asked whether the child was using any medication for asthma with response options Never, Sometimes and Often. Of the 3751 mothers who had responded to the two questions described above that we used to define our asthma cases at age 14, 70% also answered this question (the first 1000 or so participants did not get these supplementary questions at 14 years follow-up) about medication and of those who responded 23% indicated that their child sometimes or often used medication for asthma. In addition to our main analyses in which asthma at age 14 was defined as answering yes to both of the questions described above (has your child ever had asthma and what best describes your child in the last 6 months) we conducted three sensitivity analyses: (i) where a positive response to the first question only was used to define a case; (ii) where a positive response to the second question only was used to define a case; (iii) where a case was defined as a child whose mother indicated that they sometimes or often used medication for asthma, with all other children defined as healthy. The results for these three sensitivity analyses did not differ importantly from the main analyses presented here.

In this study, the main exposure was the child's BMI at the 5 and 14 year follow-up examinations. In both assessments, the average of two measures of the child's weight, lightly clothed with a scale accurate to 0.2 kg, was used. A portable stadiometer was used to measure the height. z-score of BMI at age 5 and 14 and the change in BMI z-score between two time points 5 and 14 year follow-ups were used as continuous exposures. The change in BMI z-score was estimated subtracting 5-year score from 14 years.

Confounder measurements

The potential confounders considered in this study were birth weight (in kg), maternal age at birth (grouped as 13–19; 20–34 and 35 or more), mothers level of education (did not complete secondary school, completed secondary school, completed further/higher education), gross family income around pregnancy (consistently poor; mid-income and high-income), maternal smoking during pregnancy (non-smoker, 1–20 cigarettes per day and 20 or more cigarettes per day) and duration of breastfeeding (never, less than 4 months and more than 4 months).

Other important factors such as physical activity, diet and puberty are known to be important determinants of childhood BMI and asthma[16, 17, 18, 19] We are not in a position to assess the associations of these exposures to the change in BMI because information on them was not available in this study before the age of 14 years. However, in a sensitivity analyses, we further adjusted the multivariable regression models for maternal response to food frequency questions at 14 years follow-up, relating to the child's diet, about fast food, soft drinks and red meat (all with response options of rarely or never, at least two or three times a week, most days), her report of the amount of time the child spent watching television (<1 h per day, 1 to <3 h per day, 3 to <5 h per day and 5 or more hour per day) and time spent on sports or exercise (4–7 days per week; 0–3 days per week) per week and pubertal status

Pubertal status was assessed using Tanner's classification.[20] The participants were shown pictures of breasts and genitalia representative of Tanner's classification and asked to report which was the best picture of their current status of development. The results further controlling for these factors did not differ substantially from those presented here; instead, the inclusion of these factors in the multivariate model increases the missing cases.

Statistical analyses

As comparisons of absolute values of BMI between age 5 and 14 years is not useful (children will with normal growth have increased their BMI over this 9-year period) we undertook all analyses based on internally age- and sex-standardized BMI s.d. (z-scores). The mean z-score of BMI at age 5 and 14 and the change in BMI z-score between two ages by adolescents asthma symptoms were compared by one-way analysis of variance and computing an F-test (Table 2). Unadjusted odds ratios (OR) were estimated to assess the association of potential confounding factors with asthma symptoms at age 14 using logistic regression (Table 3). Multivariable associations of BMI z-score and change in z-score of BMI between age 5 and 14 with asthma symptoms at age 14 were estimated using multivariable logistic regression models (Table 4). Analyses were performed separately for male subjects, female subjects and for both sexes combined. Statistical evidence for a difference in association between male and female subjects was assessed by computing a likelihood ratio test of the interaction with sex.

Because of loss to follow-up and hence missing data on the outcome variable the main analyses were conducted on 40% of the original birth cohort. Participants lost to follow-up were more likely to weigh 2.50 kgs or less, to be male subjects and of Asian and Aboriginal/Torres Strait Islander background (all P-values <0.001). Their mothers were more likely to be teenagers, less educated, single or cohabitating, have three or more children, use tobacco and alcohol during pregnancy and be anxious and depressed at their first antenatal visit (all P-values <0.001). To determine whether this affected the validity of our findings we undertook a weighted analysis using inverse probability (IPW) (of having missing outcome data) weights.[21] The probability weights were computed by using a logistic regression model with the outcome being complete or partial data. The influence of all other covariates used in our primary analyses on having complete or partial data was assessed in combination in a logistic regression model. The results using the IPW did not differ from those presented here. All analyses were undertaken using Stata version 9.0 (Stata inc., Tx, USA).

