



Early View

Research letter

Healthcare costs and resources utilization in bronchiectasis *versus* asthma *versus* COPD

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TITLE

Healthcare costs and resources utilization in bronchiectasis *versus* asthma *versus* COPD

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Take-home message: Direct healthcare costs for patients with asthma are less than half (-52%) and for patients with COPD are 41% higher if compared to those of patients with bronchiectasis. The leading expense items in bronchiectasis are hospitalizations and antibiotics.

Bronchiectasis is a chronic respiratory disease characterized by persistent airway dilation, mucus hypersecretion and recurrent exacerbations.[1] Although still underdiagnosed, bronchiectasis has received increasing attention in recent years with studies showing high incidence and prevalence, especially in the elderly, and high healthcare costs, particularly in those with frequent exacerbations and *P. aeruginosa* colonization.[2-4] In light of that, the assessment of resource requirements for bronchiectasis management among the different European healthcare systems is important, especially if compared to other chronic airway diseases, such as chronic obstructive pulmonary disease (COPD) and asthma. The aim of the present study is to evaluate the healthcare utilization and direct costs in patients with only bronchiectasis compared to matched cohorts of those with sole asthma or COPD.

The healthcare utilization databases of Lombardy,[5] an Italian region with 10 million inhabitants, were queried. 103,912 adults with a diagnosis of bronchiectasis, COPD or asthma made between 2016 and 2018 were identified. Patients were excluded if they had i) more than one chronic airway disease (e.g., bronchiectasis and COPD, or COPD and asthma, or bronchiectasis and asthma), ii) a concomitant pulmonary malignancy, or iii) insufficient data available in the year before or after the original diagnosis. This resulted in 940 patients with a sole diagnosis of bronchiectasis, 16,304 with a sole diagnosis of COPD, and 84,205 with a sole diagnosis of asthma. Information about hospital and emergency-room (ER) admissions, drug prescriptions, exemptions, and outpatient services were collected. Healthcare costs were assessed from the amount that the region reimbursed to health providers for healthcare services during the year following the index diagnosis and expressed in mean euros yearly spent *per patient*. Specific costs included: (i) hospitalizations and ER admissions related to and not-related to a respiratory diagnosis; (ii) all-cause outpatient services; (iii) all medication costs.

Among the 940 patients with bronchiectasis as sole chronic airway disease included in the original cohort, 891 (64% women, mean age 69 years) were matched 1:1:1 to patients with COPD and asthma for gender, age groups (± 3 years), year of diagnosis, categories of multisource comorbidity score (MCS,[6] an index of patients' clinical status, which can be derived from the hospital admissions and the drugs prescribed in the 1-year period before the index date), nationality, and prior cardiovascular (CV) events. In the bronchiectasis group, 48.8%, 43.1% and 8.1% of patients had, respectively, a good, intermediate and compromised clinical profile according to MCS. Almost the entire cohort was Italian (97.9%) and only 7.9% patients had prior CV events, while the most prescribed medications (other than respiratory) were anti-hypertensives (53%) and antithrombotics (33.3%).

