Remission of adult-onset asthma is rare: a 15-year follow-up study

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ABSTRACT

Background: There are few long-term clinical follow-up studies of adult-onset asthma. The aim of this article was to study clinical characteristics of adult-onset asthma in relation to remission and persistence of the disease in a 15-year follow-up.

Methods: A cohort of 309 adults aged 20–60 years with asthma onset during the last 12 months verified by bronchial variability, was recruited between 1995 and 1999 from the general population in northern Sweden. The cohort was followed-up in 2003 (n=250) and between 2012 and 2014 (n=205). Structured interviews and spirometry were performed at recruitment and the follow-ups. Bronchial hyperreactivity (BHR) and skin-prick tests were performed at recruitment and blood samples were collected at the last follow-up. Remission of asthma was defined as no asthma symptoms and no use of asthma medication during the last 12 months.

Results: Of eight individuals in remission in 2003, five had relapsed between 2012 and 2014 and in total, 23 (11%) were in remission, while 182 had persistent asthma. Those in remission had higher mean forced expiratory volume in 1 s % predicted at recruitment than those with persistent asthma (94.6 versus 88.3, p=0.034), fewer had severe BHR (27.3% versus 50.9%, p=0.037) and they had less body mass index increase (+1.6 versus +3.0, p=0.054). Of those with persistent asthma, 13% had uncontrolled asthma and they had higher levels of blood neutrophils than those with partly controlled or controlled asthma.

Conclusion: Higher forced expiratory volume in 1 s % predicted and less-severe BHR was associated with remission of adult-onset asthma, but still, the proportion in remission in this 15-year follow-up was low.
Introduction

Asthma has increased in prevalence worldwide [1, 2], which also has been well documented in the Nordic countries since the 1950s [2–6]. Depending on geographical area and different definitions of asthma, the prevalence of asthma among adults varies and has been estimated at about 10% in western Europe [1, 6, 7]. The epidemiology of asthma also differs by age at onset, for instance with a higher incidence among children and teenagers at around 10 in 1000 per year [8, 9], than among adults, at 2–3 in 1000 per year [10–13]. Also remission of asthma is higher among children [8, 14–16], whereas the remission rate among adults is considered to be low, at around 1–2% per year, when defined as no symptoms common in asthma and no use of asthma medication for at least 1 year [10, 15–19]. However, the remission rate varies depending on the definition of remission and studies seldom differentiate between asthma with onset in childhood and adulthood.

The few available studies about prognosis of adult-onset asthma indicate that remission is associated with a mild disease, better lung function [18, 20], lower IgE levels [20] and absence of allergic sensitisation [18], whereas a higher degree of bronchial hyperreactivity (BHR) and nasal polyps predicted persistence of the disease [21]. There are also some modifiable factors that may predict the remission of asthma. Substantial weight loss seems to improve asthma control and increase the remission rate [22, 23]. Studies of the association between smoking and remission show inconclusive results; however, some studies indicate that nonsmoking and smoking cessation favours remission [17, 21, 24]. The knowledge of clinical characteristics of importance for the prognosis of asthma with onset in adulthood is however, limited as there are few long-term clinical follow-up studies.

The aim of this paper was to study clinical characteristics of adult-onset asthma in relation to remission and persistence of the disease in a 15-year follow-up.

Materials and methods

Study design and sample

The study was performed within the research program for Obstructive Lung Disease in Northern Sweden (OLIN). A cohort including 309 individuals aged 20–60 years with onset of asthma within the last 12 months was recruited between 1995 and 1999. The study design and recruitment procedure of the...
participants has previously been described in detail [13]. In short, the strict inclusion criteria included a convincing history of asthma onset within the last 12 months and a physiological test showing bronchial variability was required. Subjects with asthma in childhood and teenage were excluded as well as subjects reporting asthma-like symptoms more than 12 months before recruitment. The cohort has been followed-up twice with clinical examinations: in 2003 [18] and between 2012 and 2014 (figure 1) [25]. The mean follow-up time from asthma onset to the last follow-up was 15.3 years (SD 1.4) and ranged from 12.4 to 18.6 years. The study sample in the current paper is focused on the 205 individuals who participated both at recruitment and the last follow-up. The Regional Ethical Review Board in Umeå, Sweden, approved the studies.