Results

Table 1 shows the prevalence of asthma symptoms reported by mother and average BMI of offspring at age 5 and 14 years. The mean BMI at age 5 and 14 -years for female and male subjects presented in this table are similar to the distributions for these age groups in the 1999 National Nutrition Survey of Australia.

Table 1. Prevalence of asthma symptoms by maternal report and average BMI at age 5 and 14 years

	Males (%)	*Females (%)*	*Total (%)*	N
Asthma/bronchitis at age 5 years	8.80	7.39	8.13	3861
Asthma at age 14 years				
Ever had asthma	29.74	27.93	28.87	3751
Asthma in the last 6 months	22.97	21.52	22.28	3744
Medication for asthma	23.59	22.85	23.24	2638
Mean BMI at age 5 years	16.04	15.99	16.02	3861
Mean BMI at age 14 years	20.26	21.05	20.64	3759

Table 2 shows the associations of asthma symptoms among adolescents by BMI z-scores at age 5 and 14 years and the change in scores between these two ages. BMI z-score at age 14 and the change in BMI z-score from age 5 to 14 years were positively associated with asthma symptoms at age 14. BMI z-score at age 5 was not associated with asthma symptoms at age 14. The association between the change in BMI z-score with asthma symptoms at 14 years appeared stronger for male subjects compared with female subjects but there was no statistical evidence for a sex difference (*P*=0.36).

Table 2. Body mass index Z score and change of body mass index Z score at age 5 and 14 years by adolescent asthma symptoms

	No asthma	*Asthma*	*P-value*
Total (N=2911)			
Z score of BMI at age 5 years	0.003	0.005	0.9
Z score of BMI at age 14 years	-0.023	0.095	0.009
Change in BMI z score	-0.025	0.093	0.004
Males (N=1517)			
Z score of BMI at age 5 years	0.031	-0.099	0.04
Z score of BMI at age 14 years	-0.007	0.038	0.04
Change in BMI z score	-0.035	0.141	0.002
Females (N=1394)			
Z score of BMI at age 5 years	-0.023	0.100	0.06
Z score of BMI at age 14 years	-0.041	0.159	0.002
Change in BMI z score	-0.017	0.053	0.20

Abbreviation: BMI, body mass index.
P-value: the differences in mean z-score of BMI at age 5 and 14 and the change in BMI Z score between two ages by adolescents asthma symptoms were compared by one-way analysis of variance and computing an F-test

Table 3 shows the associations between potential confounding and mediator factors and asthma at age 14 years. Children from younger mothers, poorer socioeconomic backgrounds, exposure of maternal smoking during pregnancy and watching TV in adolescence were more likely to have asthma symptoms at age 14 years.

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Table 3. Association of potential confounding factors with asthma symptoms at age 14

