Articles

Opportunities to diagnose chronic obstructive pulmonary disease in routine care in the UK: a retrospective study of a clinical cohort

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Summary

Background Patterns of health-care use and comorbidities present in patients in the period before diagnosis of chronic obstructive pulmonary disease (COPD) are unknown. We investigated these factors to inform future case-finding strategies.

Methods We did a retrospective analysis of a clinical cohort in the UK with data from Jan 1, 1990 to Dec 31, 2009 (General Practice Research Database and Optimum Patient Care Research Database). We assessed patients aged 40 years or older who had an electronically coded diagnosis of COPD in their primary care records and had a minimum of 3 years of continuous practice data for COPD (2 years before diagnosis up to a maximum of 20 years, and 1 year after diagnosis) and at least two prescriptions for COPD since diagnosis. We identified missed opportunites to diagnose COPD from routinely collected patient data by reviewing patterns of health-care use and comorbidities present before diagnosis. We assessed patterns of health-care use in terms of lower respiratory consultations (infective and non-infective), lower respiratory consultations with a course of antibiotics or oral steroids, and chest radiography. If these events did not lead to a diagnosis of COPD, they were deemed to be missed opportunities. This study is registered with ClinicalTrials.gov, number NCT01655667.

Findings We assessed data for 38859 patients. Opportunities for diagnosis were missed in 32900 (85%) of 38859 patients in the 5 years immediately preceding diagnosis of COPD; in 12856 (58%) of 22286 in the 6–10 years before diagnosis, in 3943 (42%) of 9351 in the 11–15 years before diagnosis; and in 95 (8%) of 1167 in the 16–20 years before diagnosis. Between 1990 and 2009, we noted decreases in the age at diagnosis (0.05 years of age per year, 95% CI 0.03–0.07) and yearly frequency of lower respiratory prescribing consultations (rate ratio 0.982 opportunities per year, 95% CI 0.979–0.985). Prevalence of all comorbidities present at COPD diagnosis increased except for asthma and bronchiectasis, which decreased between 1990 and 2007, from 281 (33.4%) of 842 patients to 451 of 1465 (30.8%) for asthma, and from 53 of 842 (6.3%) to 53 of 1465 (3.6%) for bronchiectasis. In the 2 years before diagnosis, of 6897 patients who had had a chest radiography, only 2296 (33%) also had spirometry.

Interpretation Opportunities to diagnose COPD at an earlier stage are being missed, and could be improved by casefinding in patients with lower respiratory tract symptoms and concordant long-term comorbidities.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive, destructive disease of the airways and lung parenchyma with no clear pathological or clinical starting points. The insidious and progressive nature of the disease can result in severe, irreversible damage by the time symptoms present and a diagnosis is made.¹ The earlier the diagnosis of COPD is made, the greater the potential to reduce damage to the lungs^{2,3} through addressing lifestyle factors such as smoking and lack of physical activity,⁴ and the prevention of COPD exacerbations, which are associated with disease progression. The National Outcomes Strategy for COPD, published by the UK Department of Health, provides a framework for improving outcomes of COPD in England.⁵ The Strategy estimated that 835000 people have a diagnosis of COPD, with a further $2 \cdot 2$ million people living with undiagnosed COPD.⁵ Early COPD diagnosis followed by appropriate intervention has the potential to save the UK National Health Service more than f_1 billion over 10 years.⁶

The onset of signs of lung disease should prompt appropriate investigations, such as spirometry. However, both patients and doctors often fail to recognise the significance of symptoms.⁵ In addition, some patients (particularly men) are reluctant or slow to express concern and seek advice.⁷ A holistic disease management approach—in which all present and potential comorbidities are assessed—has been suggested as an approach to evaluate those at risk of developing COPD.⁵ Compared with control populations without this disease, patient populations with COPD



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See Comment page 248

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See Online for appendix

have higher prevalence of cardiovascular disease, diabetes, peptic ulcer, gastro-oesophageal reflux disease, and lung cancer.⁸⁻¹² Shared risk factors between comorbidities, including lifestyle (eg, cigarette smoking), environmental and occupational exposures, and airway or generalised chronic inflammation from other causes all contribute to chronic ill-health and inactivity. These factors promote a cycle of debility, muscle wasting, increased susceptibility to COPD exacerbations, and worsening comorbidities.^{13,14} Although comorbidities are common, guidelines and governmental initiatives to improve management of chronic disease are usually disease-specific.

COPD exacerbations accelerate worsening of lung function, leading to: quicker disease progression,¹⁵ reduced mobility,¹⁶ and poorer quality of life.^{3,17} Indeed, COPD exacerbations account for a large proportion of the COPD-associated costs in primary and secondary care.¹⁸ Identification of people with as yet undiagnosed COPD, using a case-finding approach¹⁹ might facilitate earlier intervention to prevent exacerbations and slow the decline of lung function.³

Major guidelines and strategic statements assert that early diagnosis, combined with effective interventions, can reduce the health burden and financial cost of symptomatic COPD.^{120,21} However, the precise mechanisms through which this can be achieved are not yet agreed.^{120,22} In this study we assessed patterns of health-care use and comorbidities before a diagnosis of COPD to inform future case-finding strategies.

