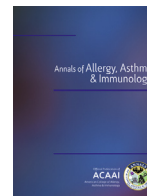




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Body mass index change and atopic diseases are not always associated in children and adolescents

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ABSTRACT

Background: Several studies have suggested an association between the increasing prevalence of allergic diseases and dietary factors.

Objective: To prospectively explore the association between changes in body mass index (BMI) and symptoms of asthma, rhinitis, rhinoconjunctivitis, and atopic dermatitis to find out whether an increase in BMI increases the risk of developing atopic diseases in adolescence.

Methods: Comprehensive questionnaires and anthropometric measurements were applied in a random subsample of the International Study of Asthma and Allergies in Childhood phase II (1995–1996, 9 to 11 years of age) in Germany. Of these participants, 1,794 could be followed up in 2002 to 2003 in the Study on Occupational Allergy Risks (16 to 18 years of age). The associations between changes of BMI from baseline to follow-up and incident and persistent respiratory diseases and atopic dermatitis were assessed.

Results: In logistic regression analyses, weight change in either direction was not statistically significantly associated with the incidence or persistence of any of the diseases of interest except for rhinitis. An increase in BMI was linked to an increased risk of incident rhinitis (odds ratio 1.9, 95% confidence interval 1.2–2.9).

Conclusion: These results indicate a nonsignificant trend between increased body weight and risk of atopic diseases. Aside from limitations owing to a small subgroup of obese participants and questionnaire-based asthma diagnosis, reasons might be related to an interaction between BMI and hormonal influences, age, and duration and severity of overweight. The results underline that BMI does not necessarily play a decisive role in the course of atopic diseases in all populations.

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Introduction

During the past 3 decades, the prevalence of overweight and obesity has steadily increased in Western countries and globally.¹ According to the German Health Interview and Examination Survey for Children and Adolescents, approximately 15% of children

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and adolescents 3 to 17 years in Germany are overweight; 6% of them have obesity.² This means a 50% increase compared with the reference populations from the 1980s and 1990s.² All over the world, obesity currently represents one of the major challenges to health care systems.³ Other health care problems that have consistently increased in recent decades are atopic and respiratory diseases, such as asthma, rhinitis, and atopic dermatitis.⁴ These are the most common chronic diseases in children and adolescents.⁵ To date, 6% to 10% of German children 11 to 17 years old have asthma.^{6,7}

Noticing this remarkable coincidence, several studies have suggested that the increasing prevalence of symptoms of asthma, rhinitis, rhinoconjunctivitis, and eczema could be associated with dietary factors⁸ because their prevalence and persistence often

increase in obese patients.⁹ There are various hypotheses trying to explain the connection between overweight and obesity, on the one hand, and between overweight and asthma or atopy, on the other.¹⁰ Obesity and asthma result from complex interactions between genetic predispositions and environmental influences. Although some investigators have suggested plausible mechanisms and provided evidence, others have questioned an association between these conditions. For example, some studies have reported a stronger or exclusive association for girls or women,^{11,12} whereas others have suggested an association for boys or men only.^{13,14} Moreover, others have proposed certain interactions of age and sex to explain this relation.^{15,16} Very few of such studies have been carried out during puberty. Therefore, the examination of weight change from childhood to adolescence or adulthood would be of great interest to possibly better understand the long-term interactions with atopic diseases.

In the present article, an analysis of longitudinal data obtained from the International Study of Asthma and Allergies in Childhood (ISAAC phase II) and the German Study on Occupational Allergy Risks (SOLAR I) is reported. The main aim was to determine whether the change in children's body mass index (BMI) was associated with the course of asthma, allergic rhinitis, rhinoconjunctivitis, and atopic dermatitis during puberty.

Methods

Study Design and Fieldwork

The ISAAC phase II was a cross-sectional study to describe the prevalence of asthma, rhinitis, and atopic dermatitis in children, which was conducted from 1995 through 1996.

