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# Five-fold increase in use of inhaled corticosteroids over 18 years in the general adult population in West Sweden

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**KEYWORDS**
Asthma medication;
Epidemiology;
Severity;
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Management

**Summary**
*Introduction:* Asthma medication was increasingly used during the second part of the past century. There are few detailed data from population studies on use of asthma medication. The current study aimed to determine the use and determinants of asthma medication in West Sweden and to assess changes during the last two decades.
*Methods:* From a random population sample participating in a survey on respiratory symptoms, 2000 individuals were randomly selected for clinical examinations and structured interviews, 1172 participated. All subjects reporting asthma ($n = 1524$) were also invited, and 834 participated. In total, 964 subjects with asthma participated. Asthma medication use was assessed in the general population and among two severity categories of asthma: multi-symptom asthma (MSA) and "other" asthma (having fewer symptoms). Current data, from 2010, was compared with data from 1992.
*Results:* Asthma medication was used by 11% of the population, 4.4% used ICS with concurrent use of LABA, 3.3% used ICS without LABA, while 3.2% only used SABA. Compared with 1992, the prevalence of asthma medication use had increased with 54%, and use of ICS had increased from 1.5% to 7.7%.

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*Conclusion:* Subjects with MSA reported using asthma medication more frequently and at higher doses, and a higher proportion used ICS.A shift in asthma medication use has occurred since 1992, with increased use of ICS and decreased use of SABA only, implying better asthma control on a population level. Multi-symptom asthma should alert the treating physician to consider under-medication and/or poor treatment adherence.


## Introduction

The prevalence of physician-diagnosed asthma has increased worldwide [1—4], and current Swedish data suggest the prevalence of asthma to be 7—10% [3,5,6]. This increase is supported by reports of a high incidence [7,8] but contrasts to reports of a stable or even decreasing prevalence of symptoms common in asthma, such as wheeze and attacks of shortness of breath when compared with results of studies performed in the 1980s and 1990s [3,9,10]. Thus there is an on-going debate whether asthma prevalence is increasing or not [6,11].

In western societies, the prevalence of users of asthma medication does not fully reflect the true prevalence of asthma [6,12]. Over the past decades an obvious increase in asthma medication use has been observed [5,6], partly as a consequence of an increased awareness of COPD. However, there are still only few large scale population surveys that have studied asthma medication use in more detail [12]. Patient reported use of asthma medication contribute to the validation of estimates of asthma prevalence and, even more importantly, give important insights into how asthma care function in society.

To contribute to the identification of asthma with more significant degrees of severity in population studies we have proposed the term multi-symptom asthma (MSA) [13]. MSA, defined as having physician-diagnosed asthma with multiple symptoms despite reporting use of asthma medication, is associated with decreased lung function, increased hyperreactivity and airway inflammation, exacerbations, emergency visits, night time awakenings [13] and chronic nasal symptoms [14]. The prevalence of MSA on a population level is 2% in West Sweden, in agreement with results from the Swedish capital Stockholm, located in the Eastern part of Sweden [3,13,14]. Tools for identifying more severe asthma in a population is important as severe asthma poses a great burden both on the individual and on society as it is associated with a decreased quality of life [15], increased morbidity with need of emergency care and life style restrictions [13] and high societal costs [16].

The present study is the first from the West Sweden Asthma Study to present clinical data from the entire cohort. The aim was to examine prevalence, distribution and determinants of asthma medication use in the general population of West Sweden. Further aims were to compare use of asthma medication in 1992 and 2010, and to determine the association between use of asthma medication in MSA versus other asthma.

## Methods

### Study population and participation

The West Sweden Asthma Study population has previously been described in detail [6]. In short, in 2008 a validated questionnaire, including the international GAL$^2$EN-questionnaire and the OLIN-questionnaire, [5,9,17] was mailed to 30 000 randomly selected subjects aged 16—75 years, living in the Swedish region of Västra Götaland. The response rate was 62%. A non-responder study showed high representativeness of the study area's population [18]. The study has been approved by the local Ethics Committee.

The results in the current paper are based on two subsamples of responders to the postal questionnaire. From the responders to the postal questionnaire, 2000 subjects were randomly selected and invited to clinical examinations, 1172 (59%) participated, 130 of whom reported asthma (11.1%). In addition, all subjects considered to have asthma according to the questionnaire, an additional 1524 subjects, were invited, 834 (55%) participated. In total, 964 asthmatics participated in the clinical examinations which were performed from winter 2009 to winter 2012. The selection procedure is described in Fig. 1.

Changes in asthma medication use were assessed by comparison with data from the European Community Respiratory Health Survey (ECRHS) I performed in 1992 in Gothenburg [19]. In the comparison only subjects aged 21—46 years, living in the city of Gothenburg were included ($n$ = 430) to match the population of ECRHS I.