Methods

Study design and dataset

We did this retrospective, cohort study with primary and secondary care data routinely collected between Jan 1, 1990, and Dec 31, 2009, in the UK. Data were pooled from the General Practice Research Database, part of the Clinical Practice Research Datalink^{21,23} and the Optimum Patient Care Research Database.²⁴ The Optimum Patient Care Research Database has been approved for clinical research use by the Trent Multi Centre Research Ethics Committee.²⁴ The study protocol was approved by the General Practice Research Database's independent scientific advisory committee and the Optimum Patient Care Research Database's anonymised data ethics and transparency committee.

Eligible patients were aged 40 years or older with an electronically coded diagnosis of COPD in their primary care records between 1990 and 2009. The minimum age was chosen because COPD predominantly affects people aged 40 years and older.²⁵ All patients had a minimum of 3 years of continuous practice data (up to a maximum of 20 years), 2 years before diagnosis and 1 year after diagnosis, and at least two prescriptions for COPD-related drugs since diagnosis. This criterion indicates continued treatment and was used as a proxy for diagnosis of symptomatic disease.²²

Procedures

We reviewed data for a maximum of 20 years before diagnosis, including demographic characteristics, data about use of health-care resources indicative of missed opportunities for diagnosis, and comorbidities. This 40-year period (1970–2009) coincided with the migration of patient records from a paper to electronic format. To avoid use of retrospectively entered routine consultation data, we examined routine data recorded only after the date the practice began to use full electronic medical records. For comorbidities, diagnostic data entered retrospectively were considered valid for the purposes of identifying a comorbidity (appendix).

We recorded demographic characteristics: sex, age at COPD diagnosis, smoking status (recorded within 12 months of date of COPD diagnosis), location of diagnosis (primary or secondary care), lung function (forced expiratory volume in 1 s as a percentage of predicted [FEV₁%], recorded before or up to 10 years after COPD diagnosis), and airflow obstruction grading at COPD diagnosis (consistent with UK and 2011 Global Initiative for Chronic Obstructive Lung Disease [GOLD] airflow obstruction severity categories: GOLD I=FEV₁% \geq 80; GOLD II=FEV₁% 50–79; GOLD III=FEV₁% 30–49; and GOLD IV=FEV₁% <30).²² The MRC dyspnoea scale²⁶ was not routinely recorded across the timeframe analysed so it was not included.

We identified missed opportunities for COPD diagnosis for each patient. We used three primary care measures of missed opportunity. First, lower respiratory consultations, defined as all consultations coded for lower respiratory complaints, including lower respiratory tract infections (such as bronchitis, tracheitis, and pneumonia, which might need antibiotic treatment), non-infective lower respiratory conditions (such as asbestosis and chronic respiratory failure), and respiratory symptoms (such as breathlessness, hyperventilation, cough, and wheezing). Second, consultations for lower respiratory symptoms with a course of antibiotic drugs or oral steroids prescribed on the same day. And third, chest radiography. We searched 919 lower respiratory Read Codes covering symptoms, diagnoses, and procedures to identify all possible consultations at which the patient would have presented with lower respiratory symptoms. Chest radiographs were included as a missed opportunity even if they were not done to look for COPD specifically, because it suggests that the patient had symptoms for which the differential diagnosis could have included COPD.

Missed opportunities during secondary care were respiratory-related outpatient and unscheduled hospital admissions that did not lead to a coded diagnosis of COPD. The 20-year period of time leading up to COPD diagnosis was stratified into four bands: 0–5 years, 6–10 years, 11–15 years, and 16–20 years. To be included in the periods 6–10 years, 11–15 years, and 16–20 years, patients had to have no less than 10 years, 15 years,

For the the General Practice Research Database see http:// www.cprd.com

For the **Optimum Patient Care Research Database** see http:// www.optimumpatientcare.org/ OPCRD.html

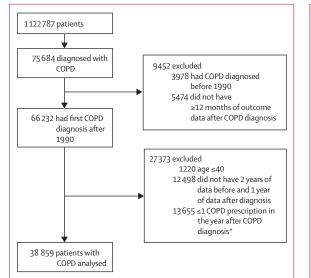


Figure 1: Study population

 * Āny of shortacting β 2 agonist, longacting β 2 agonist, inhaled corticosteroid, shortacting anticholinergic, longacting anticholinergic, leukotriene receptor antagonist, or theophylline. COPD=chronic obstructive pulmonary disease.

or 20 years of data, respectively. Patients with less than 10 years of data were included in the 0–5 year period.

We also identified recorded COPD exacerbations in the 2 years after diagnosis. Exacerbations were defined as: admission to hospital or accident and emergency attendance coded for COPD or lower respiratory prescribing consultations requiring antibiotic drugs or oral steroid treatment on the same day.

