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Study Program in Medicine KI
Degree project 30 credits
Spring 2015

Childhood Asthma and Adolescent Academic Outcome

- *A combined twin and register-based study*

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Skolresultat hos barn med astma
Bakgrund: Skolfrånvaro hos barn med astma är högre än hos friska barn och ökar med astmans svårighetsgrad. Tidigare studier har dock inte visat något samband mellan astma, dess svårighetsgrad och sämre skolresultat. *Syfte:* Att undersöka hur astma och svårighetsgraden av astma i barndomen påverkar skolresultaten i slutet av grundskolan vid 15-16 års ålder. *Material och Metoder:* Studiepopulationen deltog i Barn och ungdomsstudien i Sverige (CATSS). Av 27260 kontaktade tvillingar inkluderades 1629 stycken. 351 barn hade astma enligt förälders uppgift i CATSS. 193 barn hade astma enligt läkares uppgift i Socialstyrelsens patientregister. Deskriptiva analyser och regressionsanalyser utfördes för att undersöka sambandet mellan astma, astmans svårighetsgrad, meritvärde, gymnasiebehörighet, resultat i nationella prov och betyg i kärnämnena svenska, engelska och matematik. *Resultat:* Barn med astma enligt läkares uppgift saknade gymnasiebehörighet i högre utsträckning än friska barn efter justering (justerad OR 1.74, CI 1.02 – 2.99). Barn med astma enligt förälders eller läkares uppgift hade lägre meritvärde jämfört med friska barn (ojusterat meritvärde -8.67, CI -15.54 – -1.80), dock kunde inget negativt samband ses efter justering. *Slutsats:* Studien visar att barn med astmadiagnos riskerar att inte få gymnasiebehörighet. Framtida studier bör använda större studiepopulationer för att fastställa sambandet mellan astma och skolresultat.

Childhood asthma and adolescent academic outcome
Introduction: School absenteeism in children with asthma is higher than in healthy children and increases with asthma severity. However, previous studies have not demonstrated any association between asthma, asthma severity, and lower academic outcomes. *Aims:* To examine how asthma and asthma severity in childhood influence academic outcomes at the end of compulsory school at age 15-16. *Material and Methods:* The study population was retrieved from the Child and Adolescent Twin Study in Sweden (CATSS). Out of 27,260 contacted twins, 1,629 were included. According to CATSS, 351 children had parent-reported asthma. According to the National Patient Register, 193 children had physician-diagnosed asthma. Descriptive and regression analyses were used to examine associations between asthma, asthma severity, final grade scores, qualification for upper secondary school, national test results and final grades in core subjects Swedish, English, and Mathematics. *Results:* Children with physician-diagnosed asthma more often lacked qualification for upper secondary school compared to healthy children after adjusting for covariates (adjusted OR 1.74, CI 1.02 – 2.99). Children with either parent-reported or physician-diagnosed asthma had lower final grade scores than healthy children (unadjusted final grade score -8.67, CI -15.54 – -1.80), however this association was not significant after adjustment. *Conclusions:* Our results suggest that children with asthma diagnosis are at risk of not qualifying for upper secondary school. Further research is warranted using larger samples to determine the association between asthma and academic outcomes.

Keywords: achievement, adolescent, asthma, child, educational status, epidemiology, schools, twins.

Abbreviations

ANOVA	Analysis of Variance
CATSS	Child and Adolescent Twin Study in Sweden
CI	Confidence Interval
ICD	International Statistical Classification of Diseases and Related Health Problems
ISAAC	International Study of Asthma and Allergies in Childhood
MBR	Medical Birth Register
NPR	National Patient Register
NSR	National School Register
OR	Odds Ratio
PIN	Personal Identification Number
WHO	World Health Organization

Introduction

Asthma is a heterogeneous chronic inflammatory disease of the respiratory tract that usually begins in childhood (1). Asthma causes reversible swelling and narrowing of the airways, leading to recurrent symptoms such as shortness of breath, wheezing, coughing, chest tightness, in addition to expiratory airflow limitation; all of which vary over time and in intensity (1). Symptoms and airflow limitation vary in response to trigger factors such as allergen exposure, exercise, weather change, viral upper respiratory infections, and resolve spontaneously or by medication (1). Usually, bronchial hyper-responsiveness and chronic airway inflammation is seen, and characteristically persist even in the absence of symptoms, but may be alleviated with medication (1). Patients with asthma may have episodes of exacerbations when symptoms worsen, which carry a risk of death or hospitalization if left untreated (1).

Asthma is thought to be caused by a complex interplay of environmental and genetic factors that is not fully understood (2). However, risk factors such as atopic disease, obesity, gender, chronic stress, smoking (active and passive), viral infections, exposure to pollution, irritants, and allergens have been identified (3). It is likely that asthma susceptibility is determined by genes that interact with each other and environmental factors, along with developmental factors that modify disease risk, such as infections during the first years of life, immune response maturity, and development of atopic disease (3). A simplistic explanation of the etiology of asthma is that allergen exposure, especially early in life, produces allergic sensitization (3). Further exposure leads to development of bronchial hyper-responsiveness, airflow obstruction, and inflammation characterized by eosinophilic infiltration, leading to asthma (3). Better etiological models are warranted to account for further important factors (4).

Asthma can be categorized on the basis of etiological mechanism (3). Most commonly, there are two types classified based on whether symptoms are triggered by allergens or not, i.e. atopic and non-atopic asthma (1). Atopic asthma typically begins in childhood and is associated with allergic diseases such as eczema, allergic rhinitis, and type 1 allergy (e.g. food allergy) (1, 4). Non-atopic (non-allergic) asthma is primarily seen in adults and is not particularly associated with allergic factors (1, 4). Diagnosis is typically based on detailed

history, examination, spirometry with reversibility test, and allergy tests (1). Asthma has a number of common features that increase the likelihood of asthma diagnosis if present in the patient: respiratory symptoms often begin in childhood; usually more than one respiratory symptom is present in the patient; typically, there is a history of atopic disease, either in the patient or in the family; and respiratory viral infections are identified as common triggers in children (1). No cure for asthma currently exists, however, symptoms can be effectively managed with environmental control measures such as avoiding environmental trigger factors, and medication such as beta-agonists and inhaled glucocorticoids (1).

The World Health Organization (WHO) estimates 300 million people across all ages and ethnicities suffer from asthma (5). In the past four decades, global asthma prevalence has increased vastly in developed and developing countries (5). Until recently, asthma has been more prevalent in developed countries, but the gap is now closing due to increases in prevalence in developing countries, and plateauing in developed countries (6). Nevertheless, the prevalence of physician-diagnosed asthma varies greatly globally, from 21.0% in Australia to 0.2% in China (6). Asthma prevalence increases in parallel with allergy, and are tightly correlated with increased urbanization and adoption of a modern urban lifestyle (6). This increase is particularly pronounced in the pediatric population (6). Asthma has become the most common chronic disease in childhood (7). According to the International Study of Asthma and Allergies in Childhood (ISAAC), 14.1% of children aged 13 to 14 worldwide have symptoms of asthma, and 8% of 12 year-olds in Sweden have a physician's diagnosis of asthma (7).

