


Healthcare Service Usage and Costs for Elderly Patients with Obstructive Lung Disease

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Background: The worldwide prevalence of obstructive lung disease (OLD) is increasing, especially among people >65 years old, and nearly three in four adults with OLD have two or more comorbid conditions. This study describes the impact of such comorbidities on the healthcare service usage and related costs in a country with universal health coverage, basing on a large cohort of elderly patients with OLD and employing real-world data.

Methods: We carried out a retrospective cohort study on a large population of elderly (age >64 years) patients with OLD served by a Local Health Unit in northern Italy. Their comorbidities were assessed using the clinical diagnoses assigned by the Adjusted Clinical Group (ACG) system to individual patients by combining different information flows. Correlations between number of comorbidities and total annual healthcare service usage and costs were examined with Spearman's test. Regression models were applied to analyze the associations between the above-mentioned variables, adjusting for age and sex.

Results: All types of healthcare service usage (access to emergency care; number of outpatient visits; number of hospital admissions) and pharmacy costs increased significantly with the number of comorbidities. Average total annual costs increased steadily with the number of comorbidities, ranging from € 1158.84 with no comorbidities up to € 9666.60 with 6 comorbidities or more. Poisson regression analyses showed an independent association between the number of comorbidities and the use of every type of healthcare service.

Conclusion: These results based on real-world data provide evidence that the burden of care for OLD patients related to their comorbidities is independent of and in addition to the burden related to OLD alone and is strongly dependent on the number of comorbidities, suggesting a holistic approach to multimorbid patients with OLD is the most sound public health strategy.

Keywords: comorbidities, obstructive lung disease, healthcare costs, healthcare service usage

Introduction

Obstructive lung disease (OLD) is characterized by an obstruction in the air passages, particularly at exhalation. Asthma and chronic obstructive pulmonary disease (COPD) are by far the most common conditions responsible for OLD. The worldwide prevalence of OLD is on the rise. The WHO estimated that over 251 million adults had COPD alone in 2016, and - like most chronic conditions - it mainly affected people >65 years old.¹ Additionally, asthma affected more than 339 million people in the same year.² The incidence of COPD will likely continue to increase in the coming years due to the high prevalence of smoking and the aging of the populations in many countries. It was estimated that 3.17 million deaths

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globally were caused by the disease in 2015 (5% of all deaths around the world in that year).¹ In Italy, the prevalence of COPD among the elderly is estimated to be around 13.3%, while the prevalence of asthma is around 2.9%.³ Various studies also found that comorbidities are common in patients with COPD, and they significantly contribute to the healthcare burden, costs and mortality associated with the disease.^{3–7} This means that, with the predicted aging of the world's population (the proportion of those aged 60 years and over will nearly double from 2015 to 2050),⁸ there will be a growth in the total burden of COPD, and its associated comorbidities.⁹ A study in the Netherlands investigated comorbidities in the COPD population, finding that almost all patients had one or more comorbidities, and more than half of them had at least four.¹⁰ In particular, the Dutch analysis identified hyperglycemia, atherosclerosis, hypertension, dyslipidemia, and osteoporosis as the five most prevalent comorbidities.¹⁰ The most frequent clusters of comorbidities in patients with COPD were also identified and low-grade systemic inflammation was mostly comparable among comorbidity clusters.

The costs related to COPD worldwide amount to US\$ 2.1 trillion annually, and are expected to rise to \$ 4.8 trillion by 2030.¹¹ COPD is responsible for a considerable and growing economic burden on national healthcare systems: a recent Italian study found a total mean annual cost per patient of €3291 in 2015, 20.8% higher than had been estimated in 2008.¹² Worldwide healthcare costs related to asthma are also on the rise, and, at the individual level, appear to be closely correlated with comorbidities, age and asthma severity.¹³

In the last few years, a number of studies have examined, validated and recommended new multi-dimensional indices for assessing, managing and/or prognosticating OLD and its comorbidities, and some have measured the burden of the disease and its association with multimorbidity. However, most of those studies were carried out in the United States, where the organization and funding mechanisms of health services are quite different from Europe. For instance, an American study on 20,296 COPD patients of various ages found that comorbid diseases compounded the effect of the respiratory impairment on all-cause mortality outcomes over a 5-year follow-up, after adjusting for age, sex, race, smoking habits, education level, and body mass index.¹⁴ The study also found a significant interaction between comorbid disease, respiratory impairment and hospitalization.¹⁴

The aim of our study was to further investigate the impact of comorbidities on healthcare service usage and healthcare costs on a large cohort of elderly subjects affected by OLD, based on real-world data in a country with universal healthcare system.