The appendix shows the definitions we used to identify active chronic comorbid conditions. We used diagnostic codes present at any time before diagnosis of COPD for cardiovascular disease, osteoporosis, bronchiectasis, asthma, and diabetes (or diabetes treatment ever before COPD diagnosis, irrespective of presence of a diabetes diagnostic code). We used recent diagnostic codes (ie, within 2 years), or diagnostic codes present at any time before diagnosis of COPD and active drug management (ie, prescriptions within 2 years of date of COPD diagnosis) to identify gastrooesophageal reflux disease, allergic rhinitis, chronic pain, and depression or anxiety. The use of prescription data or diagnostic codes aimed to identify all patients who (1) might have had a current comorbidity, whether or not it was coded (eg, diabetes and chronic pain); and (2) for diseases that have a natural history of active and remission phases (eg, gastro-oesophageal reflux disease, allergic rhinitis, and depression), ensured that only patients with active disease in the 2 years before COPD diagnosis were identified. We selected these COPD concordant or related comorbidities on the basis of our clinical experience and known pathophysiology at the time of the study design because no large epidemiological studies of comorbidity were available;

| | Total (n=38859) | Patients with data for FEV ₁ (n=22 821)* | Patients with no FEV, data available (16 038) | p value |
|--|--------------------|---|--|---------|
| Age at diagnosis (years) | | | | <0.0001 |
| Mean (SD) | 67.5 (10.4) | 66.3 (10.0) | 69.1 (10.7) | |
| Median (IQR) | 68 (60–75) | 66 (59–74) | 70 (62–77) | |
| Range | 41-104 | 41-102 | 41-104 | |
| Sex (n, %) | | | | 0.006 |
| Women | 18 435 (47%) | 10693 (47%) | 7742 (48%) | |
| Men | 20 424 (53%) | 12128 (53%) | 8296 (52%) | |
| Smoking status (n, %) | | | | <0.0001 |
| Data available | 28392 (73%) | 19264 (84%) | 9128 (57%) | |
| Non-smoker | 2518 (6%) | 1894 (8%) | 624 (4%) | |
| Current smoker | 12 981 (33%) | 8468 (37%) | 4513 (28%) | |
| Ex-smoker | 12893 (33%) | 8902 (39%) | 3991 (25%) | |
| Data not available | 10 467 (27%) | 3557 (16%) | 6910 (43%) | |
| Place of diagnosis (n, %) | | | | <0.0001 |
| Primary care | 38282 (99%) | 22 617 (99%) | 15 665 (98%) | |
| Secondary care (inpatient or outpatient) | 577 (1%) | 204 (1%) | 373 (2%) | |
| GOLD FEV, impairment band* (n, %) | | | | NA |
| FEV, data‡ available | 22821(59%) | | | |
| GOLDI(FEV₁≥80%) | 2882 (7%) | | | |
| GOLD II (FEV ₁ 50–79%) | 10347 (27%) | | | |
| GOLD III (FEV ₁ 30-49%) | 5669 (15%) | | | |
| GOLD IV (FEV ₁ <30%) | 3923 (10%) | | | |
| FEV, data‡ unavailable | 16 038 (41%) | | | |

p values are for the comparison of patients with FEV, data versus those without. COPD=chronic obstructive pulmonary disease. NA=not applicable. *FEV, value recorded ever before or within 10 years of diagnosis. +For difference between means. \pm FEV, value or FEV, between total cohort and subgroup with valid FEV, values.

Table 1: COPD population demographics at time of diagnosis

the subsequent work of Barnett and colleagues²⁷ suggests that this approach was justified.

Statistical analysis

We assessed trends in missed opportunities for diagnosing COPD in both primary and secondary care over the 20 years preceding diagnosis. Missed opportunities in the 2 years immediately before diagnosis were also assessed for change over the 20-year period (1990–2009). We evaluated age at diagnosis and comorbidities present at the time of COPD diagnosis over the same 20-year period. We also assessed frequency of missed opportunities and comorbidities by severity of airway obstruction and by sex. All analyses were done with SPSS (version 18).

We used summary statistics for patient characteristics at time of COPD diagnosis. We compared age at diagnosis by year of diagnosis and by severity of airway obstruction with *F* tests; age at diagnosis between sexes with a *t* test; and severity of airway obstruction by year of diagnosis and sex with χ^2 tests.

We used a general linear model to investigate the effects of year of diagnosis, sex, place of diagnosis (secondary care or primary care), and practice (treated as

| | 0–5 years (n=38 859) | 6–10 years (n=22 286) | 11–15 years (n=9351) | 16–20 years (n=1167) |
|--|-------------------------|--------------------------|-------------------------|-------------------------|
| Lower respiratory consultation | 32 900 (85%) | 12856 (58%) | 3943 (42%) | 95 (8%) |
| Lower respiratory prescribing consultation | 26 472 (68%) | 10627 (48%) | 3185 (34%) | 31 (3%) |
| Prescribed oral steroids | 15 498 (40%) | 3869 (17%) | 928 (10%) | 1(<1%) |
| Prescribed antibiotics | 21364 (55%) | 8656 (39%) | 2544 (27%) | 1 (<1%) |
| Chest radiography | 14 675 (38%) | 3366 (15%) | 648 (7%) | 19 (2%) |
| Outpatient consultation | 4237 (11%) | 1645 (7%) | 364 (4%) | 0 (0%) |
| Admitted to hospital | 881 (2%) | 220 (1%) | 53 (1%) | 3 (<1%) |

Data are n (%). Shows the number and proportion of patients who had one or more of each event in each 5-year period. COPD=chronic obstructive pulmonary disease.