Clinical examinations at recruitment (at asthma onset)
At recruitment, the subjects participated in a clinical examination, including a structured interview with detailed questions about respiratory symptoms, asthma and comorbid conditions, including rhinitis and eczema. The participants also answered questions about environmental and lifestyle factors, including smoking habits and educational level [13].

Skin-prick tests (SPTs) were carried out for 10 airborne allergens: cat, dog, horse, birch, Timothy grass, mugwort, two mites (Dermatophagoides farinae and Dermatophagoides pteronyssinus) and two moulds (Cladosporium and Alternaria) (Soluprick, ALK, Horsholm, Denmark). A positive reaction was defined as a mean wheal diameter $\geq 3$ mm after 15 min.

Height and weight were measured prior to lung function tests, which were performed following the American Thoracic Society recommendations [26] and using a dry spirometer, the Mijnhardt Vicatest 5. Bronchial variability was verified by bronchial challenge test with methacholine, but if contraindicated, a reversibility test and/or peak flow measurements over 2 weeks was performed [13]. A positive methacholine challenge test was defined as PC$_{20}$ (provocative concentration causing a 20% fall in forced expiratory volume in 1 s (FEV$_1$)) $<8$ mg·mL$^{-1}$. In the current study, BHR is presented as two cut-offs: PC$_{20}$ $\leq 1$ mg·mL$^{-1}$ (severe) and $\leq 2$ mg·mL$^{-1}$ (moderate).

Clinical examinations at follow-up
The clinical examinations at follow-up between 2012 and 2014 [25] included a similar structured interview as at recruitment with detailed questions about the use of asthma medications. Blood samples were collected for analyses of IgE to airborne allergens, blood neutrophils (B-neu) and blood eosinophils (B-eos). Allergic sensitisation was defined as specific IgE $>0.35$ IU·mL$^{-1}$, analysed by ImmunoCAP Phadiatop (Thermo Fisher Scientific, Uppsala, Sweden). Among those with a positive Phadiatop, sensitisation to specific allergens were analysed and in the current paper defined as sensitisation to "any pollen" and "any furred animal" as sensitisation to mite and mould are uncommon in this study area [27]. Lung function tests were performed using a Jaeger Masterscope spirometer. Reversibility tests were performed after inhalation of 0.4 mg salbutamol. Reversibility was considered significant if FEV$_1$ increased $\geq 12\%$ and $\geq 200$ mL.

Lung function is presented as pre-bronchodilator FEV$_1$ and forced vital capacity (FVC) values and using the OLIN reference values both at recruitment and follow-up [28].

Definitions
The definitions used in this study are as follows.

Any respiratory symptom
Any wheeze or attacks of shortness of breath in the last 12 months.

Remission of asthma
No report of any wheeze or attacks of shortness of breath and no use of asthma medications during the last 12 months.

Body mass index
Weight/height$^2$ (kg·m$^{-2}$) and divided into categories according to the World Health Organization: normal 18.5–24.9 kg·m$^{-2}$, underweight $<18.5$ kg·m$^{-2}$, overweight 25–29.9 kg·m$^{-2}$ and obese $\geq 30$.

Stable weight
Difference of $\pm 2$ kg when comparing weight at recruitment and follow-up between 2012 and 2014.
Smoking habits
Classified as nonsmokers, ex-smokers (stopped >12 months prior to examination) and smokers (smoked at least one cigarette·day⁻¹ during the last 12 months). Ever-smokers were ex-smokers or current smokers. Pack-years: (number of cigarettes smoked per day/20)×years.

Atopic comorbidities
Affirmative answers to the following questions. Hay fever (at recruitment): "Do you have, or have you had hay fever?"; current allergic rhinitis (at follow-up): "Have you had allergic rhinitis in the last 12 months?"; eczema (at recruitment): "Do you have, or have you had eczema?"; current eczema (at follow-up): "Have you had eczema in the last 12 months?"; nasal polyps: "Do you have, or have you had nasal polyps?"; and reflux: "Do you have, or have you had heartburn or acid reflux?"