Chronic diseases, such as asthma, may have an impact on the daily functioning of affected children (8). Depending on the functional impact of a chronic disease, attention and interest in school may decrease along with academic achievement (8). Education is a natural part of a child's life and school attendance is imperative for children's social and educational development (9). Absence from school (absenteeism) disrupts learning processes and limits participation in daily activities (9). Deficits in academic achievement may increase the risk for occupational failure, low self-esteem, impaired social functioning, and mental disease in adulthood (10). Children with good health conditions are considered to have optimal prerequisites for academic achievement, since motivation to learn and attainment of learning skills are directly benefitted by health (8). With the exception of attention-deficit hyperactive

disorder and autism, the effect of chronic diseases on academic achievement is unclear (11). However, it has been shown that chronic diseases such as asthma, attention-deficit hyperactive disorder, cardiovascular disorders, diabetes, and seizures are associated with higher school absenteeism (9).

School absenteeism can be caused by asthma through a number of ways: as a result of symptoms, physician appointments, hospitalizations, sleep deprivation, asthma exacerbations, non-adherence to medications, and avoidance of environmental trigger factors (12, 13). The extent of which each of these factors contribute to the overall rate of school absenteeism in children with asthma is not completely known (13). Nevertheless, it has been established in a variety of studies that school absenteeism is correlated with asthma and increases with asthma severity (12-14). Indeed, limitations in daily activities and school attendance are used in different asthma guidelines and questionnaires as a measure of disease control in children (9). In 2003, children with asthma were estimated to miss 12.8 million school days in the United States (15). A study in a large urban school district in the United States found that children with asthma in average missed more than 10 school days per year, which is in excess of the amount of missed days that is considered to put a child at risk of grade failure according to US federal law (15). Optimal treatment of asthma, followed by appropriate school interventions, has a potential to improve school attendance for affected children through better disease control (16, 17). Strategies that aim to provide children with self-management tools in order to control asthma symptoms and manage asthma attacks may improve lung function, reduce asthma severity, give a sense of self-control, as well as increase school attendance and improve daily activities (18).

Since asthma affects individuals of all ages worldwide, there is evidence that the economic consequences of asthma are substantial due to a global loss of productivity (1). School and work absenteeism are known to constitute a source of economic and social burden of asthma overall (1). A unique, but albeit small, 25-year prospective study reported that although children with asthma were more likely to experience respiratory problems during their school years, this did not adversely affect education, employment, housing, or socioeconomic status later in life (19). However, there is little additional evidence supporting this, and generally, not much is substantiated concerning long-term social and economic outcomes of childhood asthma (20).

It has been suggested that children with asthma may be at risk for decreased academic achievement compared to their healthy peers (14). School absenteeism along with side effects of asthma medication, acute exacerbations, and asthma-related stress have been identified as factors that may put affected children at risk for decreased school functioning (21). However, the association between the presence of childhood asthma and lower academic outcomes has been inconclusive (11). Systematic reviews have suggested that childhood asthma is not associated with lower academic outcomes compared to children without asthma (12, 20). However, the cohorts in the reviewed studies consisted of homogenous populations, usually white middle-class children in suburban areas, which is a population characterized by high disease control and less severe forms of asthma (12, 20). In contrast, the results of some reviewed studies have suggested that childhood asthma is associated with lower academic outcomes (12, 20). A major drawback to these previous studies, regardless of direction of results, has been small study populations, and thereby, limited external validation (12, 20).

A systematic review on the consequences of childhood asthma by Milton et al. in 2004 has reported that although children with asthma missed more days in school, higher school absenteeism was not reflected in decreased academic outcomes (20). Besides having supported these findings, a systematic review on the school performance of childhood asthma by Taras et al. in 2005 has suggested that academic outcomes may be affected by asthma-related sleep interruptions rather than asthma severity (12). A cross-section study by Moonie et al. in a predominantly African-American urban school district has reported a significant correlation between asthma severity, higher school absenteeism, and lower academic outcome (14). However, data on asthma severity was only available for a subset of the population, and only one measure of academic outcome was used, namely a standardized test score. Interestingly, Moonie et al. did not show an association between asthma itself and lower academic outcome. Further studies were warranted by the authors to assess the relationship between asthma, asthma severity, and academic outcomes among larger urban populations with diverse cohort constitutions in order to account for a variety of population groups with different levels of disease control.

Knowledge gaps were identified in the review by Milton et al. (20). Particularly, most previous studies were found to examine only the short-term social outcomes of childhood asthma. Longitudinal cohort studies are warranted to examine the effects of asthma in

children into adolescence and adulthood (20). Such a study design would be valuable for investigating the effects of asthma over time and exploring the interaction of different exposures and outcomes, such as asthma severity and academic outcomes.

Aims

The primary aim of this study was to (i) examine the association of asthma in childhood and academic outcomes, measured by final grade score and qualification for upper secondary school at age 15-16, and (ii) investigate the impact of asthma severity on the association of asthma and academic outcomes. The secondary aim of this study was to (i) examine the association of asthma in childhood and outcomes in core subjects, measured by national test results and final grades in the subjects of Swedish, English, and Mathematics, and (ii) investigate the impact of asthma severity on the association of asthma and outcomes in core subjects.

Material and Methods

Study design and population

Overview

The present study was a national register-based longitudinal study of Swedish twins to examine the association between asthma, asthma severity, and academic outcomes at the end of compulsory school.

Child and Adolescent Twin Study in Sweden

Study participants were retrieved from the Child and Adolescent Twin Study in Sweden (CATSS). CATSS is an ongoing longitudinal study where information on 9 year-old (born since July 1995) and 12 year-old twins (born since July 1992) has been collected through parental interviews since 2004. The twins were identified through the Swedish Twin Register (22). An invitation letter served as the first contact to the parents, and the families were further contacted by phone from a professional interview company (22). A home visits was conducted if the families were not reached by phone (22). Data on the twins' somatic and mental health in addition to social environment was collected (22). Variable measurements of asthma was obtained from the International Study of Asthma and Allergies in Childhood

(ISAAC) questionnaire (23), included in CATSS, and was used in the present study as a measure to ascertain the presence and severity of asthma at age 12.

National Patient Register

The National Patient Register (NPR) contains data on in-patients and out-patients. Information on in-patients has been collected since 1964 from discharged hospitalizations in Sweden and has since 1987 had a coverage close to 100% (24). Information on out-patients in specialist care (e.g. visits to a lung clinic) has since 2001 been collected with a coverage of around 80% (25). The coverage for out-patients is lower than for in-patients, primarily due to missing data from private caregivers (25). The medical data in the register consists of primary and secondary diagnoses (up to eight diagnoses), procedures (e.g. surgical operations), injuries along with gender and age (25). Diagnoses relevant to the present study are listed according to the 9th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-9) for 1987-1996 and the 10th revision (ICD-10) for 1997-present (25). Data on asthma diagnosis by a physician was retrieved from the NPR. The medical records for asthma diagnosis in children in the NPR has been validated and the quality of childhood asthma diagnosis in the register is considered to be high (26).

National School Register

The Swedish school consists of nine years of compulsory education for children between ages of 7 to 16 years (27). After graduation at age 15-16, students receive a final grade score calculated as the sum of a total of 16 subjects (28). All participants in the present study graduated from compulsory school before or until 2011, during which a four-graded scale was in use (27). The grade of each subject was defined either as IG (fail), G (pass), VG (pass with distinction), or MVG (pass with special distinction), corresponding to a score of 0, 10, 15, and 20 respectively (27). Therefore, the final grade score ranged from a minimum of 0 to a maximum of 320 (16x20), and was used as instrument of selection for admission to upper secondary school (28).

