Benefits of Inhaled Corticosteroids (ICS) in COPD Maintenance Combinations: Real-World Evidence Using Longitudinal Targeted Maximum Likelihood Estimation

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INTRODUCTION

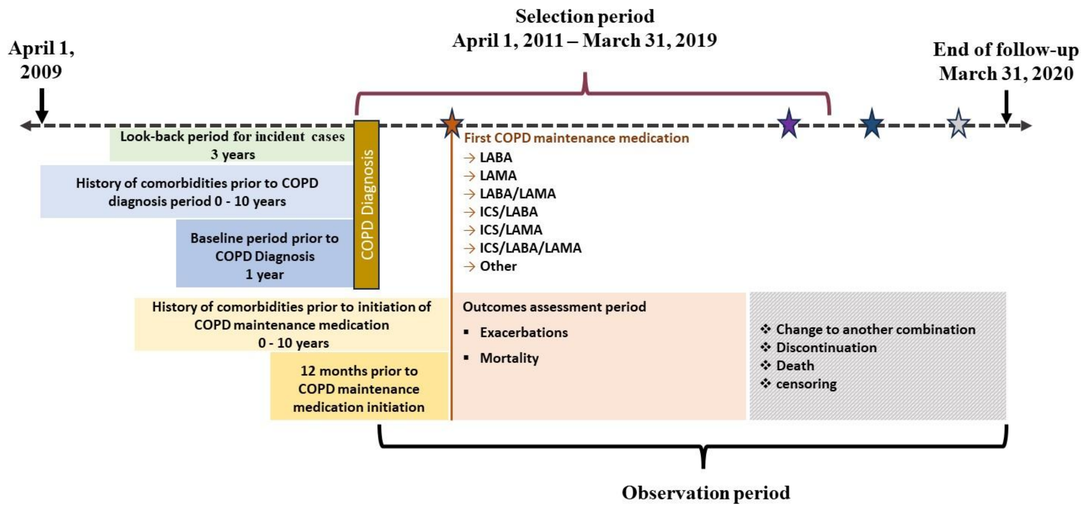
Currently, patients with symptomatic COPD and frequent exacerbations typically receive combination therapy involving inhaled corticosteroids (ICS), long-acting beta agonist (LABA) and/or long-acting muscarinic antagonist (LAMA). While pivotal randomized controlled trials have demonstrated lower exacerbation rates with ICS versus non-ICS therapy, recent RWE studies have failed to replicate these findings [1], likely due to insufficient data on confounders or use of less robust analytic methods.

OBJECTIVE

This study aims to obtain real-world evidence on the benefits of ICS-containing COPD maintenance therapy, using double-robust Longitudinal Targeted Maximum Likelihood Estimation (L-TMLE).

METHODS

- **Study Design:** Retrospective Cohort
- **Data Source:** Population-wide administrative data from Alberta, Canada
- **Study Population:** Newly diagnosed COPD patients



- **Analysis**: Longitudinal TMLE, with the 6-months follow-up period, subdivided into 15-day intervals. Using an intention-to-treat analysis, the first long-acting therapy combination in each interval was considered the treatment.
- **Parameter of interest:** average treatment effect (ATE), the mean difference in rates of exacerbations if patients were always given ICS+LABA+LAMA compared to if they were always given LABA+LAMA.
  - **Moderate exacerbations** = outpatient visit with a diagnosis code for COPD and a dispense of oral corticosteroids or an antibiotic for respiratory infection within 5 days of the visit, for <15 days
  - **Severe exacerbations** = emergency department visit with a COPD diagnosis in any position or a hospitalisation with a “most-responsible diagnosis” or post-admission COPD code

RESULTS

- 89,296 patients were included in the analysis.

Table1. Baseline Characteristics of Study Cohort

Baseline characteristic	n (%)
Age, n(%)	
40 – 74	60,193 (67.4)
75+	29,103 (32.6)
Sex, n(%)	
Male	45,298 (50.7)
Female	43,998 (49.3)
Residence at cohort entry, n(%)	
Urban(Calgary, Edmonton)	55,880 (62.6)
Rural(Central, North, South)	33,416 (37.4)
COPD Severity	
Patient category, n(%)	
Low risk	70,073 (78.5)
High risk(1+ Severe or 2+ moderate exacerbations in past 12 months)	19,223 (21.5)
Number of moderate exacerbations in prior 12 months, n(%)	
0	76,920 (86.1)
1	10,105 (11.3)
2+	2,271 (2.5)
Number of severe exacerbations in prior 12 months, n(%)	
0	71,711 (80.3)
1	14,153 (15.8)
2+	3,432 (3.8)
Comorbidities*	
Asthma	48,682 (54.5)
Diabetes mellitus type-2	29,857 (33.4)
Ischaemic heart diseases	41,615 (46.6)
Disorders of lipoprotein metabolism and other lipidaemias	48,881 (54.7)
Hypertensive diseases	67,861 (76.0)
Dyspnea	41,179 (46.1)
Initial Long-acting therapy combination	
ICS/LABA/LAMA	20,077 (22.5)
LABA/LAMA	3,017 (3.4)
Other	66,202 (74.1)

