Family Practice 2013; **30**:621–628
doi:10.1093/fampra/cmt055
Advance Access publication 10 October 2013

Predictors of exacerbations of asthma and COPD during one year in primary care

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Received 14 May 2013; Revised 4 August 2013; Accepted 25 August 2013.

Aims. To investigate the incidence of asthma and chronic obstructive pulmonary disease (COPD) exacerbations in primary care during one year and to identify risk factors for such events.

Methods. The study was carried out at seven general practice offices in Norway. Patients aged 40 years or more registered with a diagnosis of asthma and/or COPD the previous 5 years were included. After a baseline examination, the participants consulted their GP during exacerbations for the following 12 months. A questionnaire on exacerbations during the follow-up year was distributed to all. Univariable and multivariable logistic regression was performed to determine predictors of future exacerbations.

Results. Three hundred and eighty patients attended the baseline examination and complete follow-up data were retrieved from 340 patients. COPD as defined by forced expiratory volume in the first second of expiration/forced vital capacity (FEV_1/FVC) < 0.7, was found in 132 (38.8%) patients. One hundred and fifty-nine patients (46.8%) experienced one exacerbation or more and 101 (29.7%) two exacerbations or more. Patients who had an exacerbation treated with antibiotics or systemic corticosteroids or leading to hospitalization the year before baseline ($N = 88$) had the highest risk of getting an exacerbation during the subsequent year (odds ratio 9.2), whether the FEV_1/FVC was below 0.7 or not. Increased risk of future exacerbations was also related to age ≥ 65 years and limitations in social activities, but not to the FEV_1.

Conclusions. The study confirms that previous exacerbations strongly predict future exacerbations in patients with COPD or asthma. Identification and a closer follow-up of patients at risk of such events could promote earlier treatment when necessary and prevent a rapid deterioration of their condition.

Keywords. Asthma, COPD, exacerbation, primary care.

Introduction

Chronic obstructive pulmonary disease (COPD) causes a permanent decrease in lung function and causes a high degree of disability and mortality.[1–3] Asthma is a chronic reversible inflammatory disorder of the airways in which chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing. These episodes are usually associated with widespread, but variable, airway obstruction within the lung that is often reversible either spontaneously or after treatment.[4] These two obstructive lung diseases have many similarities; they may be difficult to differentiate and may co-exist in some patients.[5,6] COPD is in the top five leading causes of death in the world. The incidence of COPD increases with increasing age and the number of people aged 65 years or more is expected to double by 2025 in developed countries.[6]

The course of COPD is punctuated by periods of increased symptoms, known as exacerbations. COPD exacerbations are associated with a significant health-related and economic burden, which marks the need for early detection and treatment. Early identification and prompt treatment of exacerbations are essential to reduce not only the costs but also the consequences of such exacerbations by reducing recovery time, improving health-related quality of life and reducing risk of hospital admission.[7] COPD exacerbations increase the risk of cardiovascular events[8] that are responsible for much of the morbidity[2] and mortality[9] associated with the disease.

When it comes to the prediction of future exacerbations, not many studies have been done. The predictive value of previous COPD exacerbations has come into focus recently and Donaldson et al.[10] found, after following COPD patients for 4 years, that the number of exacerbations a patient experienced over the first year was highly and positively correlated with the number of exacerbations suffered during the following year. A large cohort study by Hurst et al.[11] found that the best predictor of exacerbations was an exacerbation the previous year.

Patients with asthma, whether they are adults or children can also suffer from acute exacerbations that range in severity from mild to life-threatening events.[12] Recent work shows interest in identifying asthma subtypes more prone to exacerbations and its associated predictive factors. Although the frequency of exacerbations can be increased in patients with severe asthma, patients with mild asthma can also experience severe asthma exacerbations.[12,13] Studies have shown that patients with a history of asthma exacerbations are at higher risk of future episodes of severe asthma exacerbations.[13–15]

More studies, especially in primary care context, are needed to validate the results of the previous studies. Hence, the aim of this study was (i) to identify exacerbation frequency among patients diagnosed with asthma and/or COPD in primary care and (ii) to evaluate the possible predictors of such exacerbations.

Methods

Design

This study was a multicenter prospective cohort study with a baseline registration and a 12 months follow-up period.