In order to qualify for upper secondary school (at the time of this study), a student had to attain prescribed learning outcomes, corresponding to at least a passed final grade in three core subjects of Mathematics, Swedish, and English (27). In grade nine, compulsory national assessment test are given to all students nationwide by the National School Agency for Education in these core subjects (27). The results of the national assessment tests have an

impact on the teacher's final grading (27). Final grades are based on the teacher's overall assessment of the student's total performance in the subject and the national tests function as a support tool for teachers when grading students (27). In common with assessment of final grades, the results of the national tests were rated on a four graded scale, with IG (fail) being the lowest result and MVG (pass with special distinction) the highest result possible (27). Discrepancies between final grades and national test results have been widely reported (27). For example, on average only 40% of nine graders who failed the national test in the Swedish subject also received a failed final grade in 2007 (27). There is a lack of explanation for these discrepancies, and there is also a lack of systematic research on the reliability and fairness of the Swedish grading system (27). However, national tests are considered to be standardized, fair and reliable assessment tools within the Swedish school system (27).

For the present study, data on school grades was retrieved from the National School Register (NSR) and used to calculate final grade scores at the end of compulsory school and to determine qualification for upper secondary school for all students. Additionally, data on national test results was also collected. Data in the register is available from all public schools since 1988 and all private schools since 1993 (28). The register is jointly administered by the Swedish National School Administration and Statistics Sweden (28). The quality of the data in the NSR is considered to be high and publications on summary statistics are regularly released (28).

Medical Birth Register

Through the Medical Birth Register (MBR), data has been available on all births since 1973 in Sweden. Information is collected prospectively on standardized records beginning at the first antenatal visit in the clinic (29).

Selection criteria

Through the Swedish Twin Register, the parents of 27,260 twins (9 and 12 year-olds) in total were contacted between August 2003 and August 2011 and asked to participate in CATSS. Twins were excluded if the parent or twin were disabled, living abroad, or not fluent in Swedish (n = 860). Of the total 26,400 eligible twins, 75% (n = 20,302) completed the interviews. The study population was further restricted to twins with complete information on asthma (n = 20,072). Data from CATSS was linked to the MBR, NSR and NPR on the basis of personal identification number (PIN), a numeric identifier that is unique for each resident

in Sweden. After linkage, 3,180 twins remained in the study populations, the rest being excluded due to not having graduated from compulsory school or missing information on school grades. The study population was further restricted to twins aged 12 at the time of the interview (n = 3,159). In order to avoid paired data, a selection protocol was followed. First, only the asthmatic member of a twin pair discordant for asthma was included in the study group (n = 269). Second, for twin pairs concordant for asthma, one member was alternatively included (n = 66). Third, for twin pairs without asthma, one member was alternatively included (n = 1,195). Finally, if data was available for only one member of a twin pair, that member was included regardless of asthma diagnosis (n = 99). All selections were made on the basis of parent-reported asthma from CATSS. Thus, the final study population consisted of 1,629 twins born between 1992 and 1994 (Figure 1). Interviews were carried out between June 2004 and September 2006.

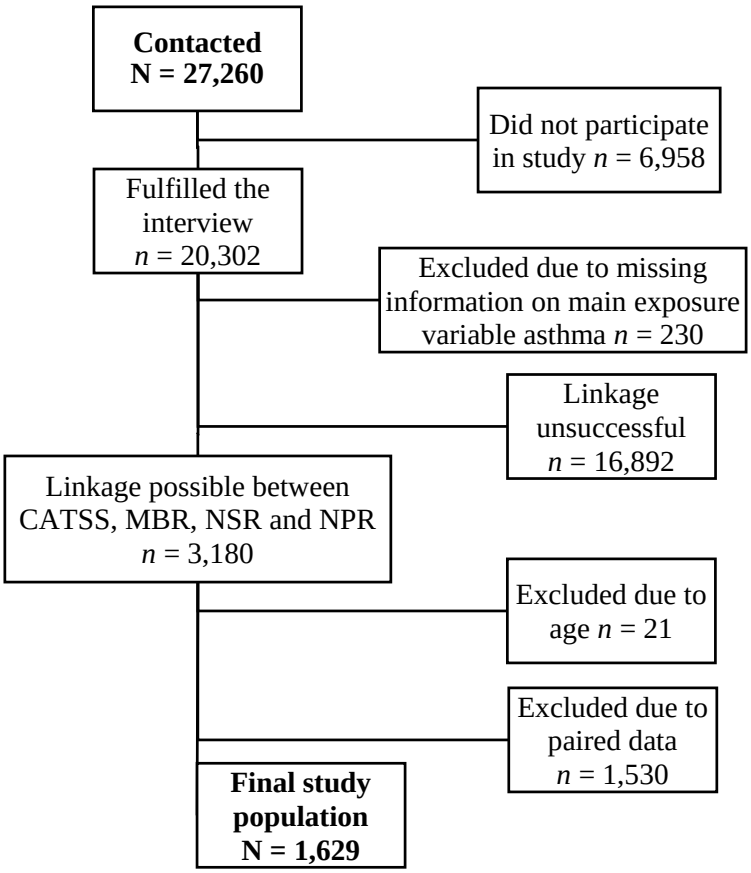

Figure 1. Final study population (N = 1,629) of the contacted twins (N = 27,026).

Variables

Asthma

The main exposure variable, “parent-reported asthma in questionnaire”, used as a measure of asthma at age 12, was ascertained through parental interviews using the questions “Has your child ever had asthma?” (yes or no) from the ISAAC questionnaire (23). The ISAAC questionnaire is widely used in epidemiological studies for evaluating the prevalence of asthma and is included as an instrument in CATSS (30). A validation study of the ISAAC questionnaire found that 40% of children with asthma in questionnaire lacked a medical record of asthma (30). Therefore, as a secondary exposure variable, “physician-diagnosed asthma based in register”, was retrieved from the NPR if a medical record had at least once been recorded with asthma as either the primary or secondary diagnosis (ICD-9 code 493 or ICD-10 codes J45 and J46). Finally, a third exposure variable, “any asthma”, was created by merging “parent-reported asthma in questionnaire” and “physician-diagnosed asthma based in register”.

Asthma severity

Number of asthma attacks according to questionnaire was used as a measure of asthma severity at age 12 in this study. If parents reported either asthma or symptoms of asthma such as wheezing in the ISAAC questionnaire, a follow-up question on asthma attacks in the last 12 months was asked. “Number of asthma attacks in the last 12 months” was categorized into five levels (no; yes, previous asthma only; yes, current asthma but no attacks in the last 12 months; 1-3 attacks in the last 12 months; ≥4 attacks in the last 12 months).

Academic outcomes

Measurements of school grades from grade nine (age 15-16) were obtained from the NSR for all children ≥15 years of age. In this study, academic outcomes were measured by final grade scores (quantitative) and qualification for upper secondary school (qualitative). Final grade scores were calculated from final grades in all 16 school subjects (0-320). Outcomes in core subjects were measured by national test results and final grades in subjects that form the basis for qualification to the next level of education. Qualification for upper secondary school was dichotomized into “qualified” if the child had passed in each of the three core subjects of Swedish, English and Mathematics, or “not qualified” if the child had failed any of these three subjects. National test results and final grades in Swedish, English and Mathematics from the NSR were also dichotomized (pass or fail).

