Chronic obstructive pulmonary disease and comorbidities

Chetty, Ula; McLean, Gary; Morrison, Deborah; Agur, Karolina; Guthrie, Bruce; Mercer, Stewart W.

Published in:
British Journal of General Practice

DOI:
10.3399/bjgp17X690605

Publication date:
2017

Document Version
Peer reviewed version

COPD and Comorbidities: A Cross- Sectional Analysis of 1.2 Million Patients from a Nationally Representative Dataset in Scotland

Corresponding Author: Professor Stewart Mercer

1 Horselethill Road, Glasgow, G12 9LX

stewart.mercer@glasgow.ac.uk

[00 44] 0141 330 8330

Authors

Ula Chetty[1], Gary Mclean [1], Deborah Morrison et al

Word count excluding title page, abstract, references, figures and tables: **2500 words**

Formatted: Font color: Red

Keywords

COPD

Primary health care

Multimorbidity

How this fits in: Comorbidities in COPD have been associated with higher ~~increased~~ mortality, hospital admission and polypharmacy but the exact prevalence of individual comorbidities varies in the literature. This is the largest cross-sectional study to date examining the extent and type of 38 comorbidities associated with COPD. Extensive comorbidities in COPD were found compared to controls, with implications for advocating for integrated primary and secondary care as well as updated guidelines reflecting the complex comorbidities encompassing COPD.

Abstract

Background

COPD is common and a major cause of morbidity and mortality worldwide. Recent studies suggest that comorbidities in COPD increase the risk of hospitalisation, polypharmacy and mortality but their estimated prevalence varies widely in the literature.

Aim

To evaluate the prevalence~~extent and type~~ of 38 physical and mental health comorbidities associated with COPD compared to controls in a large nationally representative dataset.

Design and Setting

A Cross-sectional data analysis of 314 primary care practices in Scotland including 1,272,685 adults.

Method

Data on COPD and 31 other physical and 7 mental health comorbidities was extracted. The prevalence of ~~individual and cumulative~~ comorbidities was compared in people with COPD to controls, standardised by age, gender and socioeconomic deprivation.

Results

There were 51,928 patients with COPD (4.1%). 86.0% of people with COPD had at least one additional comorbidity, compared to 48.9% of controls. 22.3% of people with COPD had five or more conditions compared to 4.9% of controls (adjusted OR 2.63, 95%CI 2.56-2.70). 29 of the 31 physical conditions and 5 of the 7 mental health conditions were more prevalent in COPD patients than controls. The six most prevalent non respiratory comorbidities in the COPD group were hypertension (35.3%), painful conditions (24.5%), coronary heart disease (20.8%) , depression (19.1%), dyspepsia (13.7%) and diabetes mellitus (12.2%.)

Conclusion

~~People~~ Patients with COPD have extensive physical and mental health comorbidities. Guidelines for COPD should reflect this complexity but optimal management will also require enhanced integration of primary and specialist health care.

Background

Chronic Obstructive Pulmonary Disease (COPD) is a major global cause of morbidity and mortality and is expected to become the third leading cause of death worldwide by 2020.(1) It has a significant impact on quality of life, even in its early often undiagnosed stages (2) and is a leading cause of unscheduled hospital admission. Comorbid conditions are commonly associated with COPD and they further increase the risk of hospitalisation.(3, 4) Comorbidity in COPD has also been associated with higher levels of polypharmacy and higher mortality.(5, 6) Estimates of the prevalence of individual comorbidities associated with COPD vary substantially in the literature (7) and studies investigating COPD and comorbidities often only consider a single or small number of comorbidities. (8, 9) Some studies have counted a larger number of comorbidities but have had limitations such as a lack of control group.(4, 10)

There have been a small number of cross-sectional studies comparing comorbidities in COPD to controls, with variation in the number and type of comorbidities assessed. One Spanish study (11)included 6357 individuals with COPD from a total sample of 198,670 and compared the prevalence of 25 additional chronic diseases in those with COPD to controls; the most prevalent of which were hypertension, dyslipidaemia and obesity in the COPD group. Another cross sectional study was the largest to date including 15,018 individuals with COPD in a population of 341,329 (12) but the analysis was limited to determining and comparing the prevalence of eleven chronic conditions. They found an increased prevalence of ischaemic heart disease, heart failure, depression, diabetes mellitus and lung cancer in COPD compared to controls.

