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# Age at asthma diagnosis is related to prevalence and characteristics of asthma symptoms

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## ABSTRACT

**Background:** Although asthma may begin at any age, knowledge about relationship between asthma age of onset and the prevalence and character of different symptoms is scarce.

**Objectives:** The aim of this study was to investigate if adult-diagnosed asthma is associated with more symptoms and different symptom profiles than child-diagnosed asthma.

**Methods:** A FinEsS postal survey was conducted in a random sample of 16 000 20-69-year-old Finnish adults in 2016. Those reporting physician-diagnosed asthma and age at asthma diagnosis were included. Age 18 years was chosen to delineate child- and adult-diagnosed asthma.

**Results:** Of responders (N = 8199, 51.5%), 842 (10.3%) reported asthma diagnosis. Adult-diagnosed asthma was reported by 499 (59.3%) and child-diagnosed by 343 (40.7%). Of responders with adult-diagnosed and child-diagnosed asthma, 81.8% versus 60.6% used asthma medication ($p < 0.001$), respectively. Current asthma was also more prevalent in adult-diagnosed asthma (89.2% versus 72.0%, $p < 0.001$). Risk factors of attacks of breathlessness during the last 12 months were adult-diagnosis (OR = 2.41, 95% CI 1.64–3.54, $p < 0.001$), female gender (OR = 1.49, 1.07–2.08, $p = 0.018$), family history of asthma (OR = 1.48, 1.07–2.04, $p = 0.018$) and allergic rhinitis (OR = 1.49, 1.07–2.09, $p = 0.019$). All the analysed asthma symptoms, except dyspnea in exercise, were more prevalent in adult-diagnosed asthma in age- and gender-adjusted analyses ($p = 0.032$-$<0.001$) which was also more often associated with 5 or more asthma symptoms ($p < 0.001$) and less often with non-symptomatic appearance ($p < 0.001$) than child-diagnosed asthma.

**Conclusion:** Responders with adult-diagnosed asthma had more often current asthma and a higher and multiform asthma symptom burden, although they used asthma medication more often compared to responders with child-diagnosed asthma.

**Keywords:** Asthma, Age of onset, Symptom, Population study, Late-onset

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## INTRODUCTION

Asthma may occur at any age, and it varies from very symptomatic to mild or symptom-free. According to earlier research, age at asthma diagnosis may influence asthma burden and prognosis.[1-4] Adult-diagnosed asthma has been reported to be more often related to environmental and lifestyle factors compared to child-diagnosed asthma, which again is frequently associated with atopy and genetic factors.[2-5] Furthermore, adult-onset asthma has been reported to be associated with poorer treatment response and prognosis,[2,6] inferior lung function,[7] weaker working ability,[8] and non-remission[9-11] more often than child-onset asthma, which usually has a good prognosis and high probability to remit.[2,12,13] Though these differences have been proposed, studies unravelling the role of age at asthma diagnosis in general population samples are still scarce.[3,10,14,15]

Common symptoms of asthma are wheezing, shortness of breath, and cough. Reporting multiple asthma symptoms is associated with decreased lung function, increased airway inflammation, and bronchial hyperresponsiveness, reflecting uncontrolled and difficult asthma.[16,17] Insufficient medication adherence, poor inhaler technique, and comorbidities may worsen asthma control and lead to difficult-to-treat asthma. If these issues have been addressed and the symptom burden is still marked, asthma is considered severe.[18] Severe asthma may reportedly begin in childhood or adulthood, but the molecular findings of bronchial inflammation seem to differentiate between them, more symptomatic disease associating especially with eosinophilic bronchial inflammation.[3,19,20]

Most of the few studies on asthma symptom burden between early- and late-onset asthma have resulted in only little or no difference.[3,4,19,21] This is in contrary to reported differences between child- and adult-diagnosed asthma severity and prognosis;[2,6,10,15] therefore, a deeper understanding of differences in asthma symptom burden in adults with asthma ever diagnosed by a physician stratified by age at asthma diagnosis is needed, especially in the population level. Therefore, firstly, we aimed to test our hypothesis that asthma diagnosed in adulthood differs in reported symptoms both in quantitative and qualitative manner from asthma diagnosed in childhood in a general adult population. Secondly, we aimed to investigate if the risk factors of having asthma symptoms differ in adults with asthma characterized by age at diagnosis.

## MATERIAL AND METHODS

### Study subjects

In 2016, a cross-sectional random sample of totally 16 000 20-69-year-old adults, 8000 from both Helsinki and Western Finland areas, were collected from the Statistics Finland. The sample was sent a FinEsS respiratory questionnaire with up to 2 reminders.

### Study design

Detailed descriptions of the study methods and questionnaire and the complete Finnish FinEsS 2016 questionnaire are available elsewhere.[14,22]

The common variables were defined as follows.

*Physician-diagnosed asthma*. *An affirmative* answer to "Have you been diagnosed by a doctor as having asthma"?

*Current asthma*. Reporting *physician-diagnosed asthma* in combination with a positive answer to at least 1 of the following questions: (1) Have you had shortness of breath during the last 12 months, (2) Have you had any wheeze during the last 12 months, or (3) Do you currently use asthma medication.