### Clinical data

The examinations included an extensive structured interview, including a detailed questionnaire on use of asthma medication. Other measurements included mainly lung function measurements, fraction of exhaled NO and skin-prick tests. The questionnaire on asthma medication use included questions on type of medication; inhaled corticosteroids (ICS only), combination treatment (i.e. ICS and long-acting beta-2-agonists (LABA), separately or as a combined inhaler), oral steroids, LABA, short-acting beta-2-agonists, (SABA), leukotriene antagonists and bronchodilators through nebuliser. For ICS, the subjects stated the name of the medication, and what daily dose they used. Questions on frequency of use included 6 options; 1) never, 2) a few times/year, 3) a few times/month, 4) no more than

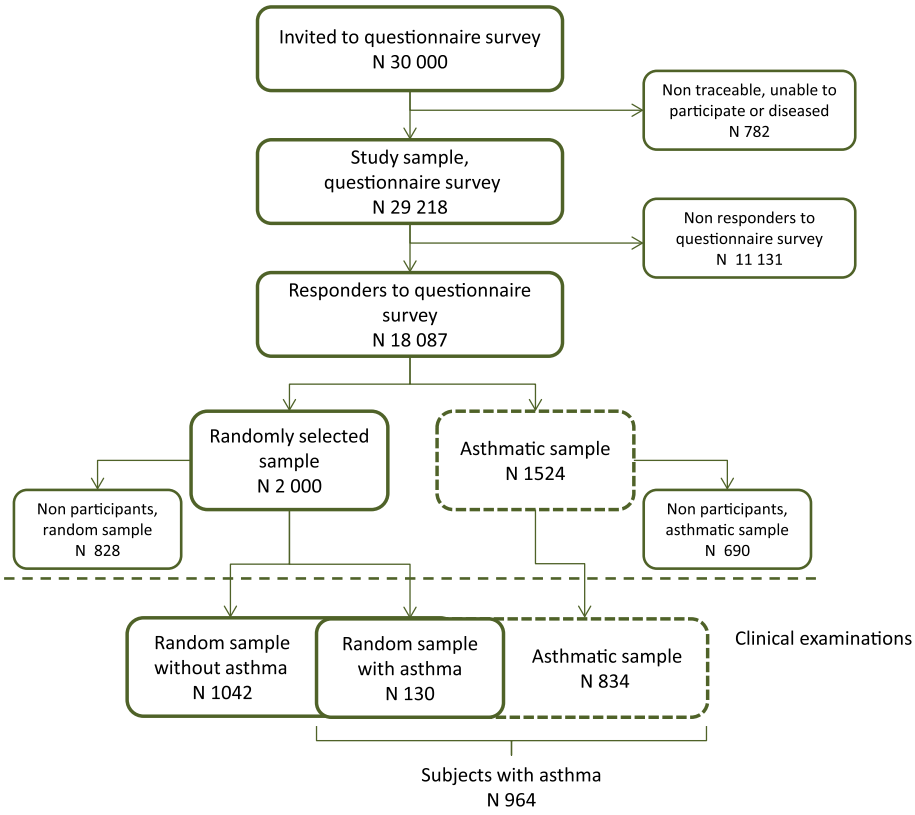


**Figure 1** Study set up. The study population was based on a questionnaire survey from which a random and an asthmatic sample were invited to clinical examinations.

twice a week, 5) at least 3 times a week and 6) daily or almost daily. In the analysis the options were condensed into three categories, 1 and 2 were considered as "never", 3 and 4 as "occasionally" and 5 and 6 as "most days". Dose of ICS is given as beclomethasone dipropionate (BDP) equipotent doses and grouped into low (200–500 μg BDP), medium (>500–1000 μg BDP) and high (>1000 μg BDP) daily doses.

## Definitions of asthma

Based on self-administrated questionnaire reports in 2008, subjects were considered as asthmatics if they reported physician-diagnosed asthma, or reported ever asthma with medication use, wheeze, or attacks of shortness of breath during the last 12 months. MSA was defined as *physician-diagnosed asthma* and *asthma medication* and *attacks of shortness of breath* and *recurrent wheeze* and at least one out of *dyspnoea, breathlessness at exertion, breathlessness in cold conditions*, and *breathlessness at exertion in cold conditions*. Asthmatic subjects not reporting MSA are referred to as having other asthma (OA).

## Analyses

Statistical analyses were performed using SPSS version 18.0. Comparisons of proportions were tested using Fischer's exact test, and the Mantel-Haenszel's test for trend was used when appropriate. *T*-tests were used to compare means between two groups. A *p*-value of $<0.05$ was regarded as statistically significant. Adjusted logistic regression analyses were performed to determine risk factors, presented as odds ratios (OR) with 95% confidence intervals (95% CI).

