

# An Exploratory Study of Physician Decision-Making When Treating Uncontrolled COPD

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**Purpose:** Current guidelines recommend triple therapy maintenance inhalers for patients with recurrent exacerbations of chronic obstructive pulmonary disease (COPD); however, these maintenance therapies are underutilized. This study aimed to understand how physicians make COPD treatment decisions, and how combination maintenance therapies are utilized in a real-world setting.

**Patients and Methods:** This exploratory, hypothesis-generating, non-interventional study used a cross-sectional online survey that was administered to a sample of practicing physicians in the United States. The survey included five fictitious vignettes detailing common symptoms experienced by patients with COPD. Survey questions included factors physicians consider in their decisions, and perceived barriers to prescribing treatments. Repeated measures multivariable analyses were conducted to evaluate how likely physicians were to switch to triple therapy versus no change to patient's current maintenance therapy or change to another maintenance therapy.

**Results:** In total, 200 physicians completed the survey. Cost of treatment and patient access to treatment were reported as the most common barriers physicians consider in their prescribing decisions. Physicians were more likely to switch a patient's maintenance inhaler to triple therapy versus no change to maintenance inhaler if they considered the patient's history of new symptoms, insurance status, and clinical guidelines in their decision. Physicians with more experience treating patients with COPD, and those who treat more patients with COPD per week, were more likely to switch to triple therapy versus no change to maintenance inhaler.

**Conclusion:** This study demonstrates the complexity of factors that can influence physicians' decisions when prescribing treatments for patients with COPD, including considerations of treatment cost, patient access and adherence, patient comorbidities, efficacy of current treatment, clinical guidelines, and provider's level of experience treating COPD. Further research may help elucidate the relative importance of the factors influencing physicians' decisions and inform what types of decision-support tools would be most beneficial.

**Plain Language Summary:** Chronic obstructive pulmonary disease (COPD) symptoms can be effectively managed with maintenance therapies, which are treatments that are taken routinely to help improve symptoms. A combination of three different therapies (triple therapy maintenance) has been shown to be more effective than a combination of two different therapies (dual therapy maintenance) in patients with moderate-to-severe COPD. However, maintenance therapies, including triple therapy, are underutilized. This study aimed to explore how physicians make their treatment decisions for patients with COPD, and how combination maintenance therapies are utilized. To do so, we administered a survey to a sample of practicing physicians in the United States. The survey included five clinically based, fictitious profiles, or vignettes, of patients with COPD, with common symptoms and patient characteristics being described. Physicians were then asked to answer questions about what treatment they would prescribe for each patient, and any factors they considered when deciding on a treatment for a patient. We found that cost of treatment and patient access to treatment were the most common barriers that physicians considered when choosing a treatment. Physicians were also more likely to switch a patient's maintenance inhaler to a triple therapy maintenance inhaler if they considered the patient's history of new symptoms, patient's insurance status, and clinical guidelines when making their decisions. Our study shows that there are many complex factors that influence physicians' decisions when deciding on a treatment for patients with COPD.

**Keywords:** maintenance therapy, patient vignette, pharmacotherapy, physician survey, real world, triple therapy

## Introduction

Chronic obstructive pulmonary disease (COPD) is a prevalent respiratory condition that affects an estimated 15 million people in the United States (US).<sup>1</sup> COPD is characterized by a gradual loss of lung function and progressive airflow limitation, which cannot always be reversed.<sup>2</sup>

Effective treatments for COPD are vital to reduce symptoms and the frequency and severity of COPD exacerbations.<sup>3</sup> COPD can be treated with a combination of an inhaled corticosteroid (ICS), long-acting  $\beta_2$ -agonist (LABA), and a long-acting muscarinic antagonist (LAMA). The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 strategy document recommends LAMA or LABA as monotherapy, LABA/LAMA as dual therapy, and ICS/LABA/LAMA as triple therapy.<sup>3</sup> Dual therapy has been shown to improve lung function compared with monotherapy<sup>4</sup> and triple therapy has been shown to reduce exacerbation rate and mortality, as well as improve lung function and quality of life compared with LAMA monotherapy or dual therapy consisting of LABA/LAMA<sup>3,5</sup> in patients with moderate-to-severe COPD. The GOLD 2023 strategy document recommends initial maintenance therapy with a LABA and a LAMA for patients with high symptom severity (modified Medical Research Council [mMRC] dyspnea scale score  $\geq 2$  and/or COPD Assessment Test [CAT] score  $\geq 10$ ) and/or for patients with  $\geq 2$  moderate exacerbations or  $\geq 1$  moderate exacerbation leading to a hospitalization.<sup>3</sup> Triple therapy with LABA/LAMA and an ICS is recommended as initial maintenance therapy for patients with recurrent exacerbations and elevated blood eosinophil counts ( $\geq 300$  cells/ $\mu\text{L}$ ), or as a step-up treatment for patients who experience persistent exacerbations while receiving dual- or mono-bronchodilator therapy.<sup>3</sup> However, GOLD recommendations are not always implemented effectively in clinical practice.<sup>6</sup>