*Age at asthma diagnosis*. "What age were you when asthma was diagnosed"?

Asthma diagnosis-age specific variables by reporting physician-diagnosed asthma and concomitantly age at diagnosis at.

0–17 years as child-diagnosed asthma and.

18–69 years as adult-diagnosed asthma.

Age 18 or 20 years is a frequently used cut-point in the age of asthma onset -studies.[3,14] It is also near the age when reimbursement right for asthma medication needs to be renewed in Finland (age 16 years) and when treatment of

asthma patients is shifted from pediatrics to pulmonology.

*Asthma medication use*. "Do you currently use asthma medication (permanently or as needed)"?

*Expenses to asthma medication*. The expenses were determined questionnaire-based in euros.

"Have you been diagnosed by a doctor as having allergic rhinitis caused by pollen (caused by, e.g., birch, grass, mugwort)" or "Have you been diagnosed by a doctor as having other allergic rhinitis (caused by, e.g., cat or dog, but not caused by pollen)"?

*Chronic rhinitis*. "Have you had longstanding nasal congestion" or "Have you had longstanding rhinitis"?

*Family history of asthma*. "Have any of your parents, brothers or sisters now or previously had asthma"?

*Co-existing chronic obstructive pulmonary disease (COPD)*. "Have you been diagnosed as having chronic bronchitis, chronic obstructive pulmonary disease (COPD) or emphysema by a doctor"?

*Occupational exposure to vapors, gases, dust, or funes (VGDF)*. "Does your working environment have now or has there previously been a lot of dusts, gases or fumes"?

"Did you live in the countryside (not in a city or suburb) during your first five years of life"?

*Living on a farm in childhood*. "Did you live on a farm during your first five years of life"?

*Exercise per week*. "Exercise in your free time: How often do you exercise at least 30 min so that you are at least slightly short of breath and get sweaty"?

*Attacks of breathlessness*. "Do you have now, or have you had asthma symptoms during the last 12 months (breathlessness with or without cough or wheezing)"?

*Wheeze*. "Have you had wheezing or whistling in your chest at any time in the last 12 months"?

*Asthmatic wheeze*. Reporting *wheeze* and affirmative responses to "Have you been at all breathless when the wheezing sound was present"? and "Have you had this wheezing or whistling when you did not have a cold"?

*Longstanding cough*. "Have you had a longstanding cough during the last 12 months"?

*Sputum production*. "Do you bring up phlegm on most days during periods of at least three successive months"?

*Dyspnea in cold*. "Do you usually have dyspnea or severe cough in cold weather"?

*Dyspnea in exercise*. "Do you usually have dyspnea or severe cough during exercise"?

*Dyspnea mMRC≥2*. "Do you have to walk slower than other people of your age because of dyspnea"?

*Morning dyspnea*. "Have you awakened with a feeling of tightness in your chest during the past 12 months"?

The *number of asthma symptoms* comprised of the following 8 symptoms: *wheeze, longstanding cough, sputum production, dyspnea in cold, dyspnea in exercise, dyspnea mMRC≥2, attacks of breathlessness,* and *morning dyspnea*.

## Methods & analysis

Statistical analyses were conducted with SPSS Statistics version 25. To compare categorical groups, chi-square test was utilized. Similarly, when comparing normally and non-normally distributed continuous variables between two categorical variables, *t*-test and Mann-Whitney test were utilized, respectively. A p-value of $<0.05$ was considered statistically significant.

Multivariable binary logistic regression was used to determine independent associations between covariates and attacks of breathlessness in $\leq$12 months in odds ratios (OR) and 95% confidence intervals (CI). The covariates were included in the model by potential confounding effect measured by individual statistical associations with the outcome variable as well as previous knowledge from the literature and clinical experience.

Subjects with incomplete data on smoking habits were excluded from analyses. Sensitivity analyses were conducted by excluding subjects with co-existing COPD and by conducting analyses also only in responders with current asthma.

## RESULTS

After 2 reminders, 51.5% (n = 8199) responded. Of responders, 10.3% (n = 842) reported an asthma diagnosis by a physician, and age at diagnosis. Responders with asthma were more often female than male, and their median age was 47 years. Almost every second patient (46.8%) was a never smoker, but 23.4% reported current smoking. Asthma medication use was reported by 73.2%. More comprehensive basic responder and non-responder analyses are reported elsewhere.[10,14,22]

Adult-diagnosed asthma was reported by 59.3% (n = 499) and child-diagnosed by 40.7% (n = 343) of responders. In adult-diagnosed asthma, allergic rhinitis (49.1% versus 70.6%, $p < 0.001$) was less frequent, and mean body mass index (BMI) was higher (27.4 versus 25.7, $P < 0.001$) compared to child-diagnosed asthma (Table 1). In addition, prevalence of current asthma was higher (89.2 versus 72.0%, $p < 0.001$), and expenses to asthma medication were higher in adult-diagnosed than child-diagnosed asthma (median 180 versus 50 euros, $p < 0.001$).