Mental health disorders are common in patients with COPD, although prevalence estimates vary substantially, for example from 10-42% for depression.(13) Hanania followed 2,118 patients with COPD and compared them to 578 controls in 12 countries and found a prevalence of depression of 26% in COPD, 2-3 fold higher than the control group.(14) Comorbid depression or anxiety in COPD has been shown to increase health care utilisation for primary and secondary care and reduce treatment adherence.(13) Given that depression and anxiety are frequently under-diagnosed in COPD; their detection and treatment is therefore essential.(8, 13)

The aim of this study was to determine the ~~extent and number~~ prevalence of physical and mental health comorbidities in people with COPD compared to controls in a large nationally representative dataset in Scotland.

Methods

We obtained data from the Primary Care Clinical Informatics Unit at the University of Aberdeen for 1,272,685 patients aged 25 and over who were alive and permanently registered with one of 314 Scottish general practices on March 31, 2007.(16) Data on the presence of COPD, 31 chronic physical health conditions and 7 mental health conditions were extracted (listed in Appendix 1). This study was a secondary data analysis using the SPICE dataset from Barnett's study. The comorbidities originally chosen were identified as important by NHS Scotland. (15) The dataset was representative of the Scottish population in terms of age, sex and socioeconomic deprivation, with a more detailed explanation available elsewhere.(16) We defined COPD using a set of read codes based on definitions used by NHS Scotland Information Services. There was no measure of severity of COPD in the data analysis.

'Controls' were defined as all patients from the 1,272,685 group who did not have COPD. To control for differences between the two populations in age, gender and deprivation levels we adopted a similar approach to that undertaken in previous papers(17)and generated standardised prevalence rates by age groups (25 to 34 years; 35 to 44; 45 to 54; 55 to 64; 65 to 74; 75 to 84 and 85 and over), gender and deprivation decile using the direct method. These age-gender-deprivation standardised rates were then used to calculate odds ratio (ORs) and 95% confidence intervals (95% CI) for the adults with COPD compared to controls without, for the prevalence of 31 physical conditions and seven mental health conditions. Furthermore, the overall number of physical and mental health conditions was documented.

Socioeconomic deprivation was measured using the Carstairs deprivation score divided into deciles from the most affluent to the most deprived. The Carstairs score is based on postcode of residence and is widely used in healthcare research as a measure of socioeconomic status.(18) We used t-tests to analyse differences between groups and one-way analysis of variance for differences across age groups and deprivation deciles. For all statistical analyses, a p-value less than 0·05 was considered statistically significant. All analyses were performed in Stata version 13. The NHS Grampian Research Ethics Service approved the anonymous use of this data for research purposes.

Results

There were 51, 928 (4.1%) people with COPD from the total sample of 1,272,685 adults aged 25 and over. People with COPD were somewhat more likely to be women than those without (46.4% vs 49.0%), were older (mean age 65.1 years vs 50.6 years for controls, p<0.001), and were more likely to live in areas of high social deprivation (24% resident in the most deprived quintile vs 17.1% of controls) (Table 1).

Overall Comorbidity

Table 2 shows that only 14% of people with COPD did not have any additional conditions compared to 48.9% of people without COPD (standardised OR 0.16, 95% CI 0.15-0.17). The COPD group after adjusting for age, gender, and deprivation standardisation were significantly more likely than controls to have one or more additional conditions with differences increasing with each additional condition. The largest difference was for 5 or more comorbidities, found in 22.3% of the COPD group compared to just 4.9% for those without COPD (standardised OR 2.63, 95% CI 2.56-2.70).

Compared to controls, individuals with COPD were significantly less likely to have no additional physical condition (COPD 17.5% vs. controls 54.7%; standardised OR 0.42 95% CI 0.41-0.43). Those with COPD were significantly more likely to have one or more non-COPD condition. The largest difference was for 5 or more physical conditions (COPD 14.8% vs. controls 2.9%; standardised OR 2.51 95% CI 2.42-2.59).

People with COPD were less likely to have no recorded mental health condition compared to controls (COPD 68.8% vs. controls 85.1%; standardised OR 0.50, 95% CI 0.49-0.51). Compared to controls, those with COPD were more likely to have one mental health condition (COPD 21.1% vs. controls 11.9%; standardised OR 1.73, 95% CI 1.69-1.77), and over twice as likely to have three or more mental health conditions (COPD 1.5% vs. controls 0.5% OR 2.51 95%CI 2.32-2.76).