Despite evidence demonstrating the effectiveness of COPD maintenance therapies in reducing exacerbations and related burdens, they are underutilized, even by patients who would be eligible to receive them according to clinical guidelines.<sup>7,8</sup> While previous research has focused on the inconsistencies between prescribing patterns for treating COPD and guideline recommendations,<sup>9</sup> the rationale behind providers' treatment decisions remains unclear. Several factors can act as barriers to treatment, including cost and lack of access to primary care and medication due to lack of health insurance coverage.<sup>10</sup> Therefore, it is important that physicians consider these factors when making their treatment decisions. This study aimed to explore how physicians make treatment decisions regarding COPD, and how they utilize combination therapies.

## Methods

### Study Design and Data Source

This exploratory, hypothesis-generating, non-interventional study used a cross-sectional online survey to explore COPD treatment preferences. The survey was administered to a sample of practicing physicians in the US, who were part of an established panel, and reflect a convenience sample. The panel comprised over 2 million physicians and healthcare professionals and the respondents' identities and credentials were validated from the American Medical Association, hospital books/directories, and verified healthcare internet sites. Approximately 400,000 of these 2 million plus healthcare professionals included in the panel were expected to be physicians working in a specialty likely to treat patients with COPD.

Potential survey respondents were identified by the panel vendor using the study protocol inclusion and exclusion criteria. A targeted sample size of 200 completed surveys was selected to balance analytic rigor, face validity, and the purpose of the study. Prior to survey administration, a power calculation confirmed the sample size was sufficient to detect statistically significant medium-to-large standardized differences for group comparisons, assuming balanced and unbalanced group sizes. All survey participation was voluntary and anonymized. Recruitment remained open until sample targets of 130 pulmonologists, and 70 non-pulmonologists and non-specified physicians were achieved.

Respondents were eligible for inclusion in the final study sample if they were a practicing physician (Doctor of Medicine or Doctor of Osteopathic Medicine) in the US with prescribing privileges, had a reported assessment or treatment of  $\geq 1$  patient with COPD in the 2 weeks prior to survey fielding and  $\geq 12$  patients with COPD in the year prior to survey fielding, and evaluated  $\geq 1$  patient per month with uncontrolled COPD or recurrent exacerbations. Physicians were excluded if they had  $< 5$  or  $> 25$  years of post-residency experience. Exclusion criteria were selected to focus the

study population on physicians who were more experienced in treating patients with COPD and also more likely to be familiar with, and use, recent therapeutic options for COPD treatment (eg, triple therapy) routinely in clinical practice.

