of budesonide/formoterol in the post-bronchodilator $FEV_1$50–<70% of predicted normal (PN) subpopulation versus the all-patient population. This analysis supported the EU label change for Symbicort® Turbuhaler® to: 'symptomatic treatment of patients with COPD with FEV_1 < 70% PN (post-bronchodilator) and an exacerbation history despite regular bronchodilator therapy'.

Methods Four randomised, double-blind, active- and/or placebo-controlled, studies in patients with moderate to very severe COPD were analysed. Key study inclusion criteria were pre-bronchodilator FEV_1 ≤50% PN; use of short-acting bronchodilator; ≥1 exacerbation in the past 12 months. Primary endpoints for the analysis were 3-month pre- and 3- and 12-months post-bronchodilator FEV_1 and exacerbation rates at 3- and 12-months. Secondary endpoints included dyspnoea score, total symptom score, reliever medication use, night-time awakening and St George's Respiratory Questionnaire. Results for the post-bronchodilator $FEV_1$50 – <70% PN subpopulation were compared with the all-patient population.

Results Of 3787 randomised patients, 832 (22.0%) had post-bronchodilator $FEV_1$50 – <70% PN. Baseline characteristics of the $FEV_1$50 – <70% subpopulation and the all-patient population were similar, except for baseline FEV_1 parameters. The benefit of budesonide/formoterol versus placebo and formoterol on the primary and secondary endpoints were generally consistent between the $FEV_1$50 – <70% subpopulation and the all-patient population across all four studies and in the pooled analysis (Figure 1). No new safety signals were identified.

Conclusions In patients with COPD, the clinical efficacy and safety of budesonide/formoterol compared with placebo and formoterol was consistent between the post-bronchodilator FEV_1 50 – <70% PN subpopulation and the all-patient population, confirming the positive benefit/risk ratio in COPD patients with a post-bronchodilator FEV_1 <70% PN and a history of exacerbations.

P59 FACTORS INFLUENCING STEP-UP TO LAMA+LABA/ICS IN COPD PATIENTS INITIALLY ON LAMA MONOTHERAPY: A THIN DATABASE STUDY

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The potentially inappropriate use of inhaled long-acting beta agonist/corticosteroid (LABA/ICS) combinations in COPD patients for whom this treatment is not recommended has clinical and economic implications.

This retrospective analysis of anonymized electronic medical records in the UK Health Improvement Network (THIN) database was conducted to identify factors associated with step-up from long-acting muscarinic antagonist (LAMA) to LAMA +LABA/ICS therapy. Secondary objectives included time to step-up, Global Initiative for Chronic Obstructive Lung Disease (GOLD) and Medical Research Council (MRC) classification. Data were included from COPD patients between 1 June 2010 and 4 September 2014, aged ≥35 years at first LAMA treatment, with continuous enrolment >360 days before the index event (date of first LAMA prescription) who received LAMA monotherapy only prior to step-up. Time to step-up was analysed using a Cox regression model with time-varying covariates using a stepwise model selection procedure.

Data from 8773 patients (6199 LAMA [136 deaths]; 2438 LAMA+LABA/ICS) were included. Multivariable analysis revealed that exacerbations (composite), elective secondary care contact, markers of COPD proactive planned care, and reactive COPD care within the primary care setting were clinically and statistically significantly associated with step-up. Statistically significant factors negatively associated with step-up were being female and having diabetes (Table). Univariate analysis revealed FEV1, COPD severity and MRC classification to be significant predictors of step-up. These were not included in the multivariable model due to reduced observations, but sensitivity analyses including each in turn confirmed the above predictors. 28% of the cohort received step-up therapy, the majority (23%) within 2 years of LAMA monotherapy initiation. Assessment per GOLD classification suggests that step-up was appropriate in most patients (group A, 18%; B, 21%; C, 26%; D, 35%). Assessment of MRC score (mean, median) in the step-up group (baseline: 2.45, 2.00; follow-up: 2.74, 3.00) suggests that patients who were stepped-up became more symptomatic prior to step-up.

These results show that COPD exacerbations were the most significant predictor of therapy step-up and that patients with initially stable disease are unlikely to require step-up. Therapy step-up appears to be appropriate in the majority of, but not all patients, and may reflect adherence to national guidelines.

Abstract P59 Table 1

Variable	Multivariate Cox Regression Analysis		
	HR	95% CI	P-value
Composite: exacerbations[a]	2.380	2.170, 2.611	<0.0001
Elective secondary care contact	1.445	1.305, 1.601	<0.0001
Markers of COPD proactive planned care within primary care setting	1.268	1.231, 1.305	<0.0001
Reactive COPD care within primary care setting	1.155	1.115, 1.198	<0.0001
Composite: cardiovascular[b]	1.150	1.025, 1.291	0.0175
Number of cough symptoms	1.086	1.046, 1.128	<0.0001
Number of short-acting bronchodilator prescriptions	1.033	1.027, 1.038	<0.0001
Age at index date[c]	0.992	0.988, 0.995	<0.0001
Sex (female)	0.798	0.735, 0.867	<0.0001
Diabetes	0.685	0.530, 0.886	0.0039

AECOPD, acute exacerbation of COPD; CI, confidence interval; HR, hazard ratio.
[a]Exacerbations (COPD emergency admission or AECOPD or lower respiratory tract infection or oral corticosteroid + antibiotic)
[b]Combined comorbidity for cardiovascular risk (heart failure, congestive heart disease, hypertensive disease, cerebrovascular disease, atrial fibrillation)
[c]HR relative to change to every 1 year difference in age.

P60 EFFECT OF INDACATEROL/GLYCOPYRRONIUM (IND/GLY) ON PATIENT-REPORTED OUTCOMES IN MEN AND WOMEN WITH COPD: A POOLED ANALYSIS FROM THE IGNITE PROGRAMME

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Introduction Literatures, although limited, suggest differences in the manifestations of COPD in terms of symptoms and health-related quality of life between men and women. Moreover, a