

Multimorbidity in Asthma, Allergic Conditions and COPD Increase Disease Severity, Drug Use and Costs: The Finnish Pharmacy Survey

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Keywords

Allergic rhinitis · Asthma costs · Asthma multimorbidity · Atopic eczema · Pharmacotherapy

Abstract

Background: Asthma, allergic conditions, and COPD overlap, but the effect of them and their combinations on disease severity, need for drugs, use of healthcare, and costs is poorly known. **Objective:** To study how different allergic diseases co-occur in asthma and allergy patients and evaluate the use of medication well as drug and healthcare costs. **Methods:** Nationwide Allergy Barometer Survey was carried out in the Finnish pharmacies during 1 week in September 2016. Altogether, 956 patients (5–75 years) who purchased asthma or allergy drugs with prescription participated in 351 pharmacies. **Results:** Of the participants, 78% reported physician-diagnosed asthma, 57% allergic rhinitis, 24% atopic eczema, 21% food allergy, 20% allergic conjunctivitis, 8% anaphylaxis, and 8% COPD. One-third of the patients had at least three

conditions, and multimorbidity was common across all age groups. Disease severity increased with the number of coexisting conditions, and asthma severity also with age. Patients with asthma alone used on average 3.8 drugs with the annual costs of EUR 661. This increased to 4.9 drugs and EUR 847 in asthmatics with multimorbidity. For all participants, costs of drugs and healthcare services together during the preceding year were on average EUR 1,214, of which 56% were drug costs. The costs doubled to EUR 2,714 in 65 subjects (7%) who had both asthma and COPD. **Conclusions:** In asthma and allergy, multimorbidity and polypharmacy are major concerns. Disease severity, drug use, and costs increased with multimorbid conditions. To reduce the burden, allergy management should be better integrated and more comprehensive.

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Introduction

One of the six goals in the Finnish Allergy Programme 2008–2018 is to improve management of severe asthma and allergies [1]. This is a prerequisite for cost reduction, both at the societal and patient level.

Many allergic conditions such as asthma, allergic rhinitis, allergic conjunctivitis, food allergy, and atopic eczema occur in same patients, and one manifestation often precedes the other as rhinitis may precede asthma [2–4]. Poor adherence to medication is a common reason for loss of asthma control [5, 6]. Clinical guidelines advise to adjust medication according to symptom severity [6–8]. At the population level, outcome of asthma improves if diagnosis is made early, treatment is started effectively, and patients are guided to proactively stop symptom increase [9, 10]. It is poorly known how asthma multimorbidities affect drug use and treatment adjustments.

Our aim was to present how different allergic diseases co-occur in asthma and allergy patients. In addition, we studied the use of medication as well as drug and healthcare costs.

Material and Methods

The study cohort consisted of 956 participants aged 5–75 years (mean 51 years, 74% females) who purchased asthma or allergy medication from 351 Finnish pharmacies (43% of all 810 pharmacies) across the country. One to 8 voluntary clients per pharmacy participated in a questionnaire survey during one week in September 2016.

The pharmacy personnel asked the participant to fill in a questionnaire, if he or she was purchasing asthma or allergy drugs with a prescription made by a physician. In the questionnaire, physician-diagnosed asthma, allergic conditions (allergic rhinitis, allergic conjunctivitis, atopic eczema, food allergy, and history of anaphylaxis), and COPD were asked for [11]. The pharmacist helped the client to answer the questions if needed. For the 55 (6%) participating children under the age of 15 years, the information was obtained from the parents.

The respondents estimated severity of their condition by using a numerical scale from 0 to 10 (0–1 no symptoms, 2–5 mild symptoms not disturbing everyday life or sleep, 6–8 moderate symptoms disturbing daily activities and causing sleep disturbances, 9–10 severe symptoms and hospitalizations) [12].