Occupational exposure to gas, dust or fumes
Affirmative answer to the question: “Have you been heavily exposed to gas, dust or fumes (GDF) at work?”

Educational level
Highest educational level achieved: primary school, high school or higher education.

Asthma control
Among subjects with persistent asthma at follow-up, level of asthma control was classified into controlled, partly controlled and uncontrolled according to Global Initiative for Asthma (GINA) 2006 [29] (table 1).

Treatment at follow-up
Use of asthma medication during the last 12 months was classified in line with GINA 2017 treatment steps [30]: short-acting β₂-agonists (SABAs) or long-acting β₂-agonists (LABAs) without inhaled corticosteroids (ICSs); SABAs or LABAs with ICSs periodically; low-dose ICSs without LABAs most days per week; combination of low-dose ICSs and LABAs most days per week; or combination of medium-/high-dose ICSs and LABAs most days per week.

Statistical analyses
The analyses were carried out using IBM Social Statistical Package for the Social Science, version 24.0 (IBM Corp, New York, USA). Comparisons of proportions were analysed using the Chi-squared test or Fisher’s exact test when appropriate. To compare means, independent sample t-test and ANOVA were used. Factors at recruitment associated with remission of asthma at follow-up between 2012 and 2014 were analysed using multivariable logistic regression analysis and expressed as odds ratios with 95% confidence intervals. A p-value <0.05 was considered statistically significant.

| TABLE 1 Classification of asthma control according to Global Initiative for Asthma 2006 |
|---------------------------------|---------------------------------|---------------------------------|
| Controlled (all of the below)   | Partly controlled (any of the below) | Uncontrolled (at least 3 of the below) |
|---------------------------------|---------------------------------|---------------------------------|
| **During the last 4 weeks:**    | **During the last 12 months:**  |                                  |
| Asthma symptoms during the day  | Twice or less per week          | Three times or more per week    | Three times or more per week    |
| Limitation of daily activities  | No                              | Yes                             | Yes                             |
| Asthma symptoms during the night| No                              | Yes                             | Yes                             |
| Reliever medication             | Used twice or less per week     | Used three times or more per week| Used three times or more per week|
| Lung function                   | FEV₁ >80% predicted            | FEV₁ <80% predicted             | FEV₁ <80% predicted             |
| **Exacerbations**               | No                              | At least one                    | At least one                    |

*: any of the following events in the last 12 months due to asthma: oral corticosteroids and/or antibiotics, emergency healthcare visit with or without hospitalisation, or not being able to work or perform daily activities due to asthma during at least 2 days. FEV₁: forced expiratory volume in 1 s. Reproduced from [29] with permission.
Results

Remission and relapse of asthma

From recruitment until the follow-up in 2003, 12 subjects were in remission [18]. In the 2012–2014 follow-up, eight subjects participated and three were still in remission, whereas five had relapsed (figure 2). Of the three with lasting remission, one was an ex-smoker (pack-years 4.3), two were overweight and none was sensitised. Of the five that relapsed, four had B-neu >4, four had controlled asthma and one had