Study patients

The study was carried out at seven general practice offices in the north and south of Norway. The practices were not randomly selected, but practices with spirometry available the previous 5 years and a certain type of the electronic medical record system (Winmed) used in this period were chosen. Out of the 43 241 patients listed at these seven offices, 18 931 (43.8%) were aged 40 years or more. Among these, 1784 patients with a diagnosis of asthma and/or COPD, registered within the 5 years previous to the start of the study, were identified. Out of these, a random sample of 1111 patients, following an alphabetical order, was invited by mail to take part and 380 patients participated in baseline registration. We asked each clinic to send invitations to at least 150 patients each to be sure to get 50 patients from each clinic, but the response rate varied between these clinics. The participants have previously been described in more detalis.[16] Participation implied a baseline examination during stable phase of disease, including spirometry, which took place between April 2009 and March 2010, and examinations during exacerbations the following 12 months.

Baseline registrations

The patients were asked to report symptoms and limitations in daily activities in the previous 7 days in the validated Clinical COPD Questionnaire (CCQ).[17] Spirometry was performed according to the American Thoracic Society/European Respiratory Society guidelines,[18] using a Spirare SPS310 Spirometer (Diagnostica AS, Oslo, Norway), both before and 20 minutes after inhalation of a short acting bronchodilator (0.4 mg salbutamol). Twelve per cent increase of forced expiratory volume in the first second of expiration (FEV_1), together with a minimum increase of 200 ml, was used as evidence of reversibility. Patients with a post-bronchodilator FEV_1/forced vital capacity (FVC) ratio < 0.7 were classified as COPD patients. C-reactive protein (CRP) was measured using Afinion AS100 Analyzer (Axis-Shield, Dundee, Scotland), Orion Quickread CRP (Orion Diagnostica Oy, Espoo, Finland) or ABX Micros CRP (HORIBA medical, Montpellier, France). These analyzers could display values down to 8 mg/l, which was used as cut-off value in the analyses. Oxygen saturation was measured by a digital handheld pulse oxymeter, Onyx II model 0550 (Nonin Medical Inc., Plymouth, MN). The best of three measurements was recorded.

Exacerbations

A COPD exacerbation is defined as an increase in dyspnea, coughing or sputum amount that is acute in onset for at least 1 day, which necessitates a dosage adjustment of medication.[1] Asthma exacerbations are defined as episodes of a progressive increase in shortness of breath, cough, wheezing, chest tightness or a combination of these symptoms.[4] The patients were asked to consult their GP within 2–3 days when they experience such an increase in symptoms.

In addition to registering consultations during 1-year follow-up, a questionnaire was sent to all participating patients after 12 months, asking about the exacerbations that had occurred during the previous year (after the baseline registration). The patients were asked how many times they had visited a doctor or had been hospitalized, because of an exacerbation or had treated themselves with antibiotics or oral corticosteroids. Patients who had either visited their GP office due to an exacerbation during the observation year or had recorded an exacerbation in the questionnaire were classified as having one or more exacerbations during the follow-up year. If they had visited the GP office two times during the follow-up year, or in addition to one

GP visit had recorded hospitalization or self-treatment with antibiotics/oral corticosteroids in the questionnaire or had recorded two or more exacerbations in the questionnaire, were classified as having two or more exacerbations the following year. Physician visits due to a perceived exacerbation were classified as 'exacerbations' independent of the treatment the patients received.

Treatment of asthma or COPD exacerbations with antibiotics and/or systemic corticosteroids (recorded by the GP) or hospitalization due to exacerbations of these diseases the year before baseline registration (registered by the patients) was used as evidence of occurrence of exacerbation the previous year (event-based exacerbation like in the ECLIPSE study).[11] We did not register the number of such exacerbations the previous year.

Statistical analysis

Descriptive data are reported as mean and percentage. The CCQ variables were dichotomized, and Receiver operating characteristic curves with future exacerbations as outcome were used to find optimal cut-off points. The possible predictors of exacerbations during the follow-up year were evaluated by univariable logistic regression. Predictors significantly associated with future exacerbations at a 10% level in the univariable analysis were entered multivariable logistic regression with future exacerbations as outcome variable. Backward stepwise elimination was applied and a P value of <0.05 was considered to be statistically significant in the final model. Statistical analyses were performed using SPSS version 19 (IBM, Armonk, NY).