Use of asthma and allergy drugs during the last 12 months was enquired. Asthma drugs were inhaled bronchodilators, inhaled corticosteroids, combination drugs, corticosteroid tablets, leukotriene antagonists, theophylline, and omalizumab. Allergy drugs were antihistamines, nasal sprays, and eye drops for allergic symptoms, creams and ointments for atopic eczema, and epinephrine auto-injectors for anaphylaxis. Depending on the purchased drug, the use was asked with the options: no, occasionally, short courses (how many courses), daily or almost daily. Medication costs were

estimated according to actual drug use and mean price of the drug in question [13]. Occasional drug use was estimated as 100 daily doses per year, and a short course as a use of 10 days. The cost of daily use was the mean price of 360 daily doses of the drug. Occasional use of topical calcineurin inhibitors was estimated as 60 g and daily use as 240 g per year. Patients with atopic eczema were estimated to use 300 g corticosteroid creams or ointments (except patients with daily use of calcineurin inhibitors) and 2 kg moisturizers per year. For omalizumab, the cost estimate was based on use of 300 mg dose per month.

Patients were asked what healthcare services they had used over the last 12 months [10]. (1) Have you had an appointment with a physician or nurse because of asthma or allergy: yes (how many times), no appointment? (2) Have you been treated at a hospital emergency unit because of asthma or allergy: yes (how many times), no? (3) Have you been hospitalized due to asthma or allergy: yes (how many days), no? The unit cost estimates were: for an appointment with a physician or nurse EUR 150/50, for an emergency visit EUR 270, and for a day at the hospital EUR 460 [14]. The healthcare costs did not include drug costs.

The study protocol was approved by the coordinating Ethics Committee of the Helsinki and Uusimaa Hospital District (HUS).

Statistical Methods

The data are presented as means with standard deviations (SD) or as counts with percentages. Differences between groups were compared using the Kruskal-Wallis test with Dunn's post hoc test for multiple comparisons. Pearson correlation was used to assess correlations with the significance level accepted at $p < 0.05$.

Principal component analysis (PCA) is used to visualize the data. This multivariate analysis emphasizes variation and brings out patterns in the dataset. PCA projects the multidimensional data into a simplified diagram without losing the significant information. In the scatterplot diagram, dots represent individual patients, and the location of dots is based on the combination of asthma and allergy drugs used by patients. The size of the dots indicates the healthcare cost including drugs.

Results

Number of Allergic Conditions

The 956 respondents had, on average, 2.2 physician-made diagnoses (asthma, rhinitis, conjunctivitis, eczema, food allergy, anaphylaxis, or COPD) (Table 1). Physician-diagnosed asthma was reported by 750 subjects (78%), and some other allergic condition by 650 subjects (68%). The study participants reporting both asthma and allergic conditions had on average 3.1 diagnoses (range 2–7), and those with allergic conditions but no asthma had on average 1.8 diagnoses (range 1–4). Seventy-five (8%) respondents had COPD, and 65 of them (67%) also reported asthma. Sixteen clients (2%) purchasing asthma or allergy medication had no diagnosis made by a physician.

Allergic rhinitis ($n = 549$, 57%) was the most common multimorbidity, as 91% of the subjects with allergic con-

