Higher parental education was associated with better asthma control

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INTRODUCTION

Asthma is one of the most common chronic diseases among children, affecting children of all ages and different ethnic groups all over the world (1).

Treatment with inhaled corticosteroids (ICS) has improved asthma control and substantially reduced the need for hospitalisation (2,3). Nevertheless, despite improved asthma medication, there are still children who carry a heavy burden of asthma morbidity and poor quality of life (4,5). Factors that have been shown to affect the severity of asthma include passive smoking, allergic rhinitis and obesity (6–9). Allergic rhinitis, passive smoking and asthma triggered by house dust mites or pets are known to impair asthma control (10). The negative effects of asthma disease are particularly profound among children from low-income and minority families, suggesting a socioeconomic factor (11).

Uncontrolled asthma and severe asthma are not synonymous (12–14). Uncontrolled asthma is not necessarily severe asthma and vice versa. Insufficient asthma control can have several reasons such as poor adherence to prescribed medication, poor inhalation technique, allergen exposure, smoking or comorbid conditions. In the ERS/ATS guidelines on severe asthma, severe asthma in patients 6 years and above is defined as asthma that requires treatment with high-dose ICS and a long-acting beta-agonist (LABA) or a leukotriene antagonist to prevent it from becoming uncontrolled or remains uncontrolled despite this therapy (13).

According to international and national guidelines, asthma control should be prioritised in clinical asthma management, guiding the level of asthma treatment and the need for asthma check-ups (15,16). Despite this, up to date data on the prevalence of uncontrolled asthma in children

### Abbreviations

ACT, Asthma Control Test; aOR, Adjusted odds ratio; ATS, American thoracic society; BAMSE, Translates as Children Allergy Milieu Stockholm Epidemiology; ERS, European respiratory society; GINA, Global initiative for asthma; ICS, Inhaled corticosteroids; IgE, Immunoglobulin E; ISAAC, International study of asthma and allergies in childhood; LABA, Long-acting beta-agonist; OR, Odds ratio.

### Key notes

- Treatment with inhaled corticosteroids has improved control of asthma but data on uncontrolled asthma in children are scarce.
- Asthma control was examined with the Asthma Control Test in 12-year-old children in a population-based longitudinal birth cohort study.
- Of children with asthma, 15% had uncontrolled asthma where cat at home and rhinitis were confirmed risk factors, while higher education in parents was associated with better asthma control in the child.
are scarce. Acquiring control of asthma could possibly reduce the risk of exacerbations and increase quality of life in asthma patients (17).

We have prospectively studied a cohort of children born in 2003. Follow-ups at six months, one, four and eight years of age have been published previously and the children in our cohort had now reached the age of 12 years. We recently published a prevalence of current doctor-diagnosed asthma among the 12-year-olds of 6.4% (18). In the current study, we wished to characterise the asthma burden in our cohort from three different perspectives: the level of asthma control, the need for hospitalisation due to asthma and the use of asthma medication.

The aim of the study was to examine the prevalence of uncontrolled asthma at the age of 12 years and factors that affect asthma control. Improved knowledge of avoidable risk factors would benefit children with asthma and aid clinicians in managing asthma in line with Global Initiative for Asthma (GINA) guidelines to ‘minimise cost and maximise safety’ (15).

METHODS
Participants
Data were obtained from a prospective, longitudinal cohort study of children born in the region of western Sweden in 2003. Of the birth cohort, 50% (8176 infants) were randomly selected and invited to participate and 5654 families entered the study. After written informed consent, the parents answered postal questionnaires at 6 months and one, four, eight and 12 years of age. Details regarding the questionnaires and earlier response rates have been previously published (18–20). At 12 years, questionnaires were distributed to the families entering the study (4777/5654), excluding those that had declared that they no longer wished to participate. The response rate at 12 years was 76%, that is 3637 of the 4777 questionnaires distributed. This equalled 64% of the families entering the study and 90% of the responders at 8 years of age.

In the present study, we focused on the children with current asthma at 12 years of age, that is 233 children (18).