Table 2: Missed opportunities to diagnose COPD in the years preceding diagnosis

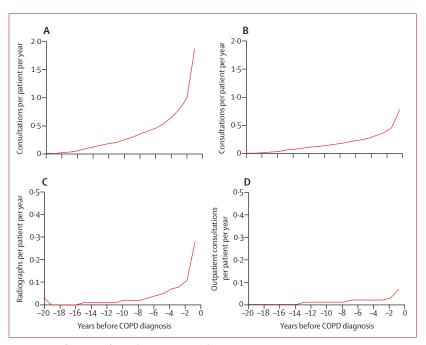


Figure 2: Mean frequency of missed opportunities to diagnose COPD

For consultations for lower respiratory symptoms (A), lower respiratory prescribing consultations (B), chest radiography (C), and outpatient consultations (D). Too few data were available to present number of admissions to hospital. COPD=chronic obstructive pulmonary disease.

a random effect to account for potential variations in clinical practice and thereby enabling results to be generalised across all practices) on age at diagnosis. We also included interactions between explanatory variables in the model. Interaction terms that were not significant were excluded and the model refitted.

We calculated the number and percentage of patients with missed opportunities for diagnosis by year before diagnosis (1–20 years before) and in 5-year bands before diagnosis. We compared the distributions by sex and place of diagnosis (primary or secondary care) with χ^2 tests. We calculated the mean number of missed opportunities per patient per year before diagnosis, the minimum, and the maximum.

We used generalised linear models to find out how missed opportunities to diagnose changed from 1990 to

2009. The frequency of missed opportunities in primary care and in secondary care recorded in the 2 years before diagnosis were each modelled as the dependent variable in a generalised linear model (with a Poisson distribution of errors and a log link) with independent variables of: year of diagnosis, age, sex, place of diagnosis (secondary care or primary care), and practice (treated as a random effect to enable results to be generalised across all practices). We also included interactions between the independent variables in the models. Interaction terms that were not significant were excluded and the model refitted. We evaluated prevalence of comorbidities by year of COPD diagnosis with a χ^2 test. For patients with data available for FEV₁%, we compared the distribution of airway obstruction severity by (1) year of diagnosis and (2) comorbidity prevalence with a χ^2 test. We tested the association between degree of airway obstruction (FEV,%) and frequency of lower respiratory prescribing consultations with Spearman's rank correlation coefficient. We analysed the prevalence of comorbidity by airway obstruction severity with the χ^2 test.

We used logistic regression to assess the odds of multiple COPD exacerbations in the first and second years after diagnosis for patients with two or more lower respiratory prescribing consultations before diagnosis compared with patients with one or no consultations. Indicator variables for two or more lower respiratory prescribing consultations in the year before diagnosis, age, sex, and year of diagnosis were included in the model as explanatory variables. We repeated the analysis using an indicator for two or more lower respiratory prescribing consultations in the 2 years before diagnosis. This study is registered with ClinicalTrials.gov, number NCT01655667.

Role of the funding source

The Department of Health and Research in Real Life designed the study, interpreted data, and revised the report. The corresponding author had full access to all of the data and the final responsibility to submit for publication.

Results

38859 patients were included in the study from a total of 1122787 patients who had a history of respiratory disease (figure 1). Average duration of longitudinal data was 10.4 years (range 3–21 years). All patients had 2 years of clinical and treatment data available before diagnosis; 33040 of 38859 (85%) patients had at least 5 years of data.

Table 1 shows the population demographic data. Data for smoking history were available for 28392 of 38859 (73%) patients and FEV₁% predicted data for 22821 of 38859 (59%) patients. Median duration between date of diagnosis and date of recording FEV₁% was 2 months (IQR 0–29 months). Of patients with an FEV₁% value available at time of COPD diagnosis, a smaller proportion of women than of men had evidence of airflow limitation (appendix). Small but significant demographic differences were present between the 22821 patients with data available for predicted FEV₁% and those without such data available (table 1). Patients with available FEV₁ data were 2.8 years (95% CI 2.6–3.1) younger (p<0.0001), were more likely to be men (odds ratio [OR] 1.06, 95% CI 1.02–1.10; p=0.006), have smoking status available (4.10, 3.91-4.30; p<0.0001), be current or ex-smokers (0.67, 0.61-0.74; p<0.0001), and were more likely to be diagnosed in primary care (2.64, 2.22–3.14; p<0.0001).

During the 20 years preceding diagnosis, opportunities to diagnose COPD related to lower respiratory events were missed in both primary and secondary care (table 2, appendix). Opportunities were missed during all four, 5-year periods (0–5, 6–10, 11–15, and 16–20 years), with many patients having opportunities missed in two or more 5-year periods in both primary and secondary care. The average number of missed opportunities per patient per year also increased leading up to the date of diagnosis (figure 2). 25 of 379 (6.6%) patients diagnosed in secondary care had one or more admissions to hospital in the 5 years before diagnosis, compared with 457 of 38480 (1.2%) diagnosed in primary care (OR 5.55, 95% CI 3.67–8.41; p<0.0001).

