asthma (> 40 years)[2,36]. Interestingly, BMI was also associated with the incidence of asthma in this study, in line with other Scandinavian studies[37]. Nevertheless, this phenomenon in women is significant and should be further investigated.

Proportion of adult-diagnosed asthma was higher than child-diagnosed, confirmed with Helsinki data. The result is in line with another study[13], which examined the whole age span and had an equivalent cut-point to our study (at 18 years). Since we had different aged responders and did not include subjects ≥ 70 years of age, although asthma can be found at any age[38], adult-diagnosed group lacked person-years and therefore underestimated the number of adult diagnoses. Nevertheless, our data probably underestimate the proportion of child-onset asthma and distinction between the two phenotypes might be overestimated. However, similar data for 70 years would be difficult to collect prospectively, and our data clearly describes adult-onset asthma as a notable phenomenon.

Understanding different asthma etiologies and their relative probabilities regarding age at onset in adult patients is important for physicians especially if the era of asthma phenotyping proceeds to clinical work. In our study, adult-onset asthma became the dominant phenotype in women by age 38 years, in line with two earlier reports[13,21]. A study from the US defined adult-onset asthma onset at ≥ 18 years of age, similarly to our study, whereas a Finnish study used a cut-point at 15 years[13,21]. The US study reported that child-onset asthma was still the dominant phenotype in 50-year-old men, differing from our result[21]. Averagely shorter recall periods and prospective design, leading to inclusion of mild asthma in the US study may explain the slightly different result. However, our result regarding men is in line with those of the previous Finnish study[13], which only included patients who had been granted with a special medication reimbursement, indicating that all patients had objectively diagnosed, more persistent asthma.

Smoking has been associated with asthma in incidence studies[20], while most cross-sectional studies have found association with ex-smoking[28,39], similarly to this study. This is presumably explained by the "healthy smoker effect": bias caused by smoking cessation because of excessive respiratory symptoms and asthma diagnosis[16]. In addition, asthma-COPD overlap (ACO) is recently identified[40]. Patients with asthma smoke as often as non-asthmatics and in adult asthma populations many have at least some smoking history[3,28,36,38]. In previous adult asthma studies the exclusion of current smokers or patients with smoking history might lower the incidence estimates in adults, and the influence is emphasized in women, in whom smoking is a higher risk factor for asthma onset[39]. In Finland COPD is diagnosed with objective lung function tests which serve as a basis for medication reimbursement, similarly as in asthma[13,33]. Nevertheless, we cannot exclude some misclassification between asthma and COPD, especially in elderly patients, since COPD usually occurs after 50 years of age. However, the majority of patients with asthma diagnosed > 40 years of age were women, in which significant smoking history is less common in Finland[41]. Thus, we consider that the bias due to misclassification of COPD as asthma does not explain the higher numbers of newly-diagnosed asthma in older women.

In the last three decades, over 130 birth cohorts on asthma and allergies have been initiated[5]. In contrast, similar adult cohort studies are scarce. Although some birth cohorts suggest that adult-onset asthma may have manifested in childhood[5,7], adult- and child-onset asthma have highly distinct characteristics and treatment response, implying that it may be appropriate to study them as separate entities[1,2,42]. In addition, adult-onset asthma is more often associated with environmental risk factors, implying that substantial potential for prevention exists[42]. In a clinical study with population from the same area as in the current study, 24% of adult patients with verified new-onset asthma had had asthma

symptoms in childhood[36] and a case-control study from Sweden found that approximately 10% of subjects with recently diagnosed asthma had been symptomatic before[37]. Therefore, it is justified to assume that most of adult-diagnosed asthma in the current study is also adult-onset asthma. Further, making asthma diagnosis in young children is complex due to lack of appropriate lung function tests and although the incidence of wheezing is substantial, it should not be too eagerly classified as asthma[43]. Furthermore, not every early wheezer develops asthma in adulthood, and neither does every adult-diagnosed asthma patient have wheezing history[7]. Small airway caliber and viral infections can also act as confounders[9]. In conclusion, we believe that adult-onset asthma is a separate entity with unidentified potential for prevention. It should not usually be considered as a reactivation of child-onset asthma, or having similar characteristics.

The response rate in the present study was 52.3%, being moderate, considering that response rates in respiratory epidemiology have declined during the last decades[44,45]. Studies investigating nonresponse bias have found non- and late responders to differ from initial responders by being more often males, younger people and current smokers, correspondingly with the data available in this study[16,44,45]. In addition, these studies report varying results on differences between proportion of asthmatics in responders versus non- and late responders. However, none of these studies stated that using reminders or nonresponse bias significantly affected the prevalence or odds ratios related to asthma, even if the response rate was < 50%. A telephone interview non-responder study was planned as a part of the current study, but ethical permission was not granted. Nevertheless, we conclude that this study might have included some non-responder bias, which mainly affects younger and males.

The main weaknesses of the current study are as follows. Firstly, recall bias is present due to the long recall periods in some asthma cases. Secondly, our responders were more

often older and women and therefore results are susceptible to nonresponse bias. Thirdly, the highest age groups (≥ 70 years) are missing. Finally, due to the inclusion of subjects with significant smoking history, we probably interpreted some COPD as asthma in older subjects. However, the present study also has many strengths. We had a large sample reflecting general population and a relatively good response rate, and used a questionnaire with well proven validity. Subjects were asked about physician-diagnosed asthma which is diagnosed with objective methods and associated to financial benefits in Finland, diminishing recall bias and securing better validity of asthma cases. Lastly, we had a very wide age span which would be extremely difficult to achieve without major drop out prospectively.

In conclusion, adult-onset asthma is a common phenotype and a major burden to the healthcare system. The incidence of adult-onset asthma peaks in middle-aged women. By investigating the poorly understood etiology of new asthma in adult subjects, new approaches to pathogenesis, preventive strategies and effective treatment methods could be discovered. This would lead to upgraded guidelines and major economical and public health improvements.

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