Information regarding parental education was collected at six months of age. A higher education was defined as reporting more than 12 years of education.

At 12 years, questions were asked regarding current health, airway symptoms, medical treatment for asthma, triggers of asthma, hospitalisation due to asthma, eczema, rhinitis, food allergy and allergic sensitisation. In addition, the answers to questions on parental smoking, both maternal and paternal, were collected at 12 years.

Definitions
Current asthma at 12 years of age was defined as reported doctor-diagnosed asthma and either current treatment or symptoms and was based on the answers to the following questions: ‘Has your child been diagnosed with asthma by a physician?’, ‘Has your child received medication for asthma during the last 12 months?’ and ‘Has your child had problems with, or symptoms of, wheezing during the last 12 months?’.

Current doctor-diagnosed allergic rhinitis was defined as reporting the medical diagnosis of allergic rhinitis (ever) plus symptoms of allergic rhinitis or medication use during the last 12 months (21).

Hospitalisation was defined as reported admission to hospital due to asthma during the past 12 months.

Asthma control was examined with the Asthma Control Test, ACT®. The test includes five questions with a score of 1–5 points per question. The questions ask for symptoms during the last 4 weeks. The maximum score is therefore 25. In accordance with recommendations, uncontrolled asthma was defined as a total score below 20 (22–24). The results from the ACT correlate well with the GINA guidelines regarding the prediction of uncontrolled asthma (25,26).

The questions asked at 12 years regarding allergic sensitisation, rhinoconjunctivitis, eczema, food allergy and asthma control are summarised in Table S1.

Statistical methods
In the statistical analysis, the methods used were frequencies, cross-tabulations, chi-square and binary logistic regression. Odds ratios (OR) were estimated with 95% confidence intervals (CI) in the binary logistic regression analysis and a p-value of <0.05 was considered to be statistically significant evaluated in the chi-square test.

Factors regarded as potential risk factors for uncontrolled asthma at 12 years are summarised in Table S2. The factors considered were based on risk factors for asthma previously identified in our cohort as well as factors identified from the literature, like, for example passive smoking.

Risk factors with a p-level of less than 0.1 in the univariate analysis were analysed in the multivariate model. A cut-off of 0.1 was chosen so that potential confounders would be included. Adjustments were made for all factors simultaneously in one multivariate model.

Uncontrolled asthma at 12 years of age was used as the primary outcome variable. Due to the expected low number of children hospitalised due to asthma, only univariate analyses of risk factors were made for that outcome.

The IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA) was used for statistical calculations.

Ethical approval
The study was approved by the ethics committee at the University of Gothenburg. All parents provided written informed consent.

RESULTS
Of the 233 children with current asthma at 12 years, we had information from 215 children regarding asthma control and 232 children regarding the need for hospitalisation due to asthma. Information on any asthma medication was available in 232 children, while 227 gave more specified information on asthma medication.
Asthma medication
The reported current asthma medication among children with current asthma at 12 years is summarised in Figure 1. It can be seen that 73% were receiving maintenance treatment with ICS, LABA or montelukast. In addition, short courses of oral corticosteroids (betamethasone) during the last 12 months were reported by 6.5% (15/232).

Asthma control
Of the children with current asthma, 15% (33/215) had an ACT value below 20, which was defined as uncontrolled asthma. Consequently, 85% (182/215) had well-controlled asthma, reporting ACT values of 20 or more. The median ACT value was 22, mean 21.9, range 12–25.

The results of the univariate analysis for uncontrolled asthma at 12 years of age (n = 215) are shown in Table 1, and the results of the multivariate analyses for uncontrolled asthma are shown in Figure 2. Independent risk factors for uncontrolled asthma at the age of 12 were wheeze triggered by exercise, cat at home and current doctor-diagnosed allergic rhinitis. Parental smoking was similar in children with controlled and uncontrolled asthma, 8% vs 9% (Table 1). A higher parental education in at least one parent independently reduced the risk of uncontrolled asthma at 12 years of age. Parental asthma did not affect the association between high parental education and uncontrolled asthma in the child and we found no interaction between parental asthma and level of parental education (p = 0.478).