	N	*Prevalence of asthma (%)*	*Unadjusted OR, 95% CI*
Maternal age at birth			
13-19	422	24.17	1.00
20-34	3130	20.96	0.83 (0.66,1.06)
35+	207	16.43	0.62 (0.40,0.95)
Family income			
Poor	206	24.27	1.00
Mid-income	2647	20.59	0.81 (0.58,1.13)
High	190	14.74	0.54 (0.32,0.90)
Maternal education			
Did not complete secondary	608	22.53	1.00
Completed secondary	2405	20.75	0.90 (0.73,1.12)
Completed further/higher	723	20.61	0.89 (0.69,1.16)
Maternal smoking during pregnancy			
Non smoker	2422	20.11	1.00
Light smoker	941	21.47	1.09 (0.90,1.31)
Heavy smoker	385	24.94	1.32 (1.03,1.70)
Duration of breastfeeding			
Never	691	21.56	1.00
Less 4 months	1355	21.55	1.00 (0.80,1.25)
4 months or more	1593	20.34	0.93 (0.75,1.16)
Fast food			
Never or rarely	2753	20.63	1.00
Most days or 2/3days per week	941	22.42	1.11 (0.93,1.33)
Pubertal stage			
Stage one or two	333	24.64	1.00
Stage three	1503	20.56	0.79 (0.60,1.05)
Stage four and more	1878	20.82	0.80 (0.61,1.06)
Soft drink			
Never or rarely	1290	19.07	1.00
2/3 days per week	1258	22.66	1.22 (0.86,1.72)
Most days	1168	21.58	1.16 (0.83,1.64)
Sports			
0-3 days per week	1809	20.95	1.00
4-7 days per week	1929	20.94	1.00 (0.85,1.17)
Watching television			
<1 h per day	304	18.09	1.00
1-<3 h per day	975	19.38	1.09 (0.78,1.52)
3-<5 h per day	1035	19.90	1.12 (0.81,1.56)
5 or more hours per day	1402	23.61	1.40 (1.02,1.92)

Table 4 shows the unadjusted and adjusted odds ratios of experiencing asthma symptoms at age 14 by BMI z-score at age 5 and 14 years and the change in BMI z-score from age 5 to 14 years. These results are for the 2812 respondents with complete data on all variables included in any of the models presented. Adjustment for a range of potential early life confounding factors did not importantly affect the positive associations between BMI z-score at age 14 and change in BMI z-score between age 5 and 14 and asthma at age 14 years. As with the unadjusted associations there was no statistical evidence that the associations of BMI z-score or its change on asthma differed between male and female subjects (*P* for interaction with sex >0.5 for all associations).

Table 4. Multivariable associations of BMI Z-score and change in z-score of body mass between ages 5 and 14 with asthma symptoms at age 14

	Unadjusted OR (95% CI)	*Adjusted [a] OR (95% CI)*
Total (N=2812)		
Z score of BMI at age 5 years	1.00 (0.91,1.10)	1.01 (0.92,1.11)
Z score of BMI at age 14 years	1.11 (1.02,1.22)	1.11 (1.02,1.22)
Change in BMI z score	1.14 (1.03,1.27)	1.13 (1.02,1.25)
Males (N=1472)		
Z score of BMI at age 5 years	0.87 (0.75,1.00)	0.87 (0.75,1.01)
Z score of BMI at age 14 years	1.04 (0.91,1.19)	1.03 (0.90,1.18)
Change in BMI z score	1.24 (1.07,1.44)	1.22 (1.06,1.41)
Females (N=1340)		
Z score of BMI at age 5 years	1.12 (0.99,1.26)	1.14 (1.00,1.29)
Z score of BMI at age 14 years	1.19 (1.05,1.34)	1.19 (1.06,1.35)
Change in BMI z score	1.08 (0.94,1.24)	1.07 (0.92,1.24)

Abbreviations: BMI, body mass index; CI, confidence interval.
[a] The association between z score of BMI and change in BMI z score with asthma symptoms at age 14 have been examined in separate models adjusted for the potential confounding factors: maternal age at birth, education, income, maternal smoking, birth weight and breastfeeding.

A prospective analysis of the change in z-score from age 5 to 14 years and the asthma symptoms at age 14 was conducted excluding the children who were overweight or obese at age 5 years (480 such children). Overweight or obesity status at age 5 was defined using Cole's[22] definition, which is equivalent to the 85th percentiles of the US CDC 2000 growth charts.[23] With those who were overweight or obese at age 5 excluded from the analyses, BMI z-score at age 14 (OR:1.14; 95% CI:1.01, 1.28) and change in BMI z-score between age 5 and 14 years (1.04; 1.01, 1.08) remained positively associated with asthma at age 14 as in the main analysis.

Finally, to examine whether reverse causation explained the association - that is the possibility that having asthma at age 5 resulted in greater weight again and was also related to asthma at age 14 years – we repeated the analyses with those children who had asthma at age 5 removed. Among children with no asthma at age 5 (*N*=2526), BMI z-score at age 14 (OR: 1.11; 95% CI: 1.00, 1.23) and change in BMI z-score between age 5 and 14 (1.12; 1.00, 1.26) years remained positively associated with asthma at age 14 with the magnitudes of these associations being similar to those in the whole cohort. These findings suggest that our main results are not largely driven by reverse causality.

