

SUPPLEMENTARY MATERIAL

Comparative Effectiveness of Fluticasone Furoate/Umeclidinium/Vilanterol and Budesonide/Glycopyrrrolate/Formoterol Fumarate in US Patients with Chronic Obstructive Pulmonary Disease

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Table S1 List of ICD-10-CM diagnosis codes

ICD-10-CM	Description	COPD	COPD exacerbation
<i>J20</i>	<i>Acute bronchitis</i>		
J20.0	Acute bronchitis due to <i>Mycoplasma pneumoniae</i>		X
J20.1	Acute bronchitis due to <i>Hemophilus influenzae</i>		X
J20.2	Acute bronchitis due to streptococcus		X
J20.3	Acute bronchitis due to coxsackievirus		X
J20.4	Acute bronchitis due to parainfluenza virus		X
J20.5	Acute bronchitis due to respiratory syncytial virus		X
J20.6	Acute bronchitis due to rhinovirus		X
J20.7	Acute bronchitis due to echovirus		X
J20.8	Acute bronchitis due to other specified organisms		X
J20.9	Acute bronchitis, unspecified		X
J40	Bronchitis, not specified as acute or chronic		X
<i>J41</i>	<i>Simple and mucopurulent chronic bronchitis</i>		
J41.0	Simple chronic bronchitis	X	X
J41.1	Mucopurulent chronic bronchitis	X	X
J41.8	Mixed simple and mucopurulent chronic bronchitis	X	X
J42	Unspecified chronic bronchitis	X	X
<i>J43</i>	<i>Emphysema</i>		
J43.0	Unilateral pulmonary emphysema [MacLeod's syndrome]	X	X
J43.1	Panlobular emphysema	X	X
J43.2	Centrilobular emphysema	X	X
J43.8	Other emphysema	X	X
J43.9	Emphysema, unspecified	X	X
<i>J44</i>	<i>Other chronic obstructive pulmonary disease</i>		
J44.0	Chronic obstructive pulmonary disease with acute lower respiratory infection	X	X
J44.1	Chronic obstructive pulmonary disease with (acute) exacerbation	X	X
J44.9	Chronic obstructive pulmonary disease, unspecified	X	X
<i>J45</i>	<i>Mild intermittent asthma</i>		
J45.20	Mild intermittent asthma, uncomplicated		X
J45.21	Mild intermittent asthma with (acute) exacerbation		X
J45.22	Mild intermittent asthma with status asthmaticus		X
J45.31	Mild persistent asthma with (acute) exacerbation		X
J45.32	Mild persistent asthma with status asthmaticus		X
J45.41	Moderate persistent asthma with (acute) exacerbation		X
J45.42	Moderate persistent asthma with status asthmaticus		X
J45.51	Severe persistent asthma with (acute) exacerbation		X
J45.52	Severe persistent asthma with status asthmaticus		X
J45.901	Unspecified asthma with (acute) exacerbation		
J45.902	Unspecified asthma with status asthmaticus		X
J45.909	Unspecified asthma, uncomplicated		X
J45.998	Other asthma		X
J47.1	Bronchiectasis with (acute) exacerbation		X
J80	Acute respiratory distress syndrome		X
<i>J96.0</i>	<i>Acute respiratory failure</i>		
J96.00	Acute respiratory failure, unspecified whether with hypoxia or hypercapnia		X
J96.01	Acute respiratory failure with hypoxia		X
J96.02	Acute respiratory failure with hypercapnia		X
<i>J96.2</i>	<i>Acute and chronic respiratory failure</i>		

J96.20	Acute and chronic respiratory failure, unspecified whether with hypoxia or hypercapnia	X
J96.21	Acute and chronic respiratory failure with hypoxia	X
J96.22	Acute and chronic respiratory failure with hypercapnia	X
<i>J96.9</i>	<i>Respiratory failure, unspecified</i>	
J96.90	Respiratory failure, unspecified, unspecified whether with hypoxia or hypercapnia	X
J96.91	Respiratory failure, unspecified with hypoxia	X
J96.92	Respiratory failure, unspecified with hypercapnia	X
R09.2	Respiratory arrest	X

COPD chronic obstructive pulmonary disease, *ICD-10-CM* International Classification of Diseases, 10th Revision, Clinical Modification

Table S2 List of drug codes for FF/UMEC/VI and BUD/GLY/FORM

NDC	Dosage strength^a	Description
<i>FF/UMEC/VI</i>		
0173-0887-10	100 µg/L, 62.5 µg/L, 25 µg/L	TRELEGY ELLIPTA 30 inhalations (60 blisters)
0173-0887-14	100 µg/L, 62.5 µg/L, 25 µg/L	TRELEGY ELLIPTA 14 inhalations (28 blisters), institutional pack
0173-0887-61	100 µg/L, 62.5 µg/L, 25 µg/L	TRELEGY ELLIPTA 14 inhalations (28 blisters)
0173-0893-10	200 µg/L, 62.5 µg/L, 25 µg/L	TRELEGY ELLIPTA 30 inhalations (60 blisters)
0173-0893-14	200 µg/L, 62.5 µg/L, 25 µg/L	TRELEGY ELLIPTA 14 inhalations (28 blisters), institutional pack
0173-0893-61	200 µg/L, 62.5 µg/L, 25 µg/L	TRELEGY ELLIPTA 14 inhalations (28 blisters)
<i>BUD/GLY/FORM</i>		
0310-4616-12	160 µg/L, 4.8 µg/L, 9 µg/L	BREZTRI AEROSPACE
0310-4616-28	160 µg/L, 4.8 µg/L, 9 µg/L	BREZTRI AEROSPACE
0310-4616-39	160 µg/L, 4.8 µg/L, 9 µg/L	BREZTRI AEROSPHERE, institutional pack

^aOnly Trelegy Ellipta with dosage 100 µg/L, 62.5 µg/L, 25 µg/L is indicated at initiation of COPD therapy

BUD/GLY/FORM budesonide/glycopyrrolate/formoterol fumarate, *COPD* chronic obstructive pulmonary disease, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *NDC* National Drug Code

Table S3 Follow-up rate of HRU in patients with Medicare FFS coverage, weighted cohorts

Follow-up HRU	Rate, PPY		RR (95% CI) ^a [A]/[B]	P value ^a
	FF/UMEC/VI N = 32,312 [A]	BUD/GLY/FORM N = 12,230 [B]		
Observation period, days, mean ± SD [median]	347 ± 272 [276]	339 ± 268 [268]		
Total person-years	30,694	11,344		
All-cause HRU^b				
Hospitalizations	0.23	0.23	0.99 (0.92–1.06)	0.714
ED visits	1.52	1.48	1.03 (0.96–1.10)	0.426
OP visits	30.04	30.13	1.00 (0.97–1.03)	0.863

^aRRs, CIs, and P values were calculated from Poisson regression models with a log-link function and robust standard errors