In the group of children with controlled asthma, 61% (107/177) reported Immunoglobulin E, IgE, sensitisation to any airborne allergen compared with 63% (20/32) in the uncontrolled asthma group (p = 0.50). Sensitisation to cats in the group of children with controlled asthma was 40% (71/177) compared with 34% (11/32) in the uncontrolled asthma group (p = 0.69). Among subjects with a cat in the home (n = 37), sensitisation to cats was reported in 40% (4/10) with uncontrolled asthma, compared with 22% (6/27) in subjects with controlled asthma (p = 0.41).

The prevalence of maintenance treatment (93% vs. 82%), combination treatment (39% vs 25%) and short courses of oral steroids (9% vs 7%) were numerically higher in the group with uncontrolled asthma, compared to children with controlled asthma. However, the differences did not reach significance (p > 0.05).

Hospitalisation due to asthma
Hospitalisation due to asthma during the past 12 months at age 12 years was reported in six patients, that is 2.6% of the 232 children with current asthma and 0.2% if we considered the total population included in the follow-up at the age of 12 years (6/3,637).

The results of the univariate analysis of risk factors for hospitalisation during the last 12 months due to asthma are shown in Table S3. The risk of hospitalisation during the last 12 months due to asthma was higher among children with uncontrolled asthma and among those who reported mites and pollen as triggers. Two thirds (67%, 4/6) of the hospitalised children reported combination treatment with ICS and LABA or a combination of ICS and montelukast vs 25% (57/226) among the other children with asthma (p = 0.043).

Moreover, the children who were hospitalised due to asthma had to a larger extent received short courses of oral...
corticosteroids (betamethasone) in the last 12 months. Having a parent with asthma or a higher education was numerically less common among children who were hospitalised for asthma, but this did not reach statistical significance (Table S3).

DISCUSSION
In this study, asthma control was examined with ACT at age 12 years in a population-based birth cohort. Our main finding was that higher parental education reduced the risk of uncontrolled asthma. Furthermore, allergic rhinitis or having a cat at home increased the risk of uncontrolled asthma. The children who were hospitalised due to asthma appeared to have more severe and more allergic disease.

Global initiative for asthma and the Swedish National Board of Health and Welfare emphasise the use of standardised ways of following asthma control in the clinical management of asthma patients (15,16). The ACT has been shown to identify partially controlled and controlled asthma in a sufficient manner, and it is comparable with the Asthma Control Questionnaire test (26). Using standardised asthma control tests to guide the level of asthma medication and the need for follow-up in the individual patient increases asthma control and quality of life, while possibly reducing the risk of exacerbations (17).
Parental education and asthma control

The ACT has become popular when assessing the level of asthma control, since the test is simple and actively involves the patient. It can be filled out just before the patient meets the doctor. As a result, it is widely used in clinical outpatient practice. The development of the ACT was described in 2004 by Nathan et al. as a reliable and validated five-item tool to identify controlled asthma with a cut-off at 19 points (22). The reliability of the ACT test and the cut-off of 19 points has been confirmed by others (23). However, the terminology of the cut-off has varied from poorly controlled to not well controlled, as the test is considered by some to better identify controlled asthma than uncontrolled asthma (17,22,23,26).

ACT is based on symptoms, limitation of activities and need for rescue medication during the past 4 weeks. However, it should be emphasised that not all aspects of asthma control are captured by ACT. As pointed out by the International consensus on paediatric asthma, lung function, exacerbations and medication side effects are also important components of asthma control (27). Furthermore, it should be emphasised that uncontrolled asthma and severe asthma are not synonymous (12). The reason that the asthma is not controlled may have several explanations such as, for example poor adherence to prescribed medication, underprescription of medication in severe asthma, chronic allergen exposure or comorbidity (12).

The prevalence of uncontrolled asthma was 15% among children with current asthma in our cohort. On the other hand, 85% appeared to have satisfactory asthma control in our population-based cohort, which is comparable to results published in other studies where the ACT was used to determine asthma control. In a Japanese population-based study, uncontrolled asthma was 14.6% (28).