From 16 years before diagnosis of COPD, and each year until diagnosis, female patients had consistently more missed opportunities in terms of lower respiratory consultations and lower respiratory prescribing consultations than did male patients (p<0.0001; data not shown). We noted that men were more likely to have a chest radiography requested in the year before diagnosis than were women (4948/20424 [24.2%] *vs* 4019/18435 [21.8%]; OR 1.11, 95% CI 1.06–1.16; p<0.0001), women were more likely to be admitted to hospital in the 2 years before diagnosis than were men (266/18435 [1.44%] *vs* 216/20424[1.06%]; OR 1.36, 95% CI 1.14–1.63; p<0.0001), but we report no significant difference for outpatient attendances (398/18435 [2.2%] women *vs* 429/20425[2.1%] men; OR 1.03, 95% CI 0.89–1.18; p=0.696).

Table 3 and figure 3 show comorbidity prevalence data at the time of COPD diagnosis from 1990 to 2009. Prevalence of all comorbidities present at COPD diagnosis significantly increased over this period, with the exception of asthma and bronchiectasis, which had small but significant decreases. The highest yearly means for active comorbidities were chronic pain (40%), asthma (34%), diabetes (18%), depression or anxiety (16%), and cardiovascular disease (15%). Presence of one or more diagnosed comorbidities at the time of COPD diagnosis was associated with less airway obstruction (22821 patients had data for airway obstruction; appendix).

Many opportunities to diagnose COPD were missed in the 2 years before diagnosis (appendix) throughout the 20-year evaluation period. The number of lower respiratory prescribing consultations per year significantly decreased from 1990 to 2009 (rate ratio 0.982 per year,

| | Mean prevalence 1990-2009 (%) | Prevalence in 1990 (%) | Prevalence in 2007 (%) |
|-----------------------------------|----------------------------------|---------------------------|---------------------------|
| Asthma | 34% | 33% | 31% |
| Bronchiectasis | 4% | 6% | 4% |
| Cardiovascular disease* | 15% | 7% | 14% |
| Gastro-oesophageal reflux disease | 7% | 1% | 7% |
| Osteoporosis | 3% | 1% | 6% |
| Diabetes | 18% | 13% | 23% |
| Sinusitus | 3% | 0% | 5% |
| Chronic pain | 40% | 17% | 48% |
| Depression and anxiety | 16% | 7% | 19% |
| Allergic rhinitis | 7% | 4% | 6% |

Because of small numbers of patients in 2008 and 2009, results for these years were inconsistent with the general trend over time and therefore results for 2007 are reported here instead. COPD=chronic obstructive pulmonary disease. *Heart failure, angina, or myocardial infarction.

Table 3: Prevalence of comorbidities at time of COPD diagnosis

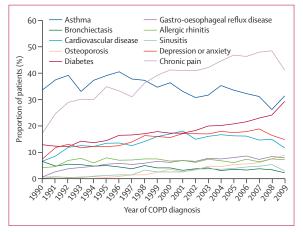


Figure 3: Prevalence of comorbidity at the time of COPD diagnosis for patients diagnosed between 1990 and 2009

95% CI 0.979-0.985), as did the number of outpatient consultations per year (0.917 per year, 95% CI 0.910-0.925;table 4). The yearly rate of all lower respiratory consultations decreased significantly for patients eventually diagnosed in secondary care (rate ratio 0.955 per year, 95% CI 0.934-0.976) but remained consistent for patients diagnosed in primary care (rate ratio 1.000 per year, 95% CI 0.998-1.003); whereas the number of chest radiographs significantly increased with year of diagnosis (rate ratio 1.093 per year, 95% CI 1.088–1.097). Because of the small numbers, change in frequency of admission to hospital over time could not be evaluated. For the 22821 patients with an FEV,% value, the frequency of lower respiratory prescribing consultations in the 5 years before diagnosis was not correlated with airway obstruction (r - 0.012; p=0.075). Of the 6897 patients who had chest radiography in the 2-24 months before diagnosis, only 2296 (33%) had evidence of having had spirometry (with or without an FEV₁% value) in the same period.

| Dependent variable | Independent variable | Rate ratio per year (95% CI) |
|---|---|--|
| Lower respiratory prescribing consultations | Year of diagnosis Age at diagnosis Men | 0·982 (0·979–0·985) 1·004 (1·002–1·006) |
| consoltations | Women | 0.992 (0.991-0.994) |
| Lower respiratory consultations | Age at diagnosis Men diagnosed in secondary care Men diagnosed in primary care Women diagnosed in secondary care Women diagnosed in primary care Year of diagnosis Secondary care Primary care | 0.990 (0.980-1.001) 1.004 (1.002-1.006) 0.982 (0.972-0.993) 0.996 (0.994-0.997) 0.955 (0.934-0.976) 1.000 (0.998-1.003) |
| Chest radiography | Year of diagnosis Age at diagnosis Diagnosed in secondary care vs primary care (reference) Men vs women (reference) | 1·093 (1·088–1·097) 1·002 (1·001–1·004) 0·73 (0·57–0·94)* 1·10 (1·06–1·14)* |
| Outpatient visits | Year of diagnosis Age at diagnosis Men Women Diagnosed in secondary care vs primary care (reference) | 0·917 (0·910–0·925) 0·998 (0·992–1·004) 0·988 (0·982–0·993) 1·49 (1·06–2·02)* |

