

Economic Burden of Cystic Fibrosis in Five Key European Countries: a Systematic Review

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INTRODUCTION

- Cystic fibrosis (CF) is an inherited condition that affects the production of mucus, sweat and digestive juices and causes severe damage to the lungs, intestines and other organs.¹ Caused by a mutation in the *CFTR* gene, CF is associated with dysregulated movement of salt in and out of cells, resulting in the presence of thick, sticky mucus throughout the body²
- Previous estimates of the incidence of CF were given as 1 in 2,500 in European population. However, the latest data indicate a reduction in its incidence, ranging between 1 in 3,000 and 1 in 6,000²
- Treatments include bronchodilators, anti-inflammatory agents, CFTR modulators, and mucus thinners¹

OBJECTIVES

This systematic literature review (SLR) aimed to comprehensively explore the economic burden of CF in terms of healthcare resource utilization and costs across five European countries.

METHODS

- A systematic literature search to identify English-language articles published between 2013 and 2023 was performed in the MEDLINE® and Embase® databases, according to pre-defined inclusion criteria (Table 1)
- Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed for reporting the SLR
- All the records retrieved from the literature search were screened against the pre-defined inclusion criteria, first based on the title and abstract and then on the full-text citations
- The eligibility of publications was assessed by two independent reviewers, with any discrepancy resolved by a third

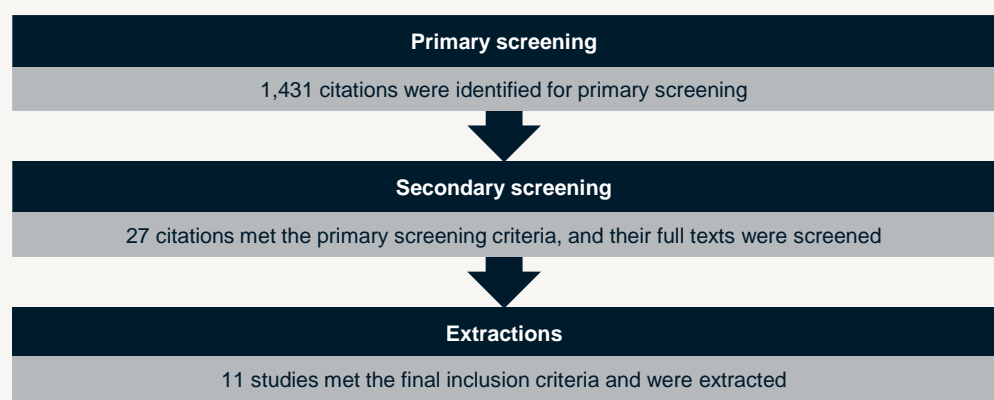
Table 1. Inclusion criteria

Language	English
Timeframe	2013–2023
Population	Adults and children with cystic fibrosis
Country	UK, France, Germany, Italy, and Spain
Outcomes	Cost and resource use
Intervention and comparator	No restriction

RESULTS

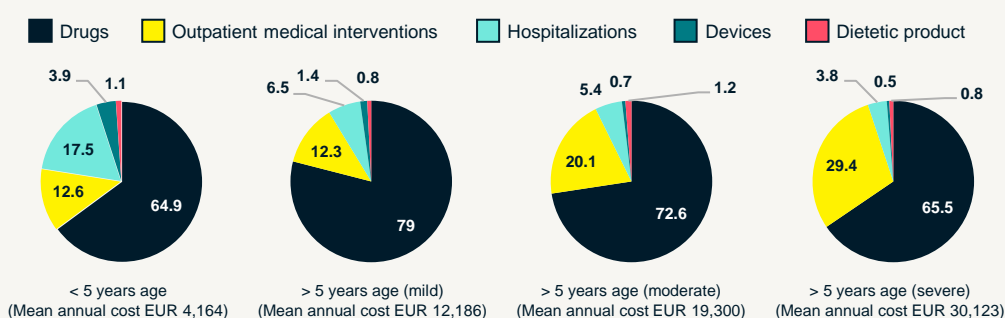
- A total of 1,431 records were screened using the pre-defined population, intervention, comparison, outcomes and study criteria. Eleven studies were identified that evaluated the economic burden of CF in the five countries of interest (Figure 1)

