




The significant global economic burden of bronchiectasis: a pending matter

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Bronchiectasis confers a considerable economic burden on healthcare services worldwide <http://ow.ly/mTkF30nbEu7>

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Bronchiectasis should no longer be considered an “orphan lung disease” in view of its prevalence globally [1]. For instance, the prevalence of bronchiectasis has been found to range from 67 to 566.1 per 100 000 inhabitants in Europe and North America (*i.e.* Germany [2], Spain [3], the UK [4] and the USA [5]), and has reached 1200 per 100 000 inhabitants among those aged 40 years or older in China [6]. In fact, bronchiectasis is one of the three most common chronic airway inflammatory diseases (along with chronic obstructive pulmonary disease (COPD) and asthma) [7] which is increasingly gaining global awareness [8, 9]. Despite accumulating appreciation of the pathogenesis and the development of novel therapeutic interventions [10], the burden (particularly, economic) of bronchiectasis remains poorly understood compared with that of COPD and asthma.

Understanding disease burden is imperative for the improvement of the global management of bronchiectasis, particularly in geographical “hotspots”. Several studies have documented the striking economic burden of bronchiectasis. In Germany, the mean age-standardised rate of bronchiectasis hospitalisations was 9.4 per 100 000 inhabitants [11], which mirrored that in Spain (16.52–16.99 hospitalisations per 100 000 inhabitants from 2004 to 2013) [12] and the USA (16.5 hospitalisations per 100 000 inhabitants) [13]. In the USA, bronchiectasis patients yielded significantly higher respiratory-related cost (mean USD 1607) than the matched controls [14]. More remarkably, the median inpatient cost accounted for USD 7827 in the USA [13], and the mean global cost was EUR 432.1 and EUR 4665.9 for emergency room visits and hospital stays in the wards (including transferrals and structural costs) in Spain, respectively [15]. Establishment of the diagnosis of *Pseudomonas aeruginosa* colonisation led to an 87% increase in the total healthcare cost (mean USD 67764 *versus* USD 36213) in the USA [16]. Importantly, greater bronchiectasis severity correlated with increased total expenditure, and most expenditure stemmed from in-hospital management with bronchodilators, inhaled steroids and inhaled antibiotics (particularly for severe exacerbation) [17]. These findings have provided crucial clues for the considerable economic burden of

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bronchiectasis worldwide (table 1). However, previous studies have been limited by the relatively small sample sizes, a lack of matched controls (particularly those with concomitant COPD) and insufficient information regarding healthcare utilisation (*i.e.* use of medication).

Reassuringly, these limitations are now being addressed. In this issue of the *European Respiratory Journal*, DIEL *et al.* [18] have comprehensively evaluated the economic burden of bronchiectasis, based on a population of greater than 4 800 000 covered by German health insurance in 2012. There are important findings that should be highlighted. Per insured bronchiectasis patient, the total direct expenditure in 2012 (mean EUR 18 634.57) was ~30% higher than that of the matched controls, and the cost of hospitalisation was ~55% higher in bronchiectasis patients than that in matched controls (mean EUR 6504.37 *versus* EUR 4183.65). In the USA, bronchiectasis patients yielded a mean of USD 2319 and USD 1607 for overall and respiratory-related costs in the first year after diagnosis [14]. Treatment is the core of bronchiectasis management, and hence, not surprisingly, constitutes an important aspect of the economic burden of bronchiectasis. The study by DIEL *et al.* [18] revealed that outpatient drug costs (41.3%), followed by hospitalisation costs (34.9%), accounted most for the expenditure of bronchiectasis management. Of all medication classes, antibiotics (including intravenous and inhaled) and bronchodilators (*i.e.* salbutamol) accounted for most of the drug costs, because eradication of pathogenic bacteria (particularly, *Pseudomonas aeruginosa*) and airway clearance are two principal dogmas for bronchiectasis management. In concert with these findings, intravenous antibiotics and inhaled bronchodilators and steroids were the three major drug classes that accounted for most of the expenditure of both emergency room visits and in-hospital management in Spain [15, 17]. Inhaled bronchodilators, but not their combination with corticosteroids, accounted for a greater proportion of drug costs in Germany [18], which might be explained by the physician's preference for prescription. As expected, the economic burden of bronchiectasis extended well beyond conventional outpatient treatment and hospitalisation. For instance, the expenditure associated with the prolonged hospital stay was significantly greater than that of matched controls [18], which echoed the findings of the recent US study [16]. In addition, there remain considerable indirect costs for bronchiectasis management. DIEL *et al.* [18] reported a noteworthy number of sick leave days (mean 40.5 days) and indirect cost (mean EUR 4230.49) associated with the loss of productivity [18]. These findings have important socioeconomic significance because such a loss of productivity may significantly reduce family income, which further predisposes to the limited access to healthcare services. We should again note that greater bronchiectasis severity correlated with significantly

TABLE 1 A summary of the current evidence regarding the global economic burden of bronchiectasis

Direct expenditure

- 31.0% higher than matched controls (mean EUR 18 634.57 *versus* EUR 14 236.99) [18]
- USD 2319 and USD 1607 increase of overall and respiratory costs compared with matched controls [14]