Table 4: General linear model derived rate ratios for missed opportunities

| Dependent variable | Independent variable | Difference in age (years) | | |
|--|--|--|--|--|
| Age at diagnosis including practice as a random effect | Increase in age per increase in year Diagnosis in secondary care vs primary care | 0·06 (0·04-0·09) 2·82 (1·77-3·87) | | |
| | Men vs women Practice Sex by practice | 0-35 (0-02–0-68) Significant (age varies across practices) Significant (age varies with sex across practices) | | |
| Age at diagnosis excluding practice as a random effect | Decrease in age per increase in year Diagnosis in secondary care vs primary care | 0.05 (0.03-0.07) 2.15 (1.10-3.20) | | |
| Data are mean (95% Cl). Table 5: Mean differences in age at diagnosis from general linear model | | | | |

Median age of the total population at diagnosis fell from 69 years (IQR 62–76) in 1990, to 67 years (62–77) in 2007. However, by contrast with the raw data, the general linear model, which included practice as a random effect, reported a yearly increase in age at diagnosis (table 5). Excluding practice from the model reversed the findings in line with the raw values. Increasing chronological year of diagnosis was associated with an increasing proportion of patients with a lesser degree of airflow obstruction at time of COPD diagnosis (appendix) and a higher frequency of multiple comorbidities (two, three, or more; appendix).

10 271 of 38 859 (26%) patients had two or more lower respiratory prescribing consultations in the year preceding diagnosis and data available for 2 years after diagnosis. Two or more lower respiratory prescribing consultations in the year preceding diagnosis were associated with an increased likelihood of having two or more exacerbations in the first year after diagnosis (OR $3 \cdot 10$, 95% CI $2 \cdot 95 - 3 \cdot 26$) and the second year

after diagnosis (2.73, 95% CI 2.59–2.87). 14730 of 38859 (38%) patients who had two or more lower respiratory prescribing consultations in the 2 years preceding diagnosis had an increased likelihood of having two or more exacerbations in the first year after diagnosis (OR 3.16, 95% CI 3.01–3.32) and the second year after diagnosis (2.81, 2.67–2.96).

Discussion

Our findings show that, during the 20 years leading up to diagnosis, the proportion of patient consultations in primary and secondary care (and the frequency of consultations) for lower respiratory symptoms, antibiotic and oral steroid prescriptions, and chest radiography increased. Indeed, 85% of patients consulted primary care for lower respiratory symptoms in the 5 years before diagnosis of COPD. This finding confirms that many opportunities exist for earlier diagnosis of COPD in the course of routine clinical practice in the UK; recognition of these opportunities could be incorporated to serve as part of a case-finding strategy for patients with COPD and associated comorbidities (panel).

Women had more missed opportunities in primary care, but not in secondary care, than did men. One explanation might be that general practitioners are less likely to suspect COPD in women than in men. However, in this study-as in others-men had more severe airway obstruction at time of diagnosis than did women.³¹ Bridevaux and colleagues³² have reported that increased weight gain in female but not male patients with COPD was associated with rapid fall of FEV;; thus, opportunities for early diagnosis and intervention including the provision of lifestyle advice are important. Contrary to the GOLD guidelines,²² which document reduced FEV, as one of the defining parameters for risk of exacerbation, we report that the frequency of lower respiratory prescribing consultations was not associated with degree of airway obstruction (FEV₁%), although a history of lower respiratory prescribing consultations before diagnosis was associated with an increased risk of exacerbations after diagnosis. The absence of association between frequency of lower respiratory prescribing consultations and degree of airway obstruction might be a result of selection bias, although since the implementation of the Quality Outcome Framework in 2005, most patients diagnosed had an FEV₁% value available. In view of our findings and those for the SAPALDIA cohort33 study- which showed an association between early symptom presentation and progression to COPD-a history of multiple lower respiratory prescribing consultations could be a useful marker for case-finding as well as predicting which patients are likely to have frequent exacerbations after diagnosis.

Recent COPD policy and practice guidance have aimed to improve COPD diagnosis. Over the 20-year study period, median age at diagnosis reduced slightly between 1990 and 2007, as did the yearly mean adjusted age at diagnosis (excluding practice). However, adjustment for practice (as a random effect) resulted in a reversal of the trend, with the yearly mean adjusted age at diagnosis increasing over time. This finding suggests that practice policy might have significantly affected age at diagnosis over the study duration. Over the same time period, we also recorded reductions in the frequency of lower respiratory events, substantial increases in the prevalence of common COPD comorbidities, and a reduction in the proportion of patients with high airflow obstruction at diagnosis, which is contrary to the accepted notion that patients with many comorbidities have severe COPD disease.³⁴

Analyses using historical primary care datasets are limited by the quality of the data. However, treatment and consultation data in UK electronic patient records are regarded to be of high quality,^{15–37} with treatment data accepted as a reliable proxy of dispensed drugs (in the UK, pharmacists are required to dispense drugs that physicians prescribe). The diagnosis of COPD in this study is based on the presence of a coded diagnosis of COPD and at least two prescriptions for COPD treatment to indicate initiation and continuation of treatment. We did not assess the different phenotypes of COPD. Because the dataset draws from a geographically and socioeconomically diverse population, we believe that the study results are widely applicable to routine clinical practice in the UK.