Materials and Methods

Context

Italy has a public national health system that guarantees access to treatment for all citizens, free of charge or against payment of a fee depending on a patient's income. The system is administered by the regional authorities, and each region is divided into several local health units (LHUs). The data used for this study refers to the LHU "Azienda ULSS 6 – Euganea", in Veneto Region, north-east of Italy, which serves a population of about 932,000 individuals.

Study Design

This is a retrospective cohort follow-up study.

Inclusion Criteria

The inclusion criteria were the following: 1) to be resident in the area served by the LHU "Azienda ULSS 6 Euganea", 2) to be over 65 years old in 2017, 3) to have been diagnosed with COPD or asthma according to data collected and processed by the ACG system (see next paragraphs). We decided to include patients diagnosed with either one of these diagnoses because they were often overlapping or difficult to tell apart using our administrative (non-clinical) database. This is mainly a result of the similarity in the pharmacological classes of drugs used to treat the conditions. Moreover, a differential diagnosis between these two conditions is difficult even at the clinical level,¹⁵ and finally there is a lot of overlapping between the two conditions among older subjects.³ No exclusion criteria have been adopted.

Identification of OLD and Comorbidities

The Adjusted Clinical Group (ACG) system is a population risk stratification method used internationally to characterize multimorbidity on the strength of routinely collected administrative data, which are pooled using record linkage.¹⁶ This tool has been adopted in the Veneto Region since 2012.^{17–19}

Based on healthcare resource usage, the ACG system automatically collapses different ACG categories into 6 Resource Utilization Bands (RUBs), from 0 ("non-user")

to 5 (“user with very high morbidity”). For the purposes of the present study, only people over 65 years old in 2017, with a diagnosis of COPD or asthma, residing in the area served by the ULSS6-Euganea LHU, with and without comorbidities, were considered. The diagnosis of OLD and other chronic diseases were established using two types of data from the ACG system:

- EDC (Expanded Diagnosis Clusters), which consists of clinical diagnoses that the ACG system’s algorithm assigns to single patients by combining different information flows, including hospital discharge records, outpatient visits, emergency department visits, homecare facility records and diagnoses assigned for exemptions from healthcare bills;
- Information available from pharmacy records, Rx-defined morbidity groups (Rx-MGs), and the clinical criteria used to prescribe medication to morbidity groups. The Rx-MGs provide further ways to describe the unique morbidity profile of a given population and form the basis of pharmacy-related predictive models, allowing for an improvement in the sensitivity of the model.

In our dataset, EDCs were based on information collected throughout a 5-year period before data extraction (2013–2017). Rx-MGs, on the other hand, were based on drug prescriptions of year 2017 alone.

The selection of which set of comorbidities to include is bound to be subjective to some degree, and to depend strongly on the data available.²⁰ This study focused on a subset of conditions including: cancer; ischemic heart disease; atrial fibrillation; cerebrovascular disease; Alzheimer’s disease; depression; asthma/bronchitis; diabetes mellitus (DM); chronic obstructive pulmonary disease; osteoporosis; hypothyroidism; and chronic kidney disease. In particular, cases of neoplastic disease, Alzheimer’s disease, atrial fibrillation, and cerebrovascular disease were only discernible from the EDC codes.

Patients were then assigned to one of 7 comorbidity classes based on how many chronic conditions they had in addition to OLD. (from “none” to “6 or more”)

Outcomes: Healthcare Service Use, Healthcare Costs and Mortality

The main outcome measures are the number of healthcare services provided to subjects (access to emergency care;

number of outpatient visits; number of hospital admissions), total healthcare costs, pharmacy costs (i.e. the cost for prescription drugs) and mortality. Costs and health care service use were measured from the perspective of the Veneto Region’s NHS using the ACG system’s data for the year 2017. Each patient was linked to all administrative data regarding their hospital admissions, day hospital visits, drug usage, outpatient visits and diagnostic procedures, and access to the emergency department (ED) in order to compute the direct costs incurred over the year 2017. For each health care service type, only the direct cost incurred by the regional public health service based on the Veneto Region tariffs was considered. The database also specified whether subjects were alive at the end of year 2017: that information was used to extrapolate mortality rates.