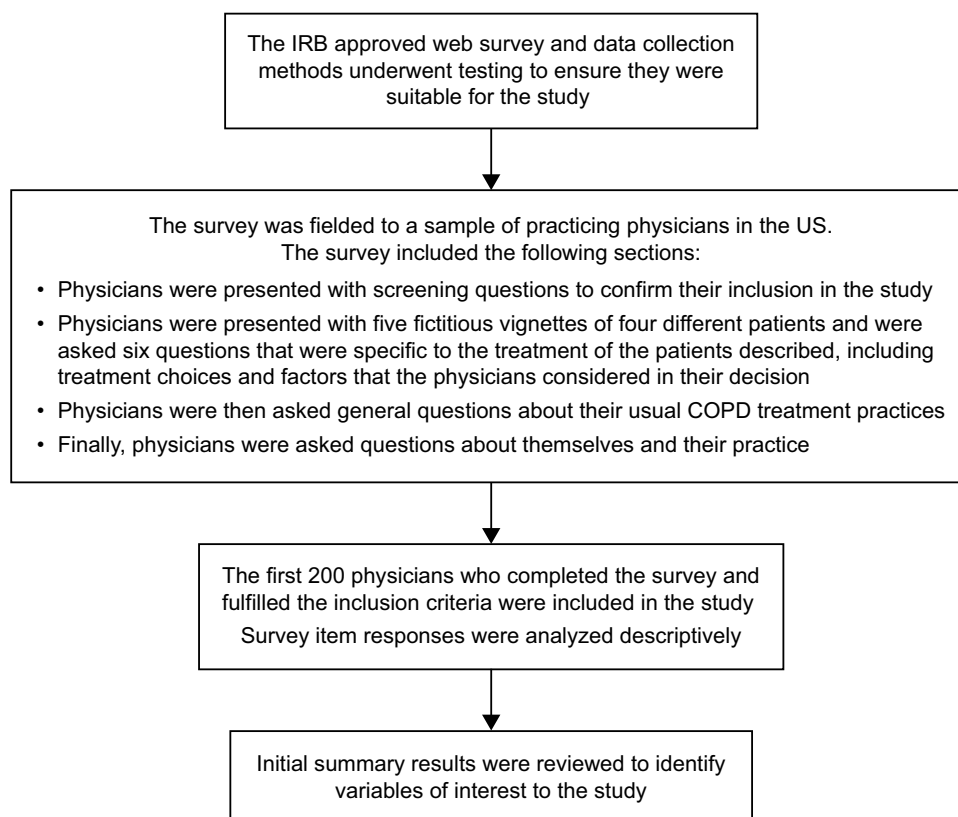
The survey was fielded on February 28, 2022, and the final dataset was received when the desired sample size had been achieved (March 4, 2022).

## Physician Survey

The physician survey was provided in English and was completed online without supervision. The survey was comprised of five fictitious vignettes of four different patients with vignette-specific questions soliciting the physician's treatment decisions. All physicians saw the same five vignettes ([Table S1](#)). The vignettes were developed with clinical input to reflect real-world patient scenarios and symptoms that the physicians surveyed are likely to encounter on a regular basis. The vignettes particularly focused on patients with recurrent or exacerbating COPD symptoms. All five vignettes described patients aged  $\geq 45$  years and both male and female patients. Vignettes are a valuable tool to accurately measure physicians' decisions regarding COPD treatments.<sup>11</sup> The survey also included general questions regarding COPD treatment in daily practice, and questions about the responding physicians' demographics, training, specialty, and practice setting ([Figure 1](#)). The survey received a critical clinical review prior to survey fielding, by  $\geq 1$  pulmonologist. Further survey details are outlined in the [Supplementary Appendix](#).

## Study Outcomes

The primary objectives of this study were to explore physicians' COPD treatment and prescribing decisions when presented with real-world patient symptoms encountered in clinical practice, to describe physician-reported use of COPD treatments, and to characterize patient characteristics considered by physicians when making COPD treatment decisions.



**Figure 1** Survey process overview.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; IRB, Institutional Review Board.

The secondary objective was to explore patient- and physician-related characteristics associated with the respondent's selection of triple therapy maintenance inhaler versus other treatment.

## Data Analysis

This was a hypothesis-generating non-interventional study, and therefore all analyses conducted were exploratory in nature. The survey responses were analyzed in three stages. First, survey responses were aggregated and pooled by all physicians. Numbers and percentages were provided for the dichotomous and polychotomous variables, and means, medians, standard deviations (SDs), and percentiles were provided for continuous variables. For the descriptive analysis, decisions on outcomes, exposures, and stratification were made following review of the pooled analyses from stage one. For the secondary objective, univariable comparisons of physician and vignette characteristics and treatment preferences among maintenance inhaler prescription patterns were performed (change to triple therapy maintenance inhaler, change to other maintenance inhaler, or no change to maintenance inhaler). Each dependent variable of interest was described as number and percentage with Clopper–Pearson exact 95% confidence intervals (CIs).

Finally, repeated measures multivariable analyses<sup>12</sup> were conducted to evaluate independent predictors of triple therapy maintenance inhaler prescription patterns, as follows: switch to triple therapy maintenance inhaler versus no change to maintenance inhaler; switch to triple therapy maintenance inhaler versus escalating current maintenance inhaler dose; and switch to triple therapy maintenance inhaler versus single- or dual-agent maintenance inhaler. The final multivariable model contained 14 predictors, involving physician decision-making factors, practice-related factors, and physician-level factors ([Supplementary Appendix](#)). Measures of association (odds ratios) and robust 95% CIs are presented for relevant independent variables.