In Germany, 3 centers (Dresden, Munich, and Leipzig) participated. Subjects were selected from grade 4 of randomly selected primary schools. A sample size of 3,000 per center and age group was obtained. A comprehensive standardized questionnaire was completed by the child's parent, and various clinical tests were conducted. To further examine the course of asthma and allergies in adolescents, SOLAR I was initiated in Dresden ($n = 1,829$, response 77%) and Munich ($n = 2,100$, response 84%) from 2002 through 2003. The 16- to 18-year-old participants of ISAAC phase II were contacted again with an adapted questionnaire (including self-reported height and weight), which was completed by the adolescents themselves. Details of the 2 studies and the examination procedures have been published previously.^{17,18}

The ISAAC phase II and SOLAR I were approved by the ethical committee of the Bavarian Chamber of Physicians (number 02071) and the ethical committee of the Department of Medicine, Technical University of Dresden (number EK96072002).

For these analyses, answers to the ISAAC Phase II and SOLAR I questionnaires were combined. Only participants with complete information on height and weight from the anthropometric measurements in ISAAC phase II and self-reports in SOLAR I were included. This resulted in a total of 1,794 subjects (852 in Dresden and 942 in Munich).

Definitions

Body mass index was calculated as weight (kilograms) divided by height (meters) squared. Baseline and follow-up BMI values were categorized as underweight, normal weight, and overweight. Overweight, which included the small group of obese participants, was defined as a BMI in at least the 90th percentile and underweight as below the 10th percentile according to the German age- and sex-specific reference values by Kromeyer-Hauschild et al.¹⁹ To obtain an unbiased estimate of prevalence, the midyear values (eg, 9.5 for the 9.0- to 10.0-year-old group) of Kromeyer-Hauschild et al were used as cutoff points. Because the entire examined population

was German, these reference curves were chosen instead of those of the World Health Organization.

Changes among the 3 BMI groups were divided into 5 categories: increased BMI, decreased BMI, unchanged underweight, unchanged overweight, and unchanged normal weight, with the latter serving as the reference. Increased BMI was defined as an "upward" change between BMI groups from underweight or normal weight at baseline to normal weight or overweight at follow-up, respectively. Accordingly, decreased BMI was defined as a "downward" change from overweight or normal weight at baseline to normal weight or underweight at follow-up, respectively. Unchanged overweight, unchanged normal weight, and unchanged underweight were assessed as being in the same weight categories at baseline and follow-up. However, the number of cases in the unchanged overweight and unchanged underweight categories was very small. Therefore, these cases are not presented.

Wheezing was assessed as self-reported wheeze or asthma attacks within the past 12 months. Asthma was defined as wheezing or use of asthma medication within the past 12 months. Rhinitis was considered present if symptoms such as "sneezing attacks" or a runny or blocked nose without having a cold were reported. Rhinoconjunctivitis was defined as rhinitis in combination with itchy, watery eyes. Atopic dermatitis was determined as an itchy rash in the typical predilection areas for at least 6 months within the past 12 months.

The course of asthma, rhinitis, rhinoconjunctivitis, and atopic dermatitis was assessed as incidence vs never reporting symptoms or persistence vs remission between ISAAC phase II and SOLAR I (eTable 1).

Dietary habits at 9 to 11 years of age were assessed as a nutrition score modified according to the Mediterranean diet score of Garcia-Marcos et al.²⁰ A higher frequency of consumption of assessed food items scored more points and the nutrition was considered healthier. A "rather healthy" nutrition was reached with at least half the maximum available score points (eTables 2 and 3).

Environmental tobacco smoke exposure was defined as being exposed to tobacco smoke of others at least once during most days or nights of the past 12 months.

