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Patterns of Comorbidities in Newly Diagnosed COPD and Asthma in Primary Care*

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Study objectives: **There is increasing interest in the frequency and nature of comorbidities in patients with obstructive lung disease: COPD and asthma. We aimed to quantify baseline rates of comorbidities in COPD and asthma patients and to compare the risks to the general population.**
Design, setting, and participants: **Within the UK General Practice Research Database, we compared incident patients with COPD (n = 2,699) and asthma (n = 7,931) physician diagnosed in 1998 with age, gender, time, and practice-matched cohorts. Rates were calculated and relative risks (RRs) were estimated for comorbidities in major organ systems and selected medical events of *a priori* interest.**
Measurements and results: **In both COPD and asthma, the total sum of diagnoses related to major organ systems was higher than in their matched population controls. Among incident COPD patients, a frequency > 1% within the first year after diagnosis was observed for angina, cataracts, bone fractures, osteoporosis, pneumonia, and respiratory infections, the highest being angina with 4.0%. Compared to the non-COPD cohort, COPD patients were at increased risk for pneumonia (relative risk [RR] = 16.0), osteoporosis (RR = 3.1), respiratory infection (RR = 2.2), myocardial infarction (RR = 1.7), angina (RR = 1.7), fractures (RR = 1.6), and glaucoma (RR = 1.3) [all $p < 0.05$]. Of note, 2.0% of COPD patients had cataracts recorded, but this rate was no different than that of the non-COPD cohort (RR = 0.9). Among incident asthma patients, the occurrence of events was generally lower, likely due to the younger age distribution, except for 4.0% with respiratory infection (RR = 1.84) and 1.7% with fractures (RR = 1.5). Angina prevalence was 0.7% in the asthma cohort and 1.4 times more common than in patients without asthma.**
Conclusion: **COPD and asthma are conditions associated with many comorbidities, albeit asthma to a lesser extent than COPD, which had not been systematically reviewed before. Baseline rates of cardiovascular-, bone-, and other smoking-related conditions are high.**
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Key words: asthma; comorbidities; COPD; general practice; incidence; obstructive lung disease; prevalence

Abbreviations: CI = confidence interval; GP = general practitioner; GPRD = General Practice Research Database; RR = relative risk

Obstructive lung disease, namely COPD and asthma, are the most frequent causes of respiratory ill health, covering all ages.[1,2] COPD produces a substantial and growing disease burden worldwide.[3] Most COPD patients are aging individuals, often with several comorbidities and multiple drug treatments.[4] Similarly, asthma is also associated with a substantial and growing disease burden worldwide. Asthma is the most common chronic disease in Western children, and asthma diagnosis can happen at all ages,[5,6] including the elderly. It is recognized that the epidemiology of both conditions, although asthma slightly better than COPD, is still behind achievements of cardiovascular or cancer epidemiology.[7]

There is interest to determine the quantity and

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quality of medical events in COPD and asthma patients from the general population. A comorbidity is usually defined as a disease coexisting with the disease of interest. Frequently used in research and practice, no definition of comorbidity is uniformly accepted. A few reports on comorbidities in COPD and asthma are found elsewhere. van Manen et al[8] reported that 22.6% of chronic airway obstruction (COPD or irreversible asthma) patients had three or more comorbid conditions. The most frequent comorbidities occurring with excessive risk in that population were locomotive diseases, insomnia, sinusitis, migraine, depression, stomach/duodenum ulcer, and cancer.[8] Comorbidities in chronic respiratory disease were also found a determinant of both general and disease-specific health-related quality of life in Dutch and American respiratory patients, respectively.[9,10] The General Practice Research Database (GPRD) can potentially help to determine baseline rates of medical events in individuals with a given condition. By using the same sampling strategy and methods in both conditions, we aimed to explore the GPRD to obtain baseline rates of comorbidities and selected medical events in COPD and asthma patients, and their relative risk (RR) vs non-COPD and nonasthma reference participants, respectively.

Materials and Methods

The GPRD database has been described elsewhere,[11,12] and has been utilized previously to obtain epidemiologic trends of COPD[13–15] and asthma.[16] Briefly, the GPRD was originally set up in May 1987, and aimed to recruit sufficient practices to build up a database containing continuing information on patients in the United Kingdom. More than 500 practices have been contributing a total population of about 6 million patients. Although not a pure population sample, the GRPD is broadly representative of the UK population in terms of gender and age structure, with an almost identical structure as the one provided by the UK Office of Population Census and Surveys. Each participating general practitioner (GP) is invited to enter all significant morbidity events regarding each individual patient in the computer record, irrespective of whether the event occurred in the practice, at a visit, or was reported over the phone.

Study Design and Case Definitions

COPD and asthma cases were defined by identification of compatible terms in Read codes only[16] (Fig 1). A cohort of COPD and a cohort of asthma cases, and matched control subjects for each condition were identified from within the GPRD. Incident cases were individuals with either COPD or asthma in 1998, and who had at least 1 year of follow-up before and after diagnosis. Control patients were matched by age, gender, practice, and a time band of ± 1 year of follow-up around the case index date. Control patients were allowed to have any medical condition including allergies and rhinitis or any other significant disease, except COPD (if they were matched in the non-COPD cohort) or except asthma (if they were matched in the nonasthma cohort).