Models were built sequentially in covariate blocks, as follows: vignette-level factors; physician decision-level factors in each vignette (eg, whether change was indicated by guidelines such as GOLD); practice-related factors (eg, practice setting); and physician-level factors (eg, demographics). All comparisons performed prior to multivariable modelling were quantified using standardized differences as opposed to significance testing to reduce the risk of type 1 error/false discovery.

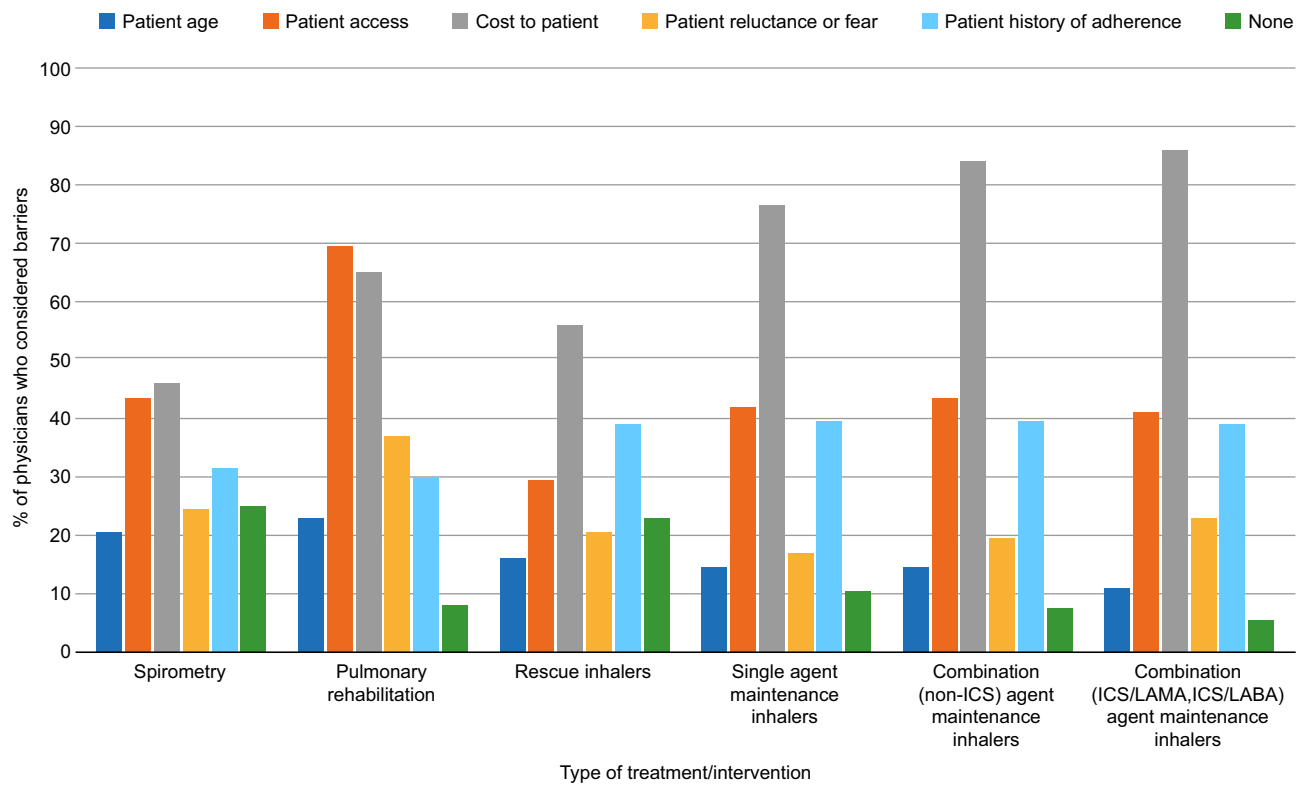
## Results

### Physician Characteristics

A total of 200 physicians completed the survey and were included in this study. Of these, 50.0% were pulmonologists who worked in a primary/ambulatory care practice setting, 18.0% were primary care physicians who worked in a primary/ambulatory care practice setting, 13.5% were internal medicine physicians who worked in a primary/ambulatory care practice setting, 12.5% were pulmonologists who worked in an inpatient practice setting, and 2.5% were internal medicine physicians working in an inpatient practice setting. Only 2.0% and 1.5% of all physicians reported that they worked in an urgent care practice setting or a telemedicine practice setting, respectively. Physicians had a mean (SD) age of 53.1 (9.5) years, and the majority were male (73.0%) ([Table S2](#)). The mean length of time that physicians reported managing patients with COPD was 20.5 years.