Statistical Analysis

Descriptive data for categorical parameters are presented as absolute and relative frequencies. The χ^2 tests were used for statistical comparison between 2 groups. Logistic regression analyses were used to assess the association between BMI change and the course of the various atopic and respiratory diseases. The following factors were considered potential confounders: dietary habits, parental education, smoking, environmental tobacco smoke exposure, computer use, and viewing television. Effect measurement modification by sex was assessed; however, because no sex-specific differences were seen for the effect of BMI, only the joined results are shown. All analyses were conducted using SPSS 11.5 (SPSS Inc, Chicago, Illinois).

Results

At baseline, approximately 13% of the study population was overweight and approximately 8.5% of participants were underweight; at follow-up, overweight had decreased to approximately 8.5% and underweight had increased to approximately 11%. The prevalence of overweight (ISAAC phase II: girls 13.8%, boys 12.0%; SOLAR I: girls 9.1%, boys 8.0%) and underweight (ISAAC Phase II: girls 7.9%, boys 9.2%; SOLAR I: girls 11.4%, boys 10.4%) did not statistically significantly differ by sex. There also were no statistically significant differences in the prevalence of overweight and underweight participants between the 2 study centers (Dresden and Munich). Approximately 50% of the study population reported

rather unhealthy nutrition at baseline (eTables 2 and 3). More than one third of the study population smoked at follow-up. Likewise, approximately one third reported more than 1 hour of computer use per day (Table 1).

Bivariate analyses did not show any statistically significant association between change of BMI and the incidence of rhinitis, rhinoconjunctivitis, asthma or eczema. There was a statistically significantly increased risk of persistent rhinitis for participants with increased BMI at follow-up (odds ratio 1.6, 95% confidence interval 1.1–2.4). No association was seen for participants with increased BMI in regard to the persistence of asthma (Table 2).

Some of these results (eg, for rhinitis incidence and persistence) changed after adjusting for potential confounders. Weight change was not statistically significantly associated with the course of any of the analyzed diseases except rhinitis. For incident rhinitis, an increase in BMI was linked to an increase in risk (odds ratio 1.9, 95% confidence interval 1.2–2.9).

Discussion

The present study could not confirm the previously described association between an increase of BMI from childhood to adolescence and a higher incidence of atopic or respiratory diseases^{21–24} but can only point to a trend of consistency with previous studies.^{21–26} In participants with increased BMI, a statistically significant increase in the risk of rhinitis incidence and rhinitis persistence was seen.

Several recent studies have described a dose–response relation between obesity and asthma^{27,28} that might support the hypothesis of an obesity threshold above and beyond which the risk of asthma incidence increases and below which asthma risk may not truly differ from that in less overweight or obese individuals. Such a threshold might help explain the present findings because the present study participants did not reach this threshold. The contrary, however, seems to be the case in the United States, where obesity prevalence is more than 2 times as high (17.1% in 2003–2004, 15.5% in 2005–2006²⁹) as in Germany (6.3% in

2003–2006²) and extreme or morbid obesity that seems to especially influence asthma^{30,31} is an increasing problem.³² Asthma in the United States remains inadequately controlled in up to 41% to 55% of patients,³¹ which might be the result of a more severe and difficult-to-control asthma phenotype owing to extreme obesity beyond that threshold.

Another possible explanation for the present findings might be the relatively small proportion of obese and overweight participants at baseline and especially at follow-up compared with German reference values² and, hence, a lack of power. Therefore, obesity was included among the overweight categories and overweight as a whole became the focus; thus, overweight or obesity applied to 12.9% of the 9- to 11-year-old children at baseline and to 8.6% of the adolescents of 16 to 18 years of age at follow-up. The number of participants who started as overweight and continued to stay in this BMI group during puberty was particularly small (1% to 3%) in the incidence and persistence groups, which resulted in too little power for some categories. Aside from the small sample of overweight participants, the use of disease definitions based only on questionnaire answers may have contributed to these findings. Another explanation might be a possible interaction between BMI and hormonal status as suggested by various researchers.^{33,34} Thus, the impact of a higher BMI in adolescence on the incidence of asthma or atopy within puberty might be attributable in part to hormonal influences.²²