^bAll-cause HRU includes many health visits unrelated to COPD (e.g., inpatient/hospital visits for cancer screening and comorbid conditions, OP visits for optometry and dental, and ED visits for falls and other conditions). Roughly one-third of OP and ED visits were associated with a diagnosis code for COPD, respectively, while slightly more than half of hospitalizations included a diagnostic code for COPD

BUD/GLY/FORM budesonide/glycopyrrolate/formoterol fumarate, *CI* confidence interval, *ED* emergency department, *FFS* Fee-for-Service, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *HRU* healthcare resource utilization, *OP* outpatient, *PPY* per patient-year, *RR* rate ratio, *SD* standard deviation

Table S4 Baseline demographic and clinical characteristics of patients with Medicare FFS coverage

Characteristics	Unweighted cohorts			Weighted cohorts ^a		
	FF/UMEC/VI N = 32,312	BUD/GLY/FORM N = 12,230	Std. diff. ^{b,c} (%)	FF/UMEC/VI N = 32,312	BUD/GLY/FORM N = 12,230	Std. diff. ^{b,c} (%)
Observation period,^d days, mean ± SD [median]	364 ± 281 [291]	333 ± 265 [263]	11.3	347 ± 272 [276]	339 ± 268 [268]	3.0
Demographics^e						
Age, years, mean ± SD [median]	74.2 ± 8.5 [74]	73.6 ± 8.4 [74]	7.2	73.8 ± 8.6 [74]	73.8 ± 8.4 [74]	0.0
Age ≥65, n (%)	28,122 (87.0)	10,482 (85.7)	3.9	27,803 (86.0)	10,530 (86.1)	0.2
Sex, n (%)						
Female	17,519 (54.2)	6567 (53.7)	1.1	17,379 (53.8)	6578 (53.8)	0.0
Male	14,791 (45.8)	5662 (46.3)	1.0	14,931 (46.2)	5651 (46.2)	0.0
Unknown	2 (0.0)	1 (0.0)	0.2	2 (0.0)	1 (0.0)	0.4
Region, n (%)						
South	14,417 (44.6)	5711 (46.7)	4.2	14,914 (46.2)	5650 (46.2)	0.1
Midwest	6821 (21.1)	2317 (18.9)	5.4	6308 (19.5)	2387 (19.5)	0.0
Northeast	6325 (19.6)	2228 (18.2)	3.5	6012 (18.6)	2276 (18.6)	0.0
West	4735 (14.7)	1973 (16.1)	4.1	5063 (15.7)	1916 (15.7)	0.0
Other/unknown	14 (0.0)	1 (0.0)	2.2	15 (0.0)	1 (0.0)	2.3
Race, n (%)						
White	28,034 (86.8)	10,476 (85.7)	3.2	27,776 (86.0)	10,513 (86.0)	0.0
Black or African American	2068 (6.4)	770 (6.3)	0.4	2169 (6.7)	758 (6.2)	2.1
Other ^f	1712 (5.3)	793 (6.5)	5.0	1840 (5.7)	773 (6.3)	2.6
Unknown	498 (1.5)	191 (1.6)	0.2	527 (1.6)	186 (1.5)	0.9
Year of index date, n (%)						
2021	12,205 (37.8)	3661 (29.9)	16.6	10,316 (31.9)	3905 (31.9)	0.0
2022	10,519 (32.6)	4176 (34.1)	3.4	10,973 (34.0)	4153 (34.0)	0.0
2023	9588 (29.7)	4393 (35.9)	13.3	11,023 (34.1)	4172 (34.1)	0.0
Prescriber specialty at index, n (%)						
Primary care ^g	13,546 (41.9)	5256 (43.0)	2.1	13,797 (42.7)	5225 (42.7)	0.1
Respiratory specialist ^h	12,371 (38.3)	4618 (37.8)	1.1	12,238 (37.9)	4632 (37.9)	0.0
Other	6143 (19.0)	2260 (18.5)	1.4	6020 (18.6)	2278 (18.6)	0.0
Missing	252 (0.8)	96 (0.8)	0.1	258 (0.8)	94 (0.8)	0.3
Pulmonary function testing^{ij}, n (%)	7689 (23.8)	3065 (25.1)	2.9	7977 (24.7)	3019 (24.7)	0.0

Quan-CCI score^{i,k}, mean ± SD						
[median]	2.77 ± 1.93 [3]	2.63 ± 1.89 [2]	7.1	2.67 ± 1.89 [2]	2.67 ± 1.91 [2]	0.0
HRU^l						
Patients with ≥1 visit, <i>n</i> (%)						
Hospitalizations	4366 (13.5)	1448 (11.8)	5.0	3964 (12.3)	1500 (12.3)	0.0
ED visit	16,706 (51.7)	5925 (48.4)	6.5	15,938 (49.3)	6032 (49.3)	0.0
OP visit	31,968 (98.9)	12,086 (98.8)	1.1	31,941 (98.9)	12,090 (98.9)	0.0
Number of HRU events, mean ± SD						
[median]						
Hospitalizations	0.20 ± 0.64 [0]	0.17 ± 0.58 [0]	5.0	0.18 ± 0.60 [0]	0.18 ± 0.60 [0]	0.3
ED visits	1.54 ± 4.94 [1]	1.40 ± 4.98 [0]	3.0	1.47 ± 4.80 [0]	1.42 ± 5.05 [0]	1.1
OP visits	28.8 ± 34.2 [20]	28.2 ± 35.0 [19]	2.0	28.2 ± 33.9 [19]	28.3 ± 35.0 [19]	0.4
Healthcare costs^{l,m}, \$US 2023, mean ± SD						
Total costs (medical and pharmacy)	22,023 ± 32,907	21,095 ± 30,870	2.9	21,337 ± 32,180	21,337 ± 31,393	0.0
Total medical costs	15,083 ± 30,073	14,052 ± 27,907	3.6	14,333 ± 29,184	14,333 ± 28,485	0.0
Hospital visit costs	3106 ± 12,331	2636 ± 11,611	3.9	2743 ± 11,316	2751 ± 11,961	0.1
ED visit costs	2015 ± 8885	1745 ± 8617	3.1	1831 ± 8416	1809 ± 8884	0.3
OP visit costs	9962 ± 23,318	9670 ± 20,803	1.3	9760 ± 23,246	9773 ± 21,024	0.1
Pharmacy costs	6941 ± 11,903	7043 ± 11,176	0.9	7004 ± 12,104	7004 ± 11,140	0.0
SITT pharmacy costs on the index date	764 ± 378	725 ± 381	10.2	736 ± 352	736 ± 391	0.0

^aPatients on FF/UMEC/VI and BUD/GLY/FORM were weighted using the overlap weighting approach based on the PS to adjust for confounding. Variables used in the PS calculation included the following: age, sex, race, year of index date, physician specialty at index, US region, pulmonary testing at baseline, Quan-CCI score, COPD exacerbations at baseline and on the index date, baseline medication use (agents with ≥5% use in either cohort), baseline HRU and medical costs, SITT pharmacy costs on the index date, and comorbidities (conditions with ≥5% prevalence in either cohort)

^bFor continuous variables, the standardized difference was calculated by dividing the absolute difference in means of the control and the case by the pooled SD of both groups. The pooled SD is the square root of the average of the squared SDs