Covariates

From the CATSS interview questions, information was obtained on child's gender, age, maternal education, and maternal country of birth, the latter two of which were categorized into the following groups (≤9 years; 10-12 years; ≥13 years and Sweden; Denmark, Finland, Norway or Iceland; other). Additional information on child characteristics (gestational age, birth weight) and maternal characteristics (smoking during pregnancy) was retrieved from MBR. Maternal smoking during pregnancy was registered at the first antenatal visit in week 8 and 12 and categorized into three levels (not smoking; 1-9 cigarettes per day; ≥10 cigarettes per day).

Statistical analysis

The study population was evaluated as a cohort (N = 1,629). First, descriptive statistics was used to describe the association of asthma measures (parent-reported asthma in questionnaire; physician-diagnosed asthma based in register; any asthma), asthma severity (number of attacks in the last 12 months), child characteristics (gender, birth weight, gestational age) and maternal characteristics (smoking during pregnancy, education, country of birth) with final grade score (mean, SD, and range with 95% confidence intervals) and qualification for upper secondary school (yes or no). In addition, the association between asthma measures and core subject outcomes (national test results; final grades) was described. Chi2-tests were used to test for differences in qualification for upper secondary school and differences in outcomes in core subjects between groups, while analysis of variance (ANOVA) was applied in assessing final grade scores. Second, logistic and linear regression analyses were performed to study if there is an association between asthma measure, asthma severity, and academic outcomes. Qualification for upper secondary school and outcomes in core subjects were used as the dependent variables in logistic regression analysis (Odds Ratio [OR]; 95% confidence intervals [CI]), and final grade scores was used as the dependent variable in linear regression models with asthma measures and asthma severity as independent variables. All regression analyses were adjusted for additional covariates (gender, birth weight, gestational age, maternal smoking during pregnancy, maternal education, and maternal country of birth) to minimize confounding. P-value of less than 0.05 was considered statistically significant. Analyses were conducted using SPSS 22.0 (IBM Corp., Armonk, NY).

Ethical considerations

The substantial amount of information collected on children and parents in the present study could infringe on the integrity of the subjects. However, participants in CATSS are thoroughly informed of the handling and collection of personal data, and have the choice to revoke their consent and participation at any given time. For the purpose of the present study, data from CATSS along with that of MBR, NPR and NSR were merged and depersonalized. All individuals included in the study were anonymized with a unique identification code ensuring that none could be traced back or identified. The present study may have a positive impact in its field, namely improving the understanding of the educational situation of children with asthma, which outweighs any risk associated with this type of study. Ethical approval has been provided by the Regional Ethics Committee at Karolinska Institutet (Dnr: 2009/939-31/5).

Results

Study population

This register-based cohort study consisted of twins born in Sweden between 1992 and 1994 (N = 1,629). Child and maternal characteristics in the present study by academic outcomes in grade nine are shown in Table 1. Among the total study population, 52.3% of the children were male, and 6.9% had a mother born outside of Scandinavia. Final grade scores ranged from 210.92 to 216.84 within a 95% confidence interval, and 92.4% of the cohort was qualified for upper secondary school. Males had lower final grade scores compared to females ($p<0.001$). No gender differences could be observed for qualification for upper secondary school. Academic outcomes did not vary significantly with any other child characteristic.

Academic outcomes varied with maternal characteristics such as smoking during pregnancy and level of education. Lower final grade scores were more common among children whose mothers had a primary education (0-9 years) or an upper secondary education (10-12 years) compared to children whose mothers had a university education (≥13 years) ($p<0.001$). Qualification for upper secondary school was lower in children whose mothers had a primary education or an upper secondary education compared to those who had a university education ($p<0.001$). Significantly lower final grade scores ($p<0.001$) and lower qualification for upper secondary school ($p<0.001$ for ≥10 cigarettes per day; $p<0.01$ for 1-9 cigarettes per day

respectively) could be seen in children to mothers who smoked during pregnancy. Academic outcomes in children did not vary with maternal country of birth.

Table 1. Child and maternal characteristics of study population with data on academic outcomes at the end of grade nine.

Child and maternal characteristics	Twins	Final grade score[1]			Qualified for upper secondary school	Not qualified[2] for upper secondary school
	N (%)	Mean	SD[†]	95% CI[‡]	N (%)	N (%)
Gender						
Male	851 (52.3)	205.08	58.91	201.11 – 209.04	778 (91.4)	73 (8.6)
Female	775 (47.7)	223.55	61.55	219.21 – 227.89	724 (93.4)	51 (6.6)
Total	1626 (100.0)	213.88	60.87	210.92 – 216.84	1502 (92.4)	124 (7.6)
Birth weight, grams						
≤1999	194 (11.9)	210.10	55.71	202.21 – 217.99	176 (90.7)	18 (9.3)
2000-2499	377 (23.2)	216.84	63.17	210.45 – 223.24	348 (92.3)	29 (7.7)
2500-2999	554 (34.1)	212.20	62.00	207.03 – 217.38	510 (92.1)	44 (7.9)
3000-3499	331 (20.4)	216.62	59.35	210.20 – 223.03	309 (93.4)	22 (6.6)
≥3500	93 (5.7)	217.90	55.37	206.50 – 229.31	89 (95.7)	4 (4.3)
Missing	77 (4.7)	204.42	66.15	189.40 – 219.43	70 (90.9)	7 (9.1)
Gestational age, weeks						
≤31	84 (5.2)	207.50	58.18	194.87 – 220.13	77 (91.7)	7 (8.3)
32-34	199 (12.2)	220.03	59.08	211.77 – 228.28	180 (90.5)	19 (9.5)
35-36	351 (21.6)	218.63	57.76	212.57 – 224.70	329 (93.7)	22 (6.3)
37-38	615 (37.8)	209.09	65.55	203.90 – 214.28	560 (91.1)	55 (8.9)
39-40	334 (20.5)	214.78	56.84	208.66 – 220.89	314 (94.0)	20 (6.0)
≥41	24 (1.5)	235.21	50.59	213.84 – 256.57	24 (100.0)	0 (0.0)
Missing	19 (1.2)	202.63	58.18	174.59 – 230.67	18 (94.7)	1 (5.3)
Maternal education, years						
≤9	129 (7.9)	188.14	58.57	177.94 – 198.34	112 (86.8)	17 (13.2)
10-12	779 (47.9)	204.06	59.67	199.87 – 208.26	707 (90.8)	72 (9.2)
≥13	654 (40.2)	232.97	55.26	228.73 – 237.22	629 (96.2)	25 (3.8)
Missing	64 (3.9)	190.23	77.91	170.77 – 209.69	54 (84.4)	10 (15.6)
Maternal smoking during pregnancy, cigarettes per day						
0	1191 (73.2)	223.08	56.02	219.89 – 226.26	1122 (94.2)	69 (5.8)
1-9	214 (13.2)	191.29	64.49	182.60 – 199.97	191 (89.3)	23 (10.7)
≥10	123 (7.6)	169.92	71.55	157.15 – 182.69	101 (82.1)	22 (17.9)
Missing	98 (6.0)	206.68	57.71	195.11 – 218.25	88 (89.8)	10 (10.2)
Maternal country of birth						
Sweden	1462 (90.0)	213.91	60.61	210.80 – 217.02	1355 (92.7)	107 (7.3)
Denmark, Finland, Norway or Iceland	51 (3.1)	197.16	77.80	175.27 – 219.04	44 (86.3)	7 (13.7)
Other	112 (6.9)	220.76	54.45	210.56 – 230.95	102 (91.1)	10 (8.9)
Missing	1 (0.0)					

[†]SD: standard deviation.
[‡]95% CI: 95% confidence intervals.
[1]Overall final grade score: possible range 0-320.
[2]Not qualified for upper secondary school; i.e. not receiving passing grades in Swedish, English and/or Mathematics.