Active long-term comorbid disease was defined a priori as a recent diagnostic code or as ever having had a diagnostic code plus recent treatment for disorders that might entail long-term treatment and no re-entry of diagnostic coding. We recorded a high prevalence of asthma across all COPD severities. A possible cause is that many patients receive an initial diagnosis of asthma on the basis of their symptoms, which is not updated (to asthma resolved) when they are subsequently diagnosed with COPD. As diagnostic accuracy improves, asthma and COPD phenotypes should be better delineated. Using population-based cohorts established in the late 1980s from the Atherosclerosis Risk in Communities Study and the Cardiovascular Health Study, Mannino and colleagues³⁴ reported that prevalence of diabetes, hypertension, and cardiovascular disease increased with increasing airflow obstruction. By contrast, across almost all the comorbidities, we report that a higher prevalence of comorbidity was associated with less airway obstruction at the time of diagnosis. This finding suggests that the presence of comorbidities leads to earlier COPD diagnosis, because those with comorbidities are more likely to visit their family doctor or nurse, leading to increased opportunities to identify symptoms and a diagnosis. Also there may be increased awareness of the risk of COPD in these patients (perhaps driven by national targets such as the UK's Quality and Outcomes Framework).³⁸ Conversely, patients with fewer comorbidities attended their family doctor less frequently,

Panel: Research in context

Systematic review

COPD is increasing in prevalence, yet studies have reported that it is often underdiagnosed or misdiagnosed. Strategies to improve COPD diagnosis in primary care, including case-finding strategies, have been proposed.²⁸ Although episodes of lower respiratory symptoms are an indicator of COPD, no studies have assessed whether measures of routinely collected resource data for lower respiratory health could be useful for identification of at-risk patients. Comorbidities are highly prevalent in COPD.²⁹ Indeed, patient-centred management, which includes assessment of current and consideration of potential comorbidities, is advocated by Fabbri and colleagues³⁰ on behalf of the American Thoracic Society. Yet, whether a patient-centred management approach could lead to diagnosis of COPD in patients with an established concordant comorbidity is unknown.

Interpretation

Opportunities to diagnose COPD are being missed in primary and secondary care despite the frequency of opportunities increasing, particularly during the 5 years immediately before diagnosis. Although we report small improvements in diagnosis of COPD for patients diagnosed at a young age, after few lower respiratory infections, and at an early stage in the course of disease, many patients were still being diagnosed with severe or very severe airway obstruction. Prevalence of concordant comorbidities (diabetes, cardiovascular disease, gastro-esophageal reflux disease, allergic rhinitis, sinusitis, depression or anxiety, and chronic pain) at the time of COPD diagnosis have significantly increased. The presence of a concordant comorbidity at diagnosis is associated with less airway obstruction at time of diagnosis, suggesting that attendance at clinics for the comorbidity is raising the possibility of the presence of COPD. COPD should be considered, and spirometry done for patients aged 40 years or older and current or ex-smoker, previously or currently presenting with lower respiratory tract symptoms in primary care, in those referred for chest radiography, or as outpatients for respiratory symptoms. Patient-centred management involving the assessment of present and potential comorbidities should be implemented to maximise opportunities for diagnosis of COPD, consistent with the findings of Barnett and colleagues.²⁷

resulting in fewer opportunities for diagnosis and therefore fewer chances to implement steps that might slow disease progression. This effect might have led to increased disease progression.

Our data searches showed that recording routine data into electronic patient records started around 15–20 years ago. During the initial years after transition from paper to electronic patient records, not all consultations were fully coded, limiting the usability of the data. The introduction in 2005 of the UK Quality and Outcomes Framework, which requires current smoking status and a valid FEV, value to be entered into the COPD patient record, has improved the frequency of data recording.34 We maximised the FEV1% data available by using the nearest recorded FEV₁ or FEV₁% value recorded either before diagnosis or within 10 years after diagnosis. Yearly decrease of lung function is 25-30 mL per year for patients aged 35-40 years, increasing to 60 mL per year for those aged 70 years and older.39 Thus, the small median duration between the date of entry of FEV, value and date of diagnosis in our dataset (2 months, IQR 0-29), suggests that the duration over which the FEV, data were identified did not significantly affect our findings. If spirometry values

were missing, we assumed that patients had spirometry done to inform the diagnosis, but results were not entered. Although small but significant differences for age at diagnosis, sex, place of diagnosis, and recording of smoking history existed between the FEV₁ subgroups and the total population, we believe our findings can be generalised to the COPD population as a whole. Indeed, the greater characterisation of the FEV₁ subgroup is consistent with management of chronic disease moving to a primary care setting and the implementation of Quality and Outcomes Framework targets for recording smoking status and FEV₁. However, questions remain about the overall quality of spirometry in primary care, and therefore the accuracy of any results.

It might be easier to identify those at risk of COPD by auditing a practice's patient records systematically rather than attempting to do so opportunistically during a consultation. Time pressure can lead to short consultations and reduced continuity of care. Casefinding strategies have been proposed as a mechanism for identifying high-risk patients. To date, these strategies have focused on patients with appropriate symptoms and risk factors including smoking,19,20,40 but have not included the number of lower respiratory consultations or chest radiographs (discrete clinical episodes). Screening asymptomatic patients for COPD with spirometry does not seem justified by current evidence²⁰ and is less useful in young people, for whom the pre-test probability of COPD is low.41 Prospective case-finding studies that include use of health-care resources are needed to establish how our findings can be used in routine primary care to help identify patients with COPD as early as possible. Such studies would require establishing background levels of use of respiratory health-care resources in the short term and long term for the healthy non-COPD population. We noted that the yearly frequency of missed opportunities increased in the 5 years immediately before diagnosis, therefore a 5-year review window of discrete clinical episodes might be appropriate for case-finding. Indeed, a 5-year window would avoid difficulties such as availability of data and changing awareness of COPD and investigations (for example following the implementation of the Quality and Outcomes Framework).