^cFor dichotomous variables, the standardized difference was calculated using the following equation where P is the respective proportion of patients in each group: $|(\text{Pcase} - \text{Pcontrol})| / \sqrt{[(\text{Pcase}(1 - \text{Pcase}) + \text{Pcontrol}(1 - \text{Pcontrol}))/2]}$

^dThe observation period spanned from the day after the index date up to the earliest end of clinical activity, end of data availability, death, or switch to the other SITT

^eEvaluated on the index date (i.e., the date of the first pharmacy claim for single-inhaler FF/UMEC/VI or BUD/GLY/FORM)

^fOther races included Hispanic or Latino, Asian or Pacific Islander, and other

^gPrimary care physician included family practice physician, general medicine physician, nurse practitioner, and internal medicine physician

^hRespiratory specialist included pulmonologist and pediatric pulmonology physician. Respiratory specialist was prioritized among patients with both a primary care and respiratory specialist (i.e., respiratory specialist and primary care are mutually exclusive)

ⁱEvaluated during the 12-month baseline period, not including the index date

^jIncluded spirometry, lung volume, diffusion capacity, and pulmonary stress testing

^kReference: Quan H et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43(11):1130–39

^lEvaluated during the 12-month baseline period, including the index date

^mCosts were inflated to \$US 2023 using the US Medical Care consumer price index from the Bureau of Labor Statistics from the US Department of Labor

BUD/GLY/FORM budesonide/glycopyrrolate/formoterol fumarate, *COPD* chronic obstructive pulmonary disease, *ED* emergency department, *FFS* Fee-for-Service, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *HRU* healthcare resource utilization, *OP* outpatient, *P* proportion of patients, *PS* propensity score, *Quan-CCI* Quan-Charlson comorbidity index, *SD* standard deviation, *SITT* single-inhaler triple therapy, *std. diff.* standardized difference

Table S5 Baseline medication use in patients with Medicare FFS coverage

Medication use, ^a <i>n</i> (%)	Unweighted cohorts					Weighted cohorts ^b				
	FF/UMEC/VI		BUD/GLY/FORM		Std. diff. ^c (%)	FF/UMEC/VI		BUD/GLY/FORM		Std. diff. ^c (%)
	<i>N</i> = 32,312		<i>N</i> = 12,230			<i>N</i> = 32,312		<i>N</i> = 12,230		
Maintenance controller medications										
Dual therapy (ICS/LABA or LAMA/LABA)	16,681	(51.6)	6784	(55.5)	7.7	17,545	(54.3)	6642	(54.3)	0.0
ICS/LABA	11,060	(34.2)	5053	(41.3)	14.7	12,696	(39.3)	4805	(39.3)	0.0
LAMA/LABA	6243	(19.3)	1975	(16.1)	8.3	5497	(17.0)	2081	(17.0)	0.0
LAMA	6494	(20.1)	2563	(21.0)	9.5	6640	(20.6)	2513	(20.6)	0.0
Leukotriene modifiers	4909	(15.2)	2293	(18.7)	2.1	5700	(17.6)	2157	(17.6)	0.0
MITT	4305	(13.3)	2010	(16.4)	8.8	5001	(15.5)	1893	(15.5)	0.0
ICS	2218	(6.9)	934	(7.6)	3.0	2387	(7.4)	904	(7.4)	0.0
PDE4 inhibitors	571	(1.8)	372	(3.0)	8.3	624	(1.9)	358	(2.9)	6.5
LABA	374	(1.2)	175	(1.4)	2.4	390	(1.2)	174	(1.4)	1.9
Methylxanthines	266	(0.8)	166	(1.4)	5.1	291	(0.9)	163	(1.3)	4.1
Mast cell stabilizers	2	(0.0)	1	(0.0)	0.2	2	(0.0)	1	(0.0)	0.3
Rescue medications										
Antibiotics	22,562	(69.8)	8965	(73.3)	7.7	23,368	(72.3)	8845	(72.3)	0.0
Guideline-recommended antibiotic ^d	20,649	(63.9)	8327	(68.1)	8.8	21,559	(66.7)	8194	(67.0)	0.6
SCS	19,969	(61.8)	8207	(67.1)	11.1	21,201	(65.6)	8024	(65.6)	0.0
SABA	19,903	(61.6)	7988	(65.3)	7.7	20,764	(64.3)	7859	(64.3)	0.0
SABA/SAMA	4769	(14.8)	2054	(16.8)	5.6	5216	(16.1)	1974	(16.1)	0.0
SAMA	876	(2.7)	396	(3.2)	3.1	939	(2.9)	389	(3.2)	1.6

^aEvaluated during the 12-month baseline period, not including the index date

^bPatients on FF/UMEC/VI and BUD/GLY/Form were weighted using the overlap weighting approach based on the PS to adjust for confounding. Variables used in the PS calculation included the following: age, sex, race, year of index date, physician specialty at index, US region, pulmonary testing at baseline, Quan-CCI score, COPD exacerbations at baseline and on the index date, baseline medication use (agents with ≥5% use in either cohort), baseline HRU and medical costs, SITT pharmacy costs on the index date, and comorbidities (conditions with ≥5% prevalence in either cohort)

^cThe standardized difference was calculated using the following equation where P is the respective proportion of patients in each group: $|(\text{Pcase} - \text{Pcontrol})| / \sqrt{[(\text{Pcase}(1 - \text{Pcase}) + \text{Pcontrol}(1 - \text{Pcontrol})) / 2]}$

^dGlobal Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. 2024. <https://goldcopd.org/2024-gold-report/>. Accessed April 29, 2024.

BUD/GLY/FORM budesonide/glycopyrrolate/formoterol fumarate, *COPD* chronic obstructive pulmonary disease, *FFS* Fee-for-Service, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *HRU* healthcare resource utilization, *ICS* inhaled corticosteroid, *LABA* long-acting β 2 agonist, *LAMA* long-acting muscarinic antagonist, *MITT* multiple-inhaler triple therapy, *P* proportion of patients, *PDE4* phosphodiesterase-4, *SABA* short-acting β 2 agonist, *SAMA* short-acting muscarinic antagonist, *SCS* systemic corticosteroid, *SITT* single-inhaler triple therapy, *std. diff.* standardized difference