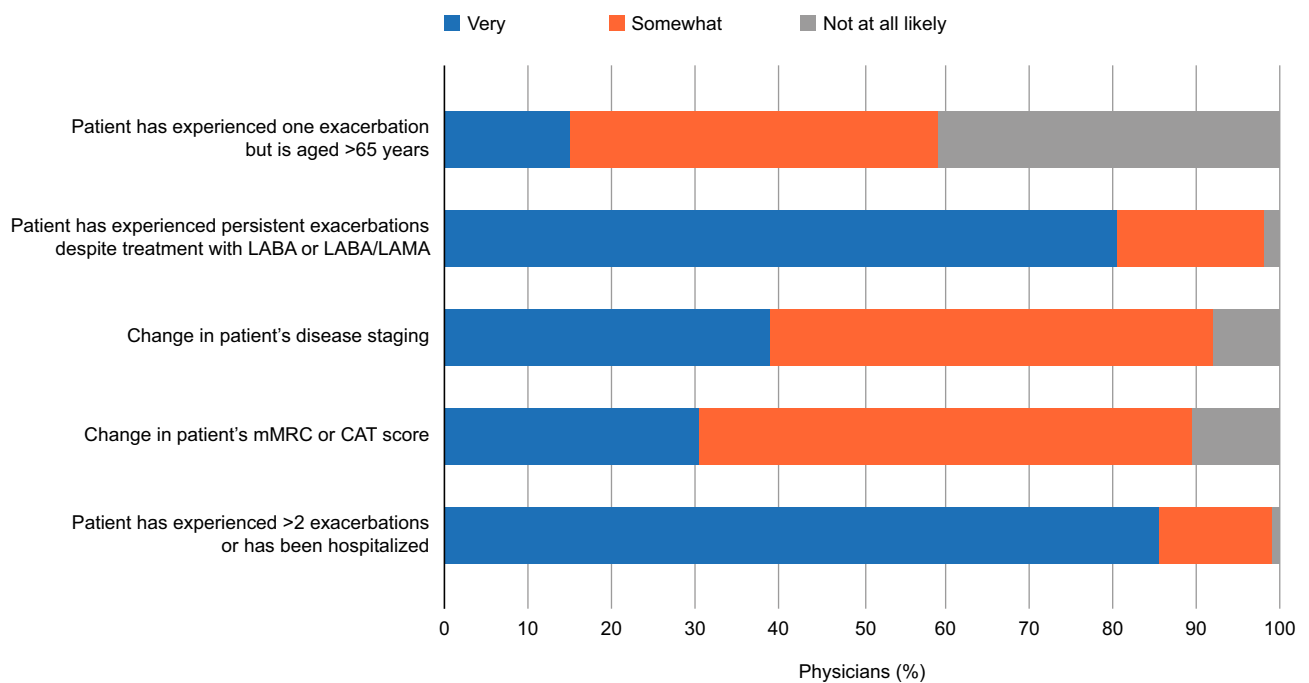
### General Treatment Preferences

When considering their general practice preferences, almost two-thirds of physicians reported “always” (22.0%) or “often” (43.0%) considering treatment guidelines when deciding on a treatment for patients. Of the 66.0% of physicians who use the mMRC questionnaire or the CAT in their practice, 73.0% responded that the patient's score affects their decisions regarding treatment options. Insurance coverage (76.5%) and the drug no longer being effective (66.5%) were the most common reasons selected by physicians for potentially switching a patient's maintenance inhaler. Cost to the patient was considered the most common reason for non-adherence (77.0%), and physicians also considered cost to patients as the most common barrier to prescribing rescue inhalers, single- or dual-agent maintenance inhalers, (non-ICS, ICS/LAMA, ICS/LABA), and spirometry to patients with COPD ([Figure 2](#)). Patient access to treatment was also considered to be a common barrier when prescribing spirometry and pulmonary rehabilitation. At least 80% of physicians reported that they were “very likely” to change a patient's COPD treatment if they experienced persistent exacerbations (despite being treated with LABA only or LAMA/LABA combination), or if they had experienced >2 exacerbations or had been hospitalized ([Figure 3](#)).