Asthma, asthma severity, and academic outcomes

Asthma measures and asthma severity are presented in relation to academic outcomes in Table 2. Parent-reported asthma and number of asthma attacks in the last 12 months were used as measures of disease prevalence and severity respectively at age 12. Children with parent-reported or physician-diagnosed asthma had lower final grade scores ($p<0.05$) and lower qualification for upper secondary school ($p<0.05$ and $p<0.01$ respectively) compared to children without asthma.

In children with parent-reported asthma, 25.0% reported at least one asthma attack in the last 12 months and 23.1% reported four or more asthma attacks. In children with parent-reported asthma, 58.7% had not been given a physician's diagnosis of asthma. Lower final grade scores were seen in children where asthma attacks had occurred previously only ($p<0.05$). No differences in academic outcomes were found for any other category of asthma severity.

Table 2. Academic outcomes at the end of grade nine in children with asthma.

Asthma measure	Twins	Final grade score[1]			Qualified for upper secondary school	Not qualified[2] for upper secondary school
	N (%)	Mean	SD[†]	95% CI[‡]	N (%)	N (%)
Parent-reported asthma in questionnaire						
No	1275 (78.4)	215.81	60.28	212.50 – 219.12	1185 (92.9)	90 (7.1)
Yes	351 (21.6)	206.89	62.57	200.33 – 213.46	317 (90.3)	34 (9.7)
Physician-diagnosed asthma based in register						
No	1433 (88.1)	215.26	60.36	212.13 – 218.39	1333 (93.0)	100 (7.0)
Yes	193 (11.9)	203.68	63.78	194.62 – 212.73	169 (87.6)	24 (12.4)
Any asthma[§]						
No	1227 (75.5)	216.01	60.47	212.62 – 219.40	1139 (92.8)	88 (7.2)
Yes	399 (24.5)	207.34	61.71	201.27 – 213.42	363 (91.0)	124 (7.6)
Asthma attacks						
No	1270 (78.9)	215.80	60.36	212.48 – 219.13	1180 (92.9)	90 (7.1)
Yes, previous asthma only	138 (8.6)	206.09	65.04	195.14 – 217.04	123 (89.1)	15 (10.9)
Yes, current asthma but no attacks in the last 12 months	33 (2.0)	193.79	74.71	167.30 – 220.28	29 (87.9)	4 (12.1)
1-3 attacks in the last 12 months	88 (5.5)	212.39	60.01	199.67 – 225.10	82 (93.2)	6 (6.8)
$\geq$4 attacks in the last 12 months	81 (5.0)	206.11	58.82	193.11 – 219.12	73 (90.1)	8 (9.9)

[†]SD: standard deviation.
[‡]95% CI: 95% confidence intervals.

[2]Overall final grade score: possible range 0-320.
[2]Not qualified for upper secondary school; i.e. not receiving passing grades in Swedish, English and/or Mathematics.
[§]Asthma reported by questionnaire and/or in register (National Patient Register).

Multivariate analyses of asthma, asthma severity, and academic outcomes

Table 3 shows the linear regression models of final grade score, asthma measures, and asthma severity. The first model is unadjusted. The second model is adjusted for gender, birth weight, gestational age, maternal education, maternal smoking during pregnancy and maternal country of birth. In model 1, children with asthma at age 12 had lower final grade scores at age 15-16 than peers with no asthma. The change in final grade score was more marked in children with a physician's diagnosis of asthma and less marked in the merged category of children with parent-reported and/or physician-diagnosed asthma. After adjusting for covariates in model 2, the change in final grade score was not significant for any of the independent variables. Final grade scores did not vary with asthma severity (number of attacks in the last 12 months) in either model.

Table 3. Difference in mean final grade score and 95% confidence intervals (CI) for parent-reported asthma in questionnaire or physician-diagnosed asthma based in registers, and asthma severity (number of attacks in the previous year).

Asthma measure	Model 1[†] Final grade score (95% CI[*])	Model 2[‡] Final grade score (95% CI)
Parent-reported asthma in questionnaire		
No	Reference	Reference
Yes	-8.91 (-16.01 – -1.73)	-3.44 (-10.59 – 3.70)
Physician-diagnosed asthma based in register		
No	Reference	Reference
Yes	-11.58 (-20.72 – -2.44)	-6.35 (-15.26 – 2.55)
Any asthma[§]		
No	Reference	Reference
Yes	-8.67 (-15.54 – -1.80)	-3.97 (-10.78 – 2.85)
Asthma attacks		
No	Reference	Reference
Yes, previous asthma only	-8.49 (-19.15 – 2.18)	-4.60 (-15.13 – 5.93)
Yes, current asthma but no attacks in the last 12 months	-20.48 (-41.53 – .58)	-18.87 (-39.31 – 1.57)
1-3 attacks in the last 12 months	-1.54 (-14.68 – 11.60)	2.94 (-9.72 – 15.60)
≥4 attacks in the last 12 months	-8.14 (-21.80 – 5.52)	-1.72 (-14.90 – 11.47)

[*]95% CI: 95% confidence intervals.
[†]Model 1 represents crude analysis of exposures.
[‡]Model 2 is adjusted for gender, birth weight, gestational age, maternal smoking during pregnancy, maternal education, maternal country of birth.
[§]Asthma reported by questionnaire and/or in register (National Patient Register).

Table 4 shows the logistic regression models of qualification for upper secondary school, asthma measures, and asthma severity, presented in 2 models. The first model is unadjusted. The second model is adjusted for the same covariates as in the linear regression model. A physician's diagnosis of asthma increased the odds of not qualifying for upper secondary school in the unadjusted models (odds ratio [OR]: 1.89; 95% confidence intervals [CI]: 1.18 – 3.04). In the adjusted analysis, the association was somewhat attenuated (OR: 1.74; CI: 1.02 – 2.99) but remained statistically significant. None of the other independent variables was associated with any significant change in odds for not qualifying to upper secondary school.

Table 4. Odds ratios (OR) and 95% confidence intervals (CI) for the association between parent-reported asthma in questionnaire or physician-diagnosed asthma based in registers, asthma severity (number of attacks in the previous year) and non-qualification for upper secondary school.

