

J. Voorham<sup>1</sup>, M. Kerkhof<sup>1</sup>, M. Scuri<sup>2</sup>, S. Vezzoli<sup>2</sup>, I. Valente<sup>2</sup>, A. Papi<sup>3</sup>, C. Vogelmeier<sup>4</sup>, D. Singh<sup>5</sup>, L.M. Fabbri<sup>6,7</sup>, J.W.H Kocks<sup>1</sup>, D.P. Price<sup>1,8</sup>

<sup>1</sup>Observational and Pragmatic Research Institute - Singapore (Singapore), <sup>2</sup>Chiesi Farmaceutici S.p.A - Parma (Italy), <sup>3</sup>University of Ferrara - Ferrara (Italy), <sup>4</sup>University of Marburg - Marburg (Germany), <sup>5</sup>University of Manchester - Manchester (United Kingdom), <sup>6</sup>University of Modena and Reggio Emilia - Modena (Italy), <sup>7</sup>University of Gothenburg – Gothenburg (Sweden), <sup>8</sup>University of Aberdeen – Aberdeen (United Kingdom)

## BACKGROUND

- The mainstay of therapeutic management in COPD is long-acting inhaled bronchodilators (LAMA and/or LABA).<sup>1</sup>
- Addition of Inhaled Corticosteroids (ICS) to LAMA+LABA is recommended in patients at risk for further exacerbations.<sup>1</sup>
- 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.<sup>2,3</sup>
- 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.

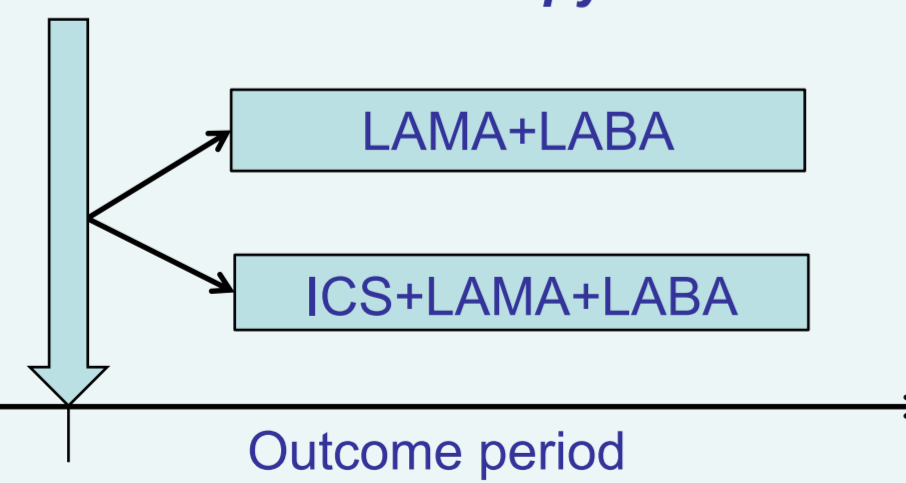
## DESIGN & METHODOLOGY

**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

- COPD diagnosis
- ≥ 2 exacerbations
- Age ≥ 40 years
- Smoking history
- No other chronic resp. conditions



**Figure 1 – Study design**

### References

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

## Primary outcome:

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

## Secondary outcomes:

- Time until 1<sup>st</sup> 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 1<sup>st</sup> 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:
- Time until 1<sup>st</sup> hospitalisation with COPD (ICD-10 J40-J44) as primary diagnosis (subpopulation with Hospital Episode Statistics (HES))
  - Time until 1<sup>st</sup> A&E attendance with COPD diagnosis (HES)