**Figure 2** Barriers considered in treatment and intervention decisions.

**Abbreviations:** ICS, inhaled corticosteroid; LABA, long-acting  $\beta_2$ -agonist; LAMA, long-acting muscarinic antagonist.



**Figure 3** Likelihood of changing a patient's COPD treatment by circumstance.

**Abbreviations:** CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; LABA, long-acting  $\beta_2$ -agonist; LAMA, long-acting muscarinic antagonist; mMRC, modified Medical Research Council.

## Responses to Patient Vignettes

Across five vignettes, the proportion of physicians who opted to prescribe a new maintenance inhaler ranged from 36.6% to 66.1%, with triple therapy as the most selected class of new maintenance inhaler (39.3–88.9%). Physicians considered updated spirometry (52.7–82.8% across all vignettes) and white blood cell/eosinophil count (30.4–56.4%) as the most selected clinical assessments they would request to help assess if change to treatment was necessary. A change in patient symptomatology was the highest ranked factor considered among physicians when deciding to change patients' treatments in the vignettes. Option of a lower cost alternative was the lowest ranked factor among providers, when considering recommendations for specific patients described in the vignettes. Physicians considered history of new symptoms (>87.0% across all vignettes), clinical guidelines (>69.0%), and medication adherence history (>46.0%) as the top three most important details in making treatment decisions.

## Stratified Descriptive Results

### Treatment Choice by Vignette

Treatment decisions by individual vignette are summarized in [Table 1](#). The lowest propensity for choice of triple therapy was observed in vignette 2, which described a female aged 60 years who had never smoked, had signs of a bacterial infection, and was using LAMA as maintenance inhaler and short-acting muscarinic antagonist when needed.

### Physician Characteristics by Treatment Choice

The unadjusted analyses for physician characteristics by treatment choice are summarized in [Table 2](#). Managing  $\geq 16$  patients with COPD per week, more years spent managing patients with COPD, more years since residency, male gender, and higher mean age of physician were demographics which favored switching to triple therapy versus no change or change to other maintenance inhaler.

**Table 1** Vignette by Treatment Choice

Vignette	Total Number of Responses (N=1000), n (%)	Respondent's Treatment Choice			Standardized Difference for Contrast, %	
		Triple Therapy Maintenance Inhaler (n=306), n (%)	Other Maintenance Inhaler Therapy (n=165), n (%)	No Change to Maintenance Inhaler Therapy (n=529), n (%)	Triple Therapy vs Other	Triple Therapy vs No
<b>Vignette 1:</b> Male, aged 67 years, current smoker, COPD diagnosis 10 years ago, hypertension. At annual visit, describes SOB with moderate activity. Inconsistent fluticasone/vilanterol (ICS/LABA) use, albuterol sulfate (SABA) use more often than usual.	200 (20.0)	63 (20.6)	51 (30.9)	86 (16.3)	-23.8	11.2
<b>Vignette 2:</b> Female, aged 60 years, never smoked, history of asthma, COPD diagnosis 5 years ago. Day 3 of a cold with SOB and low-grade fever. Pulse 83, BP 129/78. Sputum culture shows bacterial infection. Nebulized with PFT administered. FEV <sub>1</sub> /FVC 60%. Uses tiotropium bromide (LAMA) as prescribed, ipratropium bromide (SAMA) when needed.	200 (20.0)	33 (10.8)	51 (30.9)	116 (21.9)	-51.1	-30.5

(Continued)

Table 1 (Continued).

Vignette	Total Number of Responses (N=1000), n (%)	Respondent's Treatment Choice			Standardized Difference for Contrast, %	
		Triple Therapy Maintenance Inhaler (n=306), n (%)	Other Maintenance Inhaler Therapy (n=165), n (%)	No Change to Maintenance Inhaler Therapy (n=529), n (%)	Triple Therapy vs Other	Triple Therapy vs No
<b>Vignette 3:</b> Male, aged 51 years, COPD diagnosis <6 months ago. Day 14 of dyspnea, fatigue, productive cough. Not improving. Night-time awakening. FEV <sub>1</sub> /FVC <70%, FEV <sub>1</sub> % 55% predicted. Uses vilanterol/umeclidinium (LABA/LAMA) and albuterol (SABA) as prescribed.	200 (20.0)	93 (30.4)	28 (17.0)	79 (14.9)	32.0	37.6
<b>Vignette 4a:</b> Female, aged 73 years, former smoker, COPD diagnosis "a while ago". Arrived by ED/ambulance. Tachycardia, dyspnea with cyanosis, mental confusion. Prescribed oral steroids for previous exacerbation within the last year. On albuterol (SABA), fluticasone/vilanterol (ICS/LABA), naproxen (NSAID), and atorvastatin (statin).	200 (20.0)	56 (18.3)	7 (4.2)	137 (25.9)	45.6	-18.4
<b>Vignette 4b:</b> Female, aged 73 years, former smoker, COPD diagnosis "a while ago". Follow-up visit after discharge for ED visit described in 4a. No change to medication was made during that encounter. As noted above, is on albuterol (SABA), fluticasone/vilanterol (ICS/LABA), naproxen (NSAID), and atorvastatin (statin).	200 (20.0)	61 (19.9)	28 (17.0)	111 (21.0)	7.7	-2.6

