

Comparative real world effectiveness of triple therapy versus dual bronchodilation in frequently exacerbating patients with COPD

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BACKGROUND

- The mainstay of therapeutic management in COPD is long-acting inhaled bronchodilators (LAMA and/or LABA).¹
- Addition of Inhaled Corticosteroids (ICS) to LAMA+LABA is recommended in patients at risk for further exacerbations.¹
- Randomized controlled clinical trials have shown significant incremental benefit with triple therapy (ICS+LAMA+LABA) compared to dual bronchodilators (LAMA+LABA) in reducing the rate of moderate-severe exacerbations.^{2,3}
- Confirmation of this superiority of triple therapy in a representative population with a longer follow-up is needed from real world effectiveness studies.

AIM

To compare the real world effectiveness of triple therapy with ICS+LAMA+LABA vs LAMA+LABA among frequently-exacerbating COPD patients and explore the impact of exacerbation history.

DESIGN & METHODOLOGY

Design: Matched historical cohort study.

Data sources: The Clinical Practice Research Datalink (CPRD, www.cprd.com) and Optimum Patient Care Research Database (OPCRD, opcrd.co.uk).

Index date: step-up from no maintenance therapy or LAMA

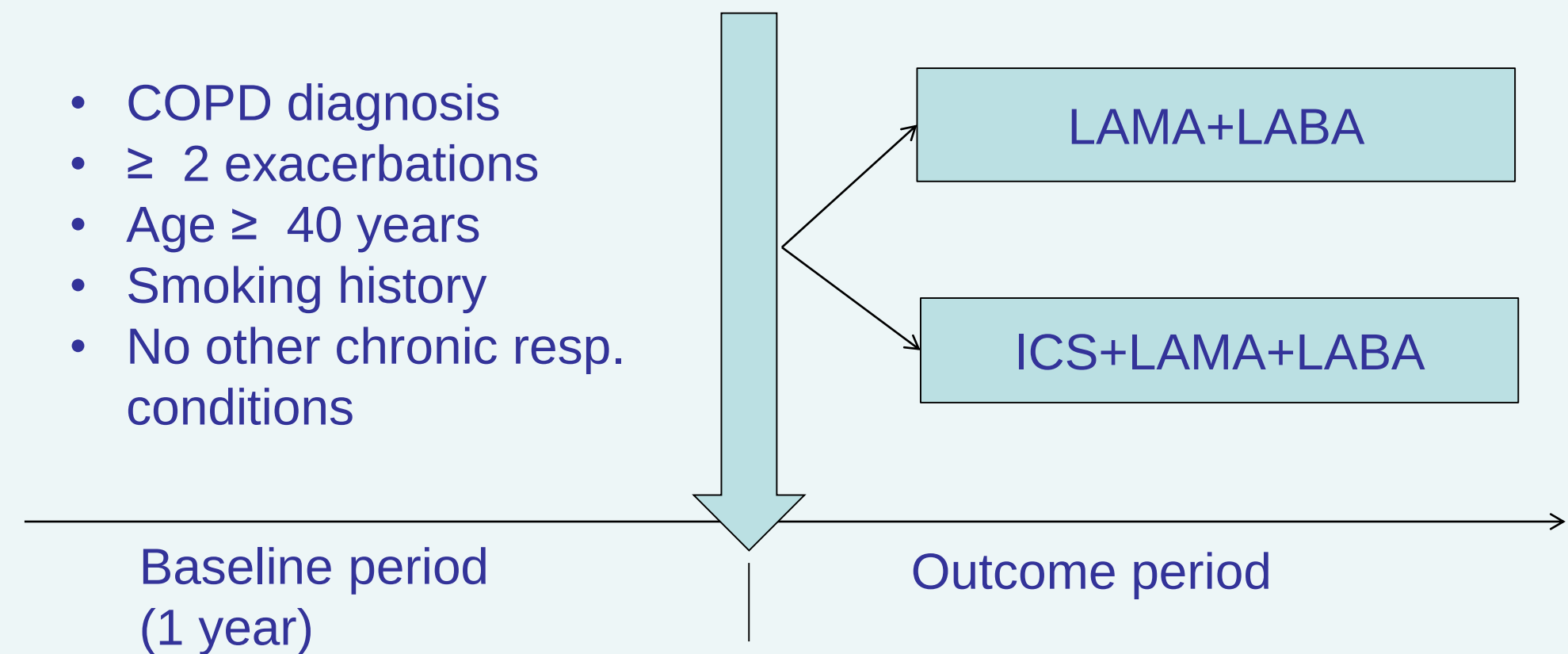


Figure 1 – Study design

Primary outcome:

- Time until 1st moderate/severe exacerbation.
Definition: respiratory-related: hospitalisation, A&E attendance, acute OCS course or antibiotics course.

Secondary outcomes:

- Time until 1st event:
 - Acute respiratory event: unplanned respiratory consultation.
 - Treatment failure: an exacerbation or additional therapy.
 - Acute OCS course.
 - Respiratory-related antibiotics courses.
 - Pneumonia diagnosis.
- Rate (number of events in 1st outcome year):
 - Moderate/severe exacerbations, Acute OCS courses, Respiratory-related antibiotics courses, Acute respiratory events.
- Recording of mMRC score ≥ 2 within 18 months (yes vs. no).

Exploratory outcomes (subpopulation with Hospital Episode Statistics):

- Time until 1st hospitalisation with COPD (ICD-10 J40-J44) as primary diagnosis.
- Time until 1st A&E attendance with COPD diagnosis.

Effect modifier:

Number of moderate/severe exacerbations in baseline year (interaction term of continuous variable and treatment in model)

Confounding handling approach:

Nearest neighbour propensity score calliper matching with a ratio of 1:3. Models were adjusted on residual confounders.