Table 1 *Characteristics at baseline of 340 patients registered with a diagnosis of asthma or COPD in primary care participating in the study*

	N (%)
Age 65 years or more	143 (42.1)
Gender	
Male	126 (37.1)
Female	214 (62.9)
Smoking status	
Never smoker	87 (25.6)
Current smoker	94 (27.6)
Ex-smoker	159 (46.8)
Diagnosis registered by GP the previous 5 years	
Asthma only	193 (56.8)
COPD only	64 (18.8)
Both asthma and COPD	83 (24.4)
Cardiovascular comorbidities	108 (31.8)
Chest findings	
Prolonged expiration	51 (15.0)
Hyperresonance to percussion	31 (9.1)
Diminished breath sounds	57 (16.8)
Wheezes/rhonchi	51 (15.0)
Crackles	34 (10.0)
Lung function	
Normal or restrictive pattern	208 (61.2)
$FEV_1/FVC < 0.7$ and $FEV_1 \geq 80\%$	15 (4.4)
$FEV_1/FVC < 0.7$ and FEV_1 50%–79%	79 (23.2)
$FEV_1/FVC < 0.7$ and $FEV_1 < 50\%$	38 (11.2)
Positive reversibility test	58 (17.1)
CRP ≥ 8 mg/l	50 (14.7)
Oxygen saturation (SpO_2) <96%	74 (21.8)
Previous exacerbations within the year before baseline	88 (25.9)

Results

Patient characteristics

Of the 380 who accepted the invitation and took part in the baseline examination, two patients were excluded from the analysis due to ongoing exacerbation that led to prescription of antibiotics, two patients were excluded as they did not perform post-bronchodilator spirometry and 36 patients were excluded as they neither attended the GP office during exacerbations nor returned the questionnaire on exacerbations in the follow-up year. The baseline characteristics of the 340 patients included in the analysis are shown in Table 1. Patients were more frequently female (62.9%) and 42.1% were ≥65 years old. Almost half of the participants were ex-smokers (46.8%) and the rest were either never smokers (25.6%) or current smokers (27.6%). Asthma was the diagnosis most frequently registered by the GPs (Table 1). COPD (post-bronchodilator FEV1/FVC < 0.7) was found in 132 (38.8%) patients. Among those with $FEV_1/FVC \geq 0.7$, 160 patients were registered with asthma only, 13 patients had been diagnosed with COPD only and 35 with both asthma and COPD. During baseline registration, 88 patients (25.9%) reported an exacerbation the year before baseline (previous exacerbation). Comparison between study population and background population is shown in Table 2.

The CCQ results at baseline are shown in Table 3. Shortness of breath doing physical activities was most frequently reported, 89.4% scored more than zero with a mean score of 2.83. Limitation in strenuous activities was scored more than zero by 82.6% of the patients, with a mean score of 2.36 (Table 3).

During the follow-up period, 159 patients (46.8%) were registered with one or more exacerbations and 101 (29.1%) with 2 or more exacerbations. As shown in Table 4, age ≥ 65 years was a significant predictor for both one or more and two or more exacerbations during the follow-up year. Prolonged expiration was a significant predictor for having one or more exacerbations, whereas all the chest findings variables except diminished breath sounds were

significant predictors for having two or more exacerbations. CRP ≥ 8 mg/l was a significant predictor of two or more exacerbations. Most of the CCQ-questionnaire variables were significant predictors with 'limitation in social activities' as the strongest predictor of one or more exacerbations [odds ration (OR) 2.92] and 'total CCQ-score' as the strongest predictor of two or more exacerbations (OR 2.69). Exacerbation the previous year was the strongest predictor of both one or more and two or more exacerbations with OR of 7.78 and 7.46, respectively. Lung function and smoking status variables were not significant predictors.

In multivariable logistic regression, we found that the best predictor of one or more or two or more exacerbations during 1-year follow-up was an exacerbation the year before baseline, OR 9.2 and OR 8.9, respectively. Age ≥ 65 years was also associated with both outcomes with OR 1.8 [95% confidence interval (CI) 1.1–2.9] for one or more exacerbation and OR 2.7 (95% CI 1.5–4.9) for two or more exacerbations. CRP ≥ 8 mg/l was only significantly predicting two or more exacerbations with OR 2.2 (95% CI 1.1–4.8). Among the CCQ items, 'common cold concern' and 'production of phlegm' were significant predictors of two or more exacerbations only with OR 1.2 and 1.3, respectively (data not shown in table).

