

Impact of the Number of Years with Exacerbations during Maintenance Therapy on Lung Function Decline in COPD

Marjan Kerkhof¹, Jaco Voorham¹, Claudia Cabrera², Patrick Darken², Paul Dorinsky², Janwillem W.H. Kocks¹, Mohsen Sadatsafavi³, Don D. Sin³, David Price¹

¹ Observational and Pragmatic Research Institute, Singapore; ²AstraZeneca; ³University of British Columbia, Vancouver, BC, Canada

Introduction

- A significant portion of patients develop COPD due to accelerated lung function decline after normal lung development¹
- Whether early intervention slows COPD progression is unclear
 - Maintenance therapy reduces exacerbation risk
 - Patients may still exacerbate despite maintenance therapy, in turn contributing to lung function decline
- Aim: To assess the impact of the number of years with COPD exacerbations on lung function decline

Methods

Study design

- Historical follow-up study of patients diagnosed with COPD followed from first to last spirometry (1980 to 2017)
- Data source: two large UK primary care record databases
 - Clinical Practice Research Datalink (CPRD)
 - Optimum Patient Care Research Database (OPCRD)
- Identified patient records with:
 - Mild-moderate COPD: FEV₁ %predicted ≥50% and ≤90%
 - First clinical diagnosis code for COPD, median year (interquartile range): 2006 (2005; 2008)

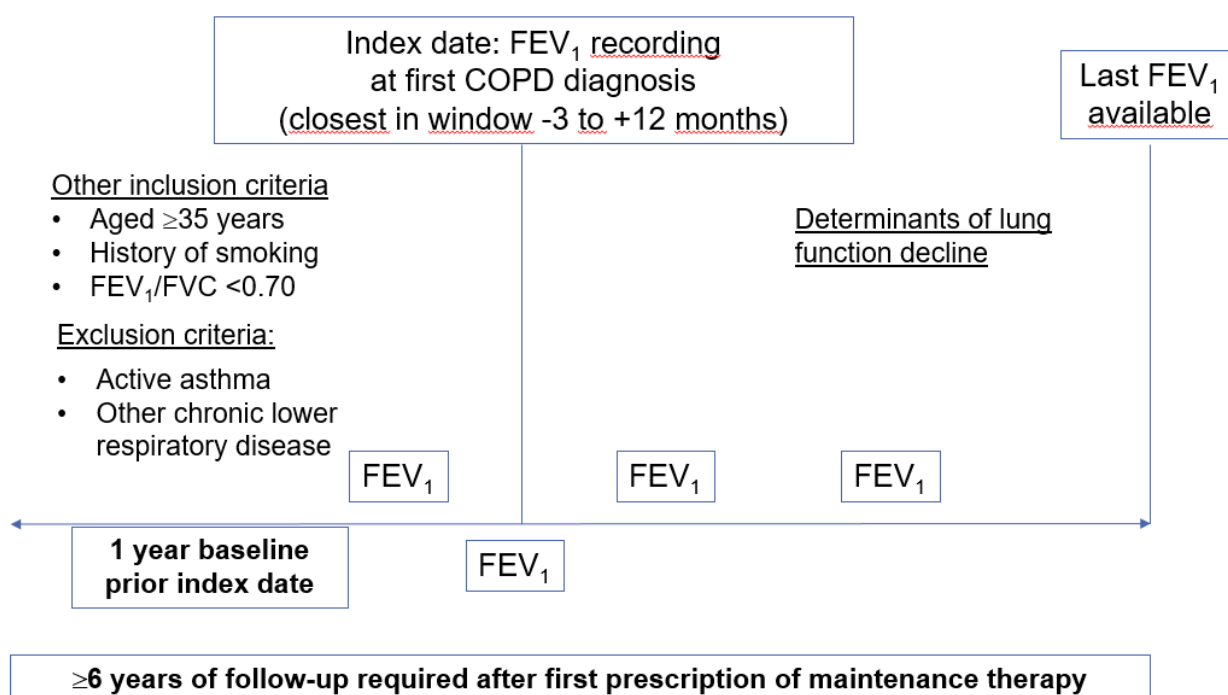


Figure 1. Study Design

Methods

Exposure

- Exacerbation burden, defined as:
 - The number of years out of 6 years a patient experienced ≥1 exacerbation after first prescription of maintenance therapy
- Exacerbation, defined as:
 - Acute oral corticosteroids, and/or
 - Antibiotics for lower respiratory consultation, and/or
 - Emergency or inpatient hospitalization for lower respiratory disease

Outcome

- Primary: Decline in FEV₁ over total time of follow-up
- Secondary: FEV₁ at time of COPD diagnosis (index date)

Data Analysis

- Multilevel random effects linear regression model to assess mean effect of exposure (exacerbation burden) on baseline FEV₁ (intercept) and change in FEV₁ over time
- Adjusted for:
 - Baseline sex, age, height, weight
 - Smoking after diagnosis
- Marginal FEV₁ decline and FEV₁ at time of diagnosis with 95% confidence intervals visualized for each possible number of years out of 6 years patients experienced exacerbations
- Exploratory analysis for number of years with ≥2 exacerbations also conducted