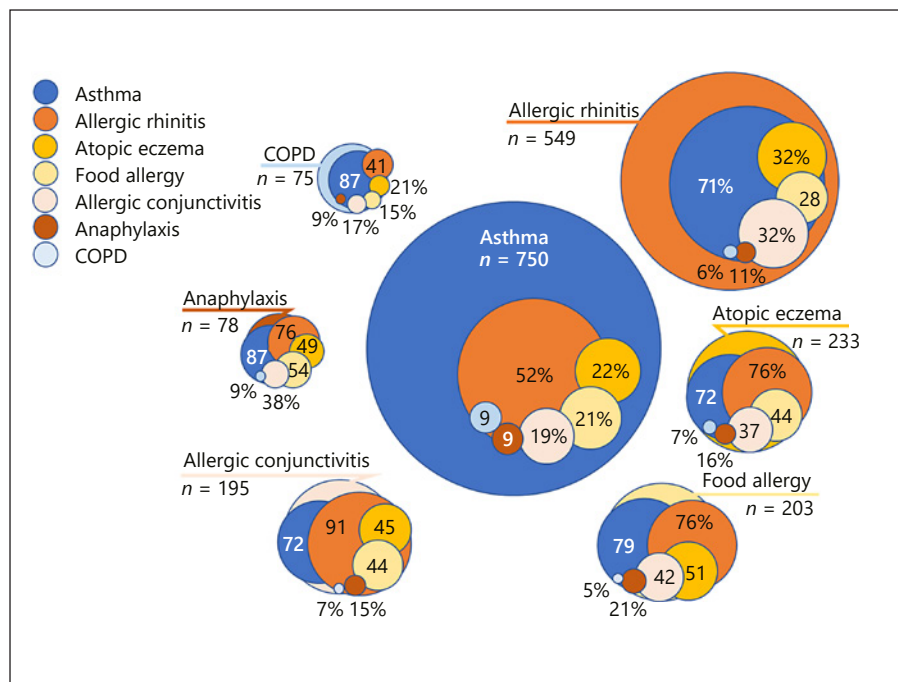


Fig. 1. Self-reported physician-diagnosed asthma, allergic conditions, COPD, and overlap of the diagnoses in the 956 subjects participating in the Pharmacy Allergy Barometer Survey. For example, 71% of patients with physician-diagnosed allergic rhinitis have also asthma diagnosis and 32% atopic eczema.

Table 1. Characteristics of participants of the Allergy Barometer Survey in the Finnish Pharmacies 2016 ($n = 956$): self-reported physician-diagnosed asthma, other allergic conditions, and COPD as well as drug use and need for healthcare during the preceding year

	All $n = 956^a$	Asthma (no allergies) $n = 284$	Asthma and allergies $n = 466$	Allergies (no asthma) $n = 184$	p
Age, years ^b	49.2 (18.3)	54.1 (16.6)	48.5 (18.6)	42.5 (18.0)	<0.001 ^{1, 2, 3}
Female, %	74.0	69.4	77.9	73.9	0.037 ¹
Diseases					
COPD, %	7.8	10.9	7.3	2.2	0.002 ^{2, 3}
Asthma, other allergic conditions, COPD, n	2.2 (1.3)	1.1 (0.3)	3.1 (1.1)	1.8 (0.9)	<0.001 ^{1, 2, 3}
Drug use					
Asthma drugs used, n	2.3 (1.3)	2.6 (1.1)	2.8 (1.1)	0.7 (0.6)	<0.001 ^{2, 3}
Allergy drugs used, n	1.9 (1.1)	1.2 (1.0)	2.1 (0.9)	2.4 (0.9)	<0.001 ^{1, 2, 3}
Drugs in total, n	4.2 (1.7)	3.8 (1.7)	4.9 (1.5)	3.1 (1.4)	<0.001 ^{1, 2, 3}
Healthcare use					
Appointments with a physician and a nurse, n	2.6 (4.3)	2.4 (3.4)	3.1 (5.3)	1.4 (1.9)	<0.001 ^{1, 2, 3}
Emergency visits, n	0.4 (1.6)	0.3 (1.4)	0.5 (2.0)	0.1 (0.6)	<0.001 ^{2, 3}
Hospitalization, days	0.3 (2.0)	0.2 (1.6)	0.4 (2.4)	0.0 (0.2)	0.031 ^{2, 3}

Data are presented as mean (SD) or as stated. ^a Sixteen participants had no self-reported physician-diagnosed allergic condition, and 6 participants had only self-reported COPD; these numbers are included in the total of 956. ^b Six percent (55) of participants were <15 years, and 23% (218) of participants >65 years. ¹ Significant asthma vs. asthma and allergies. ² Significant asthma vs. allergies. ³ Significant asthma and allergies vs. allergies.

junctivitis and 41–76% of those with other conditions reported rhinitis (Fig. 1). COPD and anaphylaxis were the least frequent multimorbidities, but even they were present in 5–21% of the subjects with other conditions. 33% of the patients ($n = 319$) had at least 3 allergic conditions, and multimorbidity was common across all age groups.

The numerical rating of self-reported asthma severity was 4.2 (SD 2.4) on a scale from 0 to 10, and of multimorbidities 3.7 (SD 2.3). Severity of asthma increased along with the number of coexisting conditions ($r = 0.158$, $p < 0.01$) (Fig. 2). Likewise, severity of the other allergic conditions increased with their numbers ($r = 0.310$, $p < 0.01$). Older age also increased asthma severity ($r = 0.139$, $p < 0.01$).

Drug and Healthcare Use

Respondents used on average 2.3 asthma drugs and 1.9 allergy drugs, i.e. 4.2 drugs per patient (Table 1). Asthma patients with other allergic conditions used on average 4.9 drugs per patient (range 1–9), while allergic patients without asthma used 3.1 drugs (range 1–8). The most widely used drugs were inhaled bronchodilators. Their use varied from 71 to 95% in the various diagnostic categories (Fig. 3). The use of antihistamines varied from 59 to 93%.