Different asthma symptoms by age at diagnosis are shown in Table 2 in all responders with asthma diagnosed by a physician. In age and gender-adjusted analysis, all the individually analysed symptoms, except dyspnea in exercise, were more prevalent in those with adult-diagnosis compared to those with child-diagnosis. In addition, the number of asthma symptoms was higher in adult-diagnosed asthma than child-diagnosed (median 4 versus 3 symptoms, $p < 0.001$). There were also significantly more responders with 5 or more reported asthma symptoms in responders with adult-diagnosis ($p < 0.001$) (Fig. 1).

To exclude the possibility that the differences in asthma symptoms would be due to co-existing COPD, which prevalence was 9.5% in subjects with ever having asthma diagnosed by a physician, we made sensitivity analysis by excluding co-existing COPD. As a result, only asthmatic wheeze and dyspnea mMRC≥2 lost their significance while all the other significant differences stayed the same (Supplementary Table 1). We also did a logistic regression analysis in which longstanding cough was the outcome variable and age, age at asthma diagnosis, hypertension, coronary artery disease, heart failure, atrial fibrillation, and gastro-esophageal reflux disease independent variables. In this analysis, adult-diagnosed asthma was still significantly associated with longstanding cough ($p < 0.001$).

A gender disparity is reported in asthma,[23] and was present also in our results as male gender was more prevalent in child-diagnosed compared to adult-diagnosed asthma ($p < 0.001$). Therefore, we studied if asthma symptoms differentiated in age at asthma diagnosis defined groups between genders, and also if asthma symptoms differentiated in males and females by age at asthma diagnosis. Gender-specific differences in age-adjusted analyses were found in child-diagnosed asthma in dyspnea in cold, dyspnea in exercise, dyspnea mMRC≥2 and attacks of breathlessness. In adult-diagnosed asthma, significant findings were seen in wheeze, and dyspnea in cold (Table 3). All the symptoms with a statistically significant difference were more common in females, except wheeze in adult-diagnosed asthma in males. In males, more and stronger significant differences were found when asthma symptoms were analysed between child- and adult-diagnosed asthma.

As asthma remission is reportedly more common in child-diagnosed asthma,[2,11,13] we wanted to find out if the responders with remitted child-diagnosed asthma would explain the results and the comparisons were also performed in patients with current asthma. Demographics of responders with current asthma are reported in Supplementary Table 2. Longstanding cough and attacks of breathlessness were significantly more prevalent in adult-diagnosed current asthma (Fig. 2), and excluding co-existing COPD in current asthmatics did not change the result (data not shown). Reporting 8 asthma symptoms was more common in responders with adult-diagnosed current asthma than in child-diagnosed ($p = 0.005$) (Supplementary Fig. 1).

We also did an analysis of asthma symptoms in which asthma was categorized by age at diagnosis using age 60 years as the delineation point (Supplementary Table 3) and in adjusted analysis not any symptom prevalence differed between these age at diagnosis strata.

| | All with physician-diagnosed asthma N = 842 | | Child-diagnosed asthma N = 343 | | Adult-diagnosed asthma N = 499 | | P |
|---|---|---|---|---|---|---|---|
| | med | $Q_1$-$Q_3$ | med | $Q_1$-$Q_3$ | med | $Q_1$-$Q_3$ | |
| Age | 47 | 32–61 | 33 | 26–43 | 56 | 44–64 | **<0.001** |
| Age at diagnosis | 23 | 10–40 | 8 | 4–12 | 38 | 27–49 | **<0.001** |
| Years since diagnosis | 19 | 10–28 | 25 | 18–36 | 14 | 6–23 | **<0.001** |
| Expenses to asthma medication per year (€)[a] | 100 | 20–230 | 50 | 0–100 | 180 | 70–300 | **<0.001** |
| | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | |
| BMI[b] | 26.7 | 5.3 | 25.7 | 4.8 | 27.4 | 5.5 | **<0.001** |
| | **N** | **%** | **N** | **%** | **N** | **%** | |
| Male | 369 | 43.8 | 183 | 53.4 | 186 | 37.3 | **<0.001** |
| Co-existing COPD | 80 | 9.5 | 9 | 2.6 | 71 | 14.2 | **<0.001** |
| Smoking | | | | | | | **<0.001** |
| • Never | 394 | 46.8 | 176 | 51.3 | 218 | 43.7 | |
| • Current | 197 | 23.4 | 89 | 25.9 | 108 | 21.6 | |
| • Ex | 251 | 29.8 | 78 | 22.7 | 173 | 34.7 | |
| Allergic rhinitis | 487 | 57.8 | 242 | 70.6 | 245 | 49.1 | **<0.001** |
| Chronic rhinitis | 479 | 56.9 | 168 | 49.0 | 311 | 62.3 | **<0.001** |
| Asthma medication use | 616 | 73.2 | 208 | 60.6 | 408 | 81.8 | **<0.001** |
| Current asthma | 692 | 82.2 | 247 | 72.0 | 445 | 89.2 | **<0.001** |
| Family history of asthma | 375 | 44.5 | 153 | 44.6 | 222 | 44.5 | 0.973 |