Statistical Methods

A descriptive analysis was conducted, estimating the mean, median and standard deviation for continuous variables, and the absolute and relative frequency for categorical variables.

The difference in median values for numerical variables that were not normally distributed was tested with the Kruskal-Wallis or Friedman test. The presence of an association between comorbidity classes and categorical variables was tested with Pearson’s chi-squared. Using Spearman’s test, we also checked the non-parametric correlation between annual healthcare service usage and healthcare costs on the one hand, and comorbidity classes on the other. We tested the difference in crude death rate for each comorbidity class with Pearson’s chi-squared. A Poisson model was used to study the associations between healthcare service usage as a continuous variable and the number of comorbidities. To deal with the high skewness of cost data we performed a GLM model with Gamma distribution and logarithmic link. Patients with zero cost were a restricted number, so we decided to simply add them a symbolic cost of 0.01 € in order to use the logarithmic transformation. The association between mortality and number of comorbidities was tested with a logistic regression model. All regression models were adjusted for covariates as age and sex.

Ethical Issues

The data analysis was performed on anonymized aggregate data with no chance of individuals being identifiable. The study complied with the Declaration of Helsinki and

with resolution No. 9/2016 of the Italian Guarantor for the Protection of Personal Data, which also confirmed the allowability of processing personal data for medical, biomedical and epidemiological research, and that data concerning people's health status can be used in aggregate form in scientific studies.

Permission to use unidentifiable individual data extracted from administrative databases was granted by the LHU (ULSS 6 - Euganea). To ensure confidentiality and anonymity, the Veneto Regional Authority removes all direct identifiers (e.g. NHS code numbers) and replaces them with a code number in all datasets to retain the opportunity to link data from different administrative databases.

Results

In 2017, there were 37,915 elderly patients with a diagnosis of OLD in the Veneto Region served by the LHU "ULSS6 – Euganea". Table 1 shows the characteristics of these patients. The mean age of the sample population was 77.3 years old and 54.5% of them were female. More than 76% had hypertension, and almost 38% had lipid metabolism disorders. The average total annual per patient healthcare cost was €4261.2. Table 2 shows the distribution of their healthcare service usage, costs and death rate by comorbidity class. All measured outcomes differed significantly among different comorbidity classes.

Analyzing the distribution of OLD patients by number of comorbidities, it emerged that the proportion of females was higher than 50% for all comorbidity classes, except for the no comorbidity class, where their proportion was just 42.9%.

The analyses also revealed that all types of healthcare service usage (e.g. access to emergency care; number of outpatient visits; number of hospital admissions) correlated significantly with comorbidity class. A significant correlation was also found for total annual costs and pharmacy costs with comorbidity class which increased steadily with the number of comorbidities, from € 1158.84 in the no comorbidities group up to € 9666.60 in the group with 6 comorbidities or more.

Regression analyses (Table 3) showed that female patients were associated with a lower healthcare resource usage, lower healthcare costs, and a lower crude death rate than males. The main differences concerned the costs (with a difference of € 748.6 in total costs and € 23.6 in pharmacy costs), and the number of hospital admissions, outpatient visits, and ED visits. (with differences of 27%, 14% and 13%, respectively)

Table 1 Characteristics of the Study Sample with Obstructive Lung Disease

Patients with BPCO			37,915
Sex	% (n)	Female	54.55% (20,684)
	% (n)	Male	45.45% (17,231)
Age	mean (±SD)		77.29 (±8,1)
RUB	% (n)	1	77.33% (8,05)
	% (n)	2	11.58% (4389)
	% (n)	3	17.61% (6675)
	% (n)	4	47.58% (18,040)
	% (n)	5	14.43% (5470)
Cancer	% (n)		14.88% (5641)
Arhythmia	% (n)		19.35% (7338)
Cerebrovascular Disease	% (n)		9.69% (3673)
Dementia and delirium	% (n)		6.32% (2398)
Diabetes mellitus	% (n)		19.41% (7358)
Lipid Metabolism disorders	% (n)		37.82% (14,341)
Hypothyroidism	% (n)		7.35% (2787)
Chronic kidney failure	% (n)		4.05% (1537)
Hypertension	% (n)		76.45% (28,986)
Congestive heart failure	% (n)		30.47% (11,553)
Ischemic heart disease	% (n)		13.88% (5262)
Depression	% (n)		18.38% (6967)
Parkinson's Disease	% (n)		3.01% (1143)
Rheumatoid arthritis	% (n)		1.79% (680)
Osteoporosis	% (n)		36.86% (13,974)
Total Costs	mean (±SD)		4261.20 (8155.30)
Pharmacy Costs	mean (±SD)		1099.14 (3555.51)
Emergency department visits, No.	mean (±SD)		0.51 (1.08)
Outpatient visits, No.	mean (±SD)		9.57 (10.61)
Hospital admissions, No.	mean (±SD)		0.39 (0.86)