Figure 1. Study flow diagram



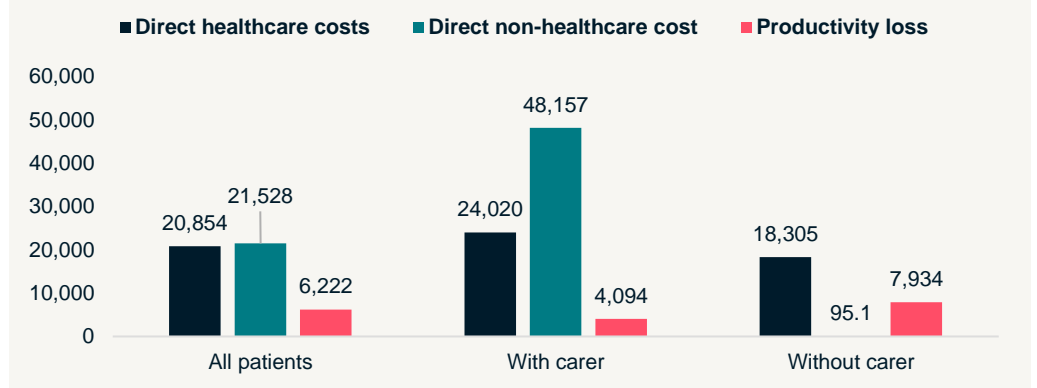
- Cost and resource use data were reported for France in four studies, Italy in three studies, the UK in two studies, and Germany in one study. One study reported data for all five countries together
- Six of the included studies were retrospective in nature, while the rest were prospective. The cost of CF management was reported in six studies, while resource use data were reported in nine studies
- In France, the mean total cost per patient increased from EUR 14,174 in 2006 to EUR 44,585 in 2017, of which medications and hospital stays accounted for > 87% of the total costs³
- A study in Italy indicated that cost of illness increases significantly with age and disease severity, with medication and hospitalizations being major cost drivers (Figure 2)⁴

Figure 2. Mean annual per patient costs by age and CF severity



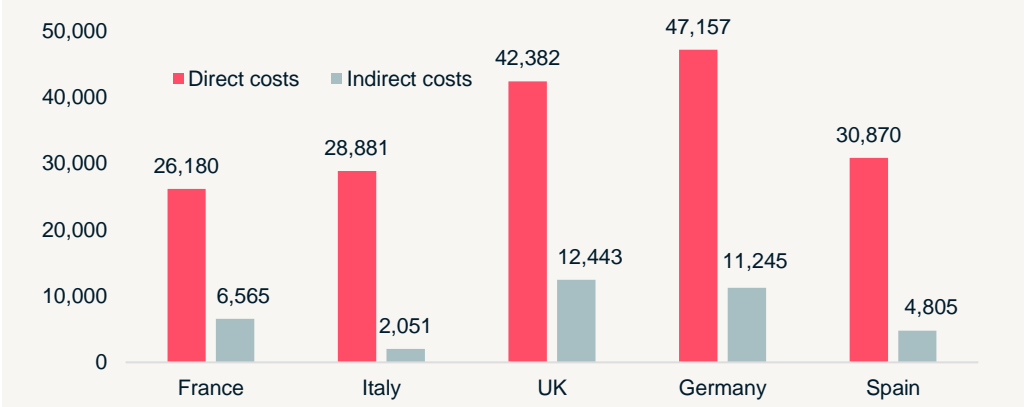
- The mean annual costs per patient with CF in the UK were EUR 48,603, which ranged from EUR 76,270 for patients who required caregiver help to EUR 26,335 for patients who did not (Figure 3)⁵. The major cost drivers observed were informal care (44%) followed by medications (14.5%), acute hospitalizations (13.9%), early retirement (9.1%) and healthcare visits (7.9%)

Figure 3. Direct and indirect costs associated with CF in the UK (2012, in €)



- The total annual direct cost burden of CF in Germany in year 2016 was estimated to be EUR 159 million, which is further expected to increase to EUR 594 million if more patients required the expensive CF-mutation specific drugs. Additionally, significant differences were observed in the cost of treatment of younger versus older patients and in patients with mild or severe form of disease⁶
- Across the key five European countries, the UK and Germany incurred higher annual per-patient direct and indirect costs (Figure 4). The adults incurred a higher direct cost, while children had a significantly higher informal care cost ($p < 0.0001$)

Figure 4. Comparison of costs across key European countries (2012, EUR)



- CFTR modulators like ivacaftor significantly reduce the event rate of number of hospitalizations per patient per year, mean number of hospitalization days, and the use of acute and inhaled antibiotics⁷
- Mean annual cost tend to increase with age and severity of disease. Children > 5 years of age and with severe CF had an approximately nine times higher rate of hospitalization per patient per year and a significantly longer duration of hospitalization, when compared to children < 5 years of age⁴
- A study from Wales indicated that patients who initiated their CFTR modulator therapy with elxacaftor, tezacaftor or ivacaftor had an even higher reduction in hospitalization rate compared with patients who received other CFTR modulators⁸

LIMITATIONS

- The identified publications may vary in terms of study design, patient population and timing of outcome measurement
- The included studies had different approaches for collecting and synthesizing evidence, which lead to diverse findings and underestimate the true impact on socio-economic burden

CONCLUSIONS

- CF is a life-limiting condition with a significant economic burden
- The burden of CF increases with the associated co-morbidities and complications
- Children with CF are associated with a considerable level of healthcare resource use across all age groups
- Hospitalization contributes significantly to the economic burden of CF
- The cost of medication (specially CFTR modulators), hospitalization and premature retirement were the major sources of cost and resource burden

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