(continued)

| | All with physician-diagnosed asthma N = 842 | | Child-diagnosed asthma N = 343 | | Adult-diagnosed asthma N = 499 | | P |
|---|---|---|---|---|---|---|---|
| | med | $Q_1$-$Q_3$ | med | $Q_1$-$Q_3$ | med | $Q_1$-$Q_3$ | |
| Living in rural area in childhood[c] | 393 | 47.2 | 133 | 38.9 | 260 | 53.1 | **<0.001** |
| Living on a farm in childhood[d] | 226 | 27.3 | 59 | 17.3 | 167 | 34.4 | **<0.001** |
| Exercise ≥2 times per week[e] | 573 | 69.9 | 233 | 68.3 | 340 | 69.5 | 0.713 |
| Occupational exposure to VGDF[f] | 318 | 39.0 | 106 | 31.5 | 212 | 44.3 | **<0.001** |

**Table 1. (Continued)** Demographics of responders ever been diagnosed with asthma by a physician and of adult-diagnosed and child-diagnosed asthma strata and statistical comparison of the strata. *Statistical comparison between adult- and child-diagnosed asthma by chi-square test in categorical, t-test in normally and Mann-Whitney test in non-normally distributed continuous variables. Bolded text indicates a statistically significant P-value (P < 0.05). Missing: [a] = 231, [b] = 12, [c] = 10, [d] = 15, [e] = 22, [f] = 27. Abbreviations: BMI, Body Mass Index; COPD, Chronic Obstructive Pulmonary Disease; Med, Median; Q1-Q3, Quartiles; SD, Standard Deviation*

| | All with physician-diagnosed asthma N = 842 | | Child-diagnosed asthma N = 343 | | Adult-diagnosed asthma N = 499 | | P[a] |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | |
| Wheeze | 452 | 53.7 | 158 | 46.1 | 294 | 58.9 | **<0.001** |
| Longstanding cough | 297 | 35.3 | 88 | 25.7 | 209 | 41.9 | **<0.001** |
| Sputum production | 257 | 30.5 | 75 | 21.9 | 182 | 36.5 | **0.005** |
| Asthmatic wheeze | 489 | 58.1 | 82 | 23.9 | 145 | 29.1 | **0.032** |
| Dyspnea in cold | 437 | 51.9 | 152 | 44.3 | 285 | 57.1 | **0.009** |
| Dyspnea in exercise | 444 | 52.7 | 162 | 47.2 | 282 | 56.5 | 0.084 |
| Dyspnea mMRC≥2 | 228 | 27.1 | 52 | 15.2 | 176 | 35.3 | **0.023** |
| Morning dyspnea | 342 | 40.6 | 119 | 34.7 | 223 | 44.7 | **0.003** |
| Attacks of breathlessness | 552 | 65.6 | 183 | 53.4 | 369 | 73.9 | **<0.001** |

**Table 2.** Asthma symptoms in responders ever been diagnosed with asthma by a physician and in child-diagnosed and adult-diagnosed asthma strata, and statistical comparison of the strata *Statistical comparison between adult- and child-diagnosed asthma by chi-square test. [a]Adjusted by age and gender. Bolded text indicates a statistically significant P-value (P < 0.05)*

As allergic asthma is more common among asthmatics diagnosed at younger age one could question whether the results seen in this study would be explained by different allergic status instead of age at diagnosis. Therefore, we did a linear regression analysis with the number of asthma symptoms as the dependant variable, and age, age at asthma diagnosis and physician-diagnosed allergic rhinitis as the independent variables. In this analysis, adult-diagnosed asthma had an odds ratio of 6.0 ($p < 0.001$) and physician-diagnosed allergic rhinitis 2.0 ($p = 0.05$).

Multivariable binary logistic regression analyses on the risk factors of attacks of breathlessness in the last 12 months in responders ever been diagnosed with asthma by a physician as well as in child and adult-diagnosed asthma are given in Table 4. Some responders had missing data in covariates included in the regression analyses, the included number of responders is indicated in Table 4. Three separate regression analyses were conducted, and gender, family history of asthma, smoking, occupational exposure to VGDF, living in rural area in childhood, living on a farm in childhood, BMI, age at asthma diagnosis, exercise per week, allergic rhinitis, age, and co-existing COPD were included in the model. Significant risk factors for attacks of breathlessness in the last 12 months in physician-diagnosed asthma were female gender, family history of asthma, adult-diagnosed asthma, and allergic rhinitis. In child-diagnosed asthma, the risk factors were family history of asthma and allergic rhinitis and in adult-diagnosed asthma, co-existing COPD.

To test if the result differs when co-existing COPD is excluded, we performed sensitivity analyses where the significant variables remained similar (Supplementary Table 3). Similar regression analysis in current asthma is reported in Supplementary Table 5.

## DISCUSSION

Adults with asthma diagnosed at adult age were more often symptomatic and had multiple asthma symptoms compared to adults with asthma diagnosed in childhood in this population-based study, even though they used asthma medication more frequently. The greatest risk factor for being symptomatic was diagnosis of asthma in adult age.