Asthma measure	Model 1[†] OR[+] (95% CI[*])	Model 2[‡] OR (95% CI)
Parent-reported asthma in questionnaire		
No	Reference	Reference
Yes	1.41 (.93 – 2.14)	1.36 (.85 – 2.19)
Physician-diagnosed asthma based in register		
No	Reference	Reference
Yes	1.89 (1.18 – 3.04)	1.74 (1.02 – 2.99)
Any asthma[*]		
No	Reference	Reference
Yes	1.28 (.86 – 1.93)	1.21 (.77 – 1.94)
Asthma attacks		
No	Reference	Reference
Yes, previous asthma only	1.54 (.87 – 2.73)	1.44 (.76 – 2.74)
Yes, current asthma but no attacks in the last 12 months	1.69 (.58 – 4.89)	2.28 (.78 – 6.89)
1-3 attacks in the last 12 months	.88 (.38 – 2.06)	.84 (.33 – 2.17)
≥4 attacks in the last 12 months	1.35 (.63 – 2.87)	1.15 (.48 – 2.77)

[+]OR: odds ratio
[*]95% CI: 95% confidence intervals
[†]Model 1 represents crude analysis of exposures.
[‡]Model 2 is adjusted for gender, birth weight, gestational age, maternal smoking during pregnancy, maternal education, maternal country of birth.
[§]Asthma reported by questionnaire and/or in register (National Patient Register).

Asthma and outcomes in core subjects

Table 5 and 6 shows asthma measures in relation to national test results and final grades respectively in the core subjects of Swedish, English, and Mathematics. Children with physician-diagnosed asthma were more likely to have failed national test results in Swedish compared to children without asthma ($p<0.05$). No statistically significant difference was observed for national test results in the subjects of English and Mathematics for children with

physician-diagnosed asthma when compared to their non-asthmatic peers. There was no differences concerning national test results in any subject for childen with parent-reported asthma compared to children without asthma. National test results and final grades in core subjects did not vary with asthma severity, and hence, these results were not presented here. Data was missing for a subset of the study population regarding national test results for Swedish (3.0% [n=49]), English (4.3% [n=69]), and Mathematics (4.9% [n=80]).

Table 5. Dichotomized results (pass or fail) in national assessment tests for core subjects Swedish, English, and Mathematics in relation to children with asthma.

Asthma measure	Swedish national tests		English national tests		Mathematics national tests	
	Pass[1] N (%)	Fail N (%)	Pass N (%)	Fail N (%)	Pass N (%)	Fail N (%)
Parent-reported asthma in questionnaire						
No	1195 (97.2)	35 (2.8)	1190 (97.1)	36 (2.9)	1068 (87.4)	154 (12.6)
Yes	324 (95.9)	14 (4.1)	327 (97.9)	7 (2.1)	287 (87.8)	40 (12.2)
Physician-diagnosed asthma based in register						
No	1344 (97.3)	38 (2.7)	1341 (97.5)	34 (2.5)	1201 (87.9)	166 (12.1)
Yes	175 (94.1)	11 (5.9)	176 (95.1)	9 (4.9)	154 (84.6)	28 (15.4)
Any asthma[§]						
No	1152 (97.3)	32 (2.7)	1148 (97.3)	32 (2.7)	1028 (87.6)	147 (12.5)
Yes	367 (95.6)	17 (4.4)	369 (97.1)	11 (2.9)	327 (87.4)	47 (12.6)

[1]Pass or higher in national test results for core subjects Swedish, English, and Mathematics.
[§]Asthma reported by questionnaire and/or in register (National Patient Register).

Higher rates of failure in final grades for Mathematics were found in children with parent-reported asthma ($p<0.05$) and physician-diagnosed asthma ($p<0.01$). Children with parent-reported or physician-diagnosed asthma were more likely to have failed final grades in Swedish than children without asthma ($p<0.05$). Final grades in English were not found to differ for either group (parent-reported and physician-diagnosed asthma) (Table 6).

Table 6. Dichotomized final grades (pass or fail) in core subjects Swedish, English, and Mathematics in relation to children with asthma.

Asthma measure	Swedish final grades		English final grades		Mathematics final grades	
	Pass[1] N (%)	Fail N (%)	Pass N (%)	Fail N (%)	Pass N (%)	Fail N (%)
Parent-reported asthma in questionnaire						
No	1237 (97.0)	38 (3.0)	1221 (95.8)	54 (4.2)	1210 (94.9)	65 (5.1)
Yes	332 (94.6)	19 (5.4)	335 (95.4)	16 (4.6)	321 (91.5)	30 (8.5)
Physician-diagnosed asthma based in register						
No	1388 (96.9)	45 (3.1)	1375 (96.0)	58 (4.0)	1358 (94.8)	75 (5.2)
Yes	181 (93.8)	12 (6.2)	181 (93.8)	12 (6.2)	173 (89.6)	20 (10.4)
Any asthma[§]						
No	1190 (97.0)	37 (3.0)	1175 (95.8)	52 (4.2)	1163 (94.8)	65 (5.2)
Yes	379 (95.0)	57 (3.5)	381 (95.5)	18 (4.5)	368 (92.2)	31 (7.8)

[1]Pass or higher in final grades for core subjects Swedish, English, and Mathematics.
[§]Asthma reported by questionnaire and/or in register (National Patient Register).

Multivariate analyses of asthma and outcomes in core subjects

Tables 7-9 show the logistic regression analyses of asthma measures and national test results and final grades in core subjects Swedish, English, Mathematics, respectively, presented in two models. The first model is unadjusted. The second model is adjusted for child and maternal characteristics as in the previous regression models.

Table 7 shows that children with physician-diagnosed asthma had higher risk of failed national test results in Swedish (OR: 2.22; CI: 1.12 – 4.43) and failed final grades in Swedish. After adjustment, the odds remained statistically significant for failed national test results (OR: 2.50; CI: 1.16 – 5.39), but not significant for failed final grades. Children with parent-reported asthma had a higher risk of failed final grades in Swedish (OR: 1.86; CI: 1.06 – 3.27). The association remained significant after adjusting for covariates (OR: 2.2; CI: 1.16 – 4.14).

Table 7. Odds ratios (OR) and 95% confidence intervals (CI) for the association between parent-reported asthma in questionnaire or physician-diagnosed asthma based in registers and failure in national assessment tests and final grades for core subject Swedish.

Asthma measure	Swedish national tests		Swedish final grades	
	Model 1[†]	Model 2[‡]	Model 1	Model 2
	OR[+] (95% CI[*])	OR (95% CI)	OR (95% CI)	OR (95% CI)
Parent-reported asthma in questionnaire				
No	Reference	Reference	Reference	Reference
Yes	1.48 (.78 – 2.78)	1.42 (.69 – 2.95)	1.86 (1.06 – 3.27)	2.2 (1.16 – 4.14)
Physician-diagnosed asthma based in register				
No	Reference	Reference	Reference	Reference
Yes	2.22 (1.12 – 4.43)	2.50 (1.16 – 5.39)	2.05 (1.06 – 3.94)	1.81 (.85 – 3.84)
Any asthma[§]				
No	Reference	Reference	Reference	Reference
Yes	1.67 (.92 – 3.04)	1.56 (.78 – 3.14)	1.70 (.97 – 2.96)	1.86 (.99 – 3.49)

[+]OR: odds ratio
[*]95% CI: 95% confidence intervals
[†]Model 1 represents crude analysis of exposures.
[‡]Model 2 is adjusted for gender, birth weight, gestational age, maternal smoking during pregnancy, maternal education, maternal country of birth.
[§]Asthma reported by questionnaire and/or in register (National Patient Register).

No association between asthma and national test results or final grades in English was found in the logistic regression analysis. However, the results were still presented in Table 8 for the sake of completeness.

Table 8. Odds ratios (OR) and 95% confidence intervals (CI) for the association between parent-reported asthma in questionnaire or physician-diagnosed asthma based in registers and failure in national assessment tests and final grades for core subject English.