Calculations of prevalence in the population and possible determinants were based only on the random sample, representing the population of Västra Götaland. Medication use among subjects with asthma was investigated using data both from the random sample and from the enriched asthma sample. A sensitivity analysis was performed to compare subjects living on Hisingen to all subjects living in Gothenburg in regards to symptoms and risk factors by using Fischer's exact test. The sensitivity analysis revealed no significant differences between subject living on Hisingen and subjects from the whole Gothenburg area. An agreement analysis using data collected from the drug registry maintained by the National Board of Health and Welfare was performed on a subsample. Prescription refill data was collected between 2008-01-01 and 2012-06-30, and the refill prior to the visit to our clinic was used for the agreement analysis using kappa-statistic and absolute agreement.

# Results

## Prevalence of medication use in the population

The prevalence of asthma medication use was 11% in the clinically examined random sample ($n = 1172$). The most common asthma medication was SABA, which was used by

8.3% of the population, followed by a combination treatment, i.e. ICS and LABA, (4.4%) and ICS only (3.3%). The majority of SABA users (61%) used SABA in combination with ICS.

Among all users of asthma medication, 38% used ICS only with or without additional SABA or LABA, while 30% had a combined inhaler, with or without additional SABA (Fig. 2). Among users of ICS, 48% used ICS only while 52% used ICS in combination with LABA. A fixed combination inhaler was used by 85% of subjects on combination treatments. SABA only was used by 27% while 6.6% used LABA only.

## Change in asthma medication use 1992–2010

Comparison with ECRHS from 1992 showed an increased use of asthma medication in the Gothenburg population aged 21–46, from 7.8% to 12%, $p = 0.02$ (Fig. 3). The increase mainly consisted of an increased use of ICS from 1.5% to 7.7%, $p < 0.001$, while the proportion who used SABA did not change significantly. The introduction of LABA during the time between the studies was clearly visible, with 4.4% of the population of young adults using LABA in 2010 while there were no LABA users in 1992. Among asthmatics there was a strong decrease in the prevalence of using only SABA with no additional medications, from 47% to 23%, $p < 0.001$, in this younger population.

## Prevalence of medication use among asthmatics

Of the subjects with asthma ($n = 964$), 66% were currently using asthma medication. ICS only were used by 20% and combination treatment was used by 24%. The prevalence of SABA use without concomitant use of ICS was 17% (Fig. 4). Oral corticosteroids were used occasionally by 6.2%, and only 0.3% used oral corticosteroids regularly. Among users of LABA, 16% did not also use corticosteroids. Leukotriene antagonists were used by 2% of the asthmatics, 29% of which did not use ICS. Use of any asthma medication was more common in women than men (Table 1). Use of ICS and combination treatment, respectively, increased by age. Use of any asthma medication and SABA was higher among subjects with allergic rhinitis.

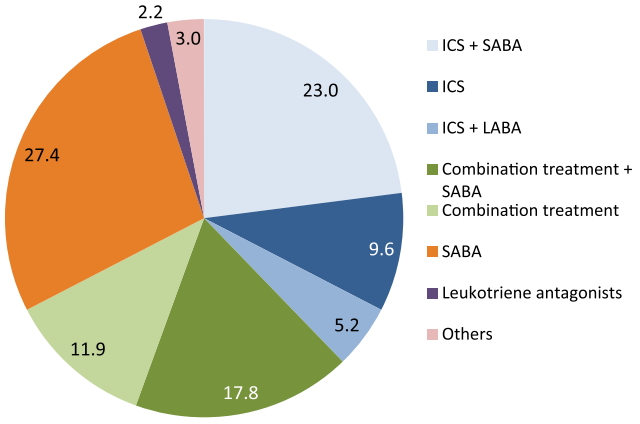


**Figure 2** Distribution (per cent) of asthma medication use among subjects with asthma in the random sample. ICS – inhaled corticosteroids, SABA – short-acting β2-agonists, LABA – long-acting β2-agonists, Combination treatment – ICS and long-acting β2-agonists as a combined inhaler.

## Medication use in multi-symptom asthma and other asthma

The prevalence of use of medication for asthma was 91% among MSA ($n = 201$) and 59% among OA ($n = 763$). Sixty-eight per cent of subjects with MSA and 40% of subjects with OA used ICS ($p < 0.001$, Fig. 4). Of subjects with MSA 42% used a combination treatment, and of these, 88% used a combination inhaler and the remaining used LABA and ICS separately. Among subjects with OA only 22% used a combination treatment including ICS. Among subjects not using ICS (32% in MSA and 54% in OA), the prevalence of SABA use was 64% in the MSA group and 29% in the OA group ($p < 0.001$, Fig. 4). Two-thirds of oral steroid users were found in the MSA group, despite MSA constituting only 21% of the whole population of asthmatics.