Among 132 patients with COPD ($FEV_1/FVC < 0.7$), 64 (48.5%) experienced one or more exacerbations during the follow-up year. Among the 208 with $FEV_1/FVC \geq 0.7$, this was experienced by 95 (45.7%). When evaluating predictors of exacerbations in these two subgroups (Table 5), age was only a significant predictor in those without COPD ($P = 0.04$). All the CCQ-variables were stronger predictors in the COPD group than in those with $FEV_1/FVC \geq 0.7$, but common cold concern and limitation in social activities were significant predictors also in those without COPD ($P = 0.007$ and $P = 0.008$, respectively). Exacerbations the previous year was the variable most strongly associated with future exacerbations in both patient groups ($P < 0.001$). In multivariable analysis, the OR of previous exacerbation as predictor of future exacerbation was 16.8 (95% CI 5.6–50.4) in patients with COPD and 5.5 (95% CI 2.3–12.7) in the other group (data not shown in table).

Table 2 *Gender, age and diagnosis in study sample compared with background population*

	Study population	Background population
	N = 340 (%)	*N* = 1781 (%)
Women	214 (62.9)	1083 (60.8)
Men	126 (37.1)	698 (39.2)
Age (years, median)	62	61
Asthma	193 (56.8)	1298 (72.9)
COPD	64 (18.8)	720 (40.4)
Both asthma and COPD	83 (24.4)	237 (13.3)

Table 3 *Symptoms and limitations in daily activities the previous seven days at baseline in 340 patients with a diagnosis of asthma or COPD using the CCQ*

	Number of patients with a higher score than 0 (%)	Mean score
CCQ-score		
Shortness of breath at rest[a]	210 (61.9)	1.20
Shortness of breath doing physical activities[a]	304 (89.4)	2.83
Common cold concern[a]	207 (60.9)	1.37
Depressed because of the breathing[a]	162 (47.6)	1.00
Coughing[a]	287 (84.4)	2.35
Phlegm[a]	259 (76.2)	2.09
Limitation in strenuous activities[b]	281 (82.6)	2.36
Limitation in moderate activities[b]	244 (71.8)	1.74
Limitation in daily activities[b]	132 (38.9)	0.66
Limitation in social activities[b]	150 (44.3)	0.85
Total score	313 (92.0)	1.63

[a]Hardly ever to almost all the time (score 1–6).
[b]Very slightly to totally limited (score 1–6).

Discussion

Main findings

This study showed that the major determinant of future exacerbations, regardless of lung function, was an exacerbation the previous year, severe enough to be hospitalized or be treated with antibiotics or systemic corticosteroids. Respiratory symptoms and limitations in daily activities were also strong predictors of future exacerbations, giving support to the new guidelines from the Global Initiatives for Chronic Obstructive Lung Disease (GOLD) with greater emphasis on symptoms and frequent exacerbations and less emphasis on lung function in the grading of COPD severity.

Strengths and limitations

The main strength of this study is that it is purely a primary care study and it is relevant for both asthma and COPD patients, and also patients that may be difficult to classify.[19] The number of patients included in the study is not very high and only one-third of the number invited participated. A probable explanation of the low participation rate is that many of the invited patients had mild asthma or COPD or no such disease at all, making them less interested in taking part in this study. Another explanation is that patients with difficult-to treat asthma or severe COPD found it difficult to participate and be followed-up for 12 months,

Table 4 *ORs for the occurrence of asthma or COPD exacerbations during the follow-up year*