Table S6 Baseline COPD exacerbations in patients with Medicare FFS coverage

COPD exacerbations, ^a <i>n</i> (%)	Unweighted cohorts			Weighted cohorts ^b		
	FF/UMEC/VI <i>N</i> = 32,312	BUD/GLY/FORM <i>N</i> = 12,230	Std. diff. ^{c,d} (%)	FF/UMEC/VI <i>N</i> = 32,312	BUD/GLY/FORM <i>N</i> = 12,230	Std. diff. ^{c,d} (%)
Patients with ≥1 event during the 12-month baseline period, not including the index date, <i>n</i> (%)						
Moderate-severe exacerbation	14,938 (46.2)	6015 (49.2)	5.9	15,640 (48.4)	5889 (48.2)	0.5
Severe exacerbation	2920 (9.0)	952 (7.8)	4.5	2610 (8.1)	988 (8.1)	0.0
Moderate exacerbation	13,208 (40.9)	5525 (45.2)	8.7	14,181 (43.9)	5368 (43.9)	0.0
Number of events during the 12-month baseline period, not including the index date, mean ± SD [median]						
Moderate-severe exacerbation	0.81 ± 1.20 [0]	0.91 ± 1.30 [0]	8.2	0.88 ± 1.28 [0]	0.88 ± 1.26 [0]	0.0
Severe exacerbation	0.11 ± 0.41 [0]	0.10 ± 0.37 [0]	4.3	0.10 ± 0.38 [0]	0.10 ± 0.38 [0]	0.0
Moderate exacerbation	0.69 ± 1.12 [0]	0.81 ± 1.23 [0]	10.2	0.77 ± 1.21 [0]	0.77 ± 1.19 [0]	0.0
Patients with ≥1 event on the index date, <i>n</i> (%)						
Moderate-severe exacerbation	1490 (4.6)	503 (4.1)	2.4	1373 (4.2)	520 (4.2)	0.0
Severe exacerbation	38 (0.1)	12 (0.1)	0.6	31 (0.1)	12 (0.1)	0.2
Moderate exacerbation	1452 (4.5)	491 (4.0)	2.4	1342 (4.2)	507 (4.1)	0.0

^aSevere exacerbations were defined as a hospitalization with a COPD exacerbation diagnosis code in the primary position. Moderate exacerbations were defined as an OP or ED visit with a COPD exacerbation diagnosis code in the primary position and at least one dispensing/administration of an SCS or guideline-recommended antibiotic within five days following, or prior to, the visit

^bPatients on FF/UMEC/VI and BUD/GLY/FORM were weighted using the overlap weighting approach based on the PS to adjust for confounding. Variables used in the PS calculation included the following: age, sex, race, year of index date, physician specialty at index, US region, pulmonary testing at baseline, Quan-CCI score, COPD exacerbations at baseline and on the index date, baseline medication use (agents with ≥5% use in either cohort), baseline HRU and medical costs, SITT pharmacy costs on the index date, and comorbidities (conditions with ≥5% prevalence in either cohort)

^cFor continuous variables, the standardized difference was calculated by dividing the absolute difference in means of the control and the case by the pooled SD of both groups. The pooled SD is the square root of the average of the squared SDs

^dFor dichotomous variables, the standardized difference was calculated using the following equation where P is the respective proportion of patients in each group: $|(P_{\text{case}} - P_{\text{control}})| / \sqrt{[(P_{\text{case}}(1 - P_{\text{case}}) + P_{\text{control}}(1 - P_{\text{control}}))/2]}$

BUD/GLY/FORM budesonide/glycopyrrolate/formoterol fumarate, *COPD* chronic obstructive pulmonary disorder, *ED* emergency department, *FFS* Fee-for-Service, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *HRU* healthcare resource utilization, *OP* outpatient, *P* proportion of patients, *PS* propensity score, *Quan-CCI* Quan-Charlson comorbidity index, *SCS* systemic corticosteroid, *SITT* single-inhaler triple therapy, *SD* standard deviation, *std. diff.* standardized difference

Table S7 Baseline comorbidities in patients with Medicare FFS coverage

Comorbidities, ^a n (%)	Unweighted cohorts					Weighted cohorts ^b				
	FF/UMEC/VI		BUD/GLY/FOR M		Std. diff. ^c (%)	FF/UMEC/VI		BUD/GLY/FOR M		Std. diff. ^c (%)
	N = 32,312		N = 12,230			N = 32,312		N = 12,230		
Select COPD-related comorbidities										
Gastroesophageal reflux disease	9888	(30.6)	3696	(30.2)	0.8	9796	(30.3)	3708	(30.3)	0.0
Anxiety disorders	7866	(24.3)	2943	(24.1)	0.7	7770	(24.0)	2941	(24.0)	0.0
Obstructive sleep apnea	7364	(22.8)	2704	(22.1)	1.6	7185	(22.2)	2719	(22.2)	0.0
Depressive disorders	6581	(20.4)	2265	(18.5)	4.7	6146	(19.0)	2326	(19.0)	0.0
Pneumonia	5934	(18.4)	2072	(16.9)	3.7	5568	(17.2)	2107	(17.2)	0.0
Acute respiratory failure	4568	(14.1)	1472	(12.0)	6.2	4056	(12.6)	1535	(12.6)	0.0
Upper respiratory tract infection	3659	(11.3)	1572	(12.9)	4.7	4017	(12.4)	1520	(12.4)	0.0
Allergic rhinitis	3351	(10.4)	1527	(12.5)	6.7	3822	(11.8)	1446	(11.8)	0.0
Sinusitis	2575	(8.0)	1155	(9.4)	5.2	2911	(9.0)	1102	(9.0)	0.0
Chronic rhinosinusitis	1177	(3.6)	547	(4.5)	4.2	1318	(4.1)	524	(4.3)	1.0
Bronchiectasis	972	(3.0)	392	(3.2)	1.1	991	(3.1)	386	(3.2)	0.5
Eosinophilic disorders	17	(0.1)	12	(0.1)	1.7	17	(0.1)	12	(0.1)	1.5
Hypereosinophilic syndrome	2	(0.0)	0	(0.0)	1.1	2	(0.0)	0	(0.0)	1.2
Eosinophilic granulomatosis with polyangiitis	0	(0.0)	2	(0.0)	1.8	0	(0.0)	2	(0.0)	1.8
Elixhauser comorbidities ^d										
Hypertension	25,338	(78.4)	9380	(76.7)	4.1	24,942	(77.2)	9440	(77.2)	0.0
Cardiac arrhythmias	11,783	(36.5)	4028	(32.9)	7.4	10,956	(33.9)	4147	(33.9)	0.0
Diabetes	11,259	(34.8)	4229	(34.6)	0.6	11,199	(34.7)	4239	(34.7)	0.0
Congestive heart failure	10,130	(31.4)	3401	(27.8)	7.8	9269	(28.7)	3508	(28.7)	0.0
Peripheral vascular disorders	9424	(29.2)	3405	(27.8)	2.9	9116	(28.2)	3451	(28.2)	0.0
Renal failure	7889	(24.4)	2764	(22.6)	4.3	7452	(23.1)	2820	(23.1)	0.0
Obesity	7039	(21.8)	2513	(20.5)	3.0	6735	(20.8)	2549	(20.8)	0.0
Fluid and electrolyte disorders	6863	(21.2)	2307	(18.9)	5.9	6292	(19.5)	2382	(19.5)	0.0
Valvular disease	5805	(18.0)	1978	(16.2)	4.8	5375	(16.6)	2035	(16.6)	0.0
Deficiency anemias	4314	(13.4)	1556	(12.7)	1.9	4169	(12.9)	1578	(12.9)	0.0
Solid tumor without metastasis	3714	(11.5)	1356	(11.1)	1.3	3623	(11.2)	1371	(11.2)	0.0
Pulmonary circulation disorder	3491	(10.8)	1233	(10.1)	2.4	3310	(10.2)	1253	(10.2)	0.0
Other neurological disorders	3300	(10.2)	1098	(9.0)	4.2	3008	(9.3)	1138	(9.3)	0.0