Regression analyses also revealed a significant increase in healthcare service usage and costs with higher comorbidity classes, compared with OLD subjects with no comorbidities. They showed rising total costs and pharmacy costs for each comorbidity class compared to the immediately lower one. The range set by confidence intervals showed the cost increments were significant for every single increase in number of comorbidities. Some overlap was present for pharmacy costs, and yet the trend was very clear. In fact, comparing subjects with no comorbidities, even those with one comorbidity had significantly higher pharmacy costs. For healthcare service usage, the Poisson regression indicated that the number of ED visits, hospital admissions and outpatient visits increased constantly and significantly with comorbidity class. The logistic regression for mortality showed that patients with OLD and 6 or

Table 2 Distribution of Healthcare Resource Usage, Costs and Death Rate by Comorbidity Class

No. of Chronic Disorders in Addition to Obstructive Lung Disease	0							1							2							3							4							5							6+							Total	Association with Comorbidity Class p-value																																	
	Female % (n)	Male % (n)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)	Mean	Median (IQR)																																																				
No. of patients in class	2681							6315							7714							7485							5804							3949							3967							37,915																																		
Sex	42.9% (1150)							51.3% (3238)							58.5% (4511)							56.5% (4231)							56.7% (3294)							55.2% (2178)							52.5% (2082)							54.5% (20,684)							<0.05 *																											
	57.1% (1531)							48.7% (3077)							41.5% (3203)							43.5% (3254)							43.2% (2510)							44.8% (1771)							47.5% (1885)							45.4% (17,231)																																		
Age	72.45							74.40							76.12							77.51							79.09							80.43							81.63							77.33							<0.01 ***																											
	71							73							75							77							79							81							82							77																																		
	9							11							11							12							12							11							10							12																																		
Total costs	1158.84							1982.26							2888.20							3796.08							5242.76							6702.69							9666.60							4261.20							<0.01***																											
	464.83							737.93							1092.19							1535.78							2195.831							3420.23							5655.97							1526.07																																		
	865							1144							1671							2569							4129							6162							9487							3322																																		
Pharmacy costs	330.23							531.97							826.39							1101.97							1388.68							1707.61							2017.39							1099.14							<0.01 ***																											
	136.06							293.13							446.34							636.11							845.8							1070							1272.41							599.53																																		
	363							459							590							750							916							1072							1283							875																																		
Emergency department visits, No.	0.27							0.33							0.40							0.49							0.59							0.71							0.87							0.51							<0.01 ***																											
	0							0							0							0							0							0							0							0																																		
	0							0							1							1							1							1							1							1							1																											
Outpatient visits, No.	4.45							6.20							7.97							9.62							11.39							12.78							15.54							9.57							<0.01 ***																											
	3							4							6							7							9							10							11							7																																		
	5							6							8							9							11							12							14							10																																		
Hospital admissions, No.	0.09							0.14							0.22							0.30							0.47							0.68							1.09							0.39							<0.01 **																											
	0							0							0							0							0							0							0							0							0																											
	0							0							0							0							1							1							1							2							0							0																				
Crude death rate	1.36%							1.89%							3.39%							4.91%							7.88%							12.14%							18.61%							6.24%							<0.01 *																											

Notes: *Chi-squared test. **Kruskal-Wallis test. ***Friedman test.

Table 3 Regression Analyses Between Dependent Variables (Healthcare Cost and Service Usage, and Mortality) and Comorbidity Class, Adjusted for Sex and Age