	1 or more exacerbations (*N* = 159)		2 or more exacerbations (*N* = 101)	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Gender—female versus male	0.8 (0.5–1.2)	0.3	0.7 (0.4–1.1)	0.1
Age ≥ 65 years	1.5 (1.1–2.4)	0.04	2.2 (1.3–3.5)	0.001
Smoking status				
Current smoker versus never smoker	1.1 (0.6–1.9)	0.9	0.8 (0.4–1.5)	0.5
Ex-smoker versus never smoker	0.9 (0.6–1.6)	0.9	0.7 (0.4–1.3)	0.3
Diagnosis registered by GP the previous 5 years				
Asthma only versus COPD only	0.8 (0.5–1.4)	0.5	0.8 (0.4–1.4)	0.4
Both asthma and COPD versus COPD only	1.2 (0.6–2.3)	0.6	1.7 (0.9–3.4)	0.1
Cardiovascular comorbidities	1.2 (0.8–1.9)	0.4	1.1 (0.7–1.8)	0.6
Lung function (FEV_1%)				
Restrictive versus normal	1.2 (0.7–2.2)	0.5	1.5 (0.8–2.8)	0.2
Mild COPD versus normal	2.5 (0.8–7.8)	0.1	2.7 (0.9–8.0)	0.07
Moderate COPD versus normal	0.9 (0.5–1.7)	0.9	1.3 (0.7–2.5)	0.3
Severe and very severe COPD versus normal	1.4 (0.7–2.9)	0.3	1.8 (0.8–3.8)	0.1
Chest findings—yes versus no				
Prolonged expiration	2.1 (1.2–3.9)	0.01	1.8 (0.9–3.4)	0.05
Hyperresonance to percussion	1.6 (0.8–3.5)	0.2	2.1 (0.9–4.4)	0.05
Diminished breath sounds	1.2 (0.7–2.1)	0.5	1.1 (0.6–2.1)	0.7
Wheezes/rhonchi	1.6 (0.9–2.9)	0.1	1.8 (0.9–3.4)	0.05
Crackles	1.5 (0.7–3.1)	0.3	2.0 (0.9–4.1)	0.05
Reversibility test—pos versus neg	0.8 (0.5–1.5)	0.5	0.9 (0.5–1.6)	0.7
CRP—pos (≥8 mg/l) versus neg	1.3 (0.7–2.3)	0.4	2.1 (1.1–3.9)	0.02
Oxygen saturation (SpO_2) <96%	1.1 (0.6–1.7)	0.9	1.4 (0.8–2.4)	0.2
CCQ-scores				
Short. of breath at rest[a]	1.4 (0.9–2.2)	0.1	1.7 (1.0–2.7)	0.03
Short. of breath doing physical activities[b]	1.3 (0.8–1.9)	0.3	1.7 (1.1–2.8)	0.02
Common cold concern[a]	2.5 (1.6–3.9)	<0.001	2.6 (1.6–4.2)	<0.001
Depressed because of the breathing[a]	1.6 (0.9–2.6)	0.05	2.3 (1.4–3.7)	0.001
Coughing[b]	1.8 (1.1–2.7)	0.01	2.1 (1.3–3.4)	0.002
Phlegm[b]	1.9 (1.2–3.1)	0.004	2.4 (1.5–3.9)	<0.001
Limitation in strenuous activities[c]	1.2 (0.8–1.8)	0.5	1.5 (0.9–2.5)	0.06
Limitation in moderate activities[c]	1.7 (1.1–2.7)	0.03	2.4 (1.5–4.0)	<0.001
Limitation in daily activities[d]	1.9 (1.1–3.3)	0.03	2.1 (1.2–3.7)	0.01
Limitation in social activities[d]	2.9 (1.7–4.9)	<0.001	2.3 (1.4–3.9)	0.002
CCQ total score ≥ 2	1.9 (1.2–3.1)	0.004	2.7 (1.8–4.9)	<0.001
Previous exacerbations within the year before baseline	7.8 (4.3–14.0)	<0.001	7.5 (4.4–12.)	<0.001

P value calculated using Pearson Chi-Square.
[a]Few times to almost all the time.
[b]Several times to almost all the time.
[c]Moderately to totally limited.
[d]Slightly to totally limited.

and also were sufficiently followed-up in secondary care. Although this may influence the representativeness of the study sample, the patient characteristics in terms of gender and age were similar to those eligible to take part, as were the frequency of patients only diagnosed with asthma.[16] We still believe that our cohort is representative in terms of primary care since the severely ill patients with comorbidities receive follow-up in secondary care in most of the cases. The majority of the patients in the COPD subgroup had moderate COPD, according to GOLD's spirometry based staging, as has also been found in previous studies from primary care.[20,21]

The classification of the patients into COPD and no-COPD subgroups may be questioned. It may look like a limitation that the majority of patients in the COPD subgroup had been diagnosed with both asthma and COPD, and even some with asthma only. Some of these patients certainly had both diagnoses.[19,22] However, some patients might have been wrongly labelled with an asthma diagnosis. There has been a change in labelling of obstructive lung diseases the last 20 years with increasing use of the COPD diagnosis and less use of the asthma diagnosis,[23] and patients with little contact with health care have probably erroneously been stuck to their old diagnosis.