Rheumatoid arthritis/collagen vascular disease	3159	(9.8)	1198	(9.8)	0.1	3170	(9.8)	1200	(9.8)	0.0
Weight loss	2441	(7.6)	943	(7.7)	0.6	2471	(7.6)	935	(7.6)	0.0
Liver disease	2407	(7.4)	884	(7.2)	0.9	2362	(7.3)	894	(7.3)	0.0
Coagulopathy	1913	(5.9)	677	(5.5)	1.7	1820	(5.6)	689	(5.6)	0.0
Drug abuse	1868	(5.8)	712	(5.8)	0.2	1894	(5.9)	717	(5.9)	0.0
Alcohol abuse	1400	(4.3)	465	(3.8)	2.7	1380	(4.3)	467	(3.8)	2.3
Blood loss anemia	953	(2.9)	293	(2.4)	3.4	886	(2.7)	302	(2.5)	1.7
Psychoses	706	(2.2)	229	(1.9)	2.2	712	(2.2)	230	(1.9)	2.3
Metastatic cancer	567	(1.8)	201	(1.6)	0.9	532	(1.6)	207	(1.7)	0.4
Peptic ulcer disease	565	(1.7)	163	(1.3)	3.4	538	(1.7)	165	(1.4)	2.6
Lymphoma	532	(1.6)	178	(1.5)	1.6	515	(1.6)	179	(1.5)	1.0
Paralysis	345	(1.1)	125	(1.0)	0.5	321	(1.0)	130	(1.1)	0.7
HIV/AIDS	127	(0.4)	44	(0.4)	0.5	127	(0.4)	44	(0.4)	0.5

^aEvaluated during the 12-month baseline period, not including the index date

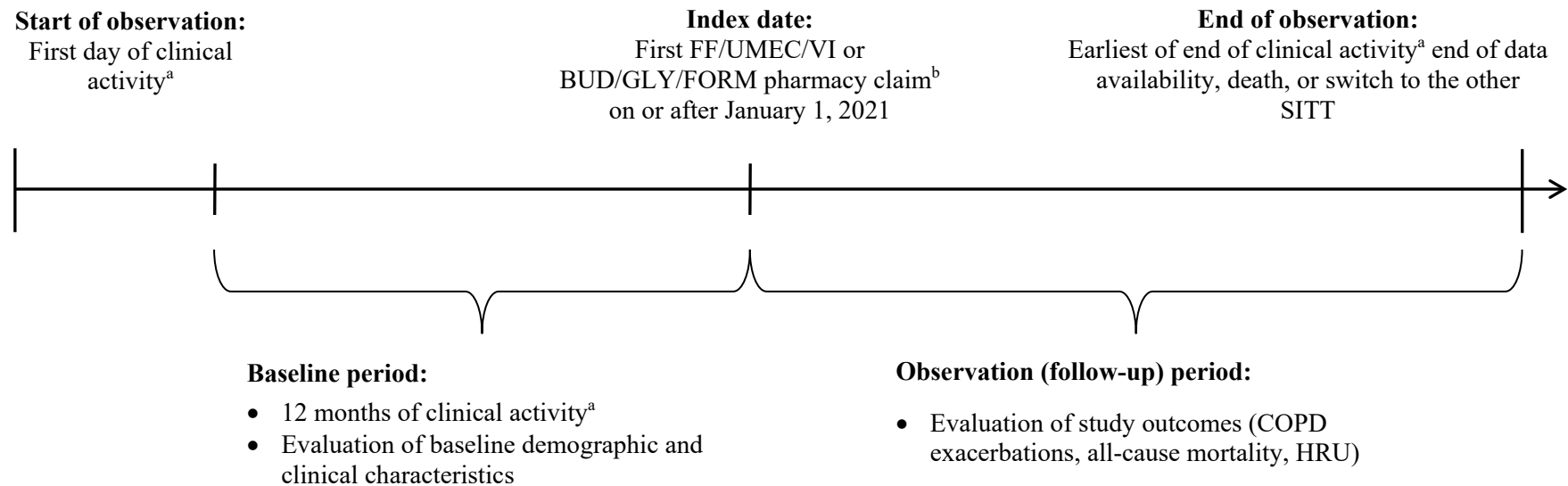
^bFF/UMEC/VI and BUD/GLY/FORM patients were weighted using the overlap weighting approach based on the PS to adjust for confounding. Variables used in the PS calculation included the following: age, sex, race, year of index date, physician specialty at index, US region, pulmonary testing at baseline, Quan-CCI score, COPD exacerbations at baseline and on the index date, baseline medication use (agents with $\geq 5\%$ use in either cohort), baseline HRU and medical costs, SITT pharmacy costs on the index date, and comorbidities (conditions with $\geq 5\%$ prevalence in either cohort)

^cThe standardized difference was calculated using the following equation where P is the respective proportion of participants in each group: $|(\text{Pcase} - \text{Pcontrol})| / \sqrt{[(\text{Pcase}(1 - \text{Pcase}) + \text{Pcontrol}(1 - \text{Pcontrol}))/2]}$

^dReference: Elixhauser A, Steiner C, Kuzik D. HCUP Comorbidity Software. Healthcare Cost and Utilization Project (HCUP). October 2015. Agency for Healthcare Research and Quality, Rockville, MD. Available from: <https://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp#download>

AIDS acquired immunodeficiency syndrome, *BUD/GLY/FORM* budesonide/glycopyrrolate/formoterol fumarate, *COPD* chronic obstructive pulmonary disease, *FFS* Fee-for-Service, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *HIV* human immunodeficiency virus, *HRU* healthcare resource utilization, *P* proportion of patients, *PS* propensity score, *Quan-CCI* Quan-Charlson comorbidity index, *SITT* single-inhaler triple therapy, *std. diff.* standardized difference