| TABLE 2 Basic and clinical characteristics at recruitment between 1995 and 1999, comparing subjects in remission and subjects with persistent asthma at follow-up |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
|                             | All                         | Persistent asthma           | Remission                   | p-value                     |
|Subjects n                   | 205                         | 182                         | 23                          |                             |
|Female sex                   | 134 (65.4)                  | 121 (66.5)                  | 13 (56.5)                   | 0.344                       |
|Age at asthma onset          | 39.3±10.3                   | 39.4±10.2                   | 38.8±11.6                   | 0.718                       |
|BMI                          | 25.9±4.5                    | 25.9±4.4                    | 26.7±4.7                    | 0.386                       |
|Family history of asthma     | 83 (40.5)                   | 77 (42.3)                   | 6 (26.1)                    | 0.135                       |
|BMI classification           |                             |                             |                             |                             |
|Normal weight                | 95 (46.3)                   | 85 (46.7)                   | 10 (43.5)                   |                             |
|Overweight                   | 79 (38.5)                   | 70 (38.5)                   | 9 (39.1)                    |                             |
|Obesity                      | 31 (15.1)                   | 27 (14.8)                   | 4 (17.4)                    | 0.717*                      |
|Smoking habits               |                             |                             |                             |                             |
|Nonsmoker                    | 105 (51.2)                  | 95 (52.2)                   | 10 (43.5)                   |                             |
|Ex-smoker                    | 64 (31.2)                   | 57 (31.3)                   | 7 (30.4)                    |                             |
|Current smoker               | 36 (17.6)                   | 30 (16.5)                   | 6 (26.1)                    | 0.276*                      |
|Occupational exposure to gas, dust or fumes | 66 (33.3)                  | 61 (34.9)                   | 5 (21.7)                    | 0.210                       |
|Educational level            |                             |                             |                             |                             |
|Primary school               | 21 (10.5)                   | 20 (11.3)                   | 1 (4.3)                     |                             |
|High school                  | 92 (46.0)                   | 81 (45.8)                   | 11 (47.8)                   |                             |
|Higher education             | 87 (43.5)                   | 76 (42.9)                   | 11 (47.8)                   | 0.417*                      |
|Lung function                |                             |                             |                             |                             |
|FEV1 % predicted            | 89.0±13.4                   | 88.3±13.7                   | 94.4±10.1                   | 0.034                       |
|FVC % predicted             | 87.1±11.6                   | 86.5±11.7                   | 92.0±9.5                    | 0.034                       |
|Bronchial hyperreactivity PC20|                             |                             |                             |                             |
|PC20 ≤1 mg·mL⁻¹              | 89 (48.1)                   | 83 (50.9)                   | 6 (27.3)                    | 0.037                       |
|PC20 ≤2 mg·mL⁻¹              | 120 (64.9)                  | 109 (66.9)                  | 11 (50.0)                   | 0.120                       |
|Atopic comorbidities         |                             |                             |                             |                             |
|Hay fever                    | 82 (40.0)                   | 73 (40.1)                   | 9 (39.1)                    | 0.928                       |
|Eczema                       | 68 (33.2)                   | 62 (34.1)                   | 6 (26.1)                    | 0.444                       |
|Nasal polyps                 | 21 (10.2)                   | 20 (11.0)                   | 1 (4.3)                     | 0.285                       |
|Positive skin-prick test†    | 85 (42.1)                   | 75 (41.9)                   | 10 (43.5)                   | 0.885                       |

Data are presented as n (%) or mean±SD, unless otherwise stated. BMI: body mass index; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; PC20: provocative concentration causing a 20% fall in FEV1; ‡: among the 185 participating in metacholine challenge test at recruitment; †: among the 202 participating in skin-prick test; *: analysis performed in a 3×2 table. Bold values indicate p<0.05.
uncontrolled asthma at follow-up. Of the 205 individuals in the follow-up between 2012 and 2014, 23 (11.2%), fulfilled the criteria for remission, yielding a remission rate between recruitment and the last follow-up of <1% per year.

**Characteristics at recruitment in relation to remission of asthma between 2012 and 2014**

Subjects in remission had higher mean FEV1 % predicted (% pred) than those with persistent asthma, both at recruitment (94.6% versus 88.3%, p=0.034, table 2) and at follow-up (96.7% versus 89.0%, p=0.014, table 3). Also, FVC % pred was significantly higher among those in remission. Severe BHR at recruitment was more common among those with persistent asthma than those in remission (50.9% versus 27.3%, p=0.037, table 2). The association between remission and FEV1 % pred and severe BHR at recruitment remained significant also after adjustment for sex, age, family history of asthma, body mass index (BMI) and smoking habits at recruitment (figure 3). There were no differences between subjects in remission and those with persistent asthma regarding sex, age at asthma onset, family history of asthma, BMI categories, smoking habits, educational level, occupational exposure to GDF, comorbidities or positive SPT at recruitment.

**Remission of asthma in relation to changes in weight, BMI and smoking habits from asthma onset to follow-up between 2012 and 2014**

Subjects with persistent asthma tended to have a greater BMI increase (3.0 versus 1.6, p=0.054) and mean per cent weight gain (10.3% versus 4.9%, p=0.059) than those in remission. Among those in remission,
26.1% had lost weight compared to 12.6% among those with persistent asthma, p=0.118 (table 3). Changes in smoking habits were not associated with remission.