Comorbidity of Individual Conditions

Table 3 demonstrates 29 out of the 31 physical conditions were significantly more prevalent in the COPD group compared to controls. The most prevalent conditions in the COPD group were hypertension (35.3%), painful conditions (24.5%), asthma (21.4%) and coronary heart disease (20.8%). The biggest differences between the COPD group and control group for individual conditions were for bronchiectasis (standardised OR 9.14, 95% CI 8.38-9.47) and asthma (standardised OR 5.07, 95% CI 4.96-5.18). Seven other physical conditions were more than twice as likely to be prevalent in those with COPD compared to controls; heart failure (OR 2.35), viral

hepatitis (OR 2.34), chronic sinusitis (OR 2.28), peripheral vascular disease (2.23), chronic liver disease (OR 2.15), psoriasis/ eczema (OR 2.03) and irritable bowel syndrome (OR 2.01).

Table 4 shows that six of the seven mental health conditions were significantly more prevalent in the COPD group than controls. The COPD group had significantly higher prevalence of alcohol misuse, anxiety, depression, schizophrenia and dementia compared to the control group. After standardisation for age, sex and deprivation, the biggest differences were found for the prevalence of alcohol misuse (COPD 7.6% vs. controls 3.0%; standardised OR 2.48, 95% CI 2.40-2.57) and anxiety (COPD 11.2% vs. controls 3.9%; standardised OR 2.14, 95% CI 2.07-2.21). The most prevalent mental health condition in COPD was depression; 19.1% compared to 10.5% of controls (standardised OR 1.77 95%CI 1.71-1.82).

Discussion

Summary of Key Findings

The prevalence of COPD was 4.1% in this study, similar to the 3.4% found by a Canadian study (12, 19) but higher than 1.4% in a study from England. (20)

Commented [UJC1]: Please let me know if anyone can find a better reference. British lung foundation quotes 2% for population, 4.5% over age 45 but this is present in a factsheet rather than a paper!

The aim was to ~~We~~ examine~~d~~ the prevalence of comorbidities in people with COPD, compared to those without, in the largest nationally representative primary care study to date. Individuals with COPD had excess physical and mental health comorbidities compared to those without, even after controlling for age, gender and deprivation. Thirty five of the thirty eight conditions examined were more common in people with COPD. The six most prevalent non-~~-~~respiratory comorbidities in people with COPD were hypertension (35.3%), painful conditions (24.5%), coronary heart disease (CHD, 20.8%), depression (19.1%), dyspepsia (13.7%) and diabetes mellitus (12.2%). The study confirms that multiple comorbidity is extremely prevalent and this is known to be associated with an increased risk of hospitalisation, polypharmacy and mortality.(7, 21)

Strengths and Limitations

To the best of our knowledge, this is the largest study to date which has evaluated the prevalence of 38 comorbidities in COPD in a nationally representative primary care sample. The data analysis was cross-sectional hence conclusions about causality cannot be made. Furthermore, the presence of a chronic illness may lead to increased diagnosis of other conditions due to closer monitoring.(22) Certain comorbidities were not specifically included in the analysis, such as lung cancer or pulmonary hypertension as this study involved a secondary data analysis and these conditions had been excluded from the primary data analysis~~.~~ Furthermore, we acknowledge that certain conditions such as viral hepatitis were associated with smaller sample sizes (42 patients with COPD had viral hepatitis) compared to commoner conditions such as diabetes.

Smoking data was not included in the data analysis therefore we have not been able to make comparisons on levels of smoking in the COPD and control groups.

Comparison with existing literature

Formatted: Normal

Within the COPD group, 86% had one or more comorbidities- similar to the prevalence ranging from 76-82% found in three ~~two~~ recent studies.(4, 19, 23) An Italian cohort study of 569 people with COPD found that 81.2% had additional comorbidity and acute exacerbations of COPD were more common in those with a higher number of comorbidities.(4)

The largest difference between the COPD group to those without was for bronchiectasis. A recent meta-analysis (24)which included fourteen observational studies found that comorbid bronchiectasis increased the risk of exacerbation and isolation of pathogenic microbes, such as pseudomonas, in the sputum. Furthermore, comorbid bronchiectasis was associated with an increased risk of severe airway obstruction and mortality.