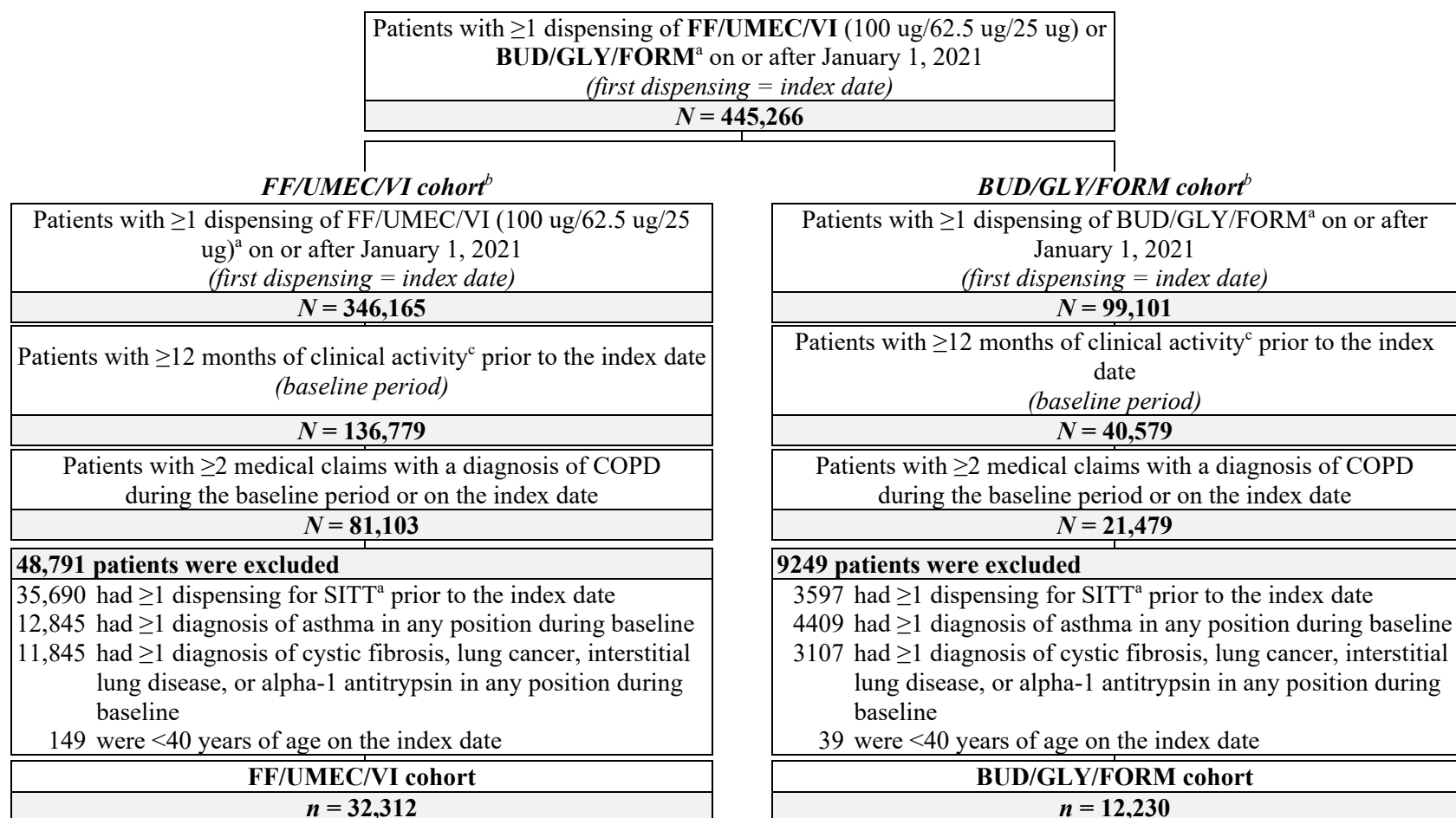
Fig. S1 Study design



Data Source: Komodo Research Data (January 1, 2016–December 31, 2023). ^aContinuous clinical activity was used for the analysis among patients with Medicare FFS coverage and was defined as consecutive quarters with ≥ 1 medical and ≥ 1 pharmacy claim in KRD open-source data and was used as a surrogate for continuous insurance coverage. In the analysis among patients with Medicare Advantage, Medicaid, or commercial coverage, continuous eligibility from KRD closed-source data was used. ^bPatients in the FF/UMEC/VI cohort were required to initiate the 100 µg/62.5 µg/25 µg formulation.

BUD/GLY/FORM budesonide, glycopyrrolate, formoterol fumarate, *COPD* chronic obstructive pulmonary disease, *FFS* Fee-for-Service, *FF/UMEC/VI* fluticasone furoate, umeclidinium, vilanterol, *HRU* healthcare resource utilization, *KRD* Komodo Research Data, *SITT* single-inhaler triple therapy

Fig. S2 Patient disposition—patients with Medicare FFS coverage



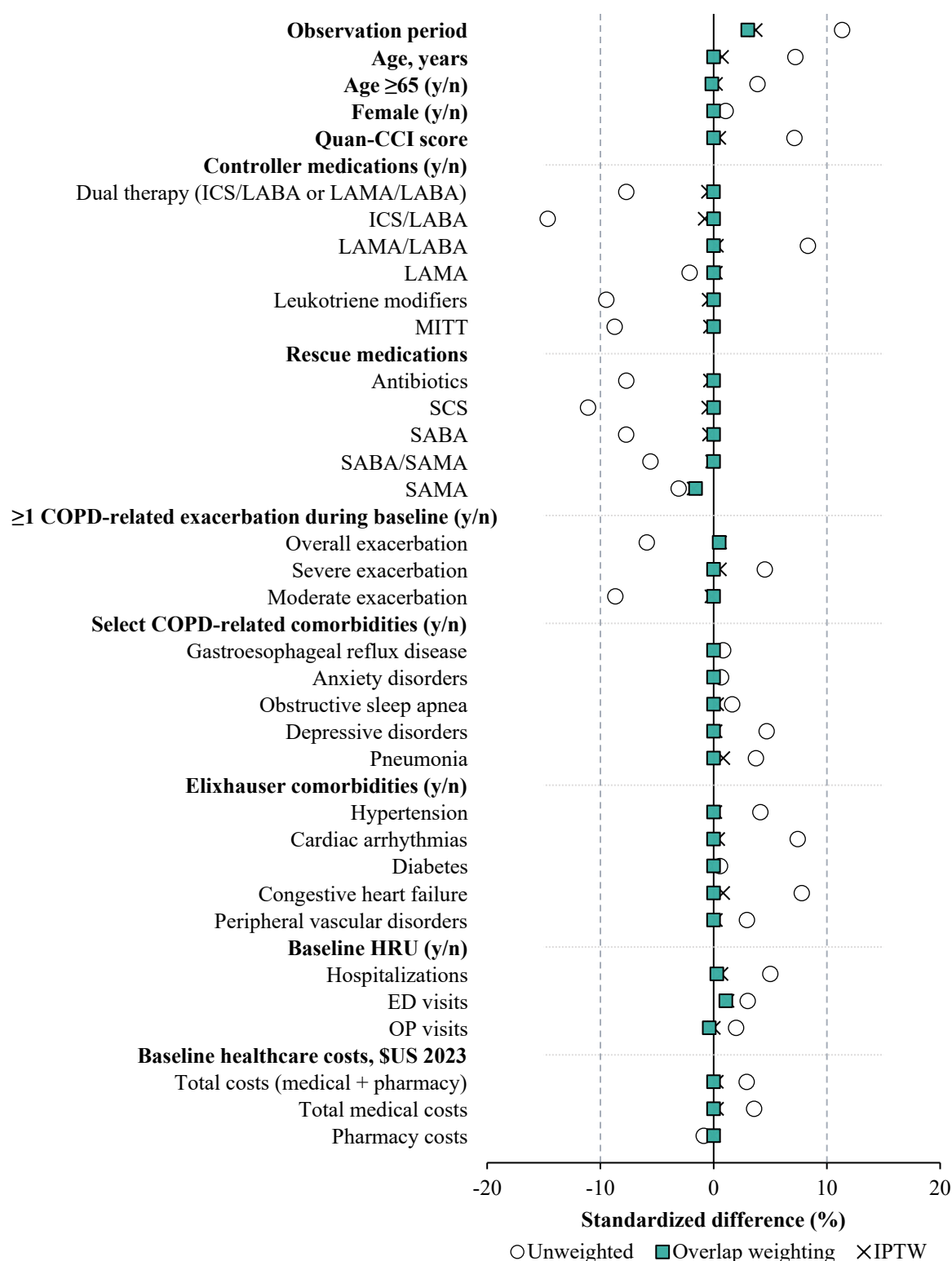
^aPatients using both SITT agents (FF/UMEC/VI and BUD/GLY/FORM) on the index date were not included