Asthma measure	English national tests		English final grades	
	Model 1[†]	Model 2[‡]	Model 1	Model 2
	OR[+] (95% CI[*])	OR (95% CI)	OR (95% CI)	OR (95% CI)
Parent-reported asthma in questionnaire				
No	Reference	Reference	Reference	Reference
Yes	.71 (.31 – 1.61)	.70 (.28 – 1.75)	1.08 (.61 – 1.91)	.97 (.50 – 1.87)
Physician-diagnosed asthma based in register				
No	Reference	Reference	Reference	Reference
Yes	2.02 (.95 – 4.28)	1.70 (.71 – 4.10)	1.57 (.83 – 2.98)	1.44 (.69 – 3.00)
Any asthma[§]				
No	Reference	Reference	Reference	Reference
Yes	1.07 (.53 – 2.14)	.86 (.38 – 1.96)	1.70 (.97 – 2.96)	1.07 (.62 – 1.85)

[+]OR: odds ratio
[*]95% CI: 95% confidence intervals
[†]Model 1 represents crude analysis of exposures.
[‡]Model 2 is adjusted for gender, birth weight, gestational age, maternal smoking during pregnancy, maternal education, maternal country of birth.
[§]Asthma reported by questionnaire and/or in register (National Patient Register).

Table 9 shows that children with parent-reported asthma had higher risk of failed grades in Mathematics (OR: 1.74; CI: 1.11 – 2.73). In the adjusted analysis, the association remained statistically significant although slightly attenuated (OR: 1.72; CI: 1.03 – 2.87). Children with physician-diagnosed also had higher risk of failed grades in Mathematics, but the association was not significant after adjusting for covariates.

Table 9. Odds ratios (OR) and 95% confidence intervals (CI) for the association between parent-reported asthma in questionnaire or physician-diagnosed asthma based in registers and failure in national assessment tests and final grades for core subject Mathematics.

Asthma measure	Mathematics national tests		Mathematics final grades	
	Model 1[†]	Model 2[‡]	Model 1	Model 2
	OR[+] (95% CI[*])	OR (95% CI)	OR (95% CI)	OR (95% CI)
Parent-reported asthma in questionnaire				
No	Reference	Reference	Reference	Reference
Yes	.97 (.67 – 1.40)	.96 (.63 – 1.46)	1.74 (1.11 – 2.73)	1.72 (1.03 – 2.87)
Physician-diagnosed asthma based in register				
No	Reference	Reference	Reference	Reference
Yes	1.32 (.85 – 2.03)	1.17 (.72 – 1.91)	2.09 (1.25 –3.51)	1.75 (.96 – 3.19)
Any asthma[§]				
No	Reference	Reference	Reference	Reference
Yes	1.01 (.71 – 1.43)	0.99 (.66 – 1.47)	1.53 (.98 – 2.39)	1.44 (.86 – 2.39)

[+]OR: odds ratio
[*]95% CI: 95% confidence intervals
[†]Model 1 represents crude analysis of exposures.
[‡]Model 2 is adjusted for gender, birth weight, gestational age, maternal smoking during pregnancy, maternal education, maternal country of birth.
[§]Asthma reported by questionnaire and/or in register (National Patient Register).

Discussion

The purpose of this study was to examine the effects of asthma and asthma severity in childhood on academic outcomes in adolescence. No association was found between the prevalence and severity of asthma at age 12 as reported by parents and lower final grade scores or qualification to upper secondary school at age 15-16. On the other hand, children with a physician's diagnosis of asthma had a higher risk of not being qualified to upper secondary school at age 15-16, however final grade scores were comparable to healthy children. Thus, the results were dependent on whether asthma was defined by parental answers in an interview or as a physician's diagnosis from a medical register. The results of this study could pave the way for increased understanding of the educational situation of children with asthma and help explore the need for educational intervention and support in order to improve their academic performance. Previous studies found that gender, birth weight, gestational age, and socio-economic factors such as maternal smoking during pregnancy, maternal education, and minority status were major predictors for lower school outcomes (31, 32). Of note, after adjusting for these covariates in the present study, a physician's diagnosis of asthma in childhood still remained predicative of increased risk for not qualifying to upper secondary school (OR: 1.74; CI: 1.02 – 2.99).

The association between asthma diagnosis in childhood and qualification for further studies was a novel finding in this study. Our results indirectly support the findings of Moonie et al. that children with asthma were at increased risk of school absenteeism associated with grade retention, as shown in a large (n = 300,881) cohort study (15). The results of this study cannot be directly interpreted in a Swedish context since grade retention is exceptionally rare in European countries (20). However, students in Sweden who wanted to pursue further studies while being unqualified for upper secondary school at the end of grade nine, had to complete a preparatory program that lasted a maximum of one year (and in rare cases two years) in order to complete failed core subjects (33). Since students in Sweden usually pursue further studies after completing compulsory school, it could be argued that being unqualified for upper secondary school had the same practical implication as having to repeat one grade, namely to fall back one year behind their peers. Thus, Swedish children with asthma may be at risk of falling back one year in studies in order to complete preparatory courses for upper secondary school. Since increased drop-out rates has been reported to be associated with grade retention (34), it may be suggested that children with asthma are at increased risk of

dropping out of school. However, this potential association must be examined by further research.

Children with asthma were found to have lower final grade scores compared to healthy children in the unadjusted analysis. However, no association between any measure of childhood asthma and lower final grade scores could be established in the present study (Table 3), which contradicted the findings of Moonie et al. that childhood asthma was associated with slightly lower grade point averages (15). This discrepancy may be the result of differences in study population size. True difference in final grade scores between children with asthma and healthy children may be too small to be demonstrated in a relatively limited sample such as ours. Given an adequately powered sample such as that of Moonie et al. (n = 300,881), there is a possibility that the association between slightly lower final grade scores in children with asthma found in our unadjusted analysis would remain after adjustment. In general, systematic reviews and previous studies have not shown an association between asthma and lower academic outcomes (12, 14, 20). On the contrary, children with asthma reportedly performed as well or better than their healthy peers on standardized test scores, grade point averages, and grade progression (12, 14, 20). Whether the data in previous studies were derived from questionnaires, parental interviews or medical registers, in addition to varying study population size and adjustment for potential confounders, may have affected results. A validation study reported that 40% of children with asthma according to the ISAAC questionnaire lacked a medical record of asthma (30). A previous study of 288 children found that parental recall of asthma during the child's lifetime agreed to 87% when compared to medical records (35). The present study used parental answers from the ISAAC questions as a measure of asthma. Our results showed that the parental reports of around 60% of children with asthma were not substantiated by a physician's diagnosis. This could suggest a possibility of over-reporting of asthma by parents, which in the case of a relatively small study population ($n \approx 1{,}000$) such as ours may be problematic. However, in this study an additional measure of asthma diagnosis based in a validated national medical register was used, and an association between asthma and lower qualification for further studies was established that was stable when adjusted for possible confounding variables.