Comorbidities

Comorbidities in major organ systems and also nine selected medical events of *a priori* interest were investigated: angina, cataracts, fractures, glaucoma, myocardial infarction, osteoporosis, pneumonia, respiratory infection, and skin bruises. Note that a comorbidity may not be a primary reason for the consultation, but secondarily recorded in the course of that consultation.

Statistical Analysis

The yearly event rate per 10,000 patients within the year after index date was obtained. Finally, the ratio of event rates or RR, COPD/non-COPD, and asthma/nonasthma, respectively, was calculated. The interpretation follows: a RR $>$ 1 indicates that a comorbidity or medical event was more frequent in respiratory patients; a RR $<$ 1 indicates that a comorbidity or medical event was less frequent in respiratory patients. Ninety-five percent confidence intervals (CIs) for the RRs were calculated.

Results

A total number of incident physician-diagnosed cases of COPD (n = 2,699) and asthma (n = 7,931) in 1998 were identified. Demographic and clinical characteristics of these patients are presented in Table 1 and are compared with their respective matched reference groups. COPD patients were older (average of 65 years) and more frequently current smokers (46%) than patients with asthma, with a mean age of 30 years and 18% of current smokers only. Because of the natural history of respiratory disease, crosslabeling of COPD and asthma in the same patient was allowed and quantified: 43% of COPD patients had a concomitant history of asthma reported, but only 8.4% of asthma patients had a concomitant history of COPD reported.

Major Organ Systems

The tabulation of comorbidities by major organ systems is presented in Table 2. This method of grouping consultations confirms that patients with COPD have more consultations in virtually all system organ classes than their matched non-COPD controls. There was heterogeneity regarding hepatobiliary disorders and all neoplasms in COPD vs asthma patients. In COPD patients, the highest medical rate was for infections and infestations with a rate of 3,923.6 per 10,000 patient-years, and the highest RR and 95% CI was for cardiac disorders: RR = 4.01 (CI, 3.6 to 4.4). This was mirrored in asthma patients in whom the highest medical rate was also for infections and infestations, with a rate of 3,995.7 per 10,000 patient-years and the highest RR and 95% CI was for cardiac disorders: RR = 3.52 (CI, 3.0 to 4.1). The pattern of consultations in the asthma cases was substantially different, but asthma