Asthma was commonly found in patients with COPD, which was expected for two reasons. First because some patients will have asthma-COPD overlap syndrome,(25) where there are chronic airway disease features overlapping both conditions. Typically, there is variable airflow obstruction which is not fully reversible.(25) Second, some people with COPD will be incorrectly coded as having asthma which may overstate the prevalence of asthma as a comorbidity. Chronic sinusitis was twice as common in the COPD group than the control group. Although a less commonly recognised phenomenon, sino-nasal involvement can impair quality of life and increase COPD exacerbations.(26)

Previous studies have established that COPD is associated with hypertension and CHD (11, 21) which this study confirmed. CHD is frequently underdiagnosed in COPD which is important as the coexistence of CHD and COPD together worsens the prognosis compared to each individually.(27) Individuals with COPD were more likely to have heart failure, peripheral vascular disease, and cerebrovascular disease consistent with higher rates of hypertension, CHD, with smoking as a common risk factor.(5, 28, 29) Research by Rutten et al identified a prevalence of 20.5% of heart failure in COPD (compared to 6.4% in this study) when screened for the condition by using a number of diagnostic tests, highlighting the issue of underdiagnosis of heart failure in COPD. (30)

Comorbid dyspepsia in patients with COPD is inkeeping with a longitudinal study by Benson et al,(31) who noted a high prevalence of gastro-oesophageal reflux disease in patients with COPD, which was

associated with an increased risk of exacerbation. Our study's finding of increased prevalence of diabetes mellitus in COPD compared to controls (12.2%) was slightly lower than the prevalence documented in two cross-sectional studies of 18.7% (12) and 20%.(11)

Our study found higher levels of alcohol misuse in patients with COPD which may in part explain the higher levels of chronic liver disease, but there were also strong associations with viral hepatitis. One small Japanese study found that chronic hepatitis C virus infection was associated with an accelerated decline in lung function in patients with COPD,(32) and hepatitis C was found to be more prevalent in people with COPD than the general population in Brazil (10.7% vs. 1.2-2%).(33). Further research is needed to evaluate whether there is a significant association between hepatitis C and COPD. Notably, our code 'viral hepatitis' did not differentiate between the hepatitis subtypes.

A recent meta-analysis identified a statistically significant association between psoriasis and COPD, with a higher risk of developing COPD with more severe psoriasis, (34) confirming this study's finding of increased risk of psoriasis in COPD compared to controls.

We found that those with COPD were more likely to have one, and more than twice as likely to have two or more mental health conditions compared to controls. The biggest difference was for alcohol misuse, with the COPD group more than twice as likely to have been coded for this. There is a lack of studies investigating alcohol misuse prevalence in COPD. There is however evidence of high rates of smoking in those who misuse alcohol.(35) The prevalence of anxiety in the COPD group was 11% and of depression 19.1%, although both may be under-diagnosed.(13) In the literature (which includes heterogeneous often selected populations), the estimated prevalence of comorbid depression varies from 10-42%, and of anxiety 10-19%.(13) Comorbid mental health conditions have significant implications such as poor compliance with treatment, increased frequency of hospital admissions as well as prolonged inpatient stay.(8, 13)

The exact mechanisms underpinning the diverse comorbidities associated with COPD are likely to be multifactorial and beyond the scope of this study. In short, some conditions may share common risk factors such as CHD and smoking.(3) However, evidence suggests that COPD is associated with chronic systemic inflammation, independent of smoking, which in turn may lead to insulin resistance (contributing to metabolic syndrome and diabetes), cachexia and a procoagulant state. (28, 36) COPD medication is also likely to exacerbate certain comorbidities; prednisolone could contribute to diabetes, osteoporosis and muscle dysfunction.(37)Further research is required to elucidate the exact mechanisms of the associated comorbidities.

Implications for Policy and Practice

This study demonstrates the high prevalence of COPD and the fact that the presence of comorbidities is the rule rather than the exception. Our current healthcare model delivers fragmented care to patients with multiple comorbidities. We postulate that optimal management for these complex patients would involve the integration of specialist and primary care services in order to provide comprehensive and holistic health care. Primary care, unique in terms of offering expert generalist care, is best placed to provide this integrated approach.

One recent Danish study (38) examining resource allocation in COPD found that multimorbidity in COPD significantly increased the annual fee for service health care expenditure. Although it is unsurprising for comorbidities to increase health care costs, this highlights evidence for the added economic burden as a result of comorbidities.