Asthma beginning in childhood is usually associated with good treatment response and prognosis, whereas asthma beginning in adulthood is more often a chronic disease.[6,10,11,13,24] We examined asthma symptom prevalence in adults ever being diagnosed with asthma by a physician. Our hypothesis was that adults with adult-diagnosed asthma would be more symptomatic than adults with child-diagnosed asthma. Our results confirmed this hypothesis. The results

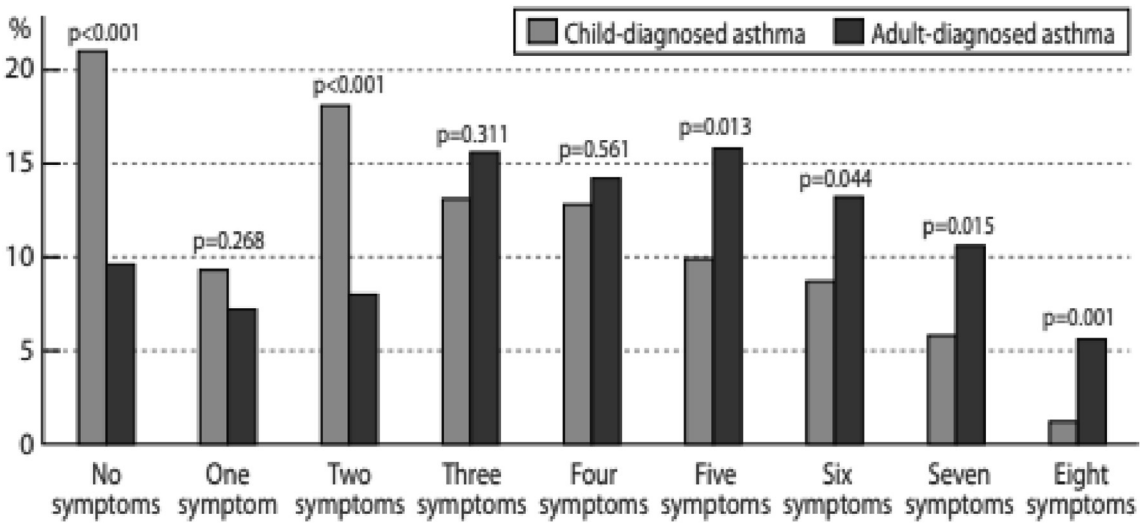


**Fig. 1** The burden of asthma symptoms in responders with child- and adult-diagnosed asthma separately as the proportion of responders (%) having zero to eight from the following asthma symptoms: wheeze, longstanding cough, sputum production, dyspnea in cold, dyspnea in exercise, dyspnea mMRC≥2, morning dyspnea and attacks of breathlessness. *P*-values are given above the columns, respectively

| | Child-diagnosed asthma N = 343 | | | | P[a] | Adult-diagnosed asthma N = 499 | | | | P[a] | P[b] | P[c] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male N = 183 | | Female N = 160 | | | Male N = 186 | | Female N = 313 | | | | |
| | N | % | N | % | | N | % | N | % | | | |
| Wheeze | 80 | 43.7 | 78 | 48.8 | 0.42 | 121 | 65.1 | 173 | 55.3 | **0.036** | **<0.001** | **0.039** |
| Longstanding cough | 41 | 22.4 | 47 | 29.4 | 0.14 | 74 | 39.8 | 135 | 43.1 | 0.44 | **<0.001** | **0.016** |
| Sputum production | 38 | 20.8 | 37 | 23.1 | 0.57 | 73 | 39.2 | 109 | 34.8 | 0.23 | **0.010** | 0.156 |
| Asthmatic wheeze | 39 | 21.3 | 43 | 26.9 | 0.26 | 61 | 32.8 | 84 | 26.8 | 0.18 | **0.021** | 0.433 |
| Dyspnea in cold | 69 | 37.7 | 83 | 51.9 | **0.009** | 90 | 48.4 | 195 | 62.3 | **0.003** | 0.196 | **0.014** |
| Dyspnea in exercise | 76 | 41.5 | 86 | 53.8 | **0.023** | 101 | 54.3 | 181 | 57.8 | 0.47 | 0.136 | 0.299 |
| Dyspnea mMRC≥2 | 19 | 10.4 | 33 | 20.6 | **0.002** | 55 | 29.6 | 121 | 38.7 | 0.085 | **0.026** | 0.261 |
| Morning dyspnea | 57 | 31.1 | 62 | 38.8 | 0.16 | 80 | 43.0 | 143 | 45.7 | 0.49 | **0.017** | 0.057 |
| Attacks of breathlessness | 86 | 47.0 | 97 | 60.6 | **0.015** | 134 | 72.0 | 235 | 75.1 | 0.53 | **<0.001** | **0.004** |

**Table 3.** Gender-specific asthma symptoms and statistical comparison of asthma symptoms in child-diagnosed and adult-diagnosed asthma by gender. *[a]Statistical comparison between males and females by age at asthma diagnosis with chi-square test, adjusted by age. [b]Statistical comparison in males and. [c]females by age at asthma diagnosis with chi-square test, adjusted by age. Bolded text indicates a statistically significant P-value ($P < 0.05$)*

remained similar when co-existing COPD was excluded. In adjusted sensitivity analysis conducted with current asthma, the results on asthmatic wheeze and some dyspnea symptoms disappeared but remained on longstanding cough and attacks of breathlessness. This indicates that asthmatics with adult-diagnosis being more symptomatic is not totally explained by asthmatics with child-diagnosis being in remission, that is, symptomless, more often.