A high number of asthma patients (69%) used some allergy drug, although they did not report any allergy diagnosis made by a physician. They commonly used antihistamines (56%), nasal sprays (45%), and eye drops (17%). 72% of them had suffered nasal congestion sometime during the past year. Oral corticosteroids were used by 36% of all asthma patients, and only 1.5% used them daily. Others had short courses (mean 2 courses during the year, range 0–20).

There were 184 patients with some allergic condition (4 patients also had COPD), but without an asthma diagnosis. Nevertheless, 45% of them ($n = 82$) used asthma drugs: 32% bronchodilators, 18% inhaled corticosteroids, and 6% combination drugs. 68% of these patients with multimorbidity, but lacking asthma diagnosis, had suffered shortness of breath, and 60% reported wheezing during the past year. For comparison, these figures were 82 and 70% in those who had physician-confirmed asthma.

Asthma patients needed more emergency visits (18 vs. 5%, $p < 0.001$) and hospitalizations (6 vs. 1%, $p = 0.010$) than those without asthma. They also needed more appointments with a physician (67 vs. 53%) or nurse (33 vs. 20%).

Drug and Healthcare Costs

In the principal component analyses, the ordination diagram shows patients with asthma (right side) and with some multimorbidity (left side), although areas of the two

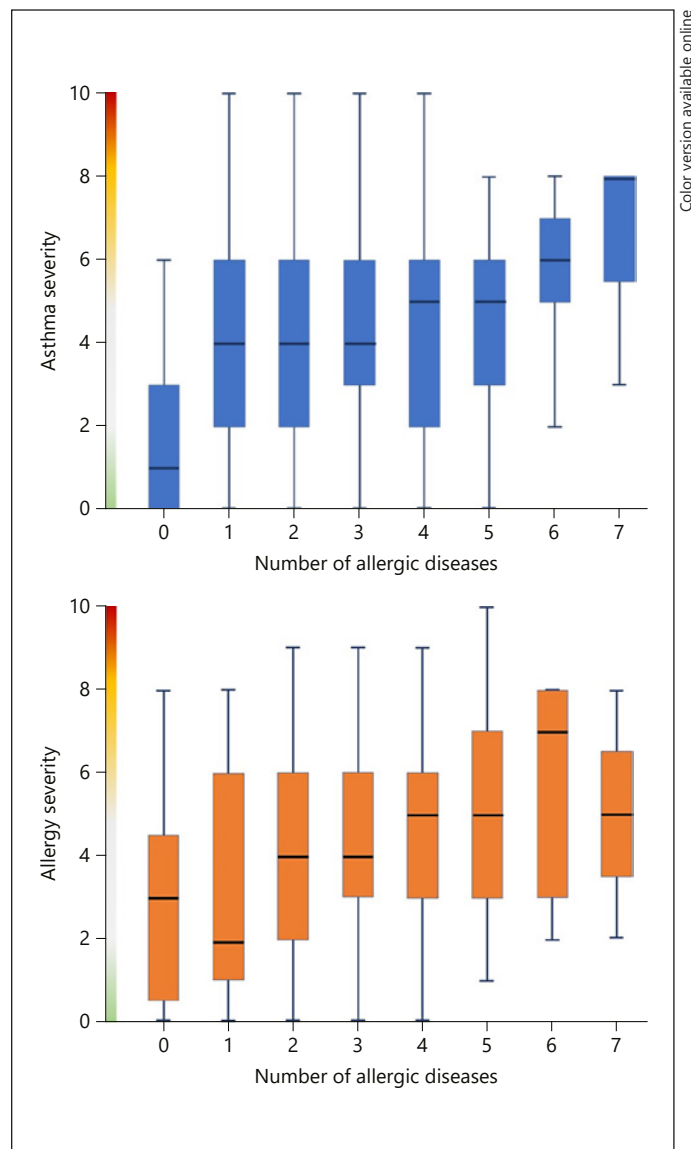


Fig. 2. Correlation of asthma severity (VAS 0–10) and number of multimorbid conditions is shown in the upper panel. Correlation of severity of the other allergic conditions and number of coexisting conditions is shown in the lower panel.

groups strongly overlap (Fig. 4). The composition in the diagram is based on drug use; thus, the overlapping area is explained by similar drug use. Patients with asthma, with or without any multimorbidity, had the highest drug and healthcare costs (Table 2).