With increasing age, all groups reported an increased prevalence of use of ICS and combination treatment. The prevalence of SABA use decreased with increasing age (Table 1).

In order to validate the self-reported use of maintenance treatment an agreement analysis using registry data was performed. A randomly selected subsample of 74 subjects revealed an absolute agreement of 82% for ICS and 91% for combination treatment, with kappa-values above 0.6.

## Frequency and dosages of medication

Of subjects with MSA, 34% used combination treatment most days versus 15% for OA ($p < 0.001$). The corresponding figures for use of ICS most days were 49% and 24%, $p < 0.001$ (Table 2). Subjects with MSA used higher doses of ICS compared with OA. High dose, i.e. >1000 μg, was used by 6.5% and 1.9% of MSA and OA, respectively ($p < 0.001$). Medium dose was used by 45% and 24% and low dose by 12% and 9.8%. Using ICS most days increased with age both among subjects with MSA and OA but was highly more prevalent among MSA in all age groups.

## Determinants of medication use

In an adjusted logistic regression model including age, BMI, population density gradient, smoking status, chronic rhinitis and allergic rhinitis the same pattern appeared for all investigated medication variables: any asthma medication; any inhaled corticosteroid; combination treatment; and high dose of any inhaled corticosteroid (Table 3). Allergic rhinitis, chronic rhinitis and having a BMI ≥30 were stable risk factors for all medication variables. For use of ICS also increasing age was a risk factor.

## Discussion

The study is the first from the West Sweden Asthma Study to present data from the clinical phase. The study reports an asthma medication use of 11% in a randomly selected

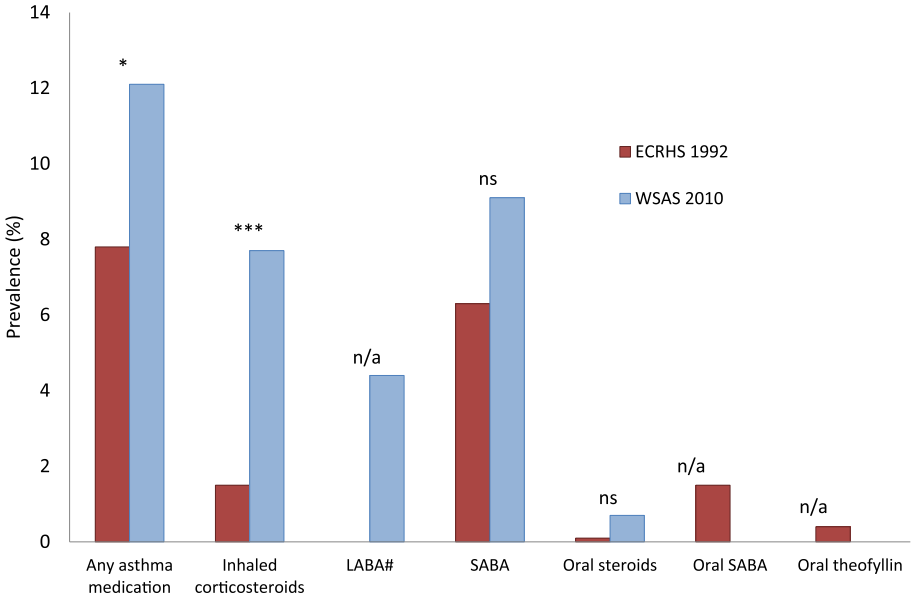


**Figure 3** Prevalence of asthma medication use in the population of Gothenburg aged 21—46 years in 1992 and 2010. *p*-Value — Fischer's exact test: *>0.05, ***<0.001, ns — non significant, N/A — not possible to calculate. #LABA in combination with ICS and taken separately. The prevalence included both regular and occasional use. WSAS — West Sweden Asthma Study. ECRHS — European Community Respiratory Health Survey.

population of adults. Of subjects with asthma, two thirds used asthma medications, the most common being ICS and SABA, and SABA alone was only used by a one fourth of these subjects. Use of ICS increased with age in all asthma groups, while the use of SABA decreased with age. The use of leukotriene antagonists was low. Between 1992 and 2010 asthma medication use had increased by 54%. The increase probably reflects a combination of the increase in prevalence of physician-diagnosed asthma during the time period [3,6] as well as the increased use of inhaled corticosteroids [20]. An increased observance of COPD has probably also contributed to the increase in asthma medication use. A major shift in asthma treatment had occurred between 1992 and 2010, with considerably more subjects in 2010 using ICS and fewer using only SABA. In addition, the changed prescriptions options and regimens could be seen in the switch from oral to inhaled SABA, and the introduction of LABA. During the time period use of evidence based