Lung function has often been the primary endpoint in clinical studies reflecting asthma control;[4,7,25] whereas the difference in asthma symptoms is less studied, especially in study settings considering age at asthma diagnosis or in the population level.[3,4,7,19] The goal of asthma treatment is to gain good asthma control,[26] meaning symptom control and prevention of disease progression. Therefore, our results are of relevance in the everyday clinic. Furthermore, asthma symptoms and different inflammation markers of asthma are shown to be in concordance,[17] suggesting that assessment of symptoms would be valid to be used as a proxy for the activity of the underlying pathological process.

Many previous studies comparing asthma by age at diagnosis have found little and controversial differences in symptoms between child- and adult-onset asthma.[3,4,19,21] However, some studies have indicated that adult-onset asthma would be less controlled[7,15] in parallel to our finding that multiple symptoms were significantly more prevalent in ever and current adult-diagnosed than child-diagnosed asthma. The controversy probably results from differences in study design–data source, asthma definition, and inclusion criteria. We studied primarily ever, not current asthma.

Gender differences in asthma symptoms are well-established in asthma.[23,27] In our study, adult females with child-diagnosed asthma reported asthma symptoms more frequently than males, which probably results somewhat from higher remission rate in males with child-diagnosed asthma in our data. In adult-diagnosed asthma, there seemed to be difference in reported symptoms; in females, dyspnea in cold and in males, wheezing, was significantly more prevalent than in the other gender, possibly indicating different pathophysiology on average between genders. Similar analysis has not been published by far to the best of our knowledge.

In the present study, the greatest independent risk factor for current attacks of breathlessness was adult-diagnosed asthma. Obesity did not increase this risk significantly. Regular physical exercise has previously been reported to improve asthma

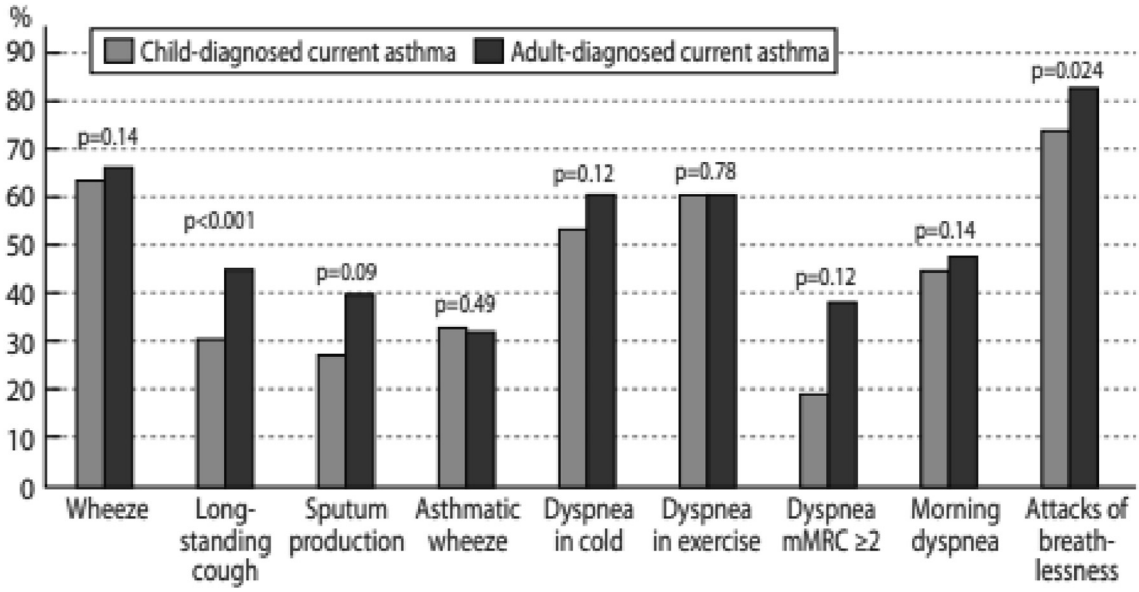


**Fig. 2** The prevalence (%) of asthma symptoms in responders with current child- and adult-diagnosed asthma defined by age at asthma diagnosis. Age-adjusted *P*-values are given above the columns, respectively