Mean costs for each group are reported in Table 1. On average, the annual expenditure for patients with bronchiectasis (€ 3,593) was 1.9 times as high as that of asthma patients (€ 1,865), while it was 29% lower than that of COPD patients (€ 5,084). This cost trend remains over the sub-categories of healthcare except for outpatient services: costs for outpatient visits and examinations were higher for patients with bronchiectasis when compared to those with asthma and COPD, both for pulmonary examinations and other services. Regarding pharmaceutical costs and consumption, the mean number of prescriptions *per* patient reflected the costs reported in Table 1. Patients with bronchiectasis received a lower number of prescriptions *per* year of inhalation therapy if compared to both patients with asthma and COPD (mean (SD) number of prescriptions 1.9 (4.2) *vs* 3.7 (7.5) *vs* 4.9 (7.1), respectively, p-values <.0001). This difference was particularly evident for inhaled corticosteroids (with or without bronchodilators) (mean (SD) number of prescriptions 0.9 (2.0) *vs* 2.4 (3.5) *vs* 2.4 (3.9), respectively, p-values <.0001), while the number of prescriptions of inhaled bronchodilators (beta-2 agonists and/or antimuscarinic agents) was similar in patients with asthma and bronchiectasis and higher in patients with COPD (mean (SD) number of prescriptions 1.0 (2.7) *vs* 1.0 (4.5) *vs* 2.3 (4.0), respectively; p-value=0.813 for patients with asthma *vs* bronchiectasis; p-value <.0001 for patients with COPD *vs* bronchiectasis). Moreover, antibiotic therapies were more frequently prescribed in patients with bronchiectasis compared to asthma and COPD (2.9 (7.0) *vs* 1.0 (2.1) *vs* 1.9 (2.5), respectively; p-values <.0001). In particular, both macrolides and fluoroquinolones were prescribed more frequently in patients with bronchiectasis: mean (SD) number of macrolides prescriptions 0.8 (2.8) *vs* 0.2 (0.6) *vs* 0.3 (0.7), respectively, p-values <.0001; mean (SD) number of fluoroquinolones prescriptions 0.8 (1.4) *vs* 0.3 (0.9) *vs* 0.7 (1.4), respectively, p-value <.0001 for patients with asthma *vs* bronchiectasis, while p-value=0.017 for patients with COPD *vs* bronchiectasis.

Finally, a Poisson regression model adjusted for baseline characteristics (multiple co-treatments and co-medications measured at the baseline) was implemented to estimate whether patients with asthma and COPD had significantly higher or lower healthcare costs compared to patients with bronchiectasis. Costs for patients with asthma were less than half compared to those of patients with bronchiectasis (-52%, 95% CI: from -53% to -51%), while those with COPD showed higher costs (+41%, 95% CI: from +40% to +42%).

Similarly to our results, a recent systematic review on the economic burden of bronchiectasis identified hospitalizations as the major driver of healthcare expenditures.[7] To our knowledge, only three studies, conducted in Germany and Spain between 2004 and 2013, reported the burden of illness and healthcare costs in population-based cohorts of patients with bronchiectasis in

Europe.[8-10] *Diel and colleagues* compared 231 new German bronchiectasis patients with 685 controls matched by age, sex and Charlson Comorbidity Index.[8] They found that total direct expenditures were nearly one-third higher in bronchiectasis patients than controls and hospitalizations contributed to 35% of the total costs, which fits with our cohort where hospitalizations accounted for 44% of the total costs. The reported annual expenditure for patients with bronchiectasis (€ 6,211) was slightly higher compared to our cohort. The two retrospective cohort studies conducted in Spain reported direct annual costs similar to those of our cohort. *Sanchez-Munoz et al.*, using data from the Spanish Health System, evaluated 70,676 patients hospitalized with bronchiectasis, as primary diagnosis, between 2004 and 2013.[9] A mean annual direct cost for patient of € 3,961 in 2004 was reported, decreasing to € 3,515 in 2013. *De la Rosa et al.* also evaluated the annual direct medical costs of 231 patients with bronchiectasis recruited from 6 Spanish hospitals in 2013.[10] The mean cost was € 4,672 per patient, which increased significantly with severity, the largest items of expenditure being hospitalizations and inhaled antibiotics. Our study is the first to directly compare costs of patients with bronchiectasis with those of matched cohorts of patients with asthma and COPD, showing higher costs in the COPD cohort except for outpatient services. A recent Korean nationwide study based on National Health Insurance data reported higher direct medical costs in patients with COPD and bronchiectasis compared to patients with COPD without bronchiectasis,[11] further suggesting the impact of bronchiectasis in generating costs.