Higher parental education was found to reduce the risk of uncontrolled asthma. In a previous Swedish study, having parents without higher education was associated with a threefold increase in odds of problematic severe asthma versus controlled persistent asthma (6). Higher parental education is a marker for higher socioeconomic status. Socioeconomic factors have been shown in other studies to affect the degree of asthma control in children (11). The reason for this association is not fully known, but it is known that higher socioeconomic status is associated with less obesity and better feeding habits like eating more fish and fruit. Moreover, it is likely that parents with a higher education are better prepared to understand and interpret information regarding the asthma disease and the medical treatment. It is possible that higher parental education is associated with better adherence to therapy and follow-up. Taken together, our results support the advice given in national and international guidelines for asthma management (15,16) carefully to educate both children with asthma and their parents. In fact, it could be that some families might be in need of more educational efforts than others to even out the chance of good asthma control in the child.

We found that it was more common in the group with uncontrolled asthma to have a cat at home, but reported sensitisation to cat did not differ between controlled and uncontrolled asthma. However, among those that reported having a cat at home, 40% of subjects with uncontrolled asthma also reported sensitisation to cat, compared with 22% among those with controlled asthma. Thus, the asthma gets worse if you are allergic to cats and the family keeps a cat (29). Even though reported sensitisation did not differ between groups there may be differences in level of sensitisation and sensitisation to different allergen components. Severe asthma has been reported to be associated with multisensitisation to furry animal allergen components (29).

In addition, current allergic rhinitis was a risk factor for uncontrolled asthma, which is in line with other studies (6,8). Furthermore, we were able to confirm the link between asthma triggered by exercise and uncontrolled asthma. A common trait of uncontrolled asthma is having symptoms of asthma while exercising and it could very well be argued that wheeze triggered by exercise is a part of the uncontrolled asthma. One of the items in ACT asks how often the child used his or her rescue inhaler or nebuliser medication. In a child prone to experience exercise-induced asthma such an increased use of rescue inhaler will increase the association between asthma triggered by exercise and a low ACT. Recording of prophylactic use of a short-acting beta-agonist could as well increase such an association but probably to a lesser extent. Parental smoking was reported in only 8%-9% and was similar in children with controlled and uncontrolled asthma. Smoking in parents is relatively uncommon in Sweden today and perhaps therefore does not come out as a risk factor in the statistical analysis.

In our study, there was no significant association between prescribed medication and asthma control. However, combination treatment tended to be more prevalent among children with uncontrolled asthma.

In our material, only six subjects reported admission to hospital due to asthma, corresponding to 0.2% of the total population included in the follow-up at 12 years of age. This low admission rate corresponds well to previous studies from Gothenburg about two decades ago, where the admission rate in 2000 was 0.2% in the age group of five to 18 years (3).

Children in the hospitalised group had poorer asthma control and reported the use of combination treatment more often than subjects not hospitalised, suggesting that this is a group of children with more severe disease. However, we do not have data on compliance.

The strengths of this prospective follow-up include the large birth cohort size and the high response rate at 12 years. We used the ACT to measure the level of asthma control and the ACT has been shown to be a valid and reliable tool (22,23,26).

Questionnaire-based studies are accompanied by limitations relating to the validity and interpretation of the answers. To avoid this, we have used validated, well-known ISAAC- and BAMSE-based questions in our questionnaires. However, as our cohort was not clinically tested,
the answers are self-reported and there could be some uncertainty about the validity of the answers.

CONCLUSIONS
Of the 12-year-old children with asthma, 15% had uncontrolled asthma, that is ACT below 20. Higher education in the parents was associated with better asthma control in the children.

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CONFLICT OF INTEREST
The authors have no conflict of interests.

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Table S1** Questions on allergic sensitisation, diagnoses, symptoms and asthma control at age 12 years.

**Table S2** Variables considered in the univariate analyses as potential risk factors for uncontrolled asthma.

**Table S3** The univariate analyses of risk factors for hospitalisation during the last 12 months due to asthma.