The average annual drug and healthcare costs for all participants were EUR 1,214, of which EUR 681 (56%) accounted for drug costs and EUR 533 healthcare costs (44%).

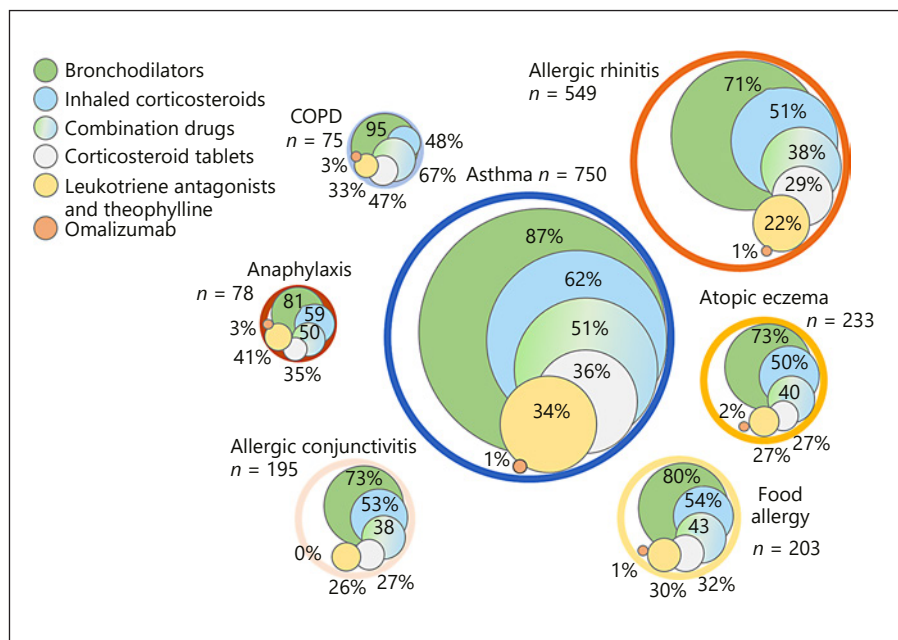


Fig. 3. Use of asthma drugs in different diagnostic categories in 956 subjects participating in the Allergy Barometer Survey. For example, 71% of those who had physician-diagnosed allergic rhinitis used inhaled bronchodilators, and 51% inhaled corticosteroids, which is explained by the high number of asthmatics among rhinitis patients.

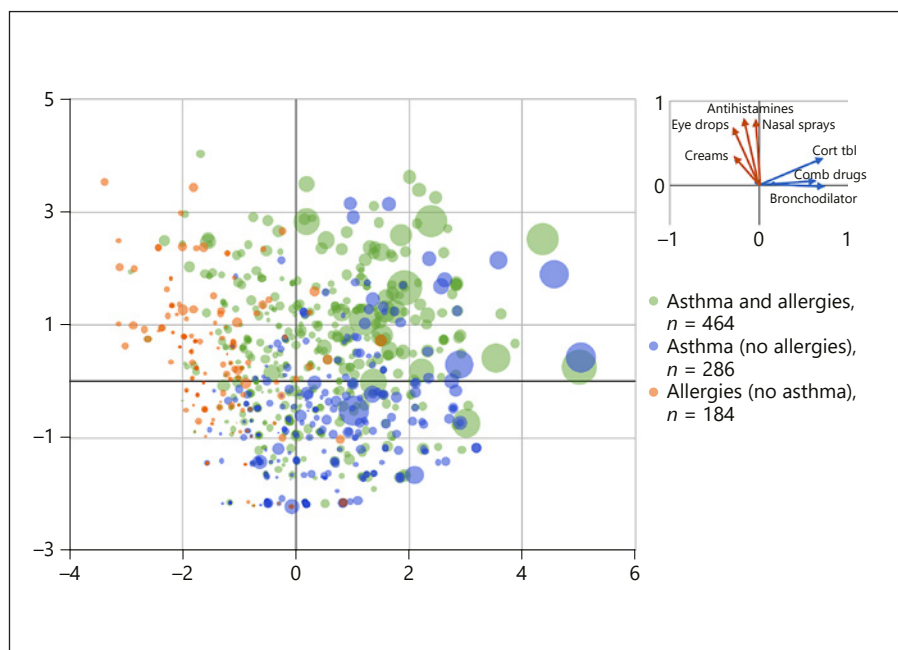


Fig. 4. Principal components analysis according to drug use and healthcare costs. One dot is one individual having a physician-diagnosed asthma and some allergic condition, asthma alone, or an allergic condition but no asthma. Composition of patients is based on their use of asthma and allergy drugs. Small panel arrows indicate increasing use of a drug. Increasing dot size indicates increasing costs of drugs and healthcare.