Previous research has not adjusted for all covariates used in the present study that affect academic outcomes such as gender, maternal education, and in utero smoking exposure

(maternal smoking during pregnancy). For example, a small cross-sectional study (n = 1,058) by Halterman et al. in 5 year-old children in kindergarten showed a lower school readiness skills in children with asthma reported by parents compared to healthy children, however this applied only to children with asthma who also had limitation of activity (36). The results were not adjusted for race and other socio-economic factors, and the results' generalizability to older children is limited. As already noted, the discrepancy in different study results may reflect the use of different measures of asthma in previous studies which define asthma diagnosis based on standardized questionnaires answered by parents with varied validation. A large epidemiological cross-sectional study from 1992 by Fowler et al. showed that children with asthma were at the same risk as non-asthmatic children of failing a grade after adjusting for gender, age, maternal education and socio-economic factors (37). Fowler et al. also found that childhood asthma was associated with learning disabilities (37). However, all exposure variables and outcomes in that study were based on subjective parental reports and were regarded as approximate by the same authors (37). This highlights the need of validated measures in studies that investigate the influence of childhood asthma on academic outcomes.

An unexpected result of this study was that academic outcomes did not vary with the influence of asthma severity, in contrast to a previous study carried out in the United States (14). This may reflect the use of different measures of asthma severity in both studies, but may also be accounted for by the higher proportion of minorities, primarily African-American children, in the US study population (95%) compared children in this study whose mothers were born outside of Scandinavia (6.8%). Poor urban minority youths are known to have both higher rates and more severe forms of asthma, to be less likely to have access to consistent medical care and use effective medication, to have higher exposure to asthma triggers and as a result have less control over asthma symptoms, more frequent exacerbations, hospitalizations and sleep-interruptions that may interfere with school performance (13). The lack of universal health care and gaps in health insurance in the United States at the time of the study (2002-2003), especially among poor urban minority youth and youth with asthma (13), may also explain this difference. Since health care is universal and free in Sweden, it is likely that children with severe asthma may have better access to health care, effective medication, and thus have a higher degree of disease control in Sweden compared to the United States.

In the descriptive analysis of national test results and final grades in core subjects for children with asthma, it appeared that children with parent-reported or physician-diagnosed asthma were more likely to have failed final grades in core subjects Swedish and Mathematics, and children with physician-diagnosed asthma had higher rates of failure in national test results for Swedish (Tables 5 and 6). The association between children with physician-diagnosed asthma and failed national test results in Swedish was stable in the adjusted analysis (OR: 2.50; CI: 1.16 – 5.39). This supports the findings of Kohen in a cohort study (n = 8,914) that children with asthma scored lower on standardized reading tests (38). However, children with physician-diagnosed asthma did not have significantly more failure in final grades in Swedish than children without asthma, which may be due to discrepancies between national test results and teacher's final grade assessment (27). Interestingly, the association between parent-reported asthma and failed final grades in Swedish and Mathematics was stable in the adjusted analysis (Tables 7 and 9). This finding was surprising, since it was expected that higher failure rates in any core subject would correspondingly be reflected in lower rates of qualification for upper secondary school and vice versa, given that core subjects form the basis of qualification to the next level of education. Nevertheless, no association was found between parent-reported asthma and qualification for upper secondary school. As noted, these disparate results may be explained by the lack of disease substantiation, in the form of a physician's diagnosis of asthma, for a high percentage of children with parent-reported asthma in this study. Our finding that these associations were not seen in children with physician-diagnosed asthma may support this explanation. Thus, the association between parent-reported asthma and higher failure rates final grades in Swedish and Mathematics may be due to parental over-reporting of asthma in children with poorer outcomes in these subjects. It may also be due to the lack of an adequately powered sample, as demonstrated by the findings of Moonie et al. that slightly lower grade point averages were found in a large cohort (n = 300,881) of children with asthma, despite the use of a reported measure of asthma in that study (15). Finally, in the unadjusted analysis, an association was found between children with physician-diagnosed asthma and failed final grades in core subjects Swedish and Mathematics. The association was not significant in the adjusted analysis. This may also be due to an inadequately powered sample, since it is improbable that lower rates of qualification should be found in children with physician-diagnosed asthma, without corresponding higher rates of failure in final grades for any core subject.

Strengths and limitations

This national longitudinal study with data from validated registers is the first of its kind to our knowledge. Validated measures of asthma diagnosis from medical records and objective measures of academic outcomes were used. Our study population was large and consisted of twins born between 1992 and 1994. Nevertheless, the results of this study should be interpreted with caution. First, data on school grades were only available for a small subset of the original cohort (around 15%). Second, the only measure of asthma severity was based on parental reports of number of asthma attack in the last 12 months. No clinical data, such as lung function, was available to serve as an objective assessment of asthma severity. Third, asthma severity was not modified by the use of medications to account for the impact of asthma control on academic outcomes. Fourth, the children in this study had to meet a set of conditions specific for the Swedish school system to qualify for upper secondary school. Thus, the qualification rate for further studies in children with asthma may vary in different school systems where other criteria are in use. Fifth, it may be possible that children with asthma, in order to compensate for missed time in school, are allocated extra pedagogical resources in school or receive extra parental support at home. The prevalence and impact of these important factors on academic outcomes were not accounted for in our study. Finally, the association between childhood asthma and academic outcomes was not adjusted for additional potential confounders, such as mental disabilities and school absence, which have been reported to negatively affect academic outcomes (11, 15, 20). Due to the nature of twin studies, the generalizability of this study to the general population may be of concern, although previous studies have noted that the risk of asthma does not differ between twins and singletons (39), and twins have been noted to have only slightly better grade point averages compared to singletons (40).

Further studies

Epidemiological studies using large cohorts need to be conducted in order to assess the association of childhood asthma and academic outcomes. Particularly, the mediating effect of school absenteeism on academic outcomes must be elucidated, and other potential mediators such as asthma-related sleep interruptions must be accounted for (12). Further studies need to identify and adjust for additional possible confounding variables such as mental diseases, use of asthma medications, and availability of extra pedagogical resources in school or extra parental support at home. Validated and objective measures of asthma diagnosis, asthma

severity (such as peak expiratory flow rate) and academic outcomes should preferentially be used in order to accurately estimate their association. Furthermore, the impact of extra pedagogical resources in school or at home on academic outcomes in children with asthma is of interest and could be explored in a prospective cohort study.

Practical implications

School failure may increase the risk for occupational failure, impaired social functioning, and mental disease later in life (10). In order to minimize major adverse effects on academic outcomes in children with asthma (e.g. qualification to upper secondary school), physicians need to make sure that the disease is well controlled and provide self-management tools to the patient in order to control asthma symptoms and manage asthma attacks. Schools need to minimize environmental factors that can provoke asthma attacks and result in school absenteeism through avoidance of triggers in children with asthma. Teachers need to allocate extra pedagogical resources to children with asthma that are at risk of school failure due to school absenteeism. Furthermore, parents to children with asthma have to provide educational support at home and help maintain high disease control.

Conclusions

This combined twin and register-based study showed an association between children with asthma diagnosis and lower qualification for upper secondary school at age 15-16. Children with asthma diagnosis were also found to be at risk of failing national tests in Swedish. Asthma severity was not found to be associated with lower academic outcomes. The results of this study suggest that further research needs to be carried out with larger cohorts in order to properly identify, quantify, and confirm factors that negatively affect the academic outcomes of children with asthma.

Acknowledgements

First and foremost, I want to extend my gratitude to my supervisor, medical doctor and paediatrician Kirsten Holmberg, for her unconditional support, advice, and guidance. I would also like to thank Tong Gong for her statistical help. Last but not least, I want to thank fellow students Rifat Chowdhury, Avan Hozali, Savas Kesen, Ahmed Subasic, and Manar Younes for their much-appreciated company during this semester.

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