Total Costs, GLM Model		Coefficient	95% CI	p-value
Sex (reference: Male)	Female	-748,6	-913,7;-583,5	<0.001
Age		10,5	-0,26;0,21	0,0557
No. of chronic disorders in addition to COPD (reference: 0)	1	905,9	525,5;1286,3	<0.001
	2	1849	1477,8;2220,2	<0.001
	3	2727	2353,6;3100,4	<0.001
	4	4163	3775,3;4550,7	<0.001
	5	5596	5181,9;6010,1	<0.001
	6+	8528	8113,1;8942,9	<0.001
Pharmacy costs, GLM model		Coefficient	95% CI	p-value
Sex (reference: Male)	Female	-23,6	-28,59;-18,61	<0.001
Age		-235,2	-311,5;-158,9	<0.001
No. of chronic disorders in addition to COPD (reference: 0)	1	298,3	124,0;472,6	<0.001
	2	648	477,8;818,2	<0.001
	3	952	780,7;1123,3	<0.001
	4	1278	1099,8;1456,2	<0.001
	5	1633	1442,4;1823,6	<0.001
	6+	1971	1779,7;2162,3	<0.001
No. of emergency department visits, Poisson regression		Exp (Coefficient) - RR	95% CI	p-value
Sex (reference: Male)	Female	0,87	0,84;0,89	<0.001
Age		1,01	1,01;1,02	<0.001
No. of chronic disorders in addition to COPD (reference: 0)	1	1,24	1,15;1,32	<0.001
	2	1,51	1,42;1,59	<0.001
	3	1,78	1,70;1,86	<0.001
	4	2,14	2,06;2,22	<0.001
	5	2,55	2,47;2,64	<0.001
	6+	3,06	2,98;3,15	<0.001
No. of outpatient visits, Poisson regression		Exp (Coefficient) - RR	95% CI	p-value
Sex (reference: Male)	Female	0,86	0,98;0,99	<0.001
Age		0,98	0,85;0,87	<0.001
No. of chronic disorders in addition to COPD (reference: 0)	1	1,47	1,45;1,49	<0.001
	2	1,98	1,96;2,00	<0.001
	3	2,46	2,44;2,48	<0.001
	4	3,01	2,99;3,03	<0.001
	5	3,47	3,45;3,49	<0.001
	6+	4,32	4,30;4,34	<0.001
No. of hospital admissions, Poisson Regression		Exp (Coefficient) - RR	95% CI	p-value
Sex (reference: Male)	Female	0,73	0,70; 0,77	<0.001
Age		1,01	1,01; 1,02	<0.001

(Continued)

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Table 3 (Continued).

Total Costs, GLM Model		Coefficient	95% CI	p-value
No. of chronic disorders in addition to COPD (reference: 0)	1	1,66	1,52; 1,81	<0.001
	2	2,58	2,44; 2,72	<0.001
	3	3,52	3,38; 3,65	<0.001
	4	5,48	5,35; 5,62	<0.001
	5	7,77	7,63; 7,90	<0.001
	6+	12,24	12,10; 12,37	<0.001
Mortality, Logistic regression		Exp (Coefficient) - OR	95% CI	p-value
Sex (reference: Male)	Female	0,64	0,55; 0,74	<0.001
Age		1,13	1,12; 1,13	<0.001
No. of chronic disorders in addition to COPD (reference: 0)	1	1,13	0,75; 1,51	0,52
	2	1,76	1,40; 2,12	0,00196
	3	2,25	1,90; 2,60	<0.001
	4	3,28	2,93; 3,63	<0.001
	5	4,82	4,47; 5,17	<0.001
	6+	7,46	7,11; 7,80	<0.001

more comorbidities were 7,46 times more likely of dying compared to patients with no comorbidities, after adjusting for age and sex.

Discussion

The present study showed a clear correlation between the number of comorbidities and the healthcare service usage in a cohort of OLD patients. Moreover, the number of comorbidities also affected both the total costs and pharmacy costs for COPD patients, which raised significantly with every rise in comorbidities count.

Gender Differences

The study found some evidence of gender disparities in the sample OLD population analyzed, the proportion of females being higher among those with at least one comorbidity. This seems to confirm the previously reported positive association between multimorbidity and female gender.²¹ However, healthcare resource usage and expenditure, and the crude death rate were lower for women than for men. The differences were seen on all major outcomes of healthcare consumption: total healthcare costs, pharmacy costs, and number of hospital admissions, outpatient visits and ED visits. Further research is needed to shed light on this discrepancy between women's higher number of comorbidities and lower healthcare resource usage. One previous study found that spirometry was prescribed less for women than for men.²² The importance of

sex as a risk factor for hospital readmissions due to respiratory disease was investigated in another previous study showing that – for COPD, pneumonia, pulmonary edema, respiratory failure, bronchitis and asthma – male patients had significantly higher odds of 30-day readmission than female patients.²³ Previous research on gender bias focused mainly on cardiovascular disease, where differences in the treatment of male and female patients have been clearly established.^{24–26} The literature on the under-usage of diagnostic procedures for women with cardiovascular disease has attributed this to the fact that this type of disease, like COPD, has been traditionally associated with men. This particularly applies to the case of the elderly, where gender bias in the use of diagnostic and therapeutic procedures is most pronounced.^{22,27}