The mean drug costs were EUR 661 for patients with asthma diagnosis alone increasing to EUR 847 in those with asthma and some multimorbid condition. Drug costs were especially high in 8 asthma patients using a biological treatment, omalizumab, with an annual cost of EUR 11,400. For patients with some allergic condi-

tions but no asthma, drug costs were markedly lower, EUR 262.

The average healthcare costs were EUR 502 for patients with asthma alone increasing to EUR 682 in those asthmatics with some coexisting condition. 14% of patients with asthma and a multimorbid condition had an annual cost of

Table 2. Drug and healthcare costs for asthma and other allergic conditions according to the Allergy Barometer Survey in the Finnish Pharmacies 2016

	All <i>n</i> = 956 ^a	Asthma (no allergies) <i>n</i> = 284	Asthma and allergies <i>n</i> = 466	Allergies (no asthma) <i>n</i> = 184	<i>p</i>
Medication costs, EUR					
Asthma drugs	547 (1,157)	614 (1,073)	677 (1,270)	74 (177)	<0.001 ^{2, 3}
Allergy drugs	134 (163)	47 (88)	170 (165)	188 (190)	<0.001 ^{1, 2}
Healthcare costs, EUR					
Asthma	392 (1,274)	448 (1,204)	497 (1,515)	35 (163)	<0.001 ^{2, 3}
Allergies	141 (372)	54 (180)	185 (473)	171 (267)	<0.001 ^{1, 2, 3}
Total costs, EUR					
Asthma	939 (1,881)	1,061 (1,723)	1,172 (2,153)	109 (265)	<0.001 ^{2, 3}
Allergies	275 (438)	100 (225)	355 (530)	359 (347)	<0.001 ^{1, 2}
In total	1,214 (2,002)	1,161 (1,752)	1,527 (2,351)	468 (436)	<0.001 ^{1, 2, 3}

Data are presented as mean (SD). ^a Sixteen participants had no self-reported physician-diagnosed allergic diseases, and 6 participants had only self-reported COPD. These numbers are included in the total of 956; ¹ Significant asthma vs. asthma and allergies; ² Significant asthma vs. allergies; ³ Significant asthma and allergies vs. allergies.

over 1,000 (max EUR 18,400). Costs for patients without asthma were again lower, EUR 206, and in all but 5 patients less than EUR 1,000 (max EUR 1,890). Asthma patients with COPD (*n* = 65) had high costs (EUR 2,714). In general, healthcare costs in the COPD patients (*n* = 75) were increased due to the high number of hospital days (mean 1.4 days vs. 0.3 days in all participants).

Both drug ($r = 0.255$, $p < 0.001$) and healthcare costs ($r = 0.314$, $p < 0.001$) increased with asthma severity.

Discussion

The study participants reporting asthma and allergic diseases had, on average, 3.1 allergic conditions, which decreased to 1.8 in patients with allergic diseases but no asthma. Allergic rhinitis was the most common allergic condition co-occurring in half of the participants with asthma. The number of allergic conditions had a marked impact on disease severity, drug and healthcare use, and costs. Asthma patients with allergies used more drugs than patients with either one of these conditions alone. The number of conditions increased the self-reported severity of asthma and allergy and not surprisingly also drug and healthcare costs.

Among conditions in which allergy plays a role, asthma is most important in terms of causing mortality, dis-

ability, and costs [15]. In the literature, the commonly analyzed asthma multimorbidities have been sinusitis, gastroesophageal reflux, and mental disorders [16, 17]. In the present study, all allergic conditions as well as COPD were analyzed. Asthma patients purchasing drugs in the Finnish pharmacies had on average two co-existing conditions and asthma severity clearly increased with the number of multimorbidities. The most prevalent multimorbidity, allergic rhinitis, co-occurred in 52% of those with asthma but was present even in 91% of patients with conjunctivitis. Asthma patients probably underreported their rhinitis, as the occurrence has been even higher in some other studies, at least 70% in severe asthma [18].