^bThe study cohorts were determined based on whether the pharmacy claim on the index date was for FF/UMEC/VI or BUD/GLY/FORM. Patients in the FF/UMEC/VI cohort were required to initiate the 100 ug/62.5 ug/25 ug formulation

^cContinuous clinical activity was defined as consecutive quarters with ≥ 1 medical and ≥ 1 pharmacy Medicare FFS claim

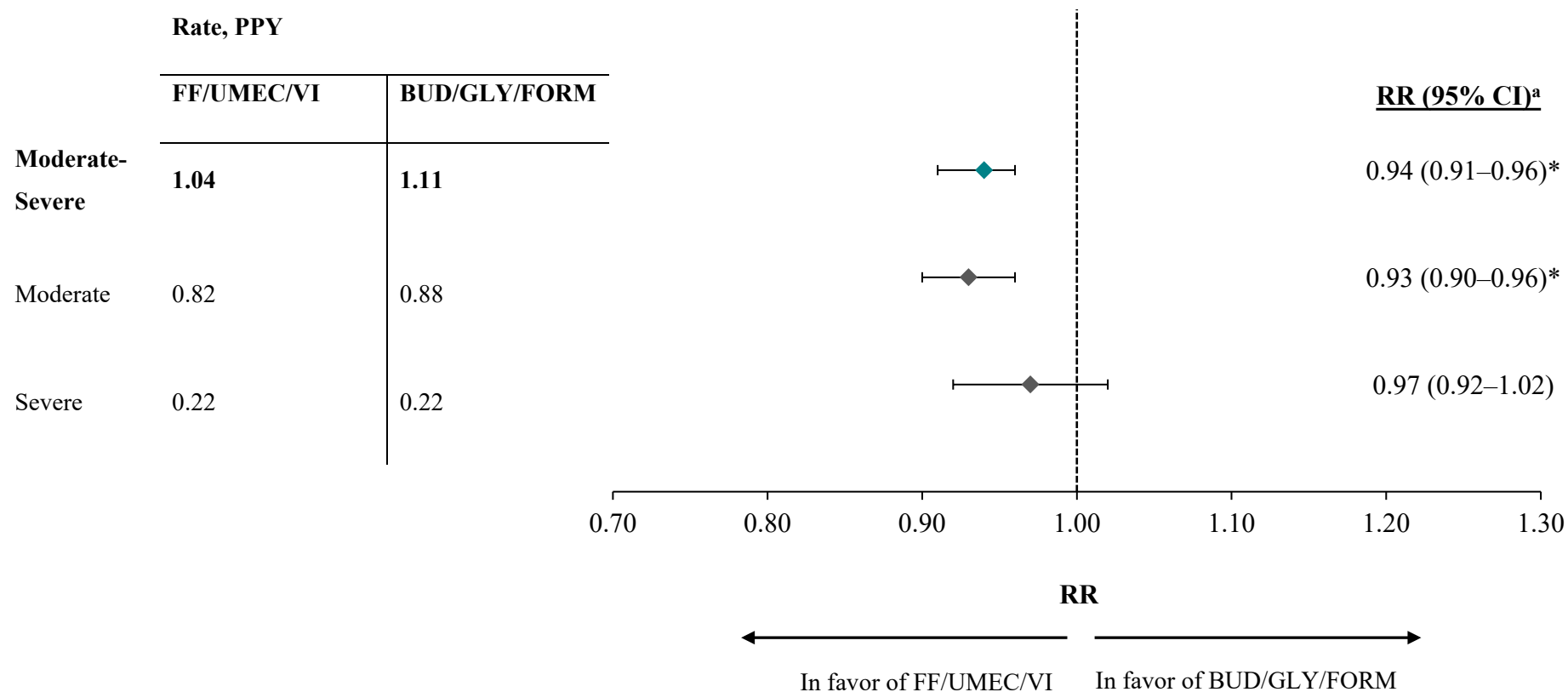
BUD/GLY/FORM budesonide/glycopyrrolate/formoterol fumarate, *COPD* chronic obstructive pulmonary disease, *FFS* Fee-for-Service, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *SITT* single-inhaler triple therapy

Fig. S3 Covariate balance before and after weighting for patients with Medicare FFS coverage



COPD chronic obstructive pulmonary disease, *ED* emergency department, *FFS* Fee-for-Service, *HRU* healthcare resource utilization, *ICS* inhaled corticosteroid, *IPTW* inverse probability of treatment weighting, *LABA* long-acting β_2 agonist, *LAMA* long-acting muscarinic antagonist, *MITT* multiple-inhaler triple therapy, *OP* outpatient, *Quan-CCI* Quan-Charlson comorbidity index, *SABA* short-acting β_2 agonist, *SAMA* short-acting muscarinic antagonist, *SCS* systemic corticosteroid

Fig. S4 Follow-up rate of patients with COPD with Medicare Advantage, Medicaid, or commercial coverage, weighted results