Decline in lung function seems to be steepest in the early stages of disease,⁴² indicating that opportunities to diagnose COPD earlier should be taken as early as possible. Our data suggest that: (1) although recurrent respiratory infections should always be assessed in their own right and treated accordingly, the possible presence of COPD should also be considered; (2) patients who smoke (current or past), are aged 40 years or older, presenting with lower respiratory symptoms requiring a prescription should be recalled after 6 weeks for spirometry to detect COPD; and (3) COPD symptoms should also be sought in patients who do or have smoked, are aged 40 years or older, and are attending clinics for

COPD concordant comorbidities with screening (handheld or similar) spirometry done as appropriate.5 The diagnosis of COPD should include clinical assessment stratification and be confirmed by postand bronchodilator spirometry done by trained staff using appropriate devices.43 Although most general practices in the UK have a spirometer, our data confirm that barriers to effective spirometric evaluation exist, probably in the form of time pressures, lack of appropriate training, and low confidence in interpretation of results.44,45 Although chest radiography might be needed to rule out cancer or tuberculosis, requesting a chest radiograph indicates that an opportunity to consider COPD might have been missed. In such cases, spirometry could have been ordered as well as chest radiography.

We noted that patients who have had recurrent lower respiratory prescribing consultations before COPD diagnosis are at a greater risk of future exacerbations. This finding is consistent with the frequent exacerbator phenotype described by Hurst and colleages.⁴⁶ Because people who have frequent exacerbations are liable to rapid decline in lung function and low quality of life,^{15,17} they have much to gain from early detection.⁴² Indeed, our results suggest that patients tended to have moderateto-severe disease at the point of diagnosis, thereby minimising the potential benefit that starting treatment could provide in terms of delayed disease progression. Prospective studies are necessary to confirm the benefit, if any, of early detection and management of COPD in primary care, based on the findings of our study.

What improvements can be made? The situation in the UK-where these data were recorded-has steadily improved over the past 20 years. This improvement might be partly related to resource allocation to encourage use of diagnostic spirometry and recent policies of the Department of Health.^{5,6} An important priority is education of primary care nurses and doctors to be aware of the possibility of COPD in people presenting with risk factors (including comorbidity) and respiratory symptoms, and to undertake quality spirometry as an early investigation. Proposals to address these priorities have included incentivisation of primary care as a means of obtaining access to quality spirometry,⁴³ coupled with knowledge and skills about disease management and an enhanced yearly structured review. Collaboration with community workers such as respiratory nurses, smoking cessation counsellors, and public health workers who provide dietary and exercise advice has the potential to improve clinical outcomes while reducing hospital admissions and treatment costs, as evidenced by the Finnish 10-year COPD Programme.⁴⁷ Because the Programme showed no improvement in the number of patients diagnosed with COPD, integration of a case-finding strategy-including analysis of routinely collected data-to identify patients at risk of COPD and who might benefit from further assessment could lead to further improvements.

We suggest that a case-finding approach should be modified to include: all patients older than 40 years with a diagnosis of asthma and who currently smoke; all smokers older than 40 years who have a lower respiratory prescribing event; and follow-up of existing recommendations for smokers aged older than 40 years with any respiratory symptoms, especially if they are male. Although we are unable to discern the principal drivers responsible for the small improvements in COPD diagnosis over the 20-year study period, our study suggests that patient outcomes could be improved when a person-centred approach to disease management is taken, including both related or concordant and unrelated disconcordant comorbidities. Decision support software could be used to automatically generate prompts for clinicians on possible next steps for patients deemed at risk. The substantial financial costs of failing to diagnose and treat COPD until a later stage would probably outweigh the costs of implementing this approach. Understanding historical patterns of respiratory symptoms, treatments, and test results, comorbidities and health-care resource use in patient-centred primary care such as we propose relies on a doctor having access to all current and past records and information. For health-care systems outside of the UK that are less focused on primary care-eg, in the USA-implemention of mechanisms to enable clinical information to be shared with family doctors is essential if diagnosis of COPD is to improve.

Contributors

RCMJ, DP, LM, DMGH, RW, DR, SH, MK, KH, AM, EDB, DF, and AC designed the study, interpreted data, and revised the report. EJS, JvZ, AB, AC, and DP analysed and interpreted data. RCMJ, DP, LM, DMGH, RW, DR, SH, MK, KH, AM, EDB, DF, EJS, JvZ, AB, and AC wrote and revised the report. All authors have given final approval of the version to be published.

Declaration of interests

We declare that we have no competing interests. RCMJ, DP, RW, DMGH, SH, MK, KH, AM, and DR were involved in the preparation of the Outcomes Strategy for COPD and Asthma in England.

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