Funding: This study is funded by AstraZeneca

Conflict of Interest:

M. Kerkhof is an employee of the Observational and Pragmatic Research Institute, which conducted this study and which has conducted paid research in respiratory disease on behalf of AstraZeneca. **D. Price** has board membership with AstraZeneca and have received grants, unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd), payment for lectures/speaking engagements, development of educational materials, travel/accommodation/meeting expenses from AstraZeneca

Reference

- Lange P, Celli B, Agusti A et al. Lung-function trajectories leading to chronic obstructive pulmonary disease. *N Engl J Med.* 2015;373(2):111-22

Results

- A total of 11,337 patients had ≥6 years of follow-up after initiation of maintenance therapy
- 43% had started inhaler maintenance therapy before diagnosis and 85% within 1 year after diagnosis

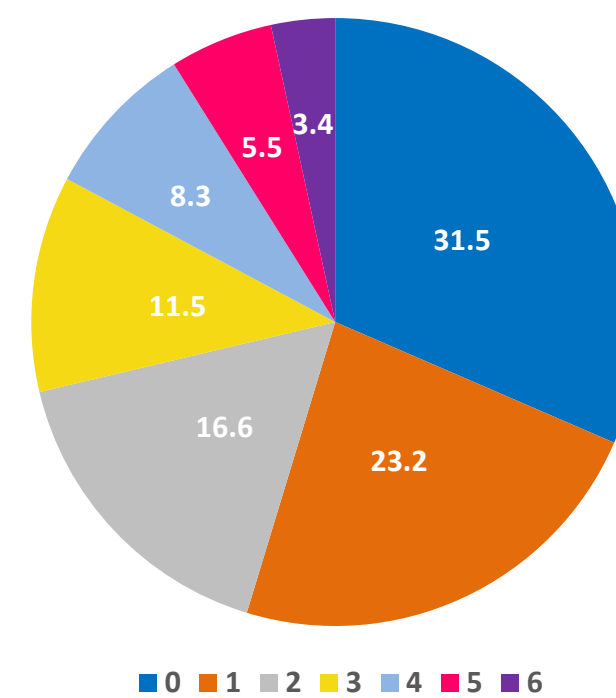


Figure 2. Distribution of number of years out of 6 years with ≥1 exacerbation

Baseline Patient Demographic		
Variable		Total (N= 11,337)
Follow-up after ID, years	Median (IQR)	8.2 (7.0;10.1)
Age (years)	Mean (SD)	65.2 (10.0)
Sex	Male, n (%)	5,771 (50.9)
BMI	Mean (SD)	27.4 (5.6)
BMI categorized	Underweight, n (%)	329 (2.9)
	Normal Weight, n (%)	3,656 (32.2)
	Overweight, n (%)	4,143 (36.5)
	Obese, n (%)	3,209 (28.3)
Baseline smoking status, closest within 5 years	N (% non-missing)	10,411 (91.8)
	Ex-smoker, n (%)	5,454 (52.4)
Smoking status up to 5 years of follow-up after ID	N (% non-missing)	10,462 (92.3)
	Sustained quitter, n (%)	3,785 (36.2)
	Intermittent quitter, n (%)	3,467 (33.1)
	Continuous smoker, n (%)	3,210 (30.7)
COPD exacerbations	Mean (SD)	0.58 (0.96)