## 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**

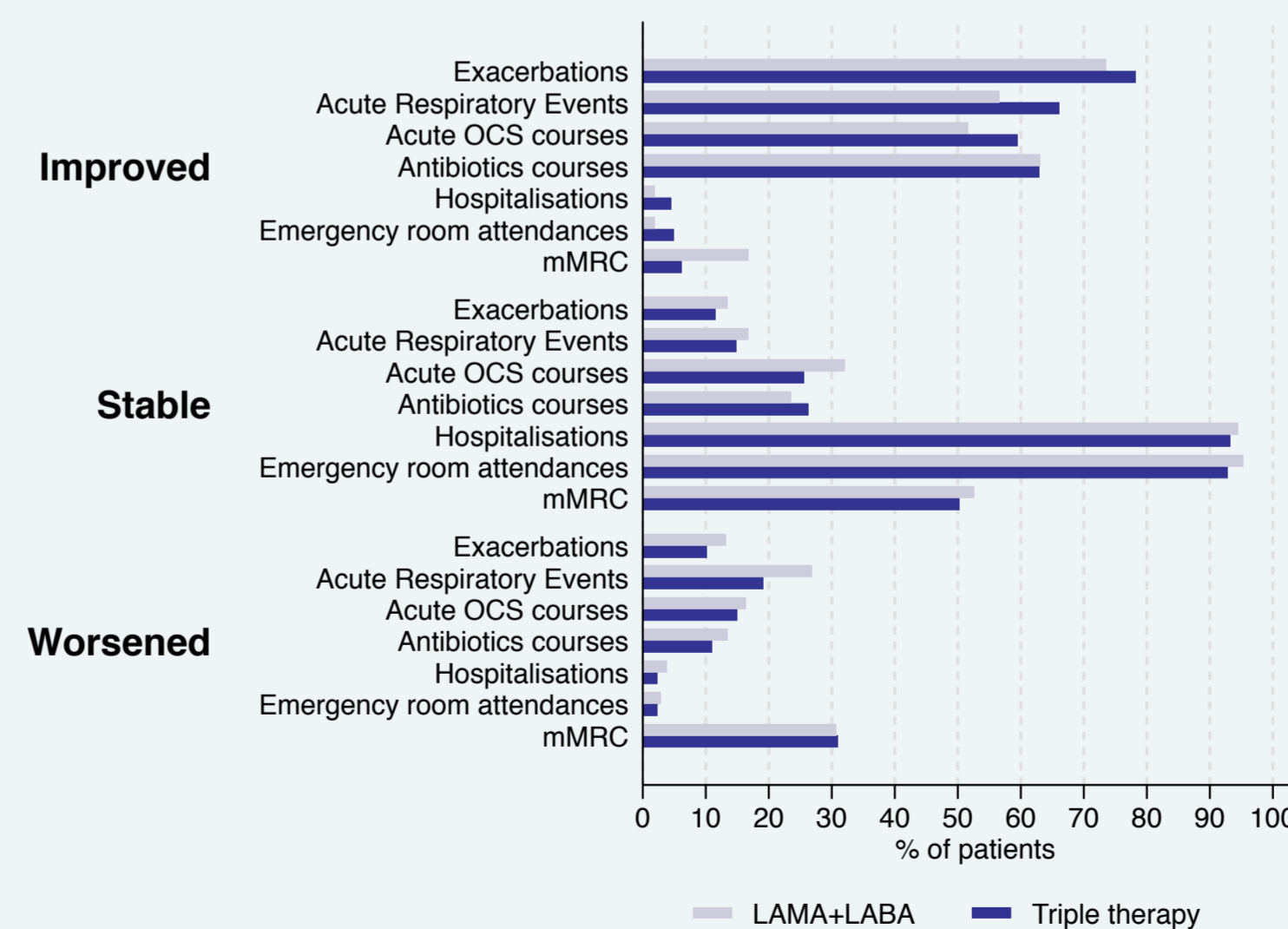
	LAMA+LABA	Triple therapy
COPD diagnosis (Read code)	299,103	
Stepped up to LAMA+LABA or Triple therapy	7,194	69,480
≥ 1 year baseline data	6,840	62,579
Age ≥40 at diagnosis	6,830	62,408
Smoking history	6,605	59,926
No other chronic respiratory diseases	5,406	40,948
Prior therapy: No maintenance or LAMA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