Burden or expenditure for hospitalisation

- 56% higher hospital costs compared with matched controls (mean EUR 6504.37 in bronchiectasis) [18]
- 16.5 hospitalisations per 100 000 inhabitants (higher in females) [13]
- 16.52–16.99 hospitalisations per 100 000 inhabitants from 2004 to 2013 in Spain [12]
- 9.4 hospitalisations per 100 000 inhabitants in the USA [11]
- Mean USD 7 respiratory-related incremental inpatient cost compared with matched controls [14]
- Mean cost of complementary explorations: EUR 147.1 for emergency room visits and EUR 331.8 for ward management [15]
- Mean global costs: EUR 432.1 for emergency room visits and EUR 4665.9 for hospital ward stay [15]

Expenditure for treatment prescription

- Mucoactive therapies: ~5 times higher than matched controls (EUR 70.11 *versus* EUR 14.15) [18]
- Inhalation and home ventilation devices: ~3 times higher than matched controls [18]
- Antibiotics: significantly higher compared with matched controls (mean EUR 87 728 *versus* EUR 56 219) [18]
- Mean annual cost per patient: EUR 2993, EUR 4732 and EUR 9999 for mild, moderate and severe bronchiectasis [17]
- Mean annual cost per patient: EUR 2041.9 and EUR 151.2 for inhaled and oral antibiotics, and EUR 759.9 for other inhaled therapy for clinically stable and exacerbation treatment [17]

Miscellaneous

- Similar sick leave (mean 40.5 *versus* 45.7 days) to matched controls [18]
- Mean sick leave: 13.4 (range 3–40) days in bronchiectasis patients [15]
- Similar productivity loss (mean EUR 4230.49 *versus* EUR 4776.50) to matched controls [18]
- Greater length of hospital stay (mean 19.6 *versus* 14.8 days) compared with matched controls [18]
- 5.8% higher annualised mortality compared to matched controls [18]

Shown are the four key aspects of the economic burden of bronchiectasis, including the direct expenditure, the cost or burden associated with hospitalisation for bronchiectasis, the expenditure for medication prescription, and other key aspects (*i.e.* mean sick leave days, length of hospital stay, loss of productivity).

increased healthcare costs [17]. Hence, more emphasis should be given to the understanding of the increased impact of severe bronchiectasis on economic burden. Moreover, the prognosis of bronchiectasis might have been influenced by the presence of co-existing diseases that may elicit significantly greater economic burden. Indeed, bronchiectasis patients (particularly those with concomitant COPD) demonstrated a greater mortality rate compared with matched controls [18]. Similarly, a recent population-based study which recruited Medicare enrollees with prescription drug plans in the USA documented a notable proportion (51%) of bronchiectasis patients with concomitant COPD who had frequent hospitalisation (due to respiratory tract infections) [19], which is known to be the risk factor of mortality. All the above-mentioned novel findings are expected to reshape our understandings of the underlying economic burden of bronchiectasis, which constitutes the cornerstone for advocating for a greater awareness of bronchiectasis healthcare worldwide.

The study, however, has some limitations that should be addressed by future investigations. For instance, the gender-adjusted mortality rate in girls aged under 15 years might have been underestimated. The difference of the prescription patterns between bronchiectasis patients and matched controls might have been diluted, given the fact that bronchiectasis frequently co-existed with COPD, which cannot be readily disentangled within the electronic database registry. More efforts are needed to systematically evaluate the post-discharge costs for bronchiectasis. Furthermore, it remains to be explored why mortality among patients with bronchiectasis without co-existing COPD was extremely low (which was significantly lower than that in controls) in the first year of follow-up.

There are some priorities and challenges for bronchiectasis research worldwide, particularly in developing countries. Incidence, prevalence and mortality remain sparsely documented in China [6], India [20] and Latin America, where the economic burden of bronchiectasis remains virtually unknown. Similarly, most economic analyses of the paediatric bronchiectasis population originated from developed, but not developing, countries [21]. Importantly, the economic burden of bronchiectasis might have been underreported in vast rural areas where recurrent respiratory tract infection and tuberculosis remain the dominant aetiologies of bronchiectasis [22]. However, the direct expenditure for bronchiectasis management might have been offset by the limited healthcare resources and relatively lower living standard in rural areas compared with urban regions. Given the significant economic burden of bronchiectasis compared with COPD, bronchiectasis should be incorporated into the list of lower respiratory tract diseases for the burden of respiratory disease report. Furthermore, establishment of a national bronchiectasis registry may facilitate assessment of how bronchiectasis contributes to the socioeconomic burden in developing countries. One way to mitigate the challenge of evaluating the economic burden of bronchiectasis in different countries and regions is the incorporation of data from the global burden of disease survey that would benefit from the collaboration with experts working in the field of epidemiology. Admittedly, population-based health insurance remains at its infancy in some developing countries, such as China; therefore, refinement of the health insurance system might provide more opportunities for further research, particularly for pilot investigations in major metropolitan areas.

Building on our expanded understanding, we have now obtained more solid evidence to justify the greater awareness of management and clinical research of bronchiectasis, which is indeed a common chronic airway inflammatory disease, aside from COPD and asthma [7]. An increase in investment in bronchiectasis research will ultimately help reduce medical expenditure *via* improved patient selection for interventions, thus saving more money [23]. Nonetheless, how best to identify the economic burden of bronchiectasis in developing countries where healthcare records are often incomplete or unavailable, still requires ongoing efforts.

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