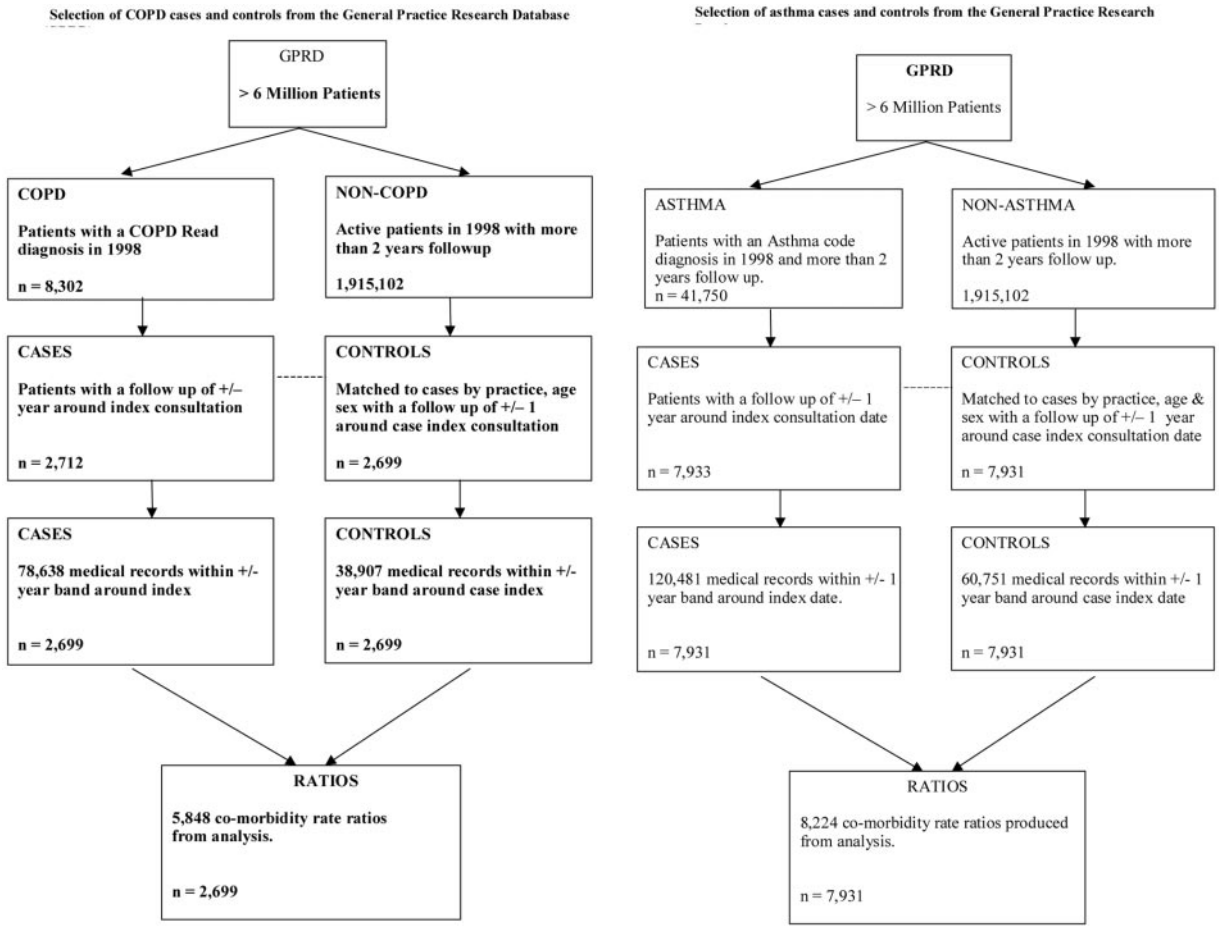

FIGURE 1. Flowchart of selection of COPD cases, asthma cases, and their respective reference groups from the GPRD.

patients have also more consultations in all systems than their matched nonasthma controls.

Selected Medical Events in COPD and Asthma

In Figures 2 and 3, selected medical events are depicted by plotting their relevance in terms of prevalence (or rate per 10,000 in the Y axis) and risk (or RR vs their matched controls in the X axis). Some events can be of importance because they are frequent in absolute terms, or more frequent than expected in that age, gender group, or both.

Among incident COPD patients, several events on

Table 1—*Demographic and Clinical Characteristics of Patients With COPD, Patients With Asthma, and Their Respective Reference Groups**

Variables	COPD	No COPD	Asthma	No Asthma
Patients, No.	2,699	2,699	7,931	7,931
Female gender	1,380 (51.1)		4,249 (53.6)	
Mean (SD) age, yr	65.0 (15.0)		29.8 (23.9)	
Smoking status				
Current smoker	1,239 (45.9)	567 (21.0)	1,468 (18.5)	1,297 (16.4)
Ex-smoker	438 (16.2)	268 (9.9)	491 (6.2)	336 (4.2)
Nonsmoker	767 (28.4)	1,231 (45.6)	2,366 (29.8)	2,205 (27.8)
Unknown	255 (9.5)	633 (23.5)	3,606 (45.5)	4,093 (51.6)
With COPD ever	2,699 (100)	0 (0)	663 (8.4)	78 (0.9)
With asthma ever	1,166 (43.2)	185 (6.9)	7,931 (100)	0 (0)
Age > 65 yr	1,488 (55.1)		855 (10.8)	

*Data are presented as No. (%) unless otherwise indicated. Matching factors were age, gender, practice, and time.

Table 2—*Rate per 10,000 and RR by Major Organ Systems in COPD and Asthma*

Disorders	COPD	RR (95% CI)	Asthma	RR (95% CI)
Blood and lymphatic system	277.8	1.74 (1.4–2.1)	216.9	1.61 (1.3–2.0)
Cardiac	2,256.3	4.01 (3.6–4.4)	648.1	3.52 (3.0–4.1)
Congenital, familial, and genetic	48.1	1.18 (0.8–1.8)	75.6	1.28 (0.9–1.8)
Ear and labyrinth	881.8	1.44 (1.3–1.6)	1,218.0	1.27 (1.2–1.4)
Endocrine	385.3	1.22 (1.1–1.4)	192.9	1.49 (1.2–1.9)
Eye	870.69	1.32 (1.2–1.5)	769.1	1.46 (1.3–1.6)
GI	2,756.5	1.69 (1.6–1.8)	1,995.9	1.49 (1.4–1.6)
General and administration site	2,252.6	1.75 (1.6–1.9)	1,457.6	1.78 (1.6–1.9)
Hepatobiliary	96.33	2.89 (1.9–4.3)	30.26	1.50 (0.8–2.6)
Immune system	481.6	1.78 (1.5–2.1)	822.1	2.54 (2.2–2.9)
Infections and infestations	3,923.6	2.13 (2.0–2.2)	3,995.7	1.52 (1.4–1.6)
Injury, poisoning	607.6	1.23 (1.1–1.4)	747.7	1.50 (1.3–1.7)
Metabolism/nutrition	485.3	1.66 (1.4–1.9)	177.8	1.72 (1.3–2.2)
Musculoskeletal and connective tissue	2,867.7	1.45 (1.4–1.5)	1,654.3	1.60 (1.5–1.7)
Neoplasms benign, malignant, and unspecified	385.3	1.09 (0.9–1.3)	363.1	1.40 (1.2–1.6)
Nervous system	1,207.8	1.48 (1.3–1.6)	800.7	1.54 (1.4–1.7)
Pregnancy, puerperium, and perinatal	11.1	0.43 (0.2–0.9)	148.8	1.27 (1.0–1.6)
Psychiatric	1,063.3	1.98 (1.8–2.2)	747.7	1.68 (1.5–1.9)
Renal and urinary	566.8	1.53 (1.3–1.7)	303.9	1.37 (1.1–1.6)
Reproductive system and breast	377.9	1.17 (1.1–1.4)	480.4	1.40 (1.2–1.6)
Respiratory, thoracic, and mediastinal	2,897.3	3.14 (2.9–3.4)	2,635.2	2.57 (2.4–2.8)
Skin and subcutaneous tissue	1,726.5	1.57 (1.4–1.7)	1,668.1	1.54 (1.4–1.7)
Social circumstances	292.7	1.80 (1.5–2.2)	184.1	2.12 (1.6–2.7)
Surgical and medical	2,315.6	1.51 (1.4–1.6)	1,480.3	1.35 (1.2–1.5)
Vascular	926.2	1.41 (1.3–1.6)	315.2	1.20 (1.0–1.4)