Clinical characteristics of subjects with persistent asthma by level of asthma control
Of the 182 individuals (88.8%) with persistent asthma at follow-up, 55% had controlled, 32% had partly controlled and 13% had uncontrolled asthma. At follow-up, the mean FEV1 % pred was significantly higher among those with controlled asthma (91.9%) than those with partly controlled (85.0%) or uncontrolled asthma (86.6%) (table 4). The proportion of subjects having B-neu ≥4.0×10^9·L^-1 was significantly higher among those with uncontrolled asthma (65.2%) than partly controlled (32.1%) or controlled asthma (37.4%). Also, the mean B-neu level was significantly higher among those with uncontrolled asthma, whereas the mean levels of B-eos were similar. Levels of asthma control were not related to sex, age at asthma onset, age at follow-up, mean BMI, BMI categories, smoking habits, occupational exposure to GDF, reversibility, allergic sensitisation (table 4) or change in weight or BMI (data not shown).

All subjects with uncontrolled asthma reported “any respiratory symptom” during the last 12 months, compared to 89.7% of those with partly controlled asthma, and 88.0% of those with controlled asthma (table 5). The majority of those with uncontrolled asthma used medium- or high-dose ICSs with LABAs most days per week (58.3%), compared with 34.5% of partly controlled and 23.0% of controlled asthma (p=0.004).

Lost to follow-up
Of the original cohort of 309 subjects, 10 individuals had died, 35 had moved from the county, 10 could not be traced, and 49 of those possible to invite declined participation (figure 1). The nonparticipants (n=49) were significantly younger than the 205 participants (mean age 32.1 versus 39.3 years, p<0.001), but there were no significant differences regarding respiratory symptoms, positive SPT, weight, BMI, smoking habits or FEV1 % pred at recruitment.

Discussion
This population-based study included a 15-year follow-up of a cohort with clinically verified adult-onset asthma. The remission rate was low and at follow-up the vast majority had persistent asthma. Lower FEV1 % pred and severe bronchial hyperreactivity at asthma onset was associated with persistent asthma. Almost every other individual with persistent asthma had uncontrolled or partly controlled disease at follow-up.

Our study is one of the few available long-term follow-up studies of adult-onset asthma where strict inclusion criteria have been used; besides verification of bronchial variability the presence of several symptom variables was also required [13]. In a previous 5-year follow-up of our cohort, the remission rate was low at 0.8 in 100 per year [18] and similar to the current follow-up. However, of those in remission, five of eight had relapsed until the current follow-up. What may seem as remission in a short-term...
follow-up, could in fact only be a temporary period with absence of symptoms, particularly among those with mild intermittent asthma [18, 20]. Thus, low remission rate of adult-onset asthma is supported by the current study. Both in the current follow-up, as well as in the 5-year follow-up [18] of our cohort, higher FEV1 pp predicted remission of adult-onset asthma. Furthermore, in this last follow-up we also found that severe BHR counteracted remission. This is in line with a similar study of 170 individuals with adult-onset asthma followed for 5 years [21]. Thus, measures to maintain good lung function and suppress hyperreactivity may increase the probability of remission.

The majority of our participants had gained weight, similar to an increase of obesity observed in the general population in high-income countries over the last decades. It has been shown that weight loss improves lung function [31], asthma control and quality of life among obese people with asthma [32, 33] and that weight loss can lead to decreased airway hyperreactivity [22, 34]. In the Finnish Seinäjoki Adult Asthma Study (SAAS), high baseline BMI was a predictor for uncontrolled asthma at a follow-up after 12 years [20]. In our study we found a trend that a greater weight gain was associated with persistent