PATIENT SELECTION

Table 1 – Patient records selection flow

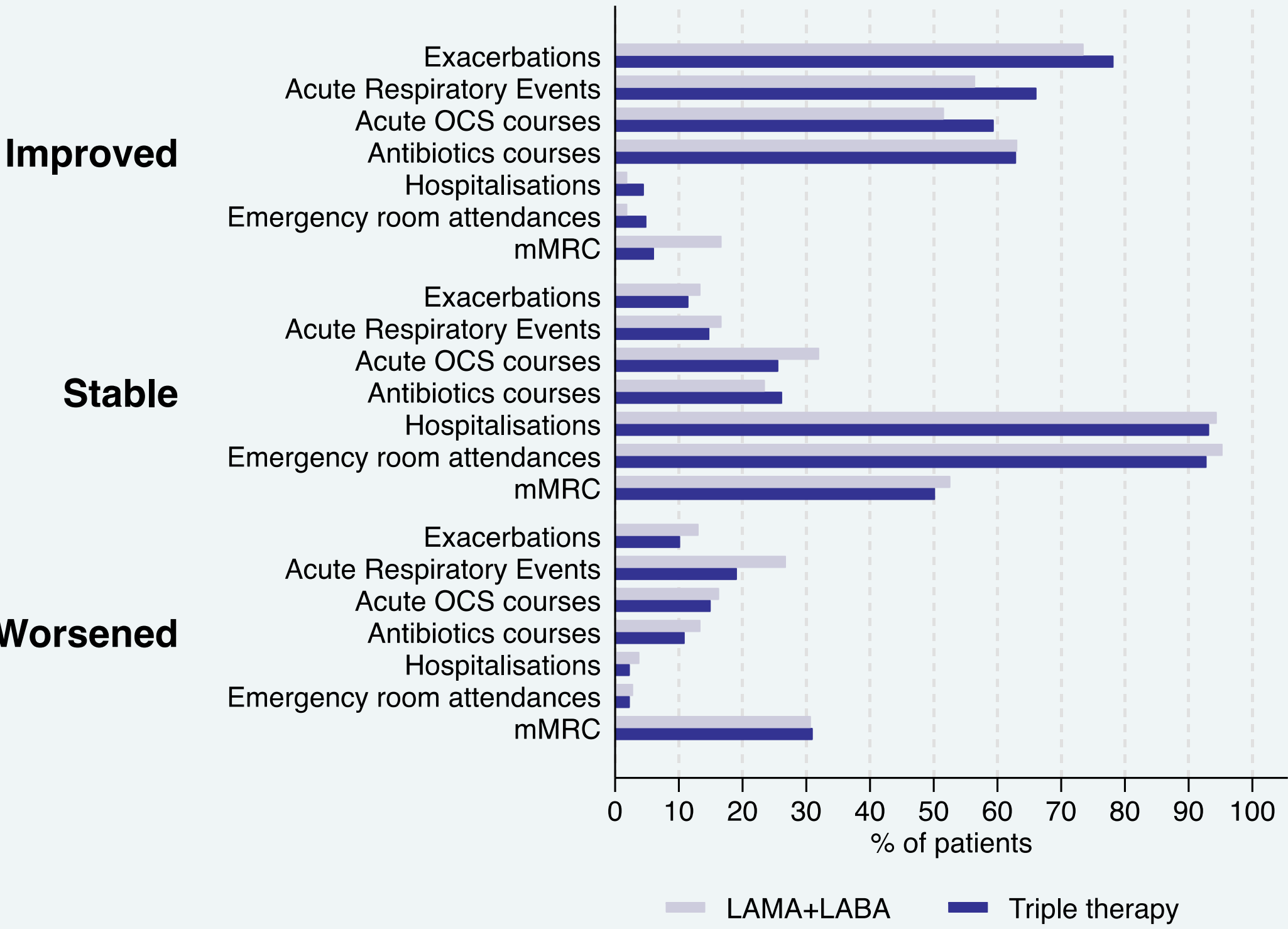
Step	LAMA+ LABA	Triple therapy
COPD diagnosis (Read code)	299,103	
Stepped up to LAMA+LABA or Triple therapy	7,194	69,480
≥ 1 year baseline data	6,840	62,579
Age ≥40 at diagnosis	6,830	62,408
Smoking history	6,605	59,926
No other chronic respiratory diseases	5,406	40,948
Prior therapy: No maintenance or LAMA	3,784	13,718
≥2 exacerbations in baseline	493	2,619
Matched patients	466	1,181

RESULTS

Table 2 – Baseline characteristics of matched patients

Variable		LAMA+ LABA (N=466)	Triple therapy (N=1,181)	SMD
Age (years)	Mean (SD)	69.2 (10.7)	69.4 (10.2)	2.0
Male gender	n (%)	233 (50.0)	603 (51.1)	2.1
Current smoker	n (%)	210 (45.1)	528 (44.7)	0.7
LAMA use	n (%)	327 (70.2)	838 (71.0)	1.8
Exacerbations	2, n (%)	287 (61.6)	698 (59.1)	3.4
	3, n (%)	105 (22.5)	284 (24.0)	
	4, n (%)	34 (7.3)	101 (8.6)	
	≥5, n (%)	40 (8.6)	98 (8.3)	
GOLD Grade	N (% non-missing)	389 (83.5)	976 (82.6)	7.9
	C, n (%)	236 (60.7)	554 (56.8)	
	D, n (%)	153 (39.3)	422 (43.2)	

SD: Standard deviation; SMD: Standardised mean difference.



Improved: Fewer events or lower score in outcome year (compared to baseline).
Stable: Same number of events or same score in outcome and baseline years.
Worsened: More events or higher score in outcome year (compared to baseline).