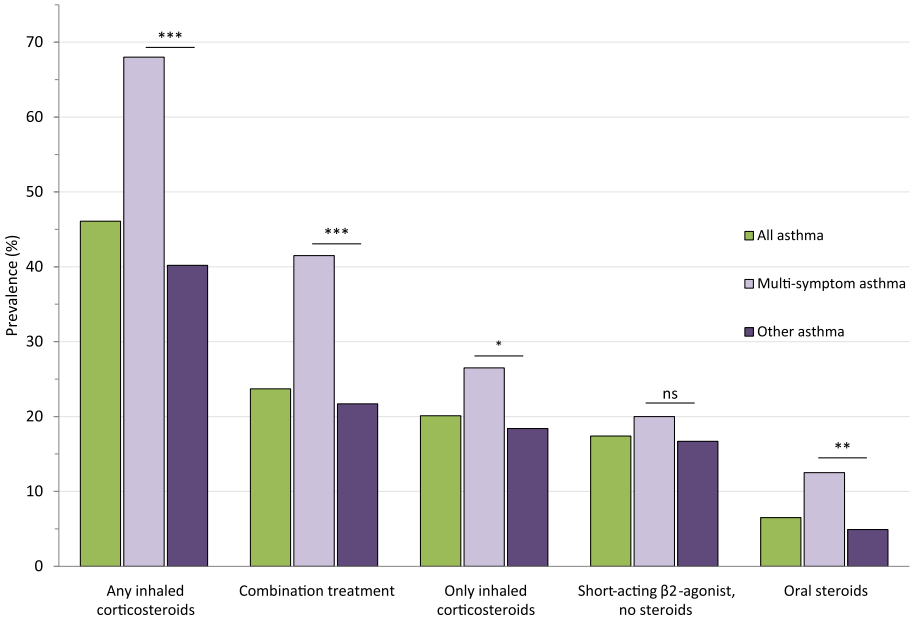


**Figure 4** Prevalence of asthma medication use among subjects with asthma, divided by degree of severity. *p*-Value — Fischer's exact test: *>0.05, **<0.01, ***<0.001, ns — non significant. The prevalence included both regular and occasional use.

**Table 1** Prevalence (%) of current use of asthma medication by gender, age group, smoking status and presence of allergic and chronic rhinitis within multi-symptom asthma. Significant *p*-vales, and associated prevalence are depicted in bold.

| | Gender | | | Allergic rhinitis | | | Chronic rhinitis | | |
|---|---|---|---|---|---|---|---|---|---|
| | Male (%) | Female (%) | *p*-Value | No (%) | Yes (%) | *p*-Value | No (%) | Yes (%) | *p*-Value |
| ***Any asthma medication*** | | | | | | | | | |
| All asthma | **61.0** | **69.1** | **0.011** | **59.1** | **70.0** | **0.001** | 63.1 | 69.3 | 0.052 |
| Multi-symptom asthma | 92.6 | 90.2 | 0.795 | 88.9 | 92.2 | 0.449 | 93.2 | 89.3 | 0.457 |
| Other asthma | **54.6** | **62.3** | **0.037** | **52.1** | **63.6** | **0.002** | 57.5 | 61.1 | 0.356 |
| ***Inhaled corticosteroids*** | | | | | | | | | |
| All asthma | **40.0** | **50.6** | **0.001** | 47.2 | 45.3 | 0.595 | 44.0 | 49.1 | 0.128 |
| Multi-symptom asthma | 64.7 | 69.7 | 0.523 | 72.2 | 65.6 | 0.349 | 68.2 | 67.9 | 1.000 |
| Other asthma | **35.0** | **44.5** | **0.009** | 41.4 | 39.4 | 0.597 | 39.5 | 41.5 | 0.643 |
| ***Inhaled corticosteroids only*** | | | | | | | | | |
| All asthma | **17.0** | **22.5** | **0.041** | 18.1 | 21.5 | 0.216 | 20.3 | 19.9 | 0.934 |
| Multi-symptom asthma | 19.1 | 30.3 | 0.094 | 23.6 | 28.1 | 0.510 | 30.7 | 23.2 | 0.261 |
| Other asthma | 16.6 | 20.0 | 0.257 | 16.8 | 19.6 | 0.389 | 18.4 | 18.5 | 1.000 |
| ***Combination treatment***[b] | | | | | | | | | |
| All asthma | 22.7 | 28.2 | 0.061 | 29.1 | 23.6 | 0.059 | 23.5 | 29.2 | 0.059 |
| Multi-symptom asthma | 45.6 | 39.4 | 0.450 | 48.6 | 37.5 | 0.137 | 37.5 | 44.6 | 0.316 |
| Other asthma | **18.1** | **24.6** | **0.033** | 24.6 | 19.6 | 0.105 | 20.9 | 22.9 | 0.521 |
| ***Short acting β2-agonists***[c] | | | | | | | | | |
| All asthma | 19.0 | 16.2 | 0.262 | **10.5** | **22.0** | **0.000** | 16.9 | 18.1 | 0.664 |
| Multi-symptom asthma | 25.0 | 17.4 | 0.263 | 13.9 | 23.4 | 0.140 | 21.6 | 18.8 | 0.722 |
| Other asthma | 17.8 | 15.8 | 0.491 | **9.7** | **21.6** | **0.000** | 16.1 | 17.8 | 0.543 |