Formatted: Left, Line spacing: Multiple 1.15 li

Current guidelines for the COPD management do not take common comorbidities into account. The research behind the guidelines frequently excludes multimorbid patients, which influences the validity and generalisability of the treatments suggested for the majority of patients with COPD. There is a real need for guidelines and healthcare to reflect the ~~complex reality of~~ COPD complexities, encompassing detection of the common physical and mental health comorbidities and management of how best to deal with them in combination. This study plays a part in determining the prevalence of comorbidities in COPD which could contribute to the creation of these appropriate comprehensive guidelines. We speculate that by achieving this, we could potentially reduce the number of admissions, improve morbidity and mortality for patients with COPD, which in turn could have a significant economic and health-care impact.

Conclusions

The current study has illustrated that the majority of patients with COPD have complex physical and mental health comorbidity. Firstly, we propose that the integration of primary and secondary care services would provide optimal holistic care for these patients. Secondly, guidelines for COPD should be based on valid generalisable evidence and need to reflect the associated comorbidities in order to provide clear management strategies for clinicians.

Table 1 Age, Gender and Deprivation status, COPD Versus Controls

Variable	COPD Number (%) N=51,928	No COPD Number (%) N=1,220,757
Mean Age (sd) in Years	65.1 (14.5%)	50.6 (16.4%)
Men	24,077 (46.4%)	598,005 (49.0%)
Age group		
25-34	1,964 (3.8)	227,432 (18.6)
35-44	3,388 (6.5)	275,605 (22.6)
45-54	5,961 (11.5)	247,833 (20.3)
55-64	11,077 (21.3)	208,256 (17.1)
65-74	14,634 (28.2)	140,646 (11.5)
75-84	11,551 (22.2)	87,769 (7.2)
85 and above	3,353 (6.5)	33,216 (2.7))
Deprivation Deciles		
1 Least Deprived	2,486 (4.8)	115,222 (9.4)
2	3,364 (6.5)	123,286 (10.1)
3	3,637 (7.0)	120,236 (9.9)
4	5,659 (10.9)	146,235 (12.0)
5	6,622 (12.8)	140,043 (11.5)
6	6,637 (12.8)	136,648 (11.2)
7	6,588 (12.7)	127,837 (10.5)
8	4,487 (8.6)	102,982 (8.4)
9	6,971 (13.4)	110,050 (9.0)
10 Most Deprived	5,477 (10.6)	98,218 (8.1)

All differences between the COPD and control group significant at $p<0.001$

Table 2 Prevalence and odds ratio for number and type of comorbidities (standardised by age, gender and deprivation score)

	COPD Number (%) with conditions other than COPD N=51,928	**No COPD** Number (%) with conditions other than COPD N=1,220,757	**Odds ratio (95% CI)** (standardised by age, gender and deprivation)
Total number of physical and mental health conditions			
None	7,264 (14.0)	597,363 (48.9)	0.16 (0.15-0.17)
One	9,305 (17.9)	271,751 (22.3)	1.16 (1.14-1.18)
Two	9,194 (17.7)	150,858 (12.4)	1.38 (1.35-1.42)
Three	8,139 (15.7)	88,888 (8.8)	1.66 (1.61-1.70)
Four	6,460 (12.4)	51,961 (4.3)	1.95 (1.89-2.01)
Five or more	11,566 (22.3)	59,936 (4.9)	2.63 (2.56-2.70)
Total number of physical conditions			
None	9,063 (17.5)	668,190 (54.7)	0.42 (0.41-0.43)
One	10,971 (21.1)	266,951 (21.9)	1.23 (1.21-1.25)
Two	10,122 (19.5)	136,637 (11.2)	1.52 (1.48-1.56)
Three	8,253 (15.9)	73,986 (6.1)	1.78 (1.73-1.83)
Four	5,834 (11.2)	39,316 (3.2)	1.95 (1.88-2.03)
Five or more	7,685 (14.8)	35,677 (2.9)	2.51 (2.42-2.59)
Total number of mental health conditions			
None	35,729 (68.8)	1,029,339 (85.1)	0.50 (0.49-0.51)
One	11,324 (21.1)	145,819 (11.9)	1.73 (1.69-1.77)
Two	4,096 (7.9)	39,160 (3.2)	2.08 (2.00-2.15)
Three or more	779 (1.5)	6,439 (0.5)	2.51 (2.32-2.76)

All differences between the COPD and control group significant at p<0.001

Commented [UJC2]: Reviewer commented on this bit- the odds ratio is greater than one here, despite a higher percentage in the Non COPD group. Please can this be checked? Is it due to the standardisation?