| | All with physician-diagnosed asthma N = 773 | P | Child-diagnosed asthma N = 325 | P | Adult-diagnosed asthma N = 448 | P |
|---|---|---|---|---|---|---|
| | OR (95% CI) | | OR (95% CI) | | OR (95% CI) | |
| Female | 1.49 (1.07–2.08) | **0.018** | 1.62 (0.99–2.66) | 0.055 | 1.40 (0.88–2.25) | 0.16 |
| Family history of asthma | 1.48 (1.07–2.04) | **0.018** | 2.04 (1.23–3.35) | **0.005** | 1.16 (0.74–1.81) | 0.52 |
| Smoking | | | | | | |
| • Never | 1 | | 1 | | 1 | |
| • Current | 1.17 (0.77–1.78) | 0.46 | 1.19 (0.66–2.15) | 0.55 | 1.13 (0.60–2.13) | 0.70 |
| • Ex | 0.91 (0.62–1.33) | 0.62 | 0.81 (0.44–1.49) | 0.50 | 0.95 (0.57–1.56) | 0.82 |
| Occupational exposure to VGDF | 1.25 (0.88–1.77) | 0.21 | 1.24 (0.73–2.11) | 0.43 | 1.18 (0.74–1.89) | 0.49 |
| Living in rural area in childhood | 1.05 (0.70–1.56) | 0.82 | 0.82 (0.45–1.48) | 0.51 | 1.27 (0.72–2.23) | 0.40 |
| Living on a farm in childhood | 1.19 (0.75–1.90) | 0.46 | 1.54 (0.70–3.36) | 0.28 | 1.10 (0.60–2.01) | 0.77 |
| BMI | | | | | | |
| • <24,99 | 1 | | 1 | | 1 | |
| • 25–29,99 | 0.94 (0.65–1.37) | 0.75 | 0.81 (0.46–1.44) | 0.48 | 0.96 (0.57–1.59) | 0.86 |
| • 30–34,99 | 1.20 (0.75–1.91) | 0.45 | 1.24 (0.63–2.44) | 0.54 | 1.11 (0.57–2.17) | 0.76 |
| • >35 | 2.07 (0.93–4.59) | 0.07 | 2.71 (0.64–11.51) | 0.18 | 1.73 (0.65–4.60) | 0.27 |
| Adult-diagnosed asthma | 2.41 (1.64–3.54) | **<0.001** | N/D | | N/D | |
| Exercise <2 times per week | 1.25 (0.88–1.79) | 0.21 | 1.13 (0.68–1.88) | 0.65 | 1.54 (0.90–2.61) | 0.11 |
| Allergic rhinitis | 1.49 (1.07–2.09) | **0.019** | 2.25 (1.33–3.79) | **0.002** | 1.12 (0.71–1.75) | 0.63 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Age | | | | | | |
| • 60-69 | 1 | | 1 | | 1 | |
| • 50-59 | 1.12 (0.66–1.89) | 0.67 | 0.47 (0.14–1.61) | 0.23 | 1.48 (0.80–2.76) | 0.22 |
| • 40-49 | 0.76 (0.45–1.29) | 0.31 | 0.48 (0.15–1.49) | 0.20 | 0.75 (0.39–1.44) | 0.39 |
| • 30-39 | 0.76 (0.45–1.29) | 0.31 | 0.50 (0.17–1.45) | 0.20 | 0.71 (0.36–1.39) | 0.32 |
| • 20-29 | 1.30 (0.73–2.32) | 0.37 | 0.75 (0.26–2.15) | 0.60 | 2.13 (0.65–7.00) | 0.21 |
| Co-existing COPD | 2.02 (1.0–4.08) | 0.052 | 1.15 (0.23–5.83) | 0.87 | 2.37 (1.05–5.35) | **0.038** |

**Table 4.** Risk factors of attacks of breathlessness in the past 12 months in binary multivariable logistic regression in responders ever been diagnosed with asthma by a physician and in its subcategories, child-diagnosed and adult-diagnosed asthma. *Three different regression analyses were conducted. All the reported variables were included in the model simultaneously. Bolded text indicates a statistically significant P-value ($P < 0.05$)*

control.[28,29] The present results were in line with this as for current adult-diagnosed asthmatics exercising less than 2–3 times a week was a risk factor for attacks of breathlessness. Smoking did not increase the risk of having asthma symptoms in asthmatic responders in the present study, somewhat in contrary to previous results,[4] in which COPD was suggested to explain some of the results. However, we did not have data on pack-years. Nevertheless, adult-diagnosed asthmatics were more symptomatic than child-diagnosed even when co-existing COPD was excluded in this study.

Associative factors with attacks of breathlessness in adult-diagnosed and child-diagnosed asthma were distinct. Allergic diseases have been recognized as a risk factor for poor asthma control in child-diagnosed asthma[15,21] which is in line with our findings as family history of asthma and allergic rhinitis were associated with attacks of breathlessness in child-diagnosed asthma, whereas the only risk factor in adult-diagnosed asthma for attacks of breathlessness was co-existing COPD.

Responders with adult-diagnosed asthma had more asthma symptoms than those with child-diagnosed asthma in our study. In previous Nordic studies, multi-symptom asthma, defined as physician-diagnosed asthma, asthma medication use, and having multiple asthma symptoms,[16] reflected more severe or uncontrolled disease. Furthermore, uncontrolled asthmatics were prone to exacerbations, and 2% of the Swedish primary health care asthma population, characterized by higher age, were seen to have frequent exacerbations.[30] Therefore, based on the results in the present and past studies, adult-diagnosis would reflect a risk for multi-symptom disease and more severe asthma. Previous studies have suggested obesity and smoking to be associated with an uncontrolled disease in adult-onset asthma and these potential risk factors for being symptomatic need an active assessment in patients with adult-onset asthma, to ensure good asthma control.[11]

One could question if there is a difference in patients' education or socioeconomic status at the time of the diagnosis if asthma is diagnosed in childhood compared to a diagnosis in adulthood,

which could potentially lead to differences in medication adherence and a difference in asthma symptom burden. Another Finnish study of adult-onset asthma reported that patients mainly followed in secondary care had poorer adherence to inhalation steroids whereas patients followed in primary health care were adherent to the treatment.[31] As most asthma patients are followed in primary care in Finland the results seen in our study seem unlikely to depend on poorer adherence in responders with adult-diagnosed asthma. Unfortunately, we did not have adherence data in our study.