This study has multiple strengths: firstly, it was based on a very large and unselected population, since the Italian healthcare system covers all citizens; secondly, healthcare utilization databases provide highly accurate data because they are collected to manage reimbursements of healthcare at regional level and incorrect reports may have legal consequences. Our investigation has also some limitations: firstly, we were not able to account for private examinations and visits, generally limited in Italy because the public healthcare service covers all the Italian population; secondly, clinical data (e.g., pulmonary function tests) and habits (e.g., smoking) were lacking in administrative databases, thus some unmeasurable confounders might be heterogeneous among groups; thirdly, the lack of adjustment for inflation may have led to a possible overestimation of the costs associated with bronchiectasis; finally, costs tracked include all those in charge of Regional Health Authority, while data on the costs of medical co-payments borne by patients and on indirect costs, such as work productivity impairment, were not available.

In conclusion, our study shows that annual direct healthcare costs in the year after diagnosis for patients with asthma were less than half (-52%) and for patients with COPD were 41% higher if compared to those of patients with bronchiectasis. The leading expense items regarding healthcare

utilization and drug dispensation for patients with bronchiectasis were hospitalizations and antibiotics, suggesting that the optimization of disease management may significantly improve the economic burden of bronchiectasis.

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Table 1. Mean (and corresponding standard deviation) healthcare costs in Euros per patient during the year following the diagnosis of bronchiectasis, asthma and COPD, respectively.

	Bronchiectasis	Asthma	COPD
Hospitalizations	1,572 (4,765)	648 (2,413)	2,700 (6,129)
Respiratory	635 (3,017)	222 (1,294)	1,468 (4,415)
Others	937 (3,427)	426 (1,845)	1,232 (4,127)
Emergency Room accesses	69 (139)	37 (117)	96 (188)
Respiratory	12 (51)	4 (27)	24 (83)
Others	56 (126)	33 (105)	72 (161)
Outpatient services	886 (1,177)	373 (654)	790 (2,022)
Pulmonology	65 (94)	28 (52)	55 (96)
Other fields	821 (1,162)	345 (638)	736 (2,012)
Drug dispensations	1,067 (3,307)	806 (2898)	1,496 (4,024)
Inhalation therapy	117 (252)	244 (357)	305 (442)
Inhaled steroids (+/- bronchodilators) ^a	61 (163)	192 (288)	170 (287)
Bronchodilators only ^β	55 (148)	41 (135)	133 (234)
Systemic steroids ^γ	0.23 (1.64)	0.33 (2.97)	0.50 (6.65)
Expectorants and mucolytics ^δ	16 (315)	0.01 (0.15)	2 (43)
Antibiotics ^ε	67 (554)	13 (27)	29 (56)
Fluoroquinolones ^ζ	10 (19)	4 (10)	9 (21)
Macrolides ^η	9 (34)	2 (8)	3 (9)
Others	865 (3,176)	548 (2,833)	1,160 (3,994)
Total	3,593 (6,336)	1,865 (4,345)	5,084 (8,276)

COPD: chronic obstructive pulmonary disease.

^α Inhaled steroids (+/- bronchodilators) ATC codes: R03AK01, R03AK04, R03AK06, R03AK07, R03AK08, R03AK09, R03AK10, R03AK11, R03AK12, R03AK13, R03AL09, R03BA01, R03BA02, R03BA03, R03BA04, R03BA05, R03BA06, R03BA07, R03BA08, R03BA09.

^β Bronchodilators only (beta-2 agonists and/or antimuscarinic agents) ATC codes: R03AC02, R03AC03, R03AC13, R03AC18, R03AC19, R03AL02, R03AL03, R03AL05, R03AL06, R03BB01, R03BB02, R03BB03, R03BB04, R03BB05, R03BB06, R03BB07, R03BB54.

γ Systemic steroids ATC codes: QH02AB-, H02BX01 and QH02BX90.

δ Expectorants and mucolytics ATC codes: R05CA and R05CB.

ε Antibiotics ATC codes: J01-.

ζ Fluoroquinolones ATC code: J01MA.

η Macrolides ATC code: J01FA.