Poster
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Microsimulation Model of Future Trends in Cystic Fibrosis (CF) Burden and Demography in France

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INTRODUCTION

- Over the past few decades, in addition to an overall improved standard of care, newborn screening, the additive use of antibiotics, mucoactive drugs, nutritional optimisation, and implementation of multidisciplinary care have led to improved survival for patients with cystic fibrosis (CF)[1]
- In France, demographic forecasts have predicted a 76% increase in the adult CF population and a 46% increase in the overall CF population between 2010 and 2025[2,3]
- However, previously described projections and trends have not factored in more recent advances in CF care, such as cystic fibrosis transmembrane conductance regulator (CFTR) modulators
- It is therefore important to accurately model future trends in CF demography (children, adults, and patients with lung transplants [LTs]) to provide insight into how health care systems may need to adapt

OBJECTIVE

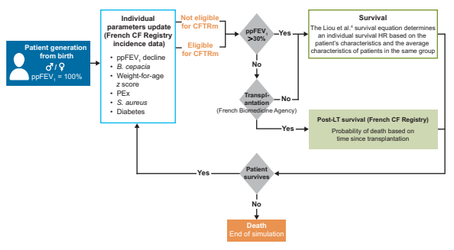
- To model future trends in CF demography and disease burden, taking into consideration the evolution of standard of care and the introduction of CFTR modulators over time (ivacaftor, ivacaftor/lumacaftor)

METHODS

Model Overview

- The model consisted of a microsimulation model that tracks virtual patients with CF by birth cohorts until death (**Figure 1**)

Figure 1. Model Structure



B. cepacia, *Burkholderia cepacia*; CF, cystic fibrosis; CFTRm, cystic fibrosis transmembrane conductance regulator modulators; HR, hazard ratio; LT, lung transplant; ppFEV$_1$, percent predicted forced expiratory volume in 1 second; PEx, pulmonary exacerbations; *S. aureus*, *Staphylococcus aureus*.

- The simulation began with patients born in 1950, with newborn patients added at a constant rate each year based on annual CF incidence until 2030
- The model was developed and validated based on the French CF Registry population
  - Patient characteristics and survival were based on the French CF Registry for patients with CF born between 1992 and 2011
  - The French CF Registry includes at least 90% of all French CF patients
- The model's main outcomes were compared for 2015 and 2030

CFTR Modulator Effect

- CFTR modulators included in the model were:
  - Ivacaftor (for *G551D*, *R117H*, and other CF populations expressing a *CFTR* mutation responsive to ivacaftor [ie non-*G551D* gating mutations and specific residual function mutations])
  - Ivacaftor/lumacaftor (for the *F508del*/*F508del* CF population)
- In addition to standard of care, the model accounted for CFTR modulator uptake in eligible patients
  - Uptake was assumed to be 50% at year 1 and 80% from year 2 onwards
- Effects of CFTR modulator treatment were based on clinical trial results and were applied to individual patient characteristics, including increase in forced expiratory volume in 1 second (FEV$_1$) and weight, reduction in pulmonary exacerbations, and impact of treatment on rate of FEV$_1$ decline
- It was assumed that patients did not interrupt treatment once initiated

Lung Transplant

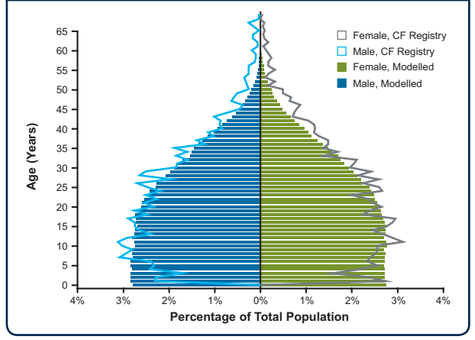
- Indication of LT was based on a percent predicted FEV$_1$ (ppFEV$_1$) of ⩽30%
- LT rates were calibrated based on the 1997-2017 French Biomedicine Agency data
- Post-LT survival was based on French CF Registry data for transplanted patients with mortality rates of 18% in the first year post-transplant and ~5% thereafter
  - Post-LT health status did not account for the effect of CFTR modulators as the post-LT survival registry data were independent of patients' clinical characteristics

RESULTS

Model Validation: Accurate Prediction of Age Distribution

- The modelled versus observed age distribution in the French CF Registry for 2015 is shown in **Figure 2**
- The model correctly reproduced real-life CF age distribution with low residual differences

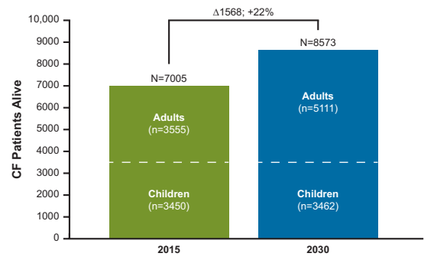
Figure 2. Modelled and French CF Registry Age Distribution of All Patients in 2015