the selected list of events had a frequency > 1% within the first year after diagnosis: angina, cataracts, bone fractures, osteoporosis, pneumonia, and respiratory infections, the highest being angina, 4% (Fig 2). Compared to the non-COPD cohort, COPD patients were at increased risk for pneumonia (RR = 16.00; 95% CI, 8.7 to 29.3), osteoporosis (RR = 3.14; 95% CI, 2.3 to 4.0), respiratory infection (RR = 2.24; 95% CI, 1.8 to 2.7), myocardial infarction (RR = 1.75; 95% CI, 1.2 to 2.5), angina (RR = 1.67; 95% CI, 1.4 to 2.0), fractures (RR = 1.58; 95% CI, 1.3 to 1.9), and glaucoma (RR = 1.29; 95% CI, 0.9 to 1.8) [all but glaucoma with $p < 0.05$]. Of note, 2% of COPD patients had

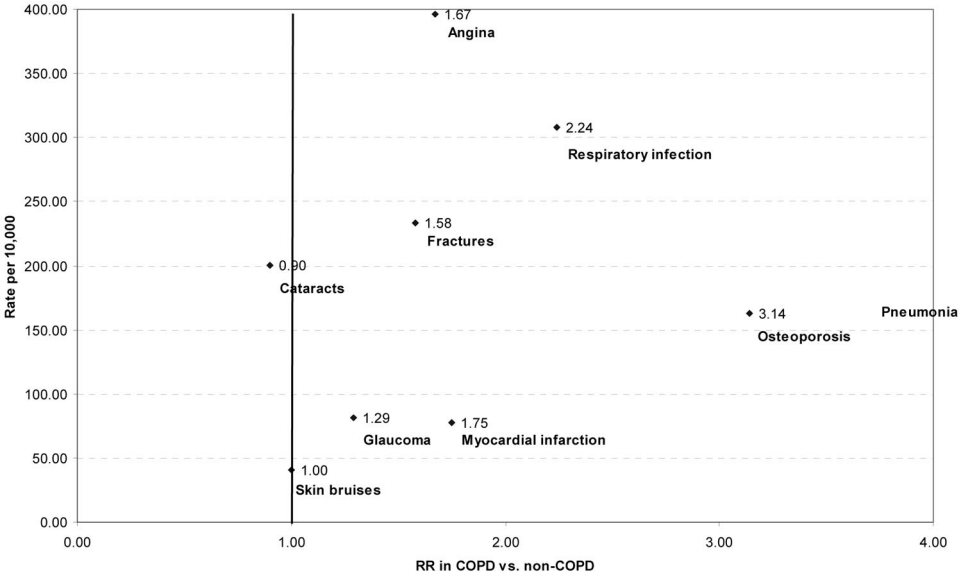

FIGURE 2. Relationship between rate per 10,000 of selected medical events and their RR in COPD vs non-COPD (GPRD, 1998).

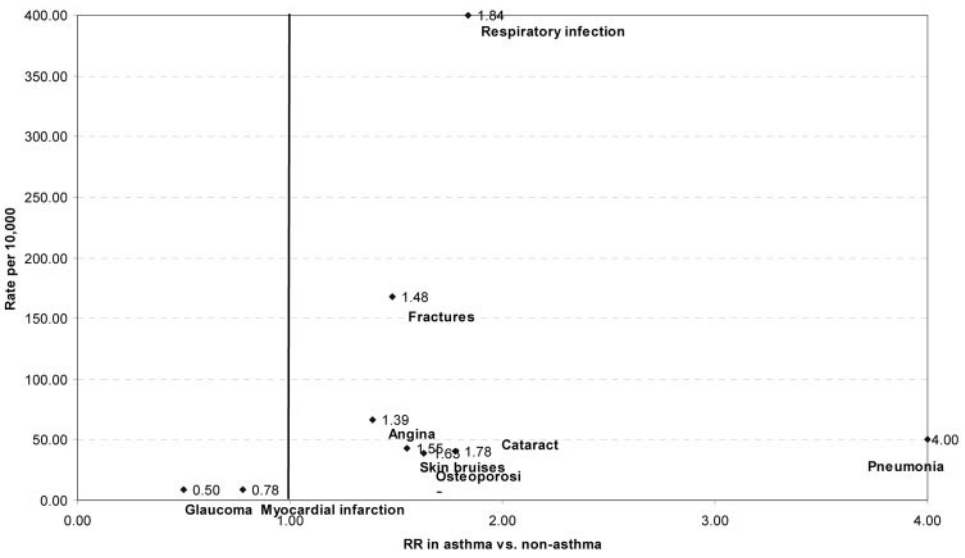

FIGURE 3. Relationship between rate per 10,000 of selected medical events and their RR in asthma vs nonasthma (GPRD, 1998).

cataracts recorded, but this rate was no different than that of the non-COPD cohort (RR = 0.90; 95% CI, 0.7 to 1.1).