| TABLE 4 Characteristics of subjects with persistent asthma at follow-up, by asthma control classified according to Global Initiative for Asthma 2006 [29] criteria |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Controlled asthma | Partly controlled asthma | Uncontrolled asthma | p-value |
| Subjects n | 100 | 58 | 24 |
| Female sex | 63 (63.0) | 40 (69.0) | 18 (75.0) | 0.476 |
| Age at follow-up | 53.7±9.7 | 55.7±10.4 | 56.3±10.1 | 0.327 |
| Age at asthma onset | 38.2±10.0 | 40.7±10.5 | 41.1±10.3 | 0.232 |
| BMI | 28.8±5.1 | 29.3±6.0 | 28.0±3.5 | 0.579 |
| BMI classification | Normal weight | 19 (19.0) | 13 (22.4) | 7 (29.2) | 0.216 |
| | Overweight | 50 (50.0) | 19 (32.8) | 10 (41.7) |
| | Obesity | 31 (31.0) | 26 (44.8) | 7 (29.2) |
| Smoking habits and occupational exposure | Nonsmoker | 50 (50.0) | 28 (48.3) | 12 (50.0) |
| | Ex-smoker | 45 (45.0) | 27 (46.6) | 11 (45.8) |
| | Current smoker | 5 (5.0) | 3 (5.2) | 1 (4.2) | 0.999 |
| | Pack-years | 11.3±12.0 | 12.1±11.1 | 9.8±12.5 | 0.846 |
| Lung function | Pre-bronchodilator FEV1 pp | 91.9±11.4 | 85.0±15.4 | 86.6±17.6 | 0.008 |
| | Pre-bronchodilator FVC pp | 97.4±12.6 | 91.1±15.1 | 91.7±16.1 | 0.015 |
| | Pre-bronchodilator FEV1/FVC <0.70 | 29 (29.9) | 22 (37.9) | 8 (33.3) | 0.588 |
| | AfterFEV1/FVC <0.70 | 13 (14.0) | 15 (26.8) | 4 (19.0) | 0.153 |
| | FEV1 reversibility ≥12% and ≥200 mL | 5 (5.4) | 6 (10.7) | 1 (4.8) | 0.425 |
| Comorbidities | Current allergic rhinitis | 37 (37.0) | 29 (50.0) | 10 (41.7) | 0.279 |
| | Current eczema | 18 (18.0) | 11 (19.0) | 5 (20.8) | 0.948 |
| | Reflux | 39 (39.0) | 25 (43.1) | 10 (41.7) | 0.875 |
| | Nasal polyps | 8 (7.1) | 5 (8.6) | 0 | 0.350 |
| Blood neutrophils 10⁶·L⁻¹ | ≥4 | 34 (37.4) | 18 (32.1) | 15 (65.2) | 0.020 |
| | ≥5 | 10 (11.0) | 5 (8.9) | 6 (26.1) | 0.092 |
| | ≥6 | 3 (3.3) | 3 (5.4) | 3 (13.0) | 0.176 |
| | mean±SD | 3.7 (1.1) | 3.6 (1.2) | 4.4 (1.5) | 0.017 |
| Blood eosinophils 10⁶·L⁻¹ | ≥0.2 | 40 (44.0) | 30 (53.6) | 0 (43.5) | 0.491 |
| | ≥0.5 | 16 (17.6) | 17 (30.4) | 6 (26.1) | 0.187 |
| | ≥0.4 | 8 (8.8) | 11 (19.6) | 4 (17.4) | 0.147 |
| | mean±SD | 0.2 (0.1) | 0.2 (0.2) | 0.2 (0.2) | 0.146 |
| Allergic sensitisation | Specific IgE >0.35 IU·mL⁻¹ | 27 (27.8) | 18 (32.7) | 5 (20.8) | 0.550 |
| | Sensitisation to any pollen | 19 (19.6) | 15 (27.3) | 3 (12.5) | 0.292 |
| | Sensitisation to any furred animal | 17 (17.5) | 10 (18.2) | 3 (12.5) | 0.812 |

Data are presented as n (%) or mean±SD, unless otherwise stated. BMI: body mass index; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; Ig: immunoglobulin. #: among the 170 participating in blood sampling for cell count; ¶: among the 176 participating in blood sampling for IgE; : analysis performed in a 3×3 table. Bold values indicate p<0.05.
asthma but not with level of asthma control. Due to the few subjects in remission, as well as few subjects losing weight, our study lacks power to fully analyse the effect of weight loss on remission of asthma.