There are various studies that have indicated that the mechanisms underlying the association between overweight and asthma and between overweight and atopy may differ with regard to the age of a person starting to become overweight,^{22,23} and that, if this assumption is correct, inconsistent findings could be accredited at least in part to the differences in the subject populations studied.²² Also, the duration and, as mentioned earlier, the degree of overweight might interact with the incidence, persistence, and severity of respiratory and atopic diseases.³⁵ For example, Silverberg et al²³ showed that obesity in early childhood, especially with a prolonged duration (>2.5 years), led to an increased risk of atopic dermatitis, and that obesity was associated in particular with severe disease.

Table 1
Descriptive data of the study population

	Dresden (n = 852)	Munich (n = 942)	P value
Mean (SD)			
Age (y), ISAAC phase II	10.4 (0.5)	9.8 (0.6)	.528
Age (y), SOLAR	17.4 (0.5)	16.8 (0.6)	.528
BMI (kg/m ²), ISAAC phase II	17.6 (2.7)	17.5 (2.7)	.285
BMI (kg/m ²), SOLAR I	21.2 (2.8)	21.2 (3.1)	.615
n, (%)			
Boys	412 (48.4)	438 (46.5)	.449
BMI, ISAAC phase II			.254
Underweight	65 (7.6)	88 (9.3)	
Overweight	104 (12.2)	128 (13.6)	
BMI, SOLAR I			.171
Underweight	94 (11.0)	102 (10.8)	
Overweight	62 (7.3)	92 (9.8)	
Dietary index, (rather) unhealthy nutrition	331 (48.4)	369 (49.9)	.596
Smoking ≥ 1 y, SOLAR I	316 (37.4)	301 (32.2)	.025
Environmental tobacco smoke exposure, SOLAR I	552 (65.2)	605 (65.1)	.960
≥ 1 h of computer use per day, SOLAR I	273 (35.5)	267 (31.6)	.113
≥ 1 h viewing television per day, SOLAR I	499 (65.0)	550 (65.0)	1.000
Parental education, ISAAC phase II			.811
University/university of applied sciences entrance qualification ^a	446 (53.3)	489 (52.8)	
Schooling of participants, SOLAR I			<.001
Grammar school for university entrance qualification ^b	366 (43.0)	426 (45.3)	
Current occupational status, SOLAR I ^c			<.001
Pupil/student	528 (63.1)	719 (77.2)	

Abbreviations: BMI, body mass index; ISAAC phase II, International Study of Asthma and Allergies in Childhood; SOLAR I, Study on Occupational Allergy Risks.

^aReference category: lower qualification.

^bReference categories: secondary general school (*Hauptschule*), intermediate secondary school (*Realschule*), other.

^cReference category: apprentice or employee.

Table 2Incidence and persistence of symptoms of atopic diseases by change in BMI from baseline to follow-up^a