Among incident asthma patients (Fig 3), the occurrence of selected medical events was generally lower compared to COPD patients, likely due to the younger age distribution, except for 4.01% with respiratory infection (RR = 1.84; 95% CI, 1.6 to 2.2) and 1.68% with fractures (RR = 1.48; 95% CI, 1.2 to 1.9). Angina prevalence was 0.67% in the asthma cohort and 1.4 times (RR = 1.39; 95% CI, 1.0 to 2.0) more common than in nonasthma patients.

Comorbidities in Elderly COPD and Asthma

In a sensitivity analysis of the subsample of individuals > 65 years old, the pattern of major organ system comorbidities (Table 3) and of selected medical events (Fig 4) in COPD was mostly unchanged, partly because half of this cohort was already > 65 years old. However, in elderly asthma patients (Fig 5), this pattern was significantly modified and resembled the pattern of COPD, with the most frequent events being for angina 3.5%, cataract 3.0%, and osteoporosis 2.7%, while the higher RRs were identified for pneumonia and respiratory infections.

DISCUSSION

We report a descriptive analysis on the quantity and quality of comorbidities in COPD and asthma patients newly diagnosed in primary care. By comparing each disorder with a set of matched controls, we present overall estimates of prevalence and RR of the comorbidities, which may provide useful in the analysis of adverse event reports.

Medications were not searched, and analyses are not corrected by drug use. This was because patients identified within the first year of their disease diagnosis would have had limited exposure to respiratory drugs and unlikely to have been exposed to long-term treatments. Therefore, it is expected that the event rates reported were not associated with adverse events of respiratory drugs.

We found that both COPD and asthma at diagnosis are conditions associated with many comorbidities, which to our knowledge were not systematically reviewed before. Rates were high, particularly for cardiovascular (angina and myocardial infarction), bone (osteoporosis and fractures), and other smoking-related conditions or diseases of the aging (respiratory infection and pneumonia). Of interest, the pattern of comorbidities comparing the COPD patients > 65 years old with the asthma patients > 65 years old was similar.

Strengths of the current research include originality, simplicity, and a large sample size. The cohort of respiratory GPRD participants matched with the same gender, age, practice, and period produces direct comparison of rates and RRs within the same study base, and not confounded by seasonality. Finally, previous reports were based on prevalent obstructive lung disease, while this is the first study on incident, newly diagnosed COPD and asthma patients.

Table 3—*Rate per 10,000 and RR by Major Organ Systems in COPD and Asthma in Patients > 65 Years Old*

Disorders	COPD	RR (95% CI)	Asthma	RR (95% CI)
Blood and lymphatic system	362.9	1.93 (1.6–2.3)	222.2	1.12 (0.9–1.3)
Cardiac	2,789.0	3.81 (3.5–4.1)	2,526.3	3.13 (2.9–3.4)
Congenital, familial, and genetic	20.2	1.00 (0.5–1.8)	46.8	
Ear and labyrinth	880.4	1.46 (1.3–1.6)	970.8	1.38 (1.3–1.5)
Endocrine	416.7	1.17 (1.0–1.3)	409.4	1.75 (1.5–2.0)
Eye	1,041.7	1.36 (1.2–1.5)	1,122.8	1.43 (1.3–1.6)
GI	2,990.6	1.75 (1.6–1.9)	2,959.1	1.69 (1.6–1.8)
General and administration site	2,520.2	1.83 (1.7–1.9)	2,339.2	1.82 (1.7–1.9)
Hepatobiliary	87.4	3.25 (2.1–5.0)	23.4	0.67 (0.4–1.1)
Immune system	396.5	1.69 (1.4–2.0)	327.5	1.12 (0.9–1.3)
Infections and infestations	3,924.7	2.29 (2.2–2.4)	3,590.6	1.74 (1.6–1.8)
Injury, poisoning	604.8	1.45 (1.3–1.6)	619.9	1.71 (1.5–1.9)
Metabolism/nutrition	551.1	1.91 (1.6–2.2)	491.2	1.17 (1.0–1.3)
Musculoskeletal and connective tissue	2,909.9	1.52 (1.4–1.6)	3,040.9	1.43 (1.3–1.5)
Neoplasms benign, malignant, and unspecified	409.9	1.07 (0.9–1.2)	514.6	1.91 (1.6–2.2)
Nervous system	1,283.6	1.36 (1.2–1.5)	1,391.8	1.43 (1.3–1.6)
Pregnancy, puerperium, and perinatal	6.7		0.0	
Psychiatric	914.0	1.92 (1.7–2.1)	771.9	1.83 (1.6–2.1)
Renal and urinary	725.8	1.93 (1.7–2.2)	701.7	1.62 (1.4–1.8)
Reproductive system and breast	282.3	1.27 (1.1–1.5)	198.8	1.13 (0.9–1.4)
Respiratory, thoracic, and mediastinal	2,836.0	3.06 (2.8–3.3)	2,982.5	2.87 (2.7–3.1)
Skin and subcutaneous tissue	1,821.2	1.46 (1.4–1.6)	1,719.3	1.44 (1.3–1.5)
Social circumstances	268.8	2.35 (1.9–2.9)	233.9	1.33 (1.1–1.6)
Surgical and medical procedures	2,560.5	1.54 (1.4–1.6)	2,397.7	1.49 (1.4–1.6)
Vascular	1,048.4	1.37 (1.2–1.5)	1,087.7	1.08 (1.0–1.2)