Abbreviations: COPD: Chronic obstructive pulmonary disease; ICS: inhaled corticosteroid; LABA: long-acting beta agonist; LAMA: long-acting muscarinic antagonist; n:number
*Only comorbidities observed in >30% of the cohort are presented here

- ATE for **severe or moderate** exacerbations = **-0.32 [-0.48,-0.17]**
- ATE for **severe** exacerbations = **-0.13 [-0.23,-0.02]**
- ATE for **moderate** exacerbations = **-0.16 [-0.27, -0.05]**

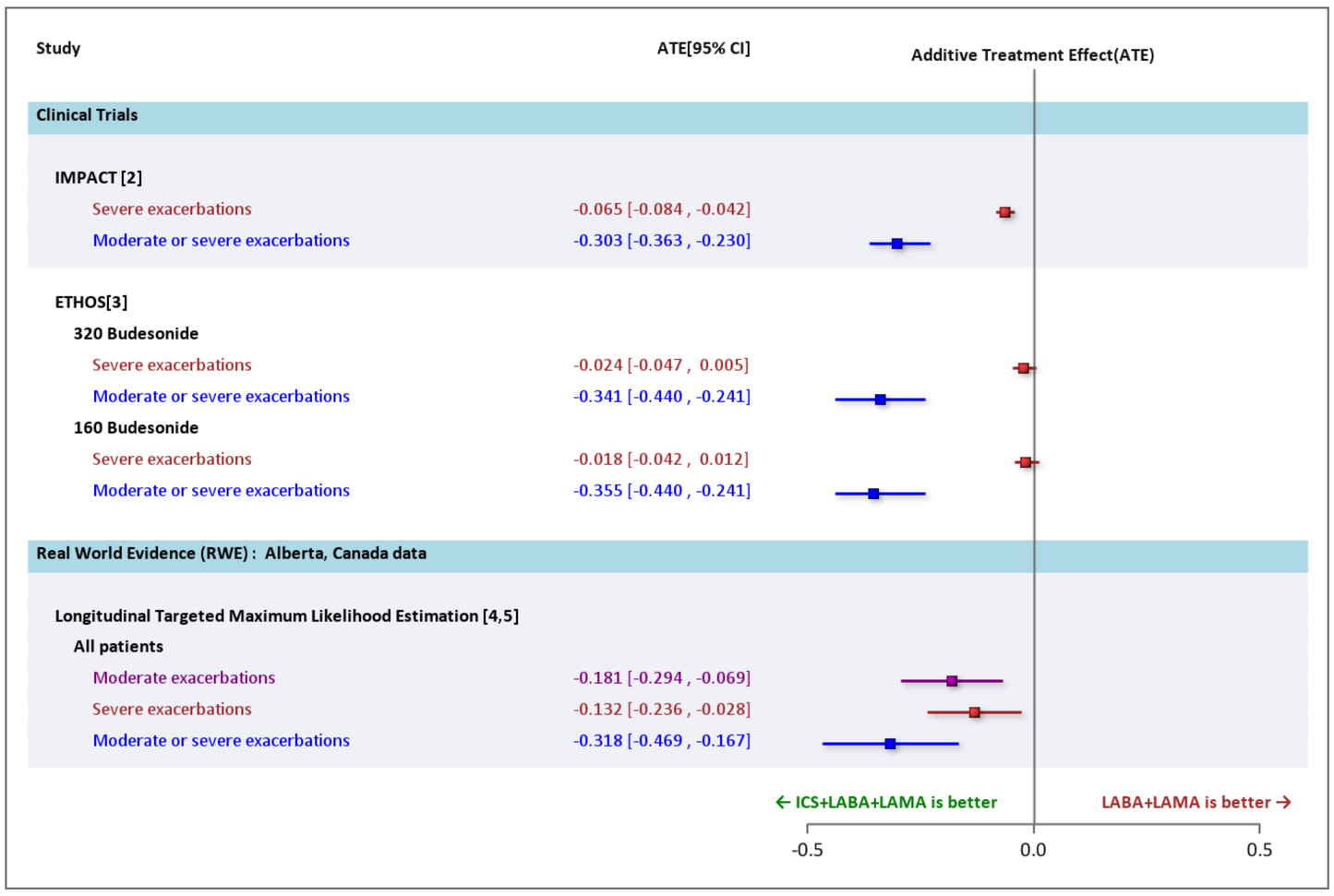


Figure 1. Additive Treatment Effect of ICD+LABA+LAMA vs LABA+LAMA

Abbreviations: ATE: additive treatment effect; CI: confidence interval; ICS: inhaled corticosteroid; LABA: long-acting beta agonist; LAMA: long-acting muscarinic antagonist; n:number; RWE: real world evidence

CONCLUSIONS

Results from this study show evidence of real-world benefits of ICS-containing COPD maintenance therapy to prevent future exacerbations.

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CONTACT INFORMATION

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