Table 5 *ORs for the occurrence of exacerbations during the follow-up year in participants with FEV1/FVC ratio below and above 0.7*

	$FEV_1/FVC < 0.7$ (COPD) ($N = 132$)*		$FEV_1/FVC \geq 0.7$ (Asthma possibly) ($N = 208$)**	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age ≥ 65 years	1.2 (0.6–2.4)	0.6	1.8 (1.0–3.3)	0.04
Gender—female versus male	0.6 (0.3–1.2)	0.1	0.9 (0.5–1.6)	0.7
Smoking status				
Current smoker versus never smoker	2.5 (0.8–8.2)	0.1	0.7 (0.4–1.5)	0.4
Ex-smoker versus never smoker	2.2 (0.7–6.3)	0.1	0.7 (0.4–1.4)	0.3
Diagnosis registered by GP the previous 5 years				
Asthma only versus COPD only	1.1 (0.5–2.7)	0.8	0.4 (0.1–1.5)	0.2
Both asthma and COPD versus COPD only	1.3 (0.6–2.9)	0.5	0.7 (0.2–2.7)	0.6
Cardiovascular comorbidities	1.3 (0.6–2.5)	0.5	1.1 (0.6–2.1)	0.7
Chest findings—yes versus no				
Prolonged expiration	1.7 (0.8–3.7)	0.2	3.6 (1.1–11.6)	0.03
Hyperresonance to percussion	1.4 (0.6–3.3)	0.4	3.6 (0.4–35.7)	0.3
Diminished breath sounds	1.4 (0.7–2.9)	0.3	0.7 (0.2–2.3)	0.6
Wheezes/rhonchi	1.1 (0.5–2.4)	0.8	2.6 (1.0–6.8)	0.04
Crackles	1.9 (0.5–7.1)	0.3	1.3 (0.6–3.2)	0.5
Reversibility test—yes versus no	0.9 (0.4–2.2)	0.9	0.7 (0.3–1.5)	0.3
CRP—pos (≥8 mg/l) versus neg	1.3 (0.5–3.1)	0.5	1.2 (0.5–2.8)	0.6
Oxygen saturation (SpO_2) <96%	1.1 (0.5–2.3)	0.8	0.9 (0.4–1.9)	0.8
CCQ-scores				
Short. of breath at rest[a]	2.2 (1.1–4.5)	0.03	1.1 (0.6–1.9)	0.8
Short. of breath doing physical activities[b]	2.3 (1.1–4.7)	0.02	0.9 (0.5–1.5)	0.6
Common cold concern[a]	2.9 (1.4–6.0)	0.003	2.2 (1.2–3.9)	0.008
Depressed because of the breathing[a]	2.1 (1.0–4.3)	0.04	1.2 (0.6–2.4)	0.5
Coughing[b]	2.7 (1.3–5.7)	0.007	1.3 (0.8–2.4)	0.3
Phlegm[b]	3.7 (1.7–8.2)	0.001	1.3 (0.8–2.4)	0.3
Limitation in strenuous activities[c]	1.4 (0.7–2.8)	0.3	1.0 (0.6–1.8)	0.9
Limitation in moderate activities[c]	1.8 (0.9–3.7)	0.1	1.6 (0.8–2.9)	0.1
Limitation in daily activities[d]	3.1 (1.3–7.5)	0.01	1.2 (0.6–2.6)	0.6
Limitation in social activities[d]	3.5 (1.5–7.9)	0.003	2.5 (1.2–5.1)	0.009
CCQ total score ≥ 2	2.7 (1.3–5.6)	0.009	1.6 (0.8–2.9)	0.1
Previous exacerbations within the year before baseline	12.5 (5.1–30.6)	<0.001	5.6 (2.5–12.5)	<0.001

P value calculated using Pearson Chi-Square.
[a]Few times to almost all the time.
[b]Several times to almost all the time.
[c]Moderately to totally limited.
[d]Slightly to totally limited.
*64 patients (48.5%) experienced an exacerbation or more the following year.
**95 patients (45.7%) experienced an exacerbation or more the following year.