On specific comorbidities, the high occurrence of angina and myocardial infarction in COPD is now well accepted, in the light of COPD as a multicomponent disease, and even therapeutic targets have been identified to tackle both conditions.[17] In asthma, the evidence for a link with coronary artery disease has been postulated, but the evidence is less clear.[18]

Limitations

A major limitation of this research is distinguishing COPD vs asthma in primary care, as these diagnoses are often established without spirometry in the United Kingdom and elsewhere. Indeed with the same symptoms, women are more likely to receive a diagnosis of asthma than COPD, while the reverse is

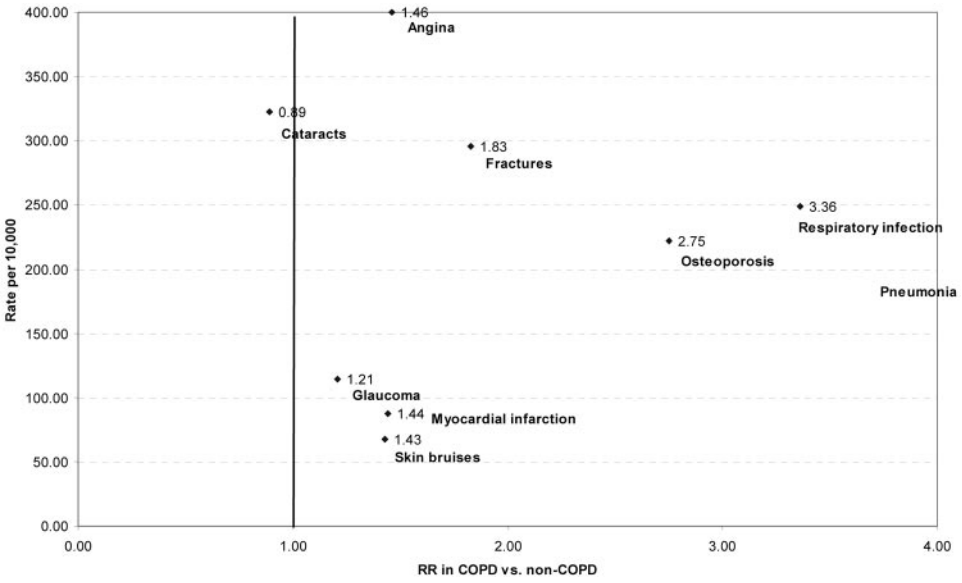

FIGURE 4. Relationship between rate per 10,000 of selected medical events and their RR in COPD vs non-COPD (GPRD, 1998) patients > 65 years old.

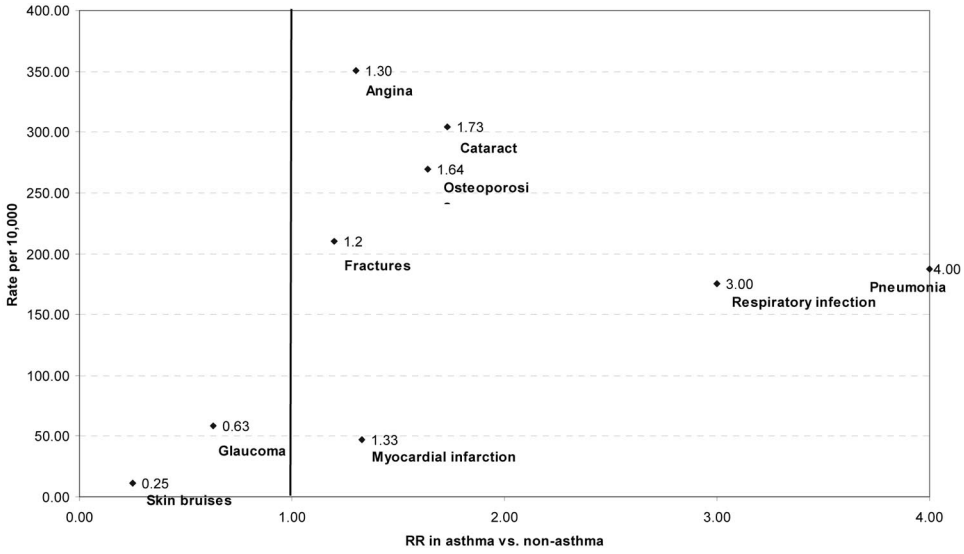

FIGURE 5. Relationship between rate per 10,000 of selected medical events and their RR in asthma vs nonasthma (GPRD, 1998) patients > 65 years old.