| | Age group | | | | | Smoking status | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 17–30 (%) | 31–45 (%) | 46–60 (%) | 61–78 (%) | *p*-Value[a] | Non-smoker (%) | Ex-smokers (%) | Smokers (%) | *p*-Value[a] |
| ***Any asthma medication*** | | | | | | | | | |
| All asthma | 62.3 | 63.9 | 68.3 | 67.5 | 0.167 | 66.1 | 65.9 | 62.5 | 0.550 |
| Multi-symptom asthma | 86.5 | 86.3 | 96.7 | 92.3 | 0.135 | 89.5 | 92.2 | 92.7 | 0.498 |
| Other asthma | 56.2 | 59.0 | 60.1 | 59.4 | 0.551 | 60.6 | 59.8 | 45.1 | 0.059 |
| ***Inhaled corticosteroids*** | | | | | | | | | |
| All asthma | **36.1** | **40.7** | **50.4** | **56.6** | **0.000** | 44.2 | 48.2 | 48.2 | 0.266 |
| Multi-symptom asthma | **56.8** | **58.8** | **68.3** | **84.6** | **0.002** | 63.2 | 75.0 | 68.3 | 0.360 |
| Other asthma | **30.8** | **36.8** | **45.2** | **47.5** | **0.001** | 39.7 | 42.0 | 36.6 | 0.971 |
| ***Inhaled corticosteroids only*** | | | | | | | | | |
| All asthma | 14.8 | 20.4 | 23.5 | 20.3 | 0.130 | 20.5 | 20.6 | 17.9 | 0.640 |
| Multi-symptom asthma | 24.3 | 19.6 | 35.0 | 25.0 | 0.512 | 23.2 | 28.1 | 31.7 | 0.276 |
| Other asthma | 12.3 | 20.5 | 20.2 | 18.8 | 0.218 | 19.8 | 18.8 | 9.9 | 0.103 |
| ***Combination treatment***[b] | | | | | | | | | |
| All asthma | **20.8** | **20.0** | **26.9** | **36.8** | **0.000** | **23.3** | **27.6** | **31.3** | **0.048** |
| Multi-symptom asthma | **32.4** | **37.3** | **33.3** | **61.5** | **0.009** | 38.9 | 46.9 | 39.0 | 0.796 |
| Other asthma | **17.8** | **16.2** | **25.0** | **28.8** | **0.002** | 19.6 | 23.2 | 26.8 | 0.116 |
| ***Short acting β2-agonists***[c] | | | | | | | | | |
| All asthma | **24.6** | **21.1** | **16.0** | **8.0** | **0.000** | **19.9** | **15.9** | **10.7** | **0.014** |
| Multi-symptom asthma | **29.7** | **23.5** | **23.3** | **5.8** | **0.006** | 23.2 | 15.6 | 19.5 | 0.469 |
| Other asthma | **23.3** | **20.5** | **13.9** | **8.8** | **0.000** | **19.1** | **15.9** | **5.6** | **0.009** |

[a] *p*-Value test for trend.
[b] Inhaled corticosteroids and long acting β2-agonists.
[c] Without use of steroids.

guidelines for the treatment of asthma was implemented and results suggests more appropriate treatment regimens in 2010 and, possibly, also better asthma control.