Gender differences in OLD also emerged when we analyzed the distribution of the most common comorbidities associated with this condition. In fact, men accounted for more cases of OLD associated with DM, hyperlipidemia, hypertension and heart failure, while more women had OLD associated with depression and osteoporosis. This is consistent with a Spanish study conducted in 2010 adopting the ECLIPSE method, which described females with COPD as being more susceptible to osteoporosis and depression than male COPD patients, but less liable to cardiovascular disease and DM.²⁸ In 2015, a Swedish study on a COPD population found that men had more comorbidities than women, except for osteoporosis and depression.²⁹

OLD Comorbidity, Total Healthcare Costs and Pharmacy Costs

The total costs of healthcare for our OLD patients rose incrementally with the number of concomitant medical conditions, as seen in other studies and different healthcare settings. A 2009 descriptive analysis of an American COPD population reported higher total Medicaid costs associated with more numerous comorbidities.³⁰ Previous research on COPD patients also found that comorbidities made an important contribution to total costs,³¹ often amounting to more than those of the respiratory condition itself.^{32,33} Confirming this, a previous study identified the comorbidities as one of the main determinants of elevated healthcare utilization in patients with COPD.³⁴ Another study did not just confirm the increase in costs as comorbidities increase, but also identified specific comorbidities among COPD patients that add significant burden with higher health care resource utilization and costs, compared to patients without these comorbidities.³⁵ In particular, congestive heart failure, coronary artery disease, and cerebrovascular disease had the strongest associations with all-cause hospitalizations, whereas chronic heart failure, anxiety, and sleep apnea had the strongest associations with COPD-related hospitalizations.³⁵

As expected, pharmacy costs also rose incrementally with comorbidity class. This result confirms a previous report on multimorbidity in asthma, allergic conditions and COPD, which highlighted multimorbid conditions and polypharmacy – along with disease severity – as major cost-multiplying factors.³⁶

OLD Comorbidity and Mortality

The distribution of crude death rates showed consistent increases going from one comorbidity class to the higher, in agreement with what was found in the literature.^{14,37} Logistic regression for mortality, adjusting for age and sex, showed the increases in death rates were statistically significant starting from two comorbidities on, whereas one single comorbidity did not significantly increase mortality. These findings are similar with the ECLIPSE study, even if they revealed that also a single comorbidity had a significant impact on mortality rate.³⁷

Strengths and Limitations

Being population-based, and using independently collected data, this study could minimize any selection bias. It was also based on real-world data, which can offer a reliable

picture of OLD patients' actual healthcare costs and healthcare service usage. On the other hand, grouping together patients with different types of OLD, such as asthma and COPD, may have resulted in missing distinct patterns of associated comorbidities and use of healthcare service. That is because of the peculiar nature of different OLD in terms of etiology and pathogenesis. Moreover, though large, our sample was limited to the population of a specific area and might not be representative of other geographical regions. Our use of administrative data may also mean that some conditions were under-represented. For instance, administrative data do not provide enough information about other highly prevalent chronic conditions, such as visual or hearing impairments, or chronic pain, thus not allowing us to include them in our study. Nonetheless, we consider the set of comorbidities included to be a sufficiently good representation of subjects' health status, and the comparisons with the relevant literature seem to back this up.

Conclusions

The present study based on real-world data indicates that all types of healthcare service usage (ED, outpatient visits, hospital admissions) and costs (total healthcare costs and pharmacy costs) correlated significantly with the number of comorbidities in OLD patients. The findings also highlighted some gender-related differences in the type and number of such patients' comorbidities, and the different impact of male and female patients on healthcare costs and healthcare service usage.

These findings point to the need for healthcare systems to be able to focus on today's aging and multi-morbid population favoring a holistic approach, which takes social and psychological dimensions into account as well. The global burden of OLD and its associated comorbidities cannot be addressed with the therapeutic option alone, but prevention must be implemented, not only of COPD and asthma but of its major comorbidities as well. This poses challenges that can only find solutions in an overarching public health strategy that aims to prevent disease, promote healthy lifestyles, slow down disease progression and prevent acute events. The development of a stronger primary healthcare seems to be a necessary step to this end.