## RESULTS

**Table 2 – Baseline characteristics of matched patients**

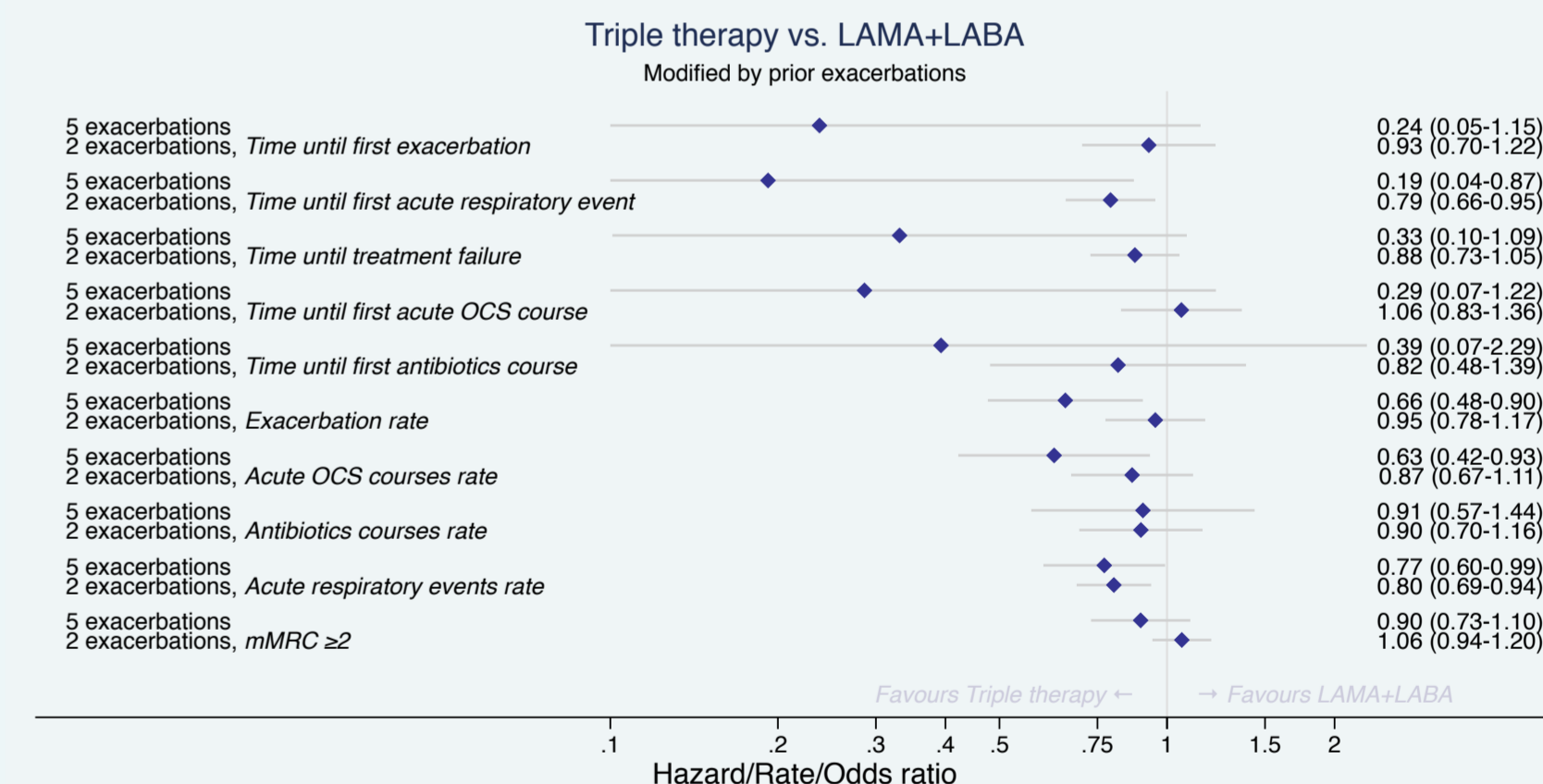
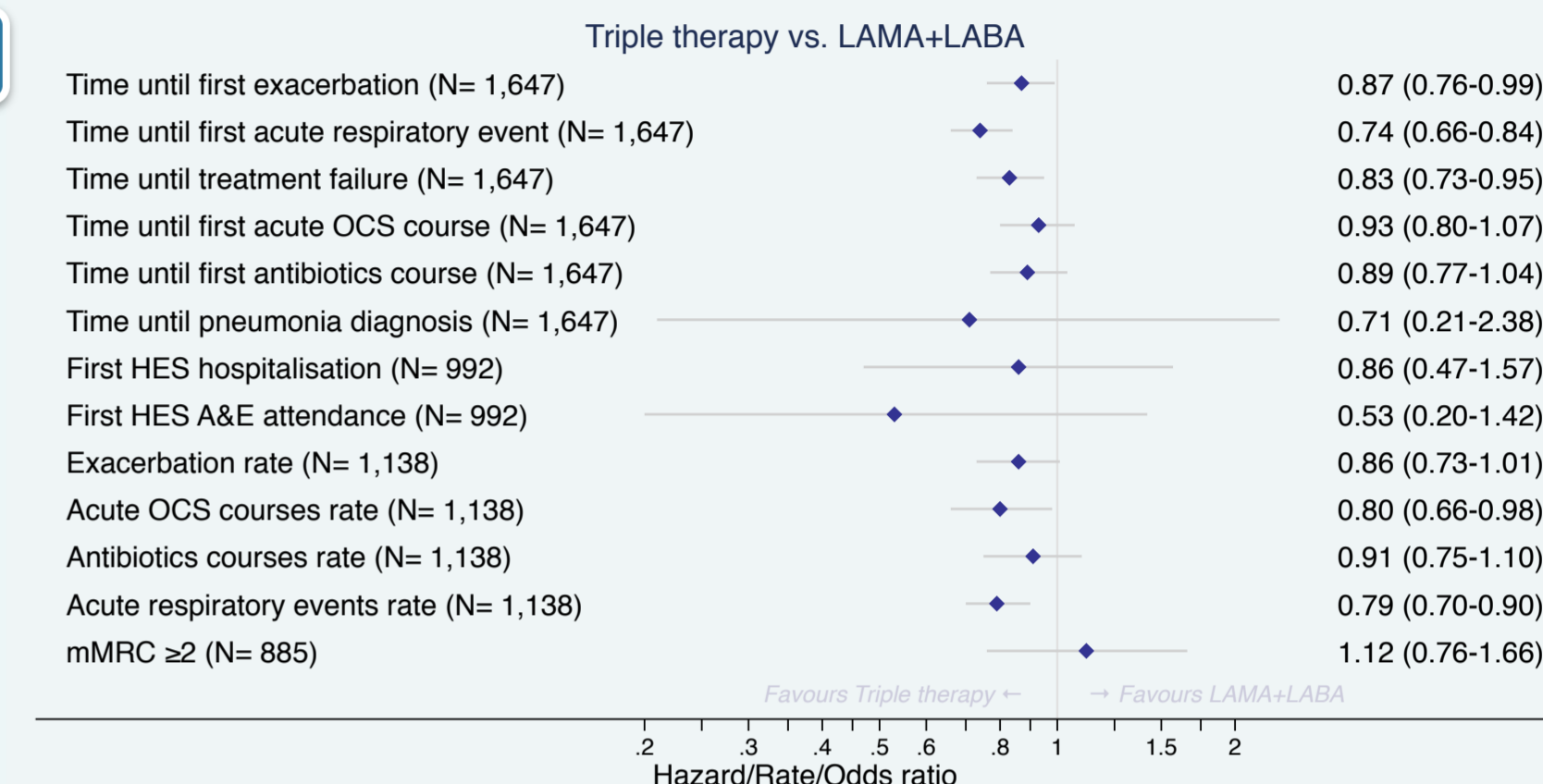
Variable		LAMA+LABA (N=466)	Triple therapy (N=1,181)	SMD
Age (years)	Mean (SD)	69.2 (10.7)	69.4 (10.2)	2.0
Male gender	n (%)	233 (50.0)	603 (51.1)	2.1
Current smoker	n (%)	210 (45.1)	528 (44.7)	0.7
LAMA use	n (%)	327 (70.2)	838 (71.0)	1.8
Exacerbations	2, n (%)	287 (61.6)	698 (59.1)	3.4
	3, n (%)	105 (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.

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