Living in a rural area or on a farm in childhood was more common among asthmatics diagnosed in adulthood. Another recent paper from the same study cohort reported that childhood exposure to a farming environment did not increase the odds for having asthma. However, it did increase the odds for having asthma diagnosed at late age (defined as age >40).[32]

It has been speculated if adult-onset asthma would be a relapse rather than initiation of the disease and whether asthma symptoms beginning in adulthood would have originated in childhood.[33,34] However, subjects with adult-onset versus child-onset asthma seem to have different basic characteristics, such as gender and BMI,[2,14] which challenges this assumption. In addition, we are beginning to understand the genetic differences between child- and adult-diagnosed asthma due to recent data[5] suggesting that there indeed is a difference in pathophysiology between these age at diagnosis defined groups. These findings show that genetic risk loci are partly similar in both asthma groups but with smaller effects in adult-onset asthma where non-genetic factors may play a more important role.[2]

A substantial part of asthma-related costs for society is caused by sickness absence, and work disability. The risk for work disability correlates with asthma diagnosis age; the later in life asthma is diagnosed, the greater the risk for work disability.[35] Having asthma has been reported to increase the risk of sickness absence markedly in Finland, and having asthma symptoms increased the risk even further.[36,37] Our results are in line with these findings, as responders with adult-diagnosed asthma were more symptomatic. In the present study, the expenses to asthma medication were almost 4-fold in adult-diagnosed compared to child-diagnosed asthmatics. These findings underline the importance of targeting treatment and control visits for this symptomatic patient group of adult-diagnosed asthma both in specialist care and in primary health care to avoid both individual and communal socioeconomic problems and inequality.

The present study has several strengths. We had a large, age comprehensive general population sample. The study sample includes responders both from the city area (Helsinki) and from the countryside (Western Finland). The FinEsS-study has been started already in 1996, and the questionnaire is empirically validated. We had a relatively good response rate considering the decline in response rates during the last decades, and we have previously discussed the matter that the response rate should not affect the results markedly.[14] Therefore, we believe that the current results are well generalizable to the general population. In addition, we asked for physician-diagnosed asthma and age at diagnosis. Considering that asthma diagnoses are based on objective lung function measurements due to the drug reimbursement system in Finland, diagnoses of asthma in this questionnaire-based study are considered reliable.[38]

This study is cross-sectional and therefore descriptive by manner. Recall bias is the main consideration regarding weaknesses in study methods. However, in an earlier study, the age of asthma onset with moderate recall periods was found to be precise, although insensitively centered on mild asthma.[39] Mislabeling of symptoms of other disorders as asthma symptoms and the other way around is also a concern, which is presumably a common problem interplaying between research and clinical practice.[40] Cohort effect is also a matter to consider since the study was cross-sectional and asthma diagnoses retrospective. These considerations could have modified the study result, but we believe that not in a critical amount considering the main results.

In conclusion, asthma diagnosed at adult age is associated with abundant and multiform individual symptoms. Being a common disease, asthma is encountered in the general primary health care population daily. Therefore, recognizing patient

groups with adult-diagnosis and those who would or would not benefit from asthma controls and specialist care is crucial both for resource optimization and for gaining comprehensively better asthma control.

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### Availability of data and materials
The datasets used and analysed in this current study are available from the corresponding author on reasonable request.

### Authors' contributions
HH-M, JH, PPi, PPa, PI and HK designed the study and wrote the report. JH and HH-M performed the statistical analyses with help from PI and PPi. PPi, PPa, AL, AS and HH-M contributed to the FinEsS Helsinki sample, population sample and questionnaires. HK, PI, HA and LT contributed to the FinEsS Western sample. All authors contributed to interpretation of the data and made critical revisions of the manuscript. All authors read and approved the final version of the publication and gave consent to publication.

### Ethics approval
The study was approved by the Coordinating Ethics Committee of Helsinki and Uusimaa Hospital District (200/13/03/00/2015).

### Potential competing interests
Päivi Piirilä reports financial support from NordForsk Foundation. Leena Tuomisto reports payments for lectures from GlaxoSmithKline, AstraZeneca and Boehringer Ingelheim. Helena Backman reports payments for scientific presentations from AstraZeneca and Boehringer Ingelheim. Hannu Kankaanranta reports personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi Pharma AB, GlaxoSmithKline, MSD, Orion Pharma, Novartis, Sanofi Genzyme and fees for lectures from AstraZeneca, Orion Pharma and Mundipharma. Lauri Lehtimäki reports payments for lectures from AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia, GSK, Mundipharma, Novartis, Sanofi, Orion Pharma and additionally Advisory Boards participation for Alk, AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, Sanofi, OrionPharma. LL reports owning stocks of Auscultching Oy and being PI in clinical trials/studies sponsored by OrionPharma. Pinja Ilmarinen reports lecture fees from GlaxoSmithKline, Novartis, Mundipharma and AstraZeneca. Pinja Ilmarinen is an employee of GlaxoSmithKline. Hanna Hisinger-Mölkänen has been an employee of GlaxoSmithKline and is an employee of Orion Pharma. The other authors have no competing interests.

### Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2022.100675.

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