Disclosure

The authors report no conflicts of interest in this work.

References

1. WHO COPD fact sheet 2017 Available from: [https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)). Accessed June 24, 2020.
2. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390(10100):1211–1259. doi:10.1016/S0140-6736(17)32154-2.
3. De Marco R, Pesce G, Marcon A, et al. The coexistence of asthma and chronic obstructive pulmonary disease (COPD): prevalence and risk factors in young, middle-aged and elderly people from the general population. *PLoS One*. 2013;8(5):e62985. doi:10.1371/journal.pone.0062985
4. Negewo NA, Gibson PG, McDonald VM. COPD and its comorbidities: impact, measurement and mechanisms. *Respirology*. 2015;20(8):1160–1171. doi:10.1111/resp.12642
5. Negewo NA, McDonald VM, Gibson PG. Comorbidity in chronic obstructive pulmonary disease. *Respir Investig*. 2015;53(6):249–258. doi:10.1016/j.resinv.2015.02.004
6. Cavallès A, Brinchault-Rabin G, Dixmier A, et al. Comorbidities of COPD. *Eur Respir Rev*. 2013;22(130):454–475. doi:10.1183/09059180.00008612
7. Smith MC, Wrobel JP. Epidemiology and clinical impact of major comorbidities in patients with COPD. *Int J Chron Obstruct Pulmon Dis*. 2014;9:871–888. doi:10.2147/COPD.S49621
8. Beard J, Ofcer A, Cassels A. *World Report on Ageing and Health*. Geneva: World Health Organization; 2015. (https://apps.who.int/iris/bitstream/handle/10665/186463/9789240694811_eng.pdf. accessed 12 January 2019).
9. World Health Organization. 2019. *Integrated Care for Older People (ICOPE) Implementation Framework: Guidance for Systems and Services*. World Health Organization. Available from: <https://apps.who.int/iris/handle/10665/325669>. License:CC BY-NC-SA3.0IGO. Accessed June 24, 2020.
10. Vanfleteren LE, Spruit MA, Groenen M, et al. Clusters of comorbidities based on validated objective measurements and systemic inflammation in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2013;187(7):728–735. doi:10.1164/rccm.201209-1665OC
11. Bloom DE, Cafiero ET, Jané-Llopis E, et al. *The Global Economic Burden of Noncommunicable Diseases*. Geneva: World Economic Forum; 2011. Available from: https://www.world-heart-federation.org/wp-content/uploads/2017/05/WEF_Harvard_HE_GlobalEconomicBurdenNonCommunicableDiseases_2011.pdf. Accessed July 15, 2020.
12. Dal Negro RW. COPD: the annual cost-of-illness during the last two decades in Italy, and its mortality predictivity power. *Healthcare (Basel)*. 2019;7:35. doi:10.3390/healthcare7010035
13. Nunes C, Pereira AM, Morais-Almeida M. Asthma costs and social impact. *Asthma Res Pract*. 2017;3(1):1. doi:10.1186/s40733-016-0029-3
14. Mannino DM, Thorn D, Swensen A, Holguin F. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. *Eur Respir J*. 2008;32(4):962–969. doi:10.1183/09031936.00012408
15. Sin BA, Akkoca O, Saryal S, Oner F, Misirligil Z. Differences between asthma and COPD in the elderly. *J Investig Allergol Clin Immunol*. 2006;16(1):44–50.
16. The Johns Hopkins University. *ACG System Version 11.0 Technical Reference Guide*. 11.0th ed. The Johns Hopkins University; 2014.
17. DGR N. 1103 del 01/07/14. Il sistema ACG (Adjusted Clinical Group) per la valutazione e gestione del case-mix territoriale nella Regione del Veneto. Approvazione dei risultati del secondo anno (DGR 498/2013) e avvio del terzo e quarto anno di attività. 2014 Lug 01, (9^a legislatura)
18. DGR N. 439 del 20/03/12. Il sistema ACG (Adjusted Clinical Group) per la valutazione e gestione del case-mix territoriale nella Regione Veneto: progetto pilota per l'adozione di strumenti innovativi di misurazione del rischio, analisi, programmazione. 2012 Mar 20.
19. DGR N. 498 del 16/04/13. Il sistema ACG (Adjusted Clinical Group) per la valutazione e gestione del case-mix territoriale nella Regione del Veneto. Approvazione dei risultati del primo anno (DGR 439/2012) e avvio del secondo anno e terzo anno di attività. 2013 Apr 16, (9^a legislatura).
20. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet*. 2012;380(9836):37–43. doi:10.1016/S0140-6736(12)60240-2
21. Violan C, Foguet-Boreu Q, Flores-Mateo G, et al. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. *PLoS One*. 2014;9(7):e102149. doi:10.1371/journal.pone.0102149
22. Watson L, Vestbo J, Postma DS, et al. Gender differences in the management and experience of chronic obstructive pulmonary disease. *Respir Med*. 2004;98(12):1207–1213. doi:10.1016/j.rmed.2004.05.004
23. Buja A, De Polo A, De Battisti E, et al. The importance of sex as a risk factor for hospital readmissions due to pulmonary diseases. *BMC Public Health*. 2020;20(1):53. doi:10.1186/s12889-019-8138-6
24. Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heart disease. *N Engl J Med*. 1991;325(4):221–225. doi:10.1056/NEJM19910725250401
25. Beery TA. Gender bias in the diagnosis and treatment of coronary artery disease. *Heart Lung*. 1995;24(6):427–435. doi:10.1016/s0147-9563(95)80020-4
26. Gan SC, Beaver SK, Houck PM, MacLehose RF, Lawson HW, Chan L. Treatment of acute myocardial infarction and 30-day mortality among women and men. *N Engl J Med*. 2000;343(1):8–15. doi:10.1056/NEJM200007063430102
27. Alter DA, Naylor CD, Austin PC, Tu JV. Biology or bias: practice patterns and long-term outcomes for men and women with acute myocardial infarction. *J Am Coll Cardiol*. 2002;39(12):1909–1916. doi:10.1016/s0735-1097(02)01892-2
28. Agusti A, Calverley PM, Celli B, et al. Characterisation of COPD heterogeneity in the ECLIPSE cohort. *Respir Res*. 2010;11(1):122. doi:10.1186/1465-9921-11-122
29. Hensch I, Strang S, Löfdahl CG, Ekberg-Jansson A. Management of COPD, equal treatment across age, gender, and social situation? A register study. *Int J Chron Obstruct Pulmon Dis*. 2016;11:2681–2690. doi:10.2147/COPD.S115238
30. Westney G, Foreman MG, Xu J, Henriques King M, Flanagan E, Rust G. Impact of comorbidities among Medicaid enrollees with chronic obstructive pulmonary disease, United States, 2009. *Prev Chronic Dis*. 2017;14:E31. doi:10.5888/pcd14.160333
31. Lisspers K, Larsson K, Johansson G, et al. Economic burden of COPD in a Swedish cohort: the ARCTIC study. *Int J Chron Obstruct Pulmon Dis*. 2018;13:275–285. doi:10.2147/COPD.S149633
32. Jansson SA, Backman H, Rönmark E, Lundbäck B, Lindberg A. Hospitalization due to co-morbid conditions is the main cost driver among subjects with COPD – a report from the population-based OLIN COPD Study. *COPD*. 2015;12(4):381–389. doi:10.3109/15412555.2014.974089
33. Lin PJ, Shaya FT, Scharf SM. Economic implications of comorbid conditions among Medicaid beneficiaries with COPD. *Respir Med*. 2010;104(5):697–704. doi:10.1016/j.rmed.2009.11.009
34. Simon-Tuval T, Scharf SM, Maimon N, Bernhard-Scharf BJ, Reuveni H, Tarasiuk A. Determinants of elevated healthcare utilization in patients with COPD. *Respir Res*. 2011;12(1):7. doi:10.1186/1465-9921-12-7

35. Schwab P, Dhamane AD, Hopson SD, et al. Impact of comorbid conditions in COPD patients on health care resource utilization and costs in a predominantly Medicare population. *Int J Chron Obstruct Pulmon Dis*. 2017;12:735–744. doi:10.2147/COPD.S112256
36. Jantunen J, Haahtela T, Salimäki J, et al. Multimorbidity in asthma, allergic conditions and COPD increase disease severity, drug use and costs: the Finnish Pharmacy Survey. *Int Arch Allergy Immunol*. 2019;179(4):273–280. doi:10.1159/000498861
37. Miller J, Edwards LD, Agustí A, et al. Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) investigators. Comorbidity, systemic inflammation and outcomes in the ECLIPSE cohort. *Respir Med*. 2013;107(9):1376–1384. doi:10.1016/j.rmed.2013.05.001

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