Discussion

Our results support emerging evidence on the importance of BMI as a predictor of asthma.[4, 5, 6] Our prospective analyses showed that a greater increase in BMI z-score from age 5 to 14 years is associated with the development of asthma symptoms amongst Australian adolescents. We found that the relationship remained robust with adjustment for the child's weight at birth, length of breastfeeding, maternal lifestyle in pregnancy, maternal education, family income around pregnancy and other factors such as diet, sports, watching TV and puberty at 14-years follow-up.

The change in BMI z-score with asthma symptoms at adolescents appeared stronger for male subjects compared with female subjects, but there was no statistical evidence for a sex difference (P=0.36).

Our results should be interpreted in the context of some limitations, the most notable of which is the reliance on maternal reports of offspring's asthma. We used the most strict definition of asthma possible in our study in the main analysis by only counting as cases those children whose mothers had indicated twice (two separate questions) in the assessment that their child had asthma. Our sensitivity analyses using the asthma definition 'medication for asthma' did not alter any results presented in this study. Nonetheless, our definition of a case is not based on a clinical diagnosis. Replications of our results in studies with clinical measurements of asthma would be valuable.

As with all population-based cohort studies, in MUSP there has been attrition over follow-up from the original cohort. Missing data owing to attrition and item non-response may cause bias in the analyses, loss of power or both.[24] The most severe case is if the data are missing not at random, that is where the probability of missing data depends on the outcome of interest. Although this is impossible to test, it seems unlikely that the probability that the data are missing is dependent on the outcome (asthma), once other exposures are taken into account. In order to assess whether those lost to follow-up produced bias in our results, we attached inverse probability weighting to subjects included in the analyses to restore the representation of those lost to follow-up. We followed the method suggested by Hogan *et al.* and used robust standard errors estimates applied to the model.[21] We found little difference between the weighted and the non-weighted results, which suggests that attrition is unlikely to have substantively biased our findings.

Comparisons with other studies

Direct comparison of our results with those of other studies is difficult because of differences in the birth years of the cohorts, the ages at which examinations were performed and the definition of asthma symptoms. However, our prevalence estimate of asthma is in the same magnitude to the prevalence of asthma reported by other studies conducted in Australia.[2] The association of greater increase in BMI during childhood with asthma is consistent with a small number of previous studies.[5, 6, 25] Authors of previous studies have sometimes emphasized stronger associations in female subjects compared with male subjects, often without formal statistical tests for a sex difference. Our point estimate, in fact, suggested a stronger association in male subjects compared with female subjects but we found no statistical evidence of a sex difference. However, the sex difference might be related to the finding in this study that male subjects with asthma at age 5 had a lower BMI. Hence, their normal growth up to age 14 would lead to a greater change in z-score BMI being associated with asthma at age 14. Subgroup analyses should be treated with caution and there is evidence that investigators present and emphasize sex-specific results when their overall associations are weak or null. Our finding of no strong evidence for a sex difference in adolescents is consistent with the recent finding among 135 000 Norwegian adults, which found no sex difference in the association between BMI and asthma.[9] Our study adds to the existing body of evidence by suggesting that the relationship between a greater increase in BMI and asthma begins in childhood.

Implications

Australia has one of the highest prevalence of asthma in the world[2] and a high prevalence of childhood and adolescent obesity.[26] Our study provides evidence that greater increases in BMI between childhood and adolescence contributes to asthma risk. Observational studies are useful for developing hypotheses but cannot prove causality. Future trials examining interventions to reduce childhood obesity or overweight status should examine whether effective interventions also affect asthma risk.

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Author contributions: AAM, DAL and RA developed the study aim and design. JN, MO, GW set up and are responsible for the conceptual development and continued management of the Mater University Study of Pregnancy and its outcomes. AAM, DAL and RA undertook the analysis and wrote the first draft of the paper. All authors contributed to the final version of the paper.

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