Formatted: Font color: Red

Formatted: Font color: Red

Formatted: Font color: Red

Formatted: Font color: Red

Formatted: Font color: Red

Table 3 Prevalence and odds ratios for individual physical conditions (standardised by age, gender and deprivation score). Conditions are ordered by size of odds ratio (largest to smallest).

Condition	**COPD** Number (%) N=51,928	**No COPD** Number (%) N=1,220,757	**Odds ratio (95% CI)** (standardised by age, gender and deprivation)
Bronchiectasis	988 (1.9)	1,782 (0.2)	9.14 (8.38-9.47)
Asthma	11,130 (21.4)	65,106 (5.3)	5.07 (4.96-5.18)
Heart failure	3,344 (6.4)	15,526 (1.3)	2.35 (2.23-2.47)
Viral hepatitis	42 (0.1)	1,096 (0.1)	2.34 (1.92-2.86)
Chronic sinusitis	721 (1.4)	8,217 (0.7)	2.28 (2.13-2.45)
Peripheral vascular disease (PVD)	3,494 (6.7)	19,437 (1.6)	2.23 (2.13-2.34)
Cirrhosis/chronic liver disease/alcoholic liver disease	307 (0.6)	2,305 (0.2)	2.15 (1.87-2.48)
Psoriasis or eczema	831 (1.6)	8,836 (0.7)	2.03 (1.88-2.18)
Irritable bowel syndrome	3,316 (6.4)	47,141 (3.9)	2.01 (1.94-2.08)
Painful condition	12,697 (24.5)	112,370 (9.2)	1.99 (1.94-2.04)
Inflammatory arthritis and related conditions including gout	5,821 (11.2)	51,461 (4.2)	1.86 (1.80-1.92)
Coronary heart disease	10,811 (20.8)	70,645 (5.7)	1.78 (1.72-1.83)
Dyspepsia	7,112 (13.7)	71,481 (5.9)	1.78 (1.73-1.83)
Constipation	4,358 (8.4)	31,737 (2.6)	1.66 (1.59-1.73)
Diverticular disease	4,273 (8.3)	29,527 (2.4)	1.63 (1.56-1.71)
Hearing loss	4,868 (9.4)	47,104 (3.9)	1.61 (1.55-1.67)
Migraine	499 (1.0)	8,508 (0.7)	1.57 (1.44-1.71)
Atrial fibrillation	3,065 (5.9)	20,894 (1.7)	1.53 (1.45-1.62)
Stroke or transient ischaemic attack	4,307 (8.3)	32,167 (2.6)	1.50 (1.43-1.57)
Epilepsy	663 (1.3)	10,886 (0.9)	1.48 (1.37-1.62)

Visual impairment	884 (1.7)	7,164 (0.6)	1.48 (1.34-1.62)
Prostate disease	1,736 (3.3)	13,484 (1.1)	1.45 (1.35-1.55)
Diabetes	6,315 (12.2)	67,410 (5.5)	1.41 (1.37-1.46)
Thyrotoxicosis/thyroid disorders inc hypothyroidism	5,185 (10.0)	65,999 (5.4)	1.34 (1.30-1.39)
Chronic kidney disease	3,842 (7.4)	29,694 (2.4)	1.33 (1.27-1.40)
Any new cancer in the last five years	3,731 (7.2)	39,275 (3.2)	1.29 (1.23-1.35)
Inflammatory bowel disease	596 (1.2)	8,812 (0.7)	1.28 (1.17-1.40)
Glaucoma	1,498 (2.9)	14,387 (1.2)	1.20 (1.11-1.29)
Hypertension	18,346 (35.3)	215,741 (17.7)	1.17 (1.14-1.20)
Multiple sclerosis	120 (0.2)	3,706 (0.3)	1.03 (0.88-1.21) p=0.62
Parkinson's disease and Parkinsonism	232 (0.5)	2,507 (0.2)	0.93 (0.77-1.13) p=0.50

All differences between the COPD and control group significant at $p<0.001$ except where stated

Table 4 Prevalence and odds ratios for Individual Mental Health Conditions (Standardised by Age, Gender and Deprivation score). Conditions are ordered by size of odds ratio (largest to smallest).