true with men.[19] Also, nonsmokers are more likely to receive an asthma diagnosis.[20] However, in a Dutch general practice study,[21] by only using simple items from the clinical history (wheeze, dyspnea, allergen-induced symptoms, smoking, female sex) and physical examination (prolonged expiration), 76% of patients could be classified "correctly" as asthma/COPD compared with "gold standards" from spirometry and methacholine provocation tests. Within the GPRD system, very similar results on sensitivity and specificity of COPD vs asthma were obtained.[22]

Other limitations that deserve consideration include very low rates of some events, coding, duration of follow-up, and smoking information. Despite the big numbers of participants involved (> 2,600 for both COPD and non-COPD), there is not enough power in determining rates and RRs of very infrequent events, that is those with a frequency of < 1 per thousand person-years. We limited the follow-up to only 1 year after diagnosis of COPD or asthma, and we can speculate that the interpretation of this simple approach is more complex when using longer periods. Finally, smoking information is limited from primary care sources; GPRD patients were not matched on smoking, and this may account at least in part for the differences observed in COPD, as discussed later. The similarity of smoking rates in asthma vs nonasthma control patients has been reported elsewhere.[23]

Potential Biases

Selection bias could have played a role within the current design and has to be considered. The use of a registration period of at least 1 year before any investigation is standard in observational research, and increases the confidence that new reports of a disease refer to new incident conditions. However, the requirement of having at least 1 year of enrollment after identification may have biased some estimates. As some patients with severe COPD may have died or been transferred within the year of diagnosis, and there is a likelihood that they had more comorbidities, this artifact could have underestimated the reported frequencies and RRs. Another type of selection bias could have occurred, as 43% of the incident COPD patients had a history of asthma and, therefore, may have been exposed to respiratory drugs for years. As the COPD/asthma mixed group might have had some exposure to inhaled and oral medications and other drugs in the past, this could explain some of the higher rates observed for some events. Therefore, the interpretation of event rates with special interest has to be done with caution. Finally, a subtle selection bias could have occurred, namely confounding by diagnosis status: patients with a diagnosis of obstructive lung disease might have a higher chance of receiving a diagnosis with other diseases due to regular, scheduled follow-up GP visits. The relationship between GP consultation and prevalence needs to be highlighted; COPD or asthma patients may have increased recording of comorbidities, as they have to attend regularly for their chest disease, giving artifactually increased comorbidity rates. Conversely, not all those with COPD/asthma seek medical care, and this may increase with age (people may think shortness of breath is due to aging) and therefore

collected data may be biased toward the more severe end of the spectrum of respiratory disease.

Smoking

The role of smoking in COPD/asthma disorders is obvious but needs to be acknowledged. Smoking as a causative factor of comorbidities in COPD and elderly asthma has to be emphasized, and all respiratory patients should quit smoking, regardless of age. The British Doctors Study, from the first publication in 1956,[24] to the latest available update with a 50-year follow-up,[25] showed that smoking was associated with increased risks of mortality for a range of conditions (cancers, vascular disorders, peptic ulcers [therefore GI], cirrhosis [therefore hepatobiliary], suicide, among others). Assessment of tobacco exposure within the GPRD is limited, reflecting medical practice in primary care. For example, smoking data are not available in many nonrespiratory control patients, in 45% of asthma patients, and in 9% of COPD patients (Table 1). Information on pack-years or age of starting smoking is not available**.** UK estimates have found a smoking prevalence of approximately 26 to 30% in population surveys in recent years, and a recent GPRD report[26] suggested underrepresentation of current smoking prevalence rates by approximately one fifth in the GPRD.

The question on whether COPD comorbidities result from tobacco smoking or COPD itself is an important etiologic and clinical question. Although COPD is seen in nonsmokers, especially in developing countries and women, most COPD in both men and women in developed countries is due to smoking. It is therefore difficult to disentangle causality due to COPD or due to tobacco, particularly with limited assessment of tobacco exposure and without validated spirometry as in the primary care database used. That is why smoking was not considering a matching factor in this study.

Comparison of COPD vs Asthma

Finally, the comparison of COPD and asthma findings has to be done only indirectly. The age distribution of both case series is very different due to the different natural history of each disorder. In the all-age group (Table 2), there are differences between COPD and asthma with hepatobiliary conditions, neoplasms and pregnancy, which may be due to younger ages in asthma. Matching COPD to asthma cases might have been misleading, as we would have been unsuccessful to find enough young COPD patients to be matched with asthmatic patients, or obtained a group of elderly asthmatic patients that would not be representative of the asthma population. However, in a sensitivity analysis, the latter was conducted in the subset of asthma patients ≥ 65 years old. The heterogeneity between COPD and asthma becomes even more apparent in this elderly subgroup (Table 3). In the elderly, while the pattern of comorbidities becomes fairly similar between COPD and asthma, patients with asthma continue to have lower rates of hepatobiliary disorders than control patients (while COPD patients have higher) and asthma patients have higher neoplasm RRs than control patients, compared with similar consulting rates to control patients for COPD patients with neoplasms. Additionally in the elderly, endocrine disorder RRs are a little higher for asthma than COPD. Also, consulting RRs for social circumstances are higher for COPD than asthma. While cataracts and glaucoma were much more prevalent in the COPD than asthma groups in the subgroup of patients > 65 years old, the prevalence of cataract was identical in elderly COPD and asthma patients, and the prevalence of glaucoma in elderly asthmatics was approaching the prevalence in elderly COPD patients.