A tendency to use the asthma diagnosis may have been strengthened by the reimbursement regulation for respiratory medication introduced in Norway in 2006. In the study period, costs of inhaled corticosteroids combined with long acting β_2-agonist were only reimbursed, as a rule, in patients with a diagnosis of asthma. Although the great majority of those with $FEV_1 \geq 0.7$ have been diagnosed with asthma only (76.9%), patients with chronic bronchitis, pre-stages of COPD and shortness of breath of other causes may also be part of this group. The fact that the same variables were strong predictors in both subgroups and that the GPs' diagnosis did not significantly predict future exacerbations tells us that the main results may be applicable in most patients with obstructive lung diseases in primary care.

Using an event-based definition of an exacerbation might have led to an under registration of exacerbations in patients who do not quickly seek medical help in periods of increased symptoms. We cannot know how the results might have been influenced by this.

The CCQ has been developed and validated for use among COPD patients and not for asthma patients. The reason for using this questionnaire in all patients was the uncertainty of the patient's diagnosis and that all the questions were also relevant for asthma patients. We could have used an asthma questionnaire in addition, like the asthma control questionnaire,[24] but the patients already had another questionnaire to fill in. The CCQ answers predicted future exacerbations more strongly in the COPD group than in those with 'possible asthma'.

However, concern about getting a common cold and limitations in social activities should raise awareness also among patients with $FEV_1/FVC \geq 0.7$.

Comparisons with previous studies

In our study, we used the event-based definition used in the ECLIPSE study to determine the occurrence of exacerbation the year before baseline. A similar event-based definition was used for the exacerbations during the study period, but specific treatment of the patients who visited a doctor was not required. In spite of this minor difference in outcome measurement from the ECLIPSE study, we came to almost identical results regarding the occurrence of one or more and two or more exacerbations during the study period (46.8% and 29.7% versus 47% and 29%) with subsequent conclusion that previous exacerbation is the strongest predictor for future exacerbation. The strong predictive value of previous exacerbations has also been found among asthma patients by Miller et al.[15] in the TENOR study, and in cluster analyses by Ortega et al.[13] including adults and children with asthma.

Self-reported shortness of breath was a significant predictor of exacerbation the follow-up year (two or more) in the univariable analysis like in the ECLIPSE study, but this symptom did not reach statistical significance in multivariate analysis in either of the studies. The CCQ items found to be significant predictors in the multivariate analysis in our study were not included in the ECLIPSE analyses. In contrast to in the ECLIPSE study we did not find reduced lung function to be a significant predictor of future exacerbations. This parallels the finding of Wan et al.[25] that lung function assessed by FEV_1% predicted was not significantly associated with frequent exacerbations, although they found that frequent exacerbations were significantly associated with lower-mid expiratory flow rates ($FEF_{25\%–75\%}$ predicted), which was not analyzed in our study. Wan et al.[25] found physician-diagnosed asthma to be a significant predictor of exacerbations in severe COPD. A similar, but not statistically significant, tendency was found among the COPD patients in this study (Table 5).

Clinical implications

Preventing asthma and COPD exacerbations may be an ambitious target; however, early identification and treatment when an exacerbation occurs may reduce the detrimental effect severe exacerbations may exert on the health of the patients.[2,3,9,26–30] Easy access to health care is crucial, and our study indicates that patients with frequent exacerbations and limitations in social activities need this kind of attention from the health care providers.

Acknowledgements

The authors thank the participating patients and Nordbyen legesenter, Tromsø, Allmed legesenter, Hammerfest, Alta legesenter, Skedsmokorset legesenter, Lillestrøm legesenter, Langbølgen legesenter, Oslo and Gransdalen legesenter, Oslo for their participation in collecting data.

Declaration

Funding: this study received a grant from the Norwegian Research Council (202650/V50).
Ethical approval: the regional committee for Medical and Health Research Ethics in North Norway approved the study.
Conflict of interest: none.

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