Mental Health Condition	**COPD** Number (%prevalence) N=51,928	**No COPD** Number (%prevalence) N=1,220,757	**Odds ratio (95% CI)** (standardised by age, gender and deprivation)
Alcohol misuse	3,952 (7.6)	36,616 (3.0)	2.48 (2.40-2.57)
Anxiety & other neurotic, stress related & somatoform disorders	5,797 (11.2)	48,318 (3.9)	2.14 (2.07-2.21)
Anorexia or bulimia	272 (0.5)	4,526 (0.4)	1.86 (1.67-2.08)
Depression	9,941 (19.1)	128,200 (10.5)	1.77 (1.71-1.82)
Schizophrenia (and related non-organic psychosis) or bipolar disorder	752 (1.5)	11,391 (0.9)	1.66 (1.54-1.78)
Dementia	1,078 (2.1)	10,602 (0.9)	1.09 (1.00-1.19) p=0.04
Learning Disability	125 (0.2)	4,311 (0.4)	1.06 (0.92 to 1.22) p=0.40

All differences between the COPD and control group at p<0.001 except where stated

Funding:
This study was funded by the Chief Scientist Office of the Scottish Government Health Directorates (Applied Research Programme Grant ARPG/07/1). Data was provided by the Primary Care Clinical Informatics Unit at the University of Aberdeen. The views in this publication are not necessarily the views of the University of Aberdeen, its agents, or employees

Ethical approval:
Specific ethical approval was not required as anonymous data was used

Competing interests: none

Acknowledgements: none

References

1. Lopez AD, Shibuya K, Rao C, et al. Chronic obstructive pulmonary disease: current burden and future projections. The European respiratory journal. 2006;27(2):397-412.
2. Dirven JA, Tange HJ, Muris JW, et al. Early detection of COPD in general practice: patient or practice managed? A randomised controlled trial of two strategies in different socioeconomic environments. Primary care respiratory journal : journal of the General Practice Airways Group. 2013;22(3):331-7.
3. Mannino DM, Thorn D, Swensen A, et al. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. The European respiratory journal. 2008;32(4):962-9.
4. Fumagalli G, Fabiani F, Forte S, et al. INDACO project: COPD and link between comorbidities, lung function and inhalation therapy. Multidisciplinary respiratory medicine. 2015;10(1):4.
5. Sin DD, Anthonisen NR, Soriano JB, et al. Mortality in COPD: Role of comorbidities. The European respiratory journal. 2006;28(6):1245-57.
6. Schnell K, Weiss CO, Lee T, et al. The prevalence of clinically-relevant comorbid conditions in patients with physician-diagnosed COPD: a cross-sectional study using data from NHANES 1999-2008. BMC pulmonary medicine. 2012;12:26.
7. Franssen FM, Rochester CL. Comorbidities in patients with COPD and pulmonary rehabilitation: do they matter? European respiratory review : an official journal of the European Respiratory Society. 2014;23(131):131-41.
8. Kunik ME, Roundy K, Veazey C, et al. Surprisingly high prevalence of anxiety and depression in chronic breathing disorders. Chest. 2005;127(4):1205-11.
9. Incalzi RA, Corsonello A, Pedone C, et al. Chronic renal failure: a neglected comorbidity of COPD. Chest. 2010;137(4):831-7.
10. O'Kelly S, Smith SM, Lane S, et al. Chronic respiratory disease and multimorbidity: prevalence and impact in a general practice setting. Respiratory medicine. 2011;105(2):236-42.
11. Garcia-Olmos L, Alberquilla A, Ayala V, et al. Comorbidity in patients with chronic obstructive pulmonary disease in family practice: a cross sectional study. BMC family practice. 2013;14:11.
12. Cazzola M, Bettoncelli G, Sessa E, et al. Prevalence of comorbidities in patients with chronic obstructive pulmonary disease. Respiration; international review of thoracic diseases. 2010;80(2):112-9.
13. Maurer J. Anxiety and depression in COPD: Current understanding, unanswered questions, and research needs. Revista portuguesa de pneumologia. 2009;15(4):740-2.
14. Hanania NA, Mullerova H, Locantore NW, et al. Determinants of depression in the ECLIPSE chronic obstructive pulmonary disease cohort. American journal of respiratory and critical care medicine. 2011;183(5):604-11.
15. Barnett K, Mercer SW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet. 2012;380(9836):37-43.
16. Elder R KM, Ramsay W, MacLeod M, Guthrie B, Sutton M, Watt G. Measuring quality in primary medical services using data from SPICE. . 2007.
17. Court H, McLean G, Guthrie B, et al. Visual impairment is associated with physical and mental comorbidities in older adults: a cross-sectional study. BMC medicine. 2014;12:181.
18. Carstairs V, Morris R. Deprivation and health in Scotland. Health bulletin. 1990;48(4):162-75.
19. Green ME, Natajaran N, O'Donnell DE, et al. Chronic obstructive pulmonary disease in primary care: an epidemiologic cohort study from the Canadian Primary Care Sentinel Surveillance Network. CMAJ open. 2015;3(1):E15-22.
20. Nacul L, Soljak M, Samarasundera E, et al. COPD in England: a comparison of expected, model-based prevalence and observed prevalence from general practice data. Journal of public health. 2011;33(1):108-16.