Evolution of Population Size

- The model predicts a 22% increase in patients with CF between 2015 and 2030 due to improved longevity (**Figure 3**)
- It is estimated that the increase in patients with CF will be driven by adults, representing ~60% of all patients in 2030

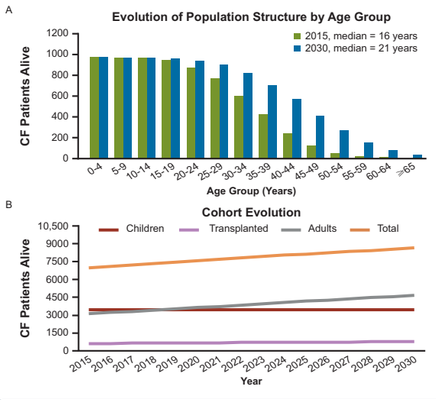
Figure 3. Number of CF Patients Predicted to be Alive in 2015 and 2030



Evolution of Population Age from 2015 to 2030

- Median age is predicted to increase from 16 years to 21 years (**Figure 4**)
- The model predicts a 184% increase in patients with CF aged >40 years
- Median age at time of death is predicted to increase by 9 years

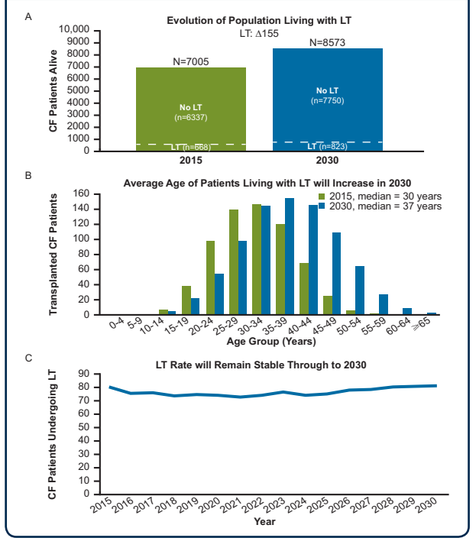
Figure 4. Evolution of Population Structure by Age Group (A); and Cohort Evolution (B)



Evolution of Lung Transplantation

- Evolution of the population living with LT is predicted to increase by Δ155 (**Figure 5A**)
- The median age of the population living with LT is predicted to increase from 30 years to 37 years (**Figure 5B**)
- The number of patients with CF living with LT is predicted to increase from 2015 to 2030 (**Figure 5C**)

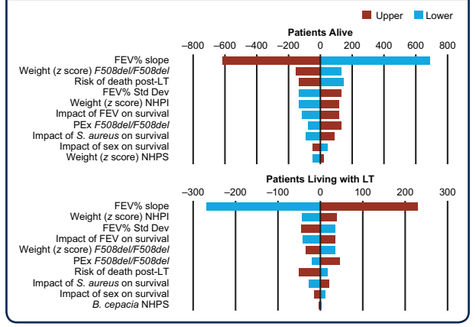
Figure 5. Evolution of the Population of Patients Living with LT: Overall (A); by Age Group (B); and by the Number of LTs per Year (C)



Deterministic Sensitivity Analysis: Total Patients Alive and Living with LT in 2030

- The model is most sensitive to changes in the slope of ppFEV$_1$ decline (**Figure 6**)
- The impact of each parameter on survival might evolve with improved care, emergence of resistant bacteria, and patient comorbidities

Figure 6. Deterministic Sensitivity Analysis – Total Patients Alive and Living with LT in 2030



B. cepacia, *Burkholderia cepacia*; FEV, forced expiratory volume; LT, lung transplant; NHPI, heterozygous with pancreatic insufficiency; NHPS, heterozygous with pancreatic sufficiency; PEx, pulmonary exacerbations; *S. aureus*, *Staphylococcus aureus*; Std Dev, standard deviation.

SUMMARY

- **The increase in the number of patients with CF is predicted to be driven by adult patients, with the number of children with CF predicted to remain stable through to 2030**
- **This increase is due to improved longevity of patients with CF, as a result of the evolving standard of care and use of CFTR modulators, leading to an ageing population in France by 2030**
- **The annual rate of LTs is predicted to remain stable, but the overall number of patients living with LT is predicted to increase between 2015 and 2030**
- **This model predicts the need for a specific increase in the future provision of care for the adult non-transplanted population, while maintaining system capacities for the paediatric and transplanted populations**
- **This model can be updated for future therapies and extended to other countries using country-specific data**

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DISCLOSURES

PRB reports personal fees for lecturing or advisory meetings from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Pfizer, Teva, Vertex Pharmaceuticals Incorporated, and Zambon. **PRB** regularly participates in advisory boards with AstraZeneca, Novartis, and Vertex Pharmaceuticals Incorporated. **BMC** is an employee of Vertex Pharmaceuticals (France) and may own stock or stock options in that company.

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