Healthcare costs and resource utilisation in bronchiectasis, asthma and COPD

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To the Editor:

Bronchiectasis is a chronic respiratory disease characterised 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 *Pseudomonas aeruginosa* colonisation [2–4]. In light of these factors, assessment of the resource requirements for bronchiectasis management among the different European healthcare systems is important, especially if compared to other chronic airway diseases, such as COPD and asthma. The aim of the present study is to evaluate the healthcare utilisation and direct costs in patients with only bronchiectasis compared to matched cohorts of those with sole asthma or COPD.

The healthcare utilisation 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 1) more than one chronic airway disease (*e.g.* bronchiectasis and COPD, or COPD and asthma, or bronchiectasis and asthma), 2) a concomitant pulmonary malignancy, or 3) 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 spent yearly per patient. Specific costs included 1) hospitalisations and ER admissions related to and not related to a respiratory diagnosis, 2) all-cause outpatient services, and 3) 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 the 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 antihypertensives (53%) and antithrombotics (33.3%).

Mean costs for each group are reported in table 1. On average, the annual expenditure for patients with bronchiectasis (EUR 3593) was 1.9 times higher than that of asthma patients (EUR 1865), while it was 29% lower than that of COPD patients (EUR 5084). This cost trend remains over the subcategories 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

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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 hospitalisations and antibiotics. https://bit.ly/3Iq8AUP

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TABLE 1 Mean±SD healthcare costs in euros per patient during the year following the diagnosis of bronchiectasis, asthma and COPD, respectively

	Bronchiectasis	Asthma	COPD
Hospitalisations	1572±4765	648±2413	2700±6129
Respiratory	635±3017	222±1294	1468±4415
Others	937±3427	426±1845	1232±4127
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±1177	373±654	790±2022
Pulmonology	65±94	28±52	55±96
Other fields	821±1162	345±638	736±2012
Drug dispensations	1067±3307	806±2898	1496±4024
Inhalation therapy	117±252	244±357	305±442
Inhaled steroids (+/− bronchodilators)[#]	61±163	192±288	170±287
Bronchodilators only[¶]	55±148	41±135	133±234
Systemic steroids[+]	0.23±1.64	0.33±2.97	0.50±6.65
Expectorants and mucolytics[§]	16±315	0.01±0.15	2±43
Antibiotics[f]	67±554	13±27	29±56
Fluoroquinolones[##]	10±19	4±10	9±21
Macrolides[¶¶]	9±34	2±8	3±9
Others	865±3176	548±2833	1160±3994
Total	3593±6336	1865±4345	5084±8276

[#]: Inhaled steroids (+/− bronchodilators) Anatomical Therapeutic Chemical (ATC) codes: R03AK01, R03AK04, R03AK06, R03AK07, R03AK08, R03AK09, R03AK10, R03AK11, R03AK12, R03AK13, R03AL09, R03BA01, R03BA02, R03BA03, R03BA04, R03BA05, R03BA06, R03BA07, R03BA08, R03BA09. [¶]: 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. [+]: Systemic steroids ATC codes: QH02AB–, H02BX01 and QH02BX90. [§]: Expectorants and mucolytics ATC codes: R05CA and R05CB. [f]: Antibiotics ATC codes: J01–. [##]: Fluoroquinolones ATC code: J01MA. [¶¶]: Macrolides ATC code: J01FA.

COPD (mean±SD number of prescriptions 1.9±4.2 *versus* 3.7±7.5 *versus* 4.9±7.1, respectively, p-values<0.0001). This difference was particularly evident for inhaled corticosteroids (with or without bronchodilators) (mean±SD number of prescriptions 0.9±2.0 *versus* 2.4±3.5 *versus* 2.4±3.9, respectively, p-values<0.0001), 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 *versus* 1.0±4.5 *versus* 2.3±4.0, respectively; p-value=0.813 for patients with asthma *versus* bronchiectasis; p-value<0.0001 for patients with COPD *versus* bronchiectasis). Moreover, antibiotic therapies were more frequently prescribed in patients with bronchiectasis compared to asthma and COPD (2.9±7.0 *versus* 1.0±2.1 *versus* 1.9±2.5, respectively; p-values<0.0001). In particular, both macrolides and fluoroquinolones were prescribed more frequently in patients with bronchiectasis: mean±SD number of macrolides prescriptions 0.8±2.8 *versus* 0.2±0.6 *versus* 0.3±0.7, respectively, p-values<0.0001; mean±SD number of fluoroquinolones prescriptions 0.8±1.4 *versus* 0.3±0.9 *versus* 0.7±1.4, respectively, p-value<0.0001 for patients with asthma *versus* bronchiectasis, while p-value=0.017 for patients with COPD *versus* 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 −53–−51%), while those with COPD showed higher costs (+41%, 95% CI +40–42%).

Similarly to our results, a recent systematic review on the economic burden of bronchiectasis identified hospitalisations 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 *et al.* [8] compared 231 new German bronchiectasis patients with 685 controls matched by age, sex and Charlson Comorbidity Index. They found that total direct expenditures were nearly one-third higher in bronchiectasis patients than controls and hospitalisations contributed to 35% of the total costs, which fits with our cohort

where hospitalisations accounted for 44% of the total costs. The reported annual expenditure for patients with bronchiectasis (EUR 6211) 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.* [9], using data from the Spanish health system, evaluated 70 676 patients hospitalised with bronchiectasis as the primary diagnosis between 2004 and 2013. A mean annual direct cost for patient of EUR 3961 in 2004 was reported, decreasing to EUR 3515 in 2013. de la Rosa *et al.* [10] also evaluated the annual direct medical costs of 231 patients with bronchiectasis recruited from six Spanish hospitals in 2013. The mean cost was EUR 4672 per patient, which increased significantly with severity; the largest items of expenditure being hospitalisations 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 utilisation databases provide highly accurate data because they are collected to manage reimbursements of healthcare at a 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 results) and information on habits (*e.g.* smoking) were lacking in the 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 charged by the regional healthcare system, 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 utilisation and drug dispensation for patients with bronchiectasis were hospitalisations and antibiotics, suggesting that the optimisation of disease management may significantly improve the economic burden of bronchiectasis.

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Author contributions: G. Corrao and P. Faverio are the guarantors of this research. P. Faverio, R. Ronco and M. Monzio Compagnoni were responsible for study concept and design. P. Faverio, R. Ronco and M. Monzio

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