The clinical, humanistic, and economic burden of obliterans bronchiolitis in Europe

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The clinical, humanistic, and economic burden of obliterans bronchiolitis (BOS) in Europe, this study summarises the clinical, humanistic and economic burden of BOS in published sources.

Introduction

- Bronchiolitis Obliterans Syndrome (BOS) is a progressive obstructive airway disease characterised by inflammation and fibrosis that reduces the internal diameter of the bronchioles and results in respiratory failure and death. BOS results from an injury to the airways that precedes the development of BOS.
- BOS occurs most frequently following lung transplantation (LTx) and allogeneic hematopoietic Stem Cell Transplantation (alloHSCT), but can also occur in patients with an injury to the airways that precedes the development of BOS, autoimmune disease and severe infections. Disease pathophysiology is not yet fully understood in adult and paediatric patients regardless of ethnicity.
- It is the leading cause of death 1-3 years after paediatric LTx, accounting for over 20% of mortality. BOS in paediatric alloHSCT patients shows a mortality rate between 11.4% and 12.5%.
- Currently, there are no approved treatments for BOS.

### Methods

A targeted literature review in Medline and Embase on the disease burden in Europe was performed in January 2019 and was supplemented with an Internet search. The studies were selected by one reviewer based on relevance to the topic but no systematic filter was applied. We were not able to identify any cost study with reported data on this topic. Data on prevalence was included wherever possible.

### Results

**Prevalence**

Post lung transplantation, the incidence of BOS is about 10% per year, with a prevalence of 30% and 50% at 3 and 5 years, respectively and a median survival of less than 6 years. The incidence of BOS in alloHSCT patients is 8.3% with a prevalence from 3.4% to 10.0%, and a 5 year survival overall of only 13%.

The reported prevalence and incidence of BOS vary significantly across countries due to differences in study design and lack of consensus regarding the clinical diagnostic criteria for BOS (Table 1).

<table>
<thead>
<tr>
<th>Country</th>
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<tr>
<td>In France, approximately 384 pulmonary transplants are performed each year, with a BOS prevalence of 45% at 5 years.</td>
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<td>The Swiss population observed for at least 2 years but less than 3 years, 22.1% of 1,263 LTx recipients developed BOS (2000 and 2014).</td>
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<td>In Italy, the estimated prevalence of BOS reached 41.2% at 119 LTx recipients at a mean interval of 5.8 years.</td>
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<td>In France between 1997 and 2016, 22.5% of patients developed BOS out of 1,457 patients followed up for 11.36 months; 60% of patients had BOS after 5 years.</td>
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**Clinical burden of BOS**

- BOS is a progressive life-threatening disease.
- 50% of LTx patients are dead by 5 years with BOS contributing to 30% of the mortality. The disease is irreversible and rapidly progressive.
- The overview of clinical burden is presented in Table 2.

### Table 2. Overview of clinical burden in Europe

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<td>In France, a cohort study monitored 3 years after BOS diagnosis, 23% of patients were alive after 3 years.</td>
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<td>In Sweden, the overall mortality rate of BOS following LTx was 24.4% at 5 years, 36.4% at 10 years, 40.4% at 15 years, and 57.6% at 20 years.</td>
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<td>In Spain, patients diagnosed with BOS after LTx had a mean survival of 31.6 months, of which 42% were alive at 1 year and 32% were alive at 3 years.</td>
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**Economic burden of BOS**

- BOS is associated with the increased use of healthcare resources due to frequent hospitalisations, extensive immunosuppressive treatment and the use of expensive medications. There is a 75% increase in cost related to lung transplant recipients developing BOS compared to those free of LTx.
- In Europe, the cost of hospitalisations due to BOS reaches up to €120 million per year.

**Humanistic burden of BOS**

- In patients following LTx, BOS significantly reduces patients’ quality of life. Examining the ability to perform daily living activities and mental domains (symptom distress, anxiety and depression) – shown in Figure 2 – was also found to increase work absence.

**Figure 2. Impact of BOS on health related quality of life**

- A number of significant gaps in knowledge of BOS contributes to robust and important limitations on the use of currently available data.
- Differences in burden according to the aetiology of BOS (LTx vs alloHSCT) has not been investigated. Also, data for other causes of BOS is lacking.
- Gathering epidemiological data on patient populations and the prevalence of BOS as well as its clinical and humanistic outcomes is key in order to create programs to treat this disease.

### Conclusions

- The median survival in LTx recipients following a BOS diagnosis is dependent on the grade of disease at the time of diagnosis, for initial diagnosis of BOS grade 1, median survival is 5.7 years; for BOS grade 2 or 3, 1.03 years.

### References

1. Garcia-Cruces L. et al. Respir Med. 2013; 107:276-83. 2. Krintzes R. and Oliver T. Treasure Island (FL): StelaPac Publishing; 2019 Jan. 3. Champs NS et al. Epub 2017. 4. Freeman Hospital, 82% survival at 1 year. 5. In Sweden, the overall mortality rate of BOS following LTx was 24.4% at 5 years, 36.4% at 10 years, 40.4% at 15 years, and 57.6% at 20 years. 6. In France, approximately 384 pulmonary transplants are performed each year, with a BOS prevalence of 45% at 5 years.

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### Figure 1. Overall BOS survival following alloHSCT [%]

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Copenhagen, Denmark. No 06 09, 2019

### Discussion

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