There is no gold standard to define remission of asthma, which is why comparisons between studies must be made cautiously. Remission of asthma from childhood to adulthood has been reported to be high at 10–65% [14–16, 35, 36]. The remission rate in our cohort of adult-onset asthma was 11% during the 15-year follow-up. Among the few other prospective studies of adult-onset asthma, higher remission rates have been shown, 16% during 5 years [21] and 20% during 10 years [24], while the previously discussed Finnish SAAS showed a lower rate of 3% during 12 years [20]. However, these studies have a different methodology and definitions. For instance, we defined adult-onset asthma based on strict inclusion criteria regarding age at onset, after 20 years of age and also required a clinically verified bronchial variability, whereas others have used 15 years as the age limit for adult onset [20] or used postal questionnaire reports to define adult-onset asthma [24]. An initial interest at the recruitment of the cohort was to study the importance of occupational exposure, therefore we used 20 years as threshold for adult asthma onset. However, as we used strict inclusion criteria, some individuals with mild asthma may have been excluded at recruitment, and as mild asthma is associated with remission, the remission rate may have been somewhat underestimated. However, taken together, the remission rate of adult-onset asthma is low and considerably lower than remission of asthma in children.

In our study, there was no significant association between current smoking and neither remission nor asthma control. Contrary to our expectations, we found that those in remission tended to have more pack-years than those with persistent asthma. This may be explained by a “healthy smoker effect” (i.e. individuals with fewer respiratory symptoms are more prone to continue smoking). However, the associations between sex, smoking and obesity in relation to asthma are difficult to disentangle. For instance, in a cross-sectional study, the association between smoking and asthma was stronger in overweight women than overweight men [37]. Further, current smoking may reduce weight gain, whereas smoking cessation increases weight gain [38]. Thus, smokers may hesitate to quit due to fear of gaining weight, which should be taken into account in smoking cessation support.

Of those with persistent asthma, subjects with uncontrolled asthma had higher B-neu levels than subjects with controlled asthma. Close to 60%, of those with uncontrolled asthma used medium/high doses of ICSs most days per week, corresponding to GINA treatment step 4. It is known that neutrophilic inflammation is associated with poor response to glucocorticoid steroids [39] and it has even been suggested that glucocorticoid steroid treatment may increase the level of sputum neutrophilia [39]. It has also been suggested that obesity in asthma could be associated with more neutrophilic inflammation [32, 40], especially among women [40]. However, in the current study there were no significant associations between overweight and asthma control but a slightly higher proportion of those with uncontrolled asthma had occupational exposure to GDF, which also could contribute to neutrophilic inflammation. On the other hand, one-quarter of those with partly controlled asthma had no treatment or merely had SABAs or LABAs without ICSs and almost 40% of those with uncontrolled asthma had low-dose ICSs with or without LABAs. Thus, these individuals would benefit from optimisation of pharmaceutical treatment but also lifestyle factors and environmental exposures.
The strengths of the current study are the strict criteria for the diagnosis of adult-onset asthma and the longitudinal study design with a long follow-up time. The validity of the study is strengthened by the high participation rate at both recruitment [13] and follow-up [18]. Even though there was a loss to follow-up, comparison of participants and nonparticipants indicated no major selection bias, thus we consider that the study population is representative of the cohort. The limited number of cases in remission did, however, not allow subgroup analyses. There was a decrease in the prevalence of allergic sensitisation from recruitment to follow-up that in part, could be explained by the use of different measuring methods of SPT and IgE levels. On the other hand, remission of allergic sensitisation to airborne allergens is common among adults [27]. Unfortunately, we lack information on IgE levels as well as B-eos and B-neu levels at recruitment. Further, another limitation is that BHR tests were not performed at follow-up. Although we lack information about the prescribed doses of asthma medication, we have detailed information about what the participants in reality are using.

In conclusion, even though better lung function and less-severe BHR was associated with remission, and those in remission tended to have less weight gain, the proportion in remission was low in this long-term cohort study of adult-onset asthma. Thus, with few exceptions, adult-onset asthma can be considered a persistent disease. Moreover, a high proportion of those with persistent asthma did not have well-controlled disease and would certainly benefit from optimised treatment.

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