Table S1. Summary of SLR protocol (broad criteria).

Objectives and research questions	
Primary objectives	• To assess the evidence supporting the relative treatment effect of inhaled therapies for the maintenance treatment of moderate-to-very severe COPD • To assess the evidence supporting the safety and tolerability profiles of different inhaled therapies for the maintenance treatment of COPD
Secondary objective	• To determine the relative treatment effect of GFF MDI compared with other LABA/LAMA FDCs in the treatment of moderate-to-very severe COPD, based on improvement in lung function (FEV_1) and other outcomes (e.g. exacerbations, SGRQ, rescue medication)
Studies to include	
Population	• Age: Adults • Gender: Any • Race: Any • Disease: Moderate-to-very severe COPD (% predicted FEV_1: ≤80%)
Interventions	**LABA** • Salmeterol • Formoterol • Bambuterol, R-bambuterol, levobambuterol • Indacaterol • Olodaterol • Abediterol • Clenbuterol • Vilanterol • Arformoterol
	LAMA • Tiotropium • Aclidinium • Glycopyrronium/glycopyrrolate • Umeclidinium
	LABA + LAMA • Vilanterol/umeclidinium • Formoterol/glycopyrrolate, GFF • Formoterol/tiotropium • Arformoterol/tiotropium • QVA149 (indacaterol/glycopyrrolate) • Olodaterol/tiotropium • Formoterol/aclidinium
Comparators	• Any included FDC or monocomponent/monotherapy • Placebo
Study design	• RCTs (irrespective of blinding status and number of arms randomized)
Language	• English language studies
Publication timeframe	• Database inception to October 2018
Databases	• Embase® • MEDLINE® • MEDLINE® In-Process • CENTRAL

	• Clinical trial registries • Conference proceedings
Information to extract	
Study information	• Study objective • Study setting • Blinding status • Randomization stratification variables • Study phase • Study country • Run-in duration • Inclusion/exclusion criteria • Study duration • Study methods • Primary and secondary endpoints, covariates used in the analysis • Safety variables • Concomitant medications • Therapies in run-in period • Statistical methods and sample size calculation • Analysis type (ITT/mITT/PP) • Number of patients enrolled • Number of patients randomized • Number of patients analyzed • Author's conclusions and comments
Treatment details	• Treatment arms • Treatment protocol and dosing details (including average dose received and administration details) • Number of patients randomized (per treatment arm) • Route of administration
Baseline characteristics	• Age • Gender • Race • Proportion of patients with disease stage (II, III, IV, II/III) • Disease duration • Comorbidities • Prior treatment, ICS use or medication history • Prior history of exacerbation • History of hospitalization • FEV_1/FVC • Baseline symptom score (TDI, mMRC) • CAT score category (≥10 *versus* <10), if reported
Efficacy and QOL outcomes	• Pre-bronchodilator FEV_1, post-bronchodilator FEV_1, peak FEV_1, trough FEV_1, AUC-FEV_1 • Use of rescue medication • Symptom-free days • Definition of exacerbation • Number of patients with exacerbations (moderate/composite of moderate and severe/severe) • Total number of exacerbations experienced over the duration of the study (moderate/composite of moderate and severe/severe) • Mean rate of exacerbations per patient per year (moderate/composite of moderate and severe/severe)

	• Time to first exacerbation (moderate/composite of moderate and severe/severe) • Exercise capacity (6MWT, ISWT) • Global Assessment of Change Questionnaire, number of respondents according to Global Assessment of Change Questionnaire • SGRQ (change from baseline and responders), SGRQ-C, CRDQ • Dyspnea measurements including symptom diary scores, TDI including proportion of patients within each group achieving a clinically meaningful change (≥1 unit) in TDI focal score, or Borg dyspnea scores • MRC/mMRC dyspnea scale • Sleep score • EQ-5D, SF-36 scores • CDLM questionnaire • EMSCI • Night-time awakenings • Symptom score (total, day-time, night-time)
Safety outcomes	• Any AEs • Any SAEs • Specific AEs (cough, dyspnea, headache, upper respiratory tract infection)
Tolerability outcomes	• All withdrawals
Critical appraisal	• NICE checklist for RCTs
Analyses	• All NMA were conducted using Bayesian NMA models available from NICE DSU

AE, adverse event; AUC, area under curve; BSC, best supportive care; CAT, COPD assessment test; CDLM, capacity of daily living during the morning; COPD, chronic obstructive pulmonary disease; CRDQ, chronic respiratory disease questionnaire; Embase, Excerpta Medica dataBASE; EMSCI, early morning symptoms of COPD instrument; EQ-5D, EuroQol-5D; FDC, fixed dose combination; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GFF MDI, glycopyrrolate/formoterol fumarate metered dose inhaler; ICS, inhaled corticosteroids; ISWT, incremental shuttle walking test; ITT, intent-to-treat; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; MEDLINE, medical literature analysis and retrieval system online; mITT, modified intent-to-treat; mMRC, modified Medical Research Council dyspnea scale; 6MWT, 6-minute walking test; NICE DSU, National Institute for Health and Care Excellence Decision Support Unit; NMA, network meta-analysis; PP, per protocol; QOL, quality of life; RCT, randomized controlled trial; SAE, serious adverse event; SF-36, Short Form-36; SGRQ, St George's Respiratory Questionnaire; SGRQ-C, COPD-specific version of SGRQ; SLR, systematic literature review; TDI, transition dyspnea index.