Figure 2 – Changes in COPD severity indicators from baseline year to first outcome year

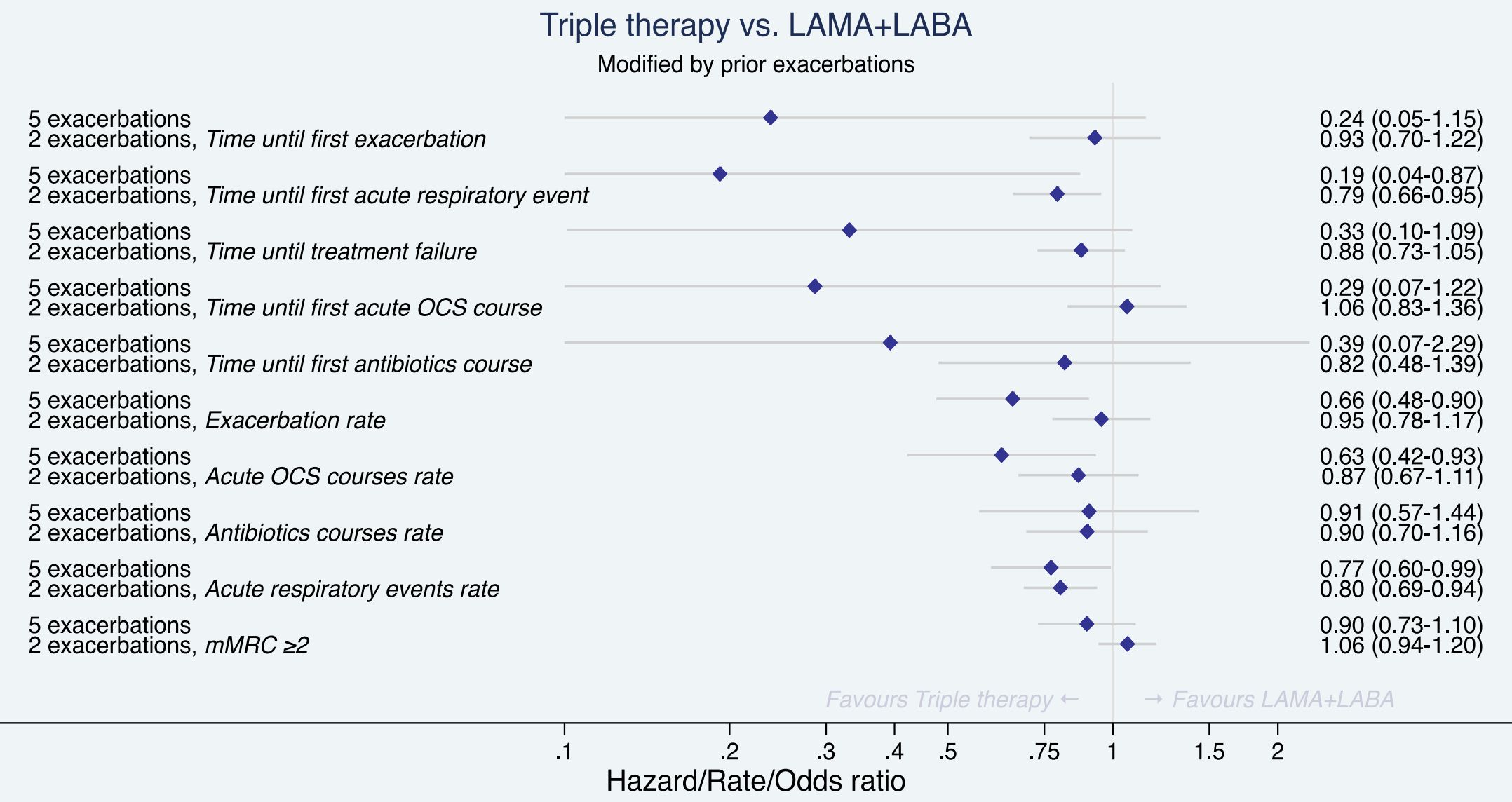
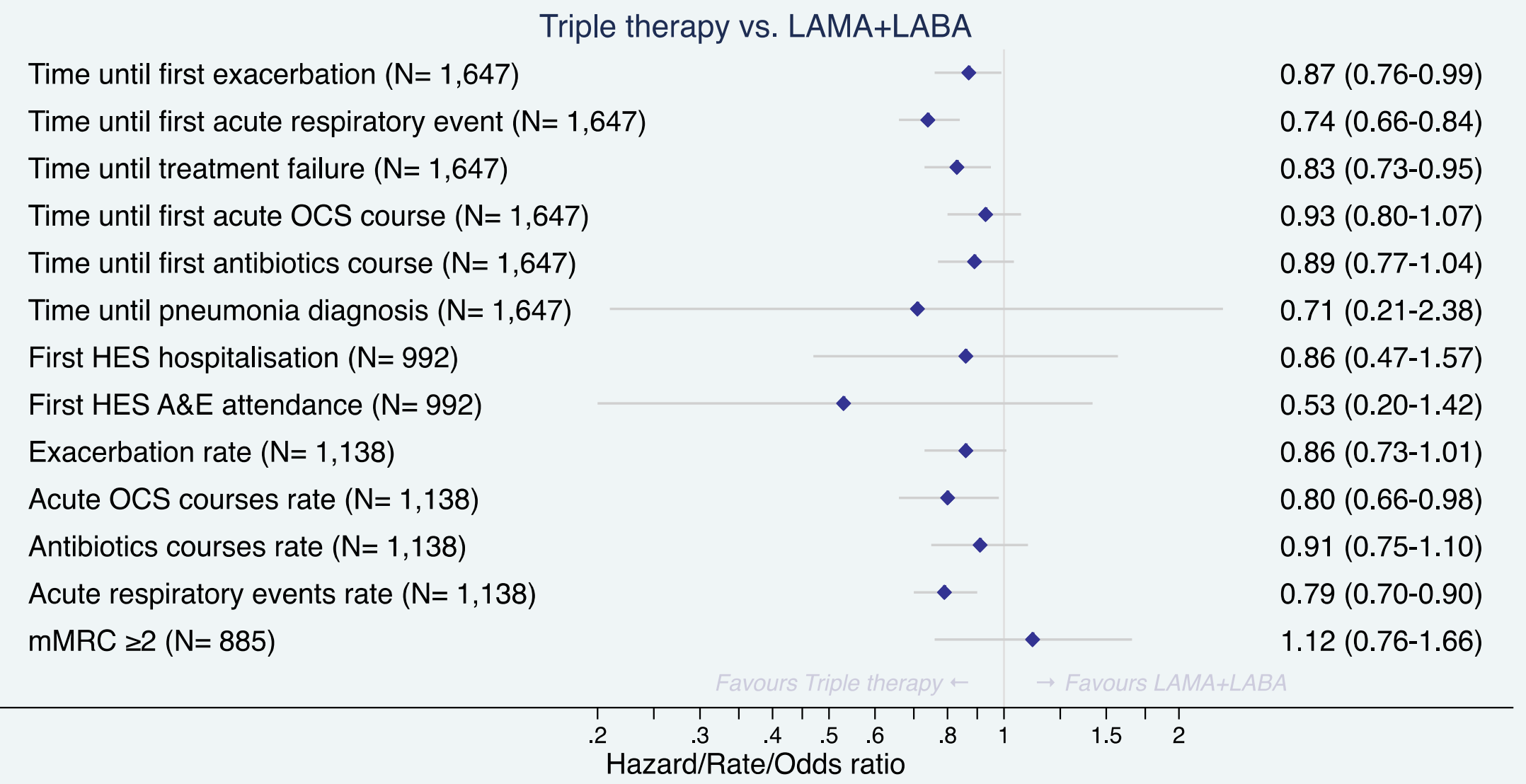


Figure 3 – Adjusted effect sizes with 95% confidence intervals

CONCLUSION

- Step-up from no maintenance therapy or LAMA to triple therapy was significantly associated with a larger reduction in the risk of exacerbation, acute respiratory event and treatment failure than a step-up to LAMA+LABA.
- This association in favor of triple therapy was significantly greater for patients with higher rates of exacerbations in the year prior to step-up.

References

1. GOLD report 2018; 2. Papi A *et al.* Lancet 2018; 391: 1076–84.
3. Lipson D *et al.* NEJM 2018;378:1671-80.

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