Severe asthma is difficult to define in epidemiology, and the prevalence in different populations depends on the definitions used. Most definitions are mainly based on symptom severity despite the highest level of treatment or required need of asthma medication to achieve controlled disease [4,21–24]. In a recent publication, the WHO defines severe asthma as "uncontrolled asthma which can result in risk of frequent severe exacerbations and/or adverse reactions to medications and/or chronic morbidity" [25], a definition that does not include use of asthma medication. We have chosen a wide definition as a proxy for severe

**Table 2** Frequency of medication use among all asthma, multi-symptom asthma and other asthma. Significant *p*-vales are depicted in bold.

| | | All asthma (%) | Multi-symptom asthma (%) | Other asthma (%) | Test for trend[c] |
|---|---|---|---|---|---|
| **Inhaled corticosteroids** | Never | 54.2 | 32.0 | 60.2 | **<0.001** |
| | Occasionally | 16.4 | 19.5 | 15.5 | |
| | Most days | 29.4 | 48.5 | 24.3 | |
| **Inhaled corticosteroids, only** | Never | 75.8 | 68.0 | 77.9 | **0.003** |
| | Occasionally | 10.1 | 12.5 | 9.5 | |
| | Most days | 14.0 | 19.5 | 12.6 | |
| ***Combination treatment***[a] | Never | 74.4 | 58.5 | 78.6 | **<0.001** |
| | Occasionally | 6.4 | 7.5 | 6.1 | |
| | Most days | 19.2 | 34.0 | 15.2 | |
| **Oral steroids** | Never | 93.5 | 87.5 | 95.1 | **<0.001** |
| | Occasionally | 6.2 | 12.0 | 4.7 | |
| | Most days | 0.3 | 0.5 | 0.3 | |
| **Short-acting β2-agonist** | Never | 49.4 | 27.5 | 55.2 | **<0.001** |
| | Occasionally | 32.6 | 38.5 | 31.0 | |
| | Most days | 18.0 | 34.0 | 13.8 | |
| **Short-acting β2-agonist**[b] | Never | 82.6 | 80.0 | 83.3 | **0.040** |
| | Occasionally | 13.6 | 12.5 | 13.9 | |
| | Most days | 3.8 | 7.5 | 2.8 | |
| **Bronchodilator through nebuliser** | Never | 97.9 | 94.0 | 98.9 | **<0.001** |
| | Occasionally | 1.6 | 4.5 | 0.8 | |
| | Most days | 0.5 | 1.5 | 0.3 | |

[a] Inhaled corticosteroids and long acting β2-agonists.
[b] Without use of steroids.
[c] Multi-symptom asthma versus other asthma.

asthma, aimed at identifying a more severe asthma in epidemiological studies and to give guidance to treatment in health care. The subjects meeting our MSA criteria report more symptoms, have a lower lung function and more airway inflammation [13]. While MSA subjects may well be under-treated, our findings underline that MSA reflects a high symptom burden despite higher use of asthma medication compared to other asthmatics. MSA could fit in the WHO severe asthma definition of "difficult-to treat" severe asthma [25], as multiple symptoms can be due to adherence issues.

Until now there has been no data on medication use in more severe asthma from population studies and we hope that our data will contribute to the understanding of this

**Table 3** Risk factors (odds ratios (95% confidence intervals)) associated with use of asthma medication. Adjusted logistic regression. Significant risk factors are depicted in bold.

| | | Any asthma medication | Any inhaled corticosteroids | Combination treatment | High dose any inhaled corticosteroids |
|---|---|---|---|---|---|
| Age | 31–45 | 0.99 (0.73–1.35) | 1.14 (0.81–1.62) | 0.92 (0.59–1.43) | 1.28 (0.85–1.94) |
| | 46–60 | 0.96 (0.70–1.33) | 1.32 (0.92–1.88) | 1.13 (0.72–1.75) | 1.27 (0.83–1.95) |
| | 61–78 | 0.89 (0.64–1.25) | 1.46 (1.01–2.11) | 1.57 (1.01–2.45) | 1.44 (0.93–2.24) |
| BMI | <20 | 0.84 (0.49–1.45) | 1.10 (0.62–1.98) | 1.50 (0.78–2.88) | 1.16 (0.59–2.27) |
| | 25–29 | 1.17 (0.92–1.48) | 1.15 (0.89–1.49) | 0.94 (0.68–1.31) | 1.14 (0.84–1.56) |
| | ≥30 | **1.69 (1.28–2.23)** | **1.64 (1.22–2.20)** | **1.50 (1.05–2.14)** | **1.73 (1.22–2.45)** |
| Population density | 500–2000 | 0.77 (0.46–1.30) | 0.70 (0.39–1.26) | 0.90 (0.44–1.86) | 0.61 (0.30–1.24) |
| | 2000–10 000 | 1.05 (0.68–1.62) | 1.43 (0.91–2.25) | 1.58 (0.90–2.79) | 1.23 (0.72–2.10) |
| | >10 000 | 0.76 (0.55–1.05) | 0.88 (0.62–1.25) | 0.99 (0.63–1.56) | 0.83 (0.55–1.26) |
| Smoking | Former | 0.98 (0.78–1.23) | 0.96 (0.75–1.22) | 1.03 (0.76–1.40) | 1.02 (0.76–1.36) |
| | Current | 0.95 (0.69–1.31) | 1.07 (0.76–1.51) | 1.27 (0.84–1.92) | 1.10 (0.73–1.65) |
| Chronic rhinitis | Yes | **1.79 (1.45–2.21)** | **1.76 (1.41–2.21)** | **1.97 (1.49–2.60)** | **1.76 (1.35–2.30)** |
| Allergic rhinitis | Yes | **3.28 (2.67–4.01)** | **2.14 (1.71–2.67)** | **1.59 (1.20–2.09)** | **2.36 (1.81–3.07)** |