21. Divo M, Cote C, de Torres JP, et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. American journal of respiratory and critical care medicine. 2012;186(2):155-61.
22. Soriano JB, Visick GT, Muellerova H, et al. Patterns of comorbidities in newly diagnosed COPD and asthma in primary care. Chest. 2005;128(4):2099-107.
23. Ajmera M, Sambamoorthi U, Metzger A, et al. Multimorbidity and COPD Medication Receipt Among Medicaid Beneficiaries With Newly Diagnosed COPD. Respiratory care. 2015;60(11):1592-602.
24. Du Q, Jin J, Liu X, et al. Bronchiectasis as a Comorbidity of Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis. PloS one. 2016;11(3):e0150532.
25. Gibson PG, Simpson JL. The overlap syndrome of asthma and COPD: what are its features and how important is it? Thorax. 2009;64(8):728-35.
26. Hurst JR. Upper airway. 3: Sinonasal involvement in chronic obstructive pulmonary disease. Thorax. 2010;65(1):85-90.
27. Sin DD, Man SF. Chronic obstructive pulmonary disease as a risk factor for cardiovascular morbidity and mortality. Proceedings of the American Thoracic Society. 2005;2(1):8-11.
28. Cavailles A, Brinchault-Rabin G, Dixmier A, et al. Comorbidities of COPD. European respiratory review : an official journal of the European Respiratory Society. 2013;22(130):454-75.
29. Pecci R, De La Fuente Aguado J, Sanjurjo Rivo AB, et al. Peripheral arterial disease in patients with chronic obstructive pulmonary disease. International angiology : a journal of the International Union of Angiology. 2012;31(5):444-53.
30. Rutten FH, Moons KG, Cramer MJ, et al. Recognising heart failure in elderly patients with stable chronic obstructive pulmonary disease in primary care: cross sectional diagnostic study. Bmj. 2005;331(7529):1379.
31. Benson VS, Mullerova H, Vestbo J, et al. Associations between gastro-oesophageal reflux, its management and exacerbations of chronic obstructive pulmonary disease. Respiratory medicine. 2015;109(9):1147-54.
32. Kanazawa H, Yoshikawa J. Accelerated decline in lung function and impaired reversibility with salbutamol in asthmatic patients with chronic hepatitis C virus infection: a 6-year follow-up study. The American journal of medicine. 2004;116(11):749-52.
33. Silva DR, Stifft J, Cheinquer H, et al. Prevalence of hepatitis C virus infection in patients with COPD. Epidemiology and infection. 2010;138(2):167-73.
34. Li X, Kong L, Li F, et al. Association between Psoriasis and Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-analysis. PloS one. 2015;10(12):e0145221.
35. Romberger DJ, Grant K. Alcohol consumption and smoking status: the role of smoking cessation. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie. 2004;58(2):77-83.
36. Fabbri LM, Luppi F, Beghe B, et al. Complex chronic comorbidities of COPD. The European respiratory journal. 2008;31(1):204-12.
37. Hillas G, Perlikos F, Tsiligianni I, et al. Managing comorbidities in COPD. International journal of chronic obstructive pulmonary disease. 2015;10:95-109.
38. Ahnfeldt-Mollerup P, Lykkegaard J, Halling A, et al. Resource allocation and the burden of co-morbidities among patients diagnosed with chronic obstructive pulmonary disease: an observational cohort study from Danish general practice. BMC health services research. 2016;16(1):121.

Authors Roles

Ula Chetty- Academic GP Fellow

Gary Mclean- research associate

Deborah Morrison - Honorary clinical lecturer

Karolina Agur -clinical lecturer

Bruce Guthrie -Professor of Primary Care Medicine

Stewart W Mercer -Professor of Primary Care

No conflict of interest for any of abovementioned authors