Results

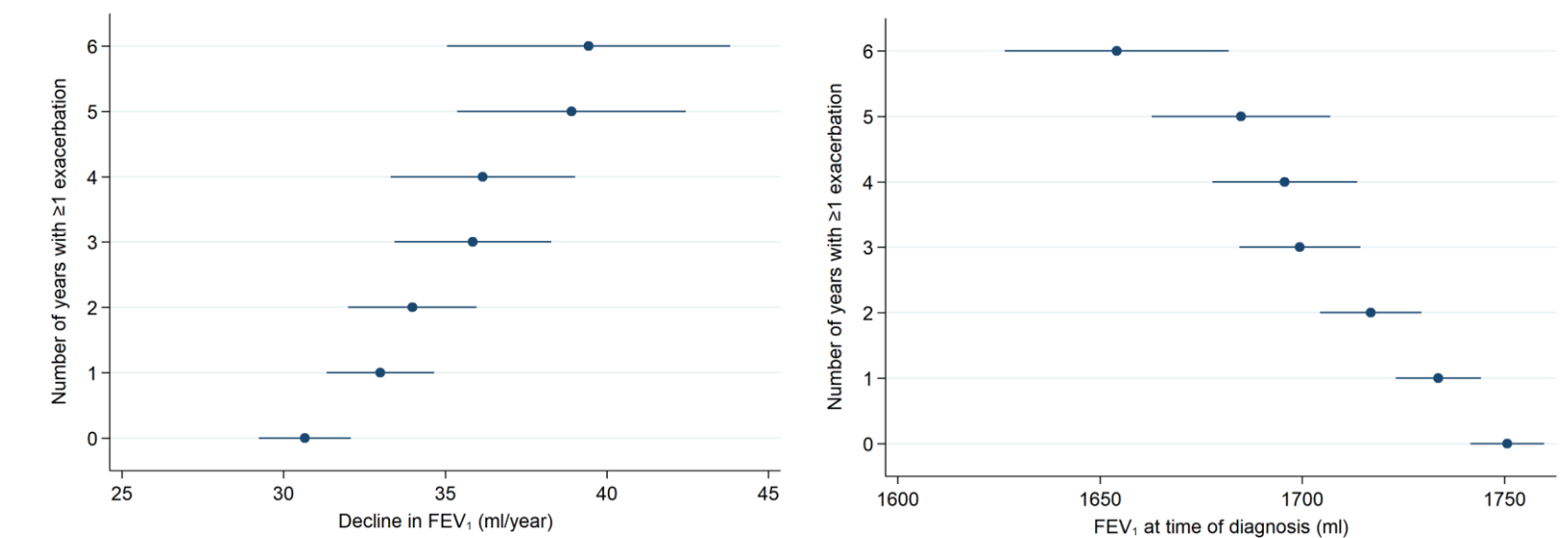


Figure 3. Marginal FEV₁ decline (left) and FEV₁ at diagnosis (right) by the number of years with ≥1 exacerbation in the first 6 years after maintenance therapy initiation

- Left:** Greater FEV₁ decline for patients who experienced more years with exacerbations after initiation of maintenance treatment
- Right:** Patients who had more exacerbation years started with lower FEV₁ value at the time of diagnosis compared to patients who had no exacerbations

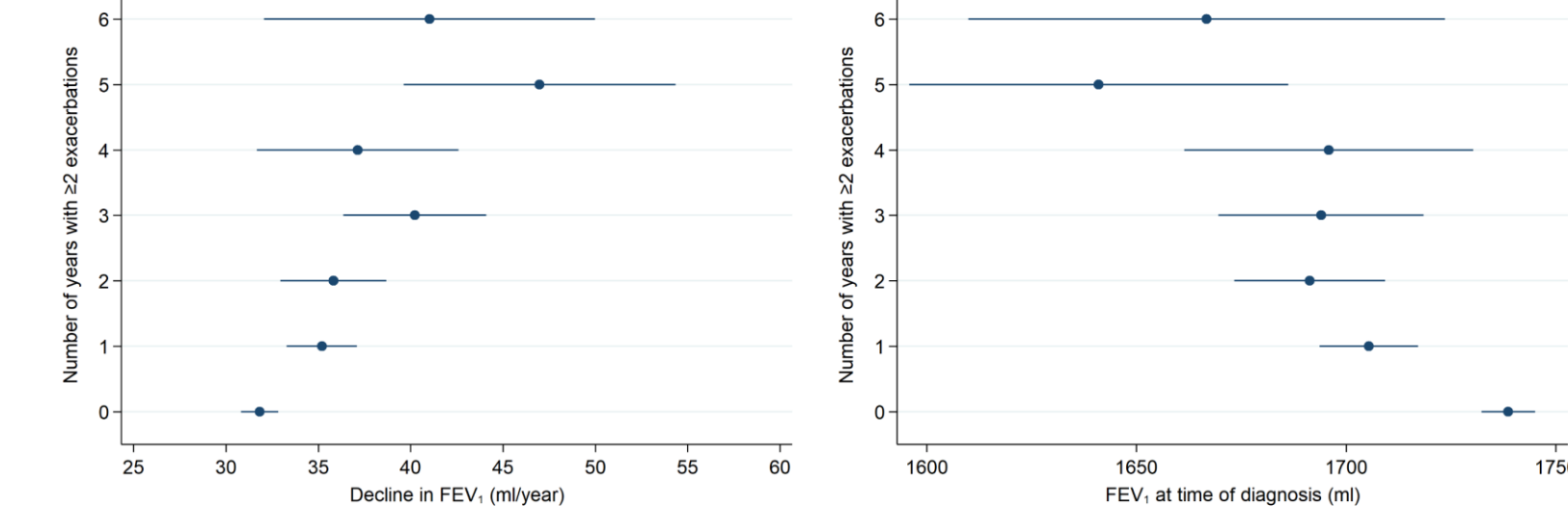


Figure 4. Marginal FEV₁ decline (left) and FEV₁ at diagnosis (right) by the number of years with ≥2 exacerbations in the first 6 years after maintenance therapy initiation

- Similar results for number of years with ≥2 exacerbations

Conclusion

- Higher number of years with exacerbations is associated with:
 - Lower lung function at time of COPD diagnosis
 - Steeper decline in lung function over time
- Our results stress the importance of therapeutic interventions earlier in the course of the disease which can effectively reduce the exacerbation burden in patients with COPD
- More research needed to understand if the lung function deterioration after exacerbation was permanent or partial reversibility of the lung function can be recouped after treatment and medication