Reference categories were: being aged 17–30, having a BMI of 20–24, non-smoking, a population density <500, not having chronic rhinitis and not having allergic rhinitis, respectively.

issue. Worldwide many subjects fall short of treatment goals [26,27]. Despite guideline recommendations, the limited reviews available suggests that control of persistent asthma remains poor [28] with combination treatment being regarded as the most effective [29]. In view of this it is discouraging that only 44% of subjects with MSA and 22% of subjects with OA report use of a combination treatment, however, this is in line with other studies [28,30].

Those classified as having MSA used their medication more frequently and in higher doses than those classified as having OA. Further, maintenance treatment was considerably more common among those with MSA, reflecting current guidelines where subjects with persistent asthma should not only use relief medication. In contrast to current guidelines, 29% of users of LABA with MSA and 11% of users of LABA with OA did not concomitantly use ICS.

The prevalence of asthma medication use varies largely in Europe. Data from the 1992 ECHRS study report prevalence of asthma medication ranging from 1% to 9% [31]. Use of broncho-pulmonary drugs was reported by 5% in a general population in Italy in early 1990s, lower than in the ECHRS study group that was used for comparison in our study [32]. The use of ICS and LABA only found in the current study is slightly higher than in a clinical sample investigated in early 2000s [28].

Issues of non-adherence are well recognised in asthma and low adherence is associated with poor asthma control and an increased risk of exacerbations [33,34]. We estimate that in our study at least 30% of MSA can be due to low adherence or under-treatment, as they do not have a maintenance treatment, or use it irregularly. This is in line with another study where 35% of asthmatics had non-adherence as the main cause of difficult-to-treat asthma [35].

The identified risk factors, with the exception of old age, reflects, as expected, risk factors previously associated with asthma [8,13]. It has previously been shown that concomitant rhinitis increases the burden of asthma results in a lower level of asthma control [36]. The association between old age and ICS could reflect a lower adherence to maintenance treatment among younger subjects [37]. Smokers used combination treatment to a greater extent than ex-smokers and non-smokers, possibly reflecting COPD, especially as these subjects were older.

A strength of the current study is the large study population drawn from the general population which results in high degree of representativeness of the population in the studied region [18]. Some of the subjects regarded as asthmatics might have COPD. Most asthmatics in the current study had an onset of disease in young adulthood or earlier but might have developed a combination of asthma and COPD. The main weakness of the study is the lack of objective measurements of medication use. However, we suggest that the results are reasonably accurate as many subjects admit non-adherence. An agreement analysis revealed high absolute agreement for ICS and combination treatment, with kappa-vales above 0.6, suggesting substantial agreement. However, an additional aim for the future should be to investigate adherence by using data from the prescription refill registry in a larger sample. The response rates of 59% and 55% in the random and asthmatic sample respectively, while comparable to many other international studies, instigated a sensitivity analysis. This analysis showed no differences in gender, smoking or reported use of asthma medication between participants and non-participants. However, participants reported somewhat more ever and physician-diagnosed asthma, any wheeze and allergic rhinitis. We do not believe these differences had any major influence on the results.

In conclusion, an increase in asthma medication use of 54% from 1992 could be observed. A shift in asthma medication use from 1992, with an increased in the use of steroids and a decreased in the use of SABA was also found. Moreover, it demonstrates that the presence of multiple asthma symptoms in a patient should alert the treating physician to the possibilities of under-medication and poor adherence to the treatment regimen.

## Conflict of interest

Dr. Ekerljung, Dr. Bjerg, Dr. Bossios, Dr. Axelsson, Dr. Torén and Dr. Wennergren have nothing to disclose. Dr. Lötvall reports grants and personal fees from AstraZeneca, grants and personal fees from GSK, personal fees from Merck/MSD, personal fees from Abdi Ibrahim, personal fees from Novartis, outside the submitted work. Dr. Lundbäck reports grants and personal fees from AstraZeneca, grants and personal fees from GSK, personal fees from Mundipharma, personal fees from MSD, personal fees from Takeda, outside the submitted work.

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