We conclude that COPD and asthma are conditions associated with many comorbidities at the time of diagnosis, particularly cardiovascular-, bone-, and other smoking-related diseases. Further research is needed to elucidate the role of smoking, medication use, and the interrelationships between asthma and COPD and other comorbidities.

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References

1 Theisen C, Bruckbauer S. Defining global health: who is responsible for the world's burden of disease? J Natl Cancer Inst 2003; 95:1568–1570
2 The World Health Report 1998. Life in the 21st century: a vision for all. Geneva, Switzerland: World Health Organization, 1998
3 Murray CJL, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. Lancet 1997; 349:1498–1504
4 Pauwels RA, Buist AS, Calverley PM, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) workshop summary. Am J Respir Crit Care Med 2001; 163:1256–1276
5 The International Study of Asthma and Allergies in Childhood Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). Eur Respir J 1998; 12:315–335
6 Janson C, Chinn S, Jarvis D, et al. Physician-diagnosed asthma and drug utilization in the European Community Respiratory Health Survey. Eur Respir J 1997; 10:1795–1802
7 Pearce N, Beasley R, Burgess C, et al, eds. Asthma epidemi-

ology: principles and methods. New York, NY: Oxford University Press, 1998
8 van Manen JG, Bindels PJ, IJzermans CJ, et al. Prevalence of comorbidity in patients with a chronic airway obstruction and controls over the age of 40. J Clin Epidemiol 2001; 54:287–293
9 Wijnhoven HA, Kriegsman DM, Hesselink AE, et al. The influence of co-morbidity on health-related quality of life in asthma and COPD patients. Respir Med 2003; 97:468–475
10 Eisner MD, Yelin EH, Trupin L, et al. The influence of chronic respiratory conditions on health status and work disability. Am J Public Health 2002; 92:1506–1513
11 Lawson DH, Sherman V, Hollowell J. The General Practice Research Database. Scientific and Ethical Advisory Group. QJM 1998; 91:445–452
12 Nazareth I, King M, Haines A, et al. Accuracy of diagnosis on general practice computer system. BMJ 1993; 307:32–34
13 Hansell A, Hollowell J, Nichols T, et al. Use of the General Practice Research Database (GPRD) for respiratory epidemiology: a comparison with the 4th Morbidity Survey in General Practice (MSGP4). Thorax 1999; 54:413–419
14 Soriano JB, Maier WC, Egger P, et al. Recent trends of physician-diagnosed COPD in women and men in the UK. Thorax 2000; 55:789–794
15 Hansell AL, Lam KA, Richardson S, et al. Medical event profiling of COPD patients. Pharmacoepidemiol Drug Saf 2004; 13:547–555
16 Soriano JB, Kiri VA, Maier WC, et al. Increasing prevalence of asthma in UK primary care during the 1990s. Int J Tuberc Lung Dis 2003; 7:415–421
17 Gan WQ, Man SF, Senthilselvan A, et al. Association between chronic obstructive pulmonary disease and systemic inflammation: a systematic review and a meta-analysis. Thorax 2004; 59:574–580
18 Iribarren C, Tolstykh IV, Eisner MD. Are patients with asthma at increased risk of coronary heart disease? Int J Epidemiol 2004; 33:743–748
19 Chapman KR, Tashkin DP, Pye DJ. Gender bias in the diagnosis of COPD. Chest 2001; 119:1691–1695
20 Bleecker ER. Similarities and differences in asthma and COPD: the Dutch hypothesis. Chest 2004; 126(suppl):93S–95S
21 Thiadens HA, de Bock GH, Dekker FW, et al. Identifying asthma and chronic obstructive pulmonary disease in patients with persistent cough presenting to general practitioners: descriptive study. BMJ 1998; 316:1286–1290
22 Soriano JB, Maier WC, Visick G, et al. Validation of general practitioner-diagnosed COPD in the UK General Practice Research Database. Eur J Epidemiol 2001; 17:1075–1080
23 Rabe KF, Adachi M, Lai CK, et al. Worldwide severity and control of asthma in children and adults: the global asthma insights and reality surveys. J Allergy Clin Immunol 2004; 114:40–47
24 Doll R, Hill AB. Lung cancer and other causes of death in relation to smoking: a second report on the mortality of British doctors. BMJ 1956; 12:1071–1081
25 Doll R, Peto R, Boreham J, et al. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ 2004; 328:1519
26 Lewis JD, Brensinger C. Agreement between GPRD smoking data: a survey of general practitioners and a population-based survey. Pharmacoepidemiol Drug Saf 2004; 13:437–441

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