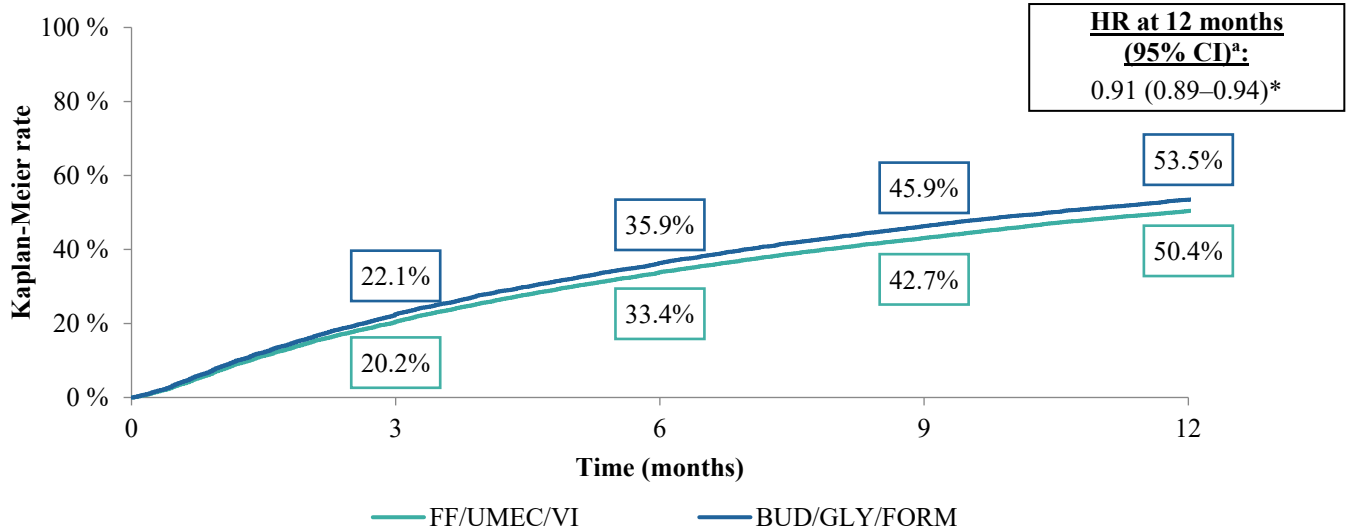


* $P < 0.001$. ^aFollow-up rate of exacerbations was compared between cohorts using RRs from Poisson regression models with a log-link function; robust SEs were used to estimate 95% CIs and P values.

BUD/GLY/FORM budesonide/glycopyrrolate/formoterol fumarate, *CI* confidence interval, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *PPY* per patient-year, *RR* rate ratio

Fig. S5 Time to first COPD exacerbation in patients with Medicare Advantage, Medicaid, or commercial coverage

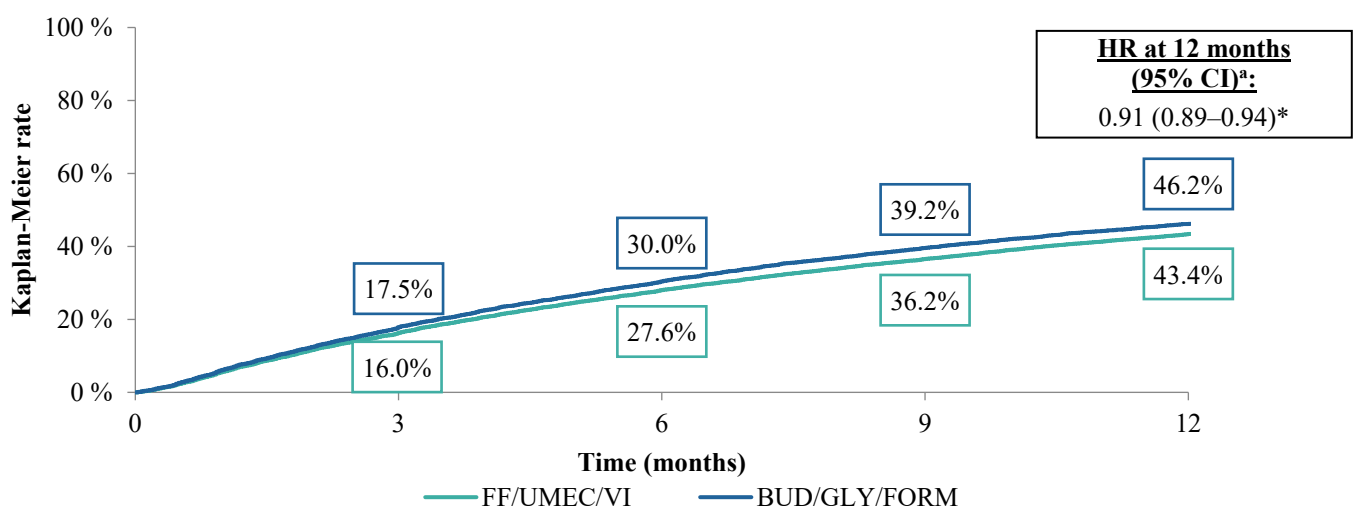
a) Moderate-severe exacerbations



Patients at risk^b:

FF/UMEC/VI	49,570	32,138	20,928	13,889	8975
BUD/GLY/FORM	17,728	10,996	7027	4588	2965

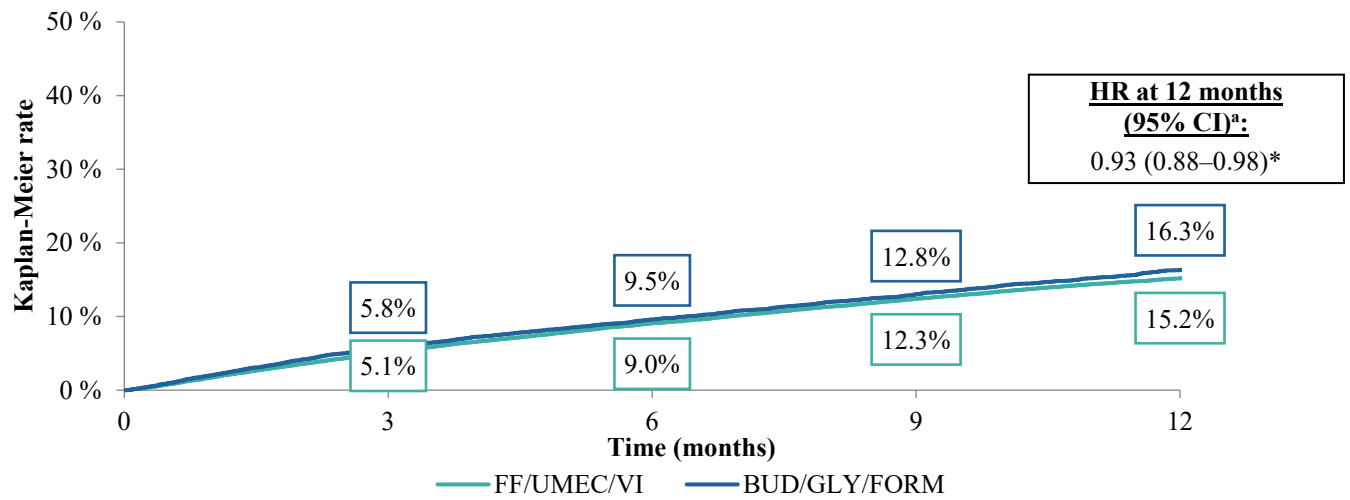
b) Moderate exacerbations



Patients at risk^b:

FF/UMEC/VI	49,570	33,739	22,582	15,305	10,108
BUD/GLY/FORM	17,728	11,594	7607	5077	3359

c) Severe exacerbations



Patients at risk^b:

FF/UMEC/VI	49,570	38,192	28,615	21,427	15,553
BUD/GLY/FOR	17,728	13,296	9921	7369	5289

* $P < 0.05$. ^aHRs and P values were calculated using Cox proportional hazards regression models;

^bNumber of patients without event still observed at the specific point in time.

BUD/GLY/FOR budesonide/glycopyrrolate/formoterol fumarate, *CI* confidence interval, *COPD* chronic obstructive pulmonary disease, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *HR* hazard ratio