Rhinitis is associated with both allergic and non-allergic asthma, but also a non-rhinitic asthma phenotype has been identified [19, 20]. Shared risk gene variants have been suggested in asthma, allergic rhinitis, and atopic eczema [21]. Monosensitization and polysensitization have been proposed as different phenotypes, especially the latter increasing the risk of multimorbidity [22, 23]. However, in a longitudinal cohort of children, the non-IgE conditions increased the risk of multimorbidity [3]. Clinical studies often focus either on airways (asthma, rhinitis) or skin-related symptoms (atopic eczema, food allergy), although they often have common background. This was exemplified in a study, where treatment of atopic

dermatitis decreased respiratory symptoms and bronchial hyperresponsiveness [24].

Oral corticosteroids are still important asthma drugs in Finland, as 36% of the asthmatics needed them, mainly as short courses. Only a few (1%) used biological treatments but at the time of the study only one biological treatment was available for asthma. Recent recommendations favor biological treatments instead of regular oral corticosteroids in severe asthma [25, 26]. In Finland, results of the public health programs for asthma (1994–2014) and for all allergic conditions (2008–2018) have shown that early treatment with conventional drugs is effective [27]. However, since 2016 biological treatments have been introduced also into atopic dermatitis, chronic urticaria, and nasal polyposis, and their role is likely to increase with the personalized medicine approach.

In asthma patients, drug and healthcare costs together were on average EUR 1,161 during the preceding year. As expected, multimorbidity increased drug use. Asthma patients with multimorbidity used on average 4.9 drugs (3.1 drugs if asthma was not present). Also, asthmatics with multimorbidity had more emergency visits, hospitalizations, and visits to a physician or nurse. If other allergic conditions were present, drug and healthcare costs (EUR 1,527) were one-third higher than in patients with asthma alone. Co-occurrence of COPD doubled the overall costs. In allergic patients, drug and healthcare costs (EUR 468) were only half of those observed in patients with asthma.

In 2 recent studies for allergic rhinitis and allergic asthma, the direct and indirect costs have clearly increased with severity and poor control of the condition [28, 29]. However, the cost effect of multimorbidity has not been analyzed in any detail.

Strengths and Limitations

The study sample was nationwide and obtained during routine pharmacy visits. All areas of Finland were represented, and both large city pharmacies and small rural pharmacies participated. Thus, the response rate of 43% was satisfactory, and the respondents represented the pharmacy clients. There were more women (74%) in the respondents than in patients with asthma in general in Finland (60%). Probably either willingness to participate in the study or purchasing asthma and allergy drugs have been greater in women than in men. The mean age of the allergic respondents (42.5 years) was close to the age of the Finnish population in general (42 years). The mean age of the asthma patients (50.6 years) was little less than in the Finnish database of existing entitlements to reimbursement of asthma

drug expenses (56 years), and thus the sample can be considered representative.

The target population was all those purchasing asthma or allergy drugs, with a physician's prescription, during a defined time period of 1 week in early autumn. At that time, the pollen season in Finland is over, and the season of respiratory infections has not yet started. This may mean that the need for drugs was at a lower level compared with the high "flu" season or start of the birch pollen season in spring. Self-reported questionnaire data have limitations as objective lung function or allergy testing are lacking. Nevertheless, physician-made diagnoses have shown to be reliable in Finland [30]. The cost calculations presented here give unique information of cumulating costs with multimorbidity.

Conclusions

Participants with asthma and allergies had on average three allergic conditions. Multimorbidity increased the severity of the overall condition. Participants used on average four drugs for asthma and allergy symptoms. This is a major concern in terms of treatment adherence and rational use of medication. The average costs of drugs and healthcare use are three times bigger in asthma than in an allergic condition without asthma. Asthma symptoms are common in allergic patients and lead to asthma drug prescriptions, even without proper diagnosis. Early detection of asthma and guidance for rational drug use in the multifaceted allergy syndrome remain a challenge in Finland. Our results call for a more comprehensive and integrated approach to asthma and allergy management.

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Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Juha Jantunen, Johanna Salimäki, and Paula Kauppi collected and processed the data. All authors participated in planning the study, interpreting the data, and writing the paper.

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