	Incidence ^b				Persistence ^c			
	n	%	Crude OR (95% CI)	Adjusted OR ^d (95% CI)	n	%	Crude OR (95% CI)	Adjusted OR ^d (95% CI)
Wheezing ^e								
BMI decreased ^f	36	18.9	0.9 (0.6–1.4)	0.7 (0.4–1.1)	18	24.7	1.2 (0.7–2.2)	1.6 (0.6–4.1)
Unchanged normal weight	119	62.6	1	1	44	60.3	1	1
BMI increased ^g	32	16.8	1.2 (0.8–1.8)	1.4 (0.8–2.3)	7	9.6	0.7 (0.3–1.6)	1.2 (0.3–4.2)
Asthma ^h								
BMI decreased ^f	44	19.6	0.9 (0.7–1.3)	0.8 (0.5–1.4)	23	24.7	1.2 (0.7–2.0)	1.5 (0.6–3.5)
Unchanged normal weight	143	63.8	1	1	59	63.4	1	1
BMI increased ^g	34	15.2	1.0 (0.7–1.5)	1.4 (0.8–2.3)	7	7.5	0.5 (0.2–1.1)	1.0 (0.3–3.5)
Rhinitis								
BMI decreased ^f	90	20.4	1.0 (0.7–1.3)	1.1 (0.7–1.3)	50	20.8	1.1 (0.7–1.5)	1.6 (0.8–3.1)
Unchanged normal weight	278	62.9	1	1	139	57.9	1	1
BMI increased ^g	66	14.9	1.2 (0.8–1.6)	1.9 (1.2–2.9)	45	18.8	1.6 (1.1–2.4)	1.2 (0.6–2.3)
Rhinoconjunctivitis								
BMI decreased ^f	55	23.2	1.2 (0.8–1.6)	1.0 (0.6–1.6)	27	20.0	1.1 (0.7–1.7)	0.6 (0.2–1.5)
Unchanged normal weight	150	63.3	1	1	81	60.0	1	1
BMI increased ^g	27	11.4	0.8 (0.5–1.3)	1.0 (0.6–1.8)	25	18.5	1.4 (0.9–2.3)	0.5 (0.2–1.3)
Atopic dermatitis								
BMI decreased ^f	22	22.0	1.1 (0.7–1.8)	1.0 (0.5–1.9)	17	21.8	1.1 (0.6–2.0)	0.6 (0.3–1.4)
Unchanged normal weight	62	62.0	1	1	47	60.3	1	1
BMI increased ^g	13	13.0	1.0 (0.5–1.8)	1.2 (0.5–2.5)	13	16.7	1.3 (0.7–2.4)	1.4 (0.6–3.7)

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.

^aPresented are absolute and relative frequencies and results of crude and adjusted logistic regression models.^bReference category: never reporting symptoms.^cReference category: remission.^dResults of logistic regression model adjusted for dietary habits, parental education, smoking, environmental tobacco smoke exposure, computer use, and viewing television selected a priori based on recent literature.^eSelf-reported wheeze, or asthma attacks within past 12 months.^fChange in BMI from overweight to normal weight or underweight or from normal weight to underweight from baseline to follow-up.^gChange in BMI from underweight to normal weight or overweight or from normal weight to overweight from baseline to follow-up.^hWheeze or use of asthma medication within past 12 months.

Conversely, Green³⁶ found that asthma levels were positively correlated with the onset of obesity and suggested that new-onset asthma may be related to subsequent weight gain over time.

The unknown information on the duration of overweight and on the diseases' severity in the present study might have contributed to the lack of statistically significant associations. Moreover, because asthma and atopy often begin in early life, the impact of changes in BMI in later years on these diseases may be less significant.²²

Still another point that might contribute to an explanation for the absence of statistically significant associations between BMI change and asthma in the present analyses could be found in the following argument. An interaction between BMI and asthma may not necessarily arise from an association between increased weight and asthma but could be attributable to a relation between BMI and other kinds of respiratory symptoms.³⁷ Because the definition of asthma used in the present study is neither a very rigorous one nor diagnosed by a physician, "other kinds of respiratory symptoms" might have interacted and might have affected the results. For example, Schachter et al³⁷ found that a higher BMI is a risk factor for atopy, wheeze ever, and cough (in girls only) but is not a risk factor for asthma or airway hyper-responsiveness (in boys or girls). Hence, overweight might result in impaired lung function but not necessarily in asthma by limiting chest mechanics or airway conductance. Impaired lung function may restrict physical activity and thus boost an increased BMI.²² Related findings were reported by Lang et al¹⁴ who found that obesity did affect airflow obstruction (in boys only), but it did not affect airway markers, asthma control, or the stability of the asthma. Whatever the precise mechanisms at work, the clinical expression of respiratory symptoms often seems to be preceded by obesity.^{21,22,24}

Various mechanisms that may explain a positive association between BMI and atopic diseases and between BMI and asthma

have been proposed, such as genetic predispositions,^{38,39} Western lifestyle,^{8,10} obesity-related inflammation,^{8,11} pulmonary dysfunction,^{10,40} and dietary habits.^{8,23} In addition, asthma has various phenotypic appearances that may result in various kinds of relations with BMI.^{41,42} Furthermore, several studies have shown that a distinction between nonatopic and atopic asthma may be helpful because nonatopic asthma seems to be more strongly affected by greater body weight than atopic asthma.⁴³ Unfortunately, the authors were unable to stratify asthma by phenotype or by the existence or nonexistence of atopy for lack of power and lack of clinical data at follow-up.

The major strength of the present study is its longitudinal approach to a general population sample using a thoroughly tested and validated questionnaire instrument.⁴⁴ This allows important insights into the development of atopic and respiratory diseases from childhood to adulthood. Nevertheless, the present report has its limitations. Definitions of respiratory and atopic diseases used in these analyses were not verified by a physician's diagnosis, medical records, or other measurements. Data assessment in ISAAC phase II and SOLAR I was not consistent regarding the source of information (parent-reported vs self-reported questionnaires) and depended in part on the recall of parents and participants who might have failed to correctly remember or interpret symptoms. Self-reported BMI might have led to a bias toward the null because it is most likely independent of the outcome. Selection bias has to be considered, because girls and children of parents of a higher socioeconomic status were more likely to participate in the follow-up. Thus, a selection toward higher educated participants with a greater likelihood of atopic diseases can be assumed. This has to be taken into account when interpreting the results.

In summary, this study shows a nonsignificant trend in the association between BMI change and the incidence of atopic diseases during puberty. Although some results indicate a link between

weight change and the incidence and persistence of rhinitis, these are rather weak associations. Therefore, this study underlines the importance of taking into account the life course of overweight and obesity in the analyses of asthma and atopy. It illustrates that although several studies have provided evidence that increased body weight might be associated with an increased risk of atopic diseases, overweight and obesity might not act a major part in all populations, which might support the hypothesis of a threshold for an association between increased BMI and asthma.

Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.anai.2014.07.011>.

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eTable 1

Course of diseases

Baseline/follow-up	Wheezing ^a	Wheezing or medication ^b	Wheezing and medication ^b	No symptoms
Wheezing ^a	wheezing persistence	wheezing persistence or asthma persistence	asthma persistence	wheezing incidence
Wheezing or medication ^b	wheezing persistence or asthma persistence	wheezing persistence or asthma persistence	asthma persistence	wheezing incidence or asthma incidence
Wheezing and medication ^b	asthma persistence	asthma persistence	asthma persistence	asthma incidence
No symptoms	wheezing remission	wheezing remission or asthma remission	asthma remission	never symptoms

^aWheezing was assessed as self-reported wheeze or asthma attacks within the past 12 months.^bAsthma was defined as wheezing and/or use of asthma medication within the past 12 months.**eTable 2**

Variables entering the nutrition score

Frequency of average consumption of the following foods	Frequency of average consumption of the following foods during winter time
Cereals or muesli/granola	spinach
Fresh grain	carrots
Whole-grain bread	cabbage
Other kinds of bread	fruit
Cold cuts	
Meat	
Fish	

eTable 3Composition of nutrition score according to Garcia-Marcos et al²⁰

Score ^a	Category
≤5 points	rather unhealthy
6–8 points	somewhat healthy
9–11 points	rather healthy
≥12 points	very healthy

^aAll mentioned nutrition, except cold cuts and meat, was considered healthy and intake was rated as none (0 point), less frequent (1 point), or more frequent (2 points). Because cold cuts and meat were considered rather unhealthy, a lower frequency was connected to more points. The nutrition score resulted from the total of points (maximum achieved score was approximately two thirds of the possibly highest reachable score of 22 points). The score represents the approximate total consumption of the examined food intake that is considered very healthy, rather healthy, somewhat healthy, or rather unhealthy.