**Notes:** Responses over all vignettes were aggregated for these analyses. The N of 1000 is calculated as 200 responses each, from vignettes 1, 2, 3, 4a, and 4b (5 vignettes x 200 respondents).

**Abbreviations:** BP, blood pressure; COPD, chronic obstructive pulmonary disease; ED, emergency department; FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity; ICS, inhaled corticosteroid; LABA, long-acting  $\beta_2$ -agonist; LAMA, long-acting muscarinic antagonist; NSAID, non-steroidal anti-inflammatory drug; PFT, pulmonary function test; SABA, short-acting  $\beta_2$ -agonist; SAMA, short-acting muscarinic antagonist; SOB, shortness of breath.

Table 2 Physician Characteristics by Treatment Choice

Physician Characteristics	Total (N=1000)	Triple Therapy Maintenance Inhaler (n=306)	Other Maintenance Inhaler Therapy (n=165)	No Change to Maintenance Inhaler Therapy (n=529)	Triple Therapy vs Other Standardized Difference, %	Triple Therapy vs No Standardized Difference, %
Mean (SD) years since residency completion <sup>a</sup>	20.4 (6.2)	21.6 (5.6)	19.4 (6.9)	20.0 (6.1)	35.9	27.4
Specialty <sup>b</sup> , n (%)						
Primary care	190 (19.0)	44 (14.4)	24 (14.5)	122 (23.1)	-0.5	-22.4
Internal medicine	160 (16.0)	32 (10.5)	33 (20.0)	95 (18.0)	-26.8	-21.6
Pulmonology	650 (65.0)	230 (75.2)	108 (65.5)	312 (59.0)	21.4	35.0
Other	0 (0)	0 (0)	0 (0)	0 (0)	-	-

(Continued)



Table 2 (Continued).

Physician Characteristics	Total (N=1000)	Triple Therapy Maintenance Inhaler (n=306)	Other Maintenance Inhaler Therapy (n=165)	No Change to Maintenance Inhaler Therapy (n=529)	Triple Therapy vs Other Standardized Difference, %	Triple Therapy vs No Standardized Difference, %
<b>Number of patients with COPD managed per week, n (%)</b>						
1–5	70 (7.0)	9 (2.9)	9 (5.5)	52 (9.8)	–12.6	–28.5
6–10	145 (14.5)	41 (13.4)	29 (17.6)	75 (14.2)	–11.6	–2.3
11–15	195 (19.5)	52 (17.0)	39 (23.6)	104 (19.7)	–16.6	–6.9
≥16	590 (59.0)	204 (66.7)	88 (53.3)	298 (56.3)	27.5	21.4
<b>Practice setting, n (%)</b>						
Primary/ambulatory care	815 (81.5)	267 (87.3)	121 (73.3)	427 (80.7)	35.6	17.9
Inpatient	150 (15.0)	35 (11.4)	31 (18.8)	84 (15.9)	–20.6	–13.0
Urgent care	20 (2.0)	3 (1.0)	4 (2.4)	13 (2.5)	–11.2	–11.4
Emergency department	0 (0)	0 (0)	0 (0)	0 (0)	–	–
Telemedicine	15 (1.5)	1 (0.3)	9 (5.5)	5 (0.9)	–31.0	–7.8
<b>Specialty type, n (%)</b>						
Single specialty	515 (51.5)	162 (52.9)	88 (53.3)	265 (50.1)	–0.8	5.7
Multispecialty group	485 (48.5)	144 (47.1)	77 (46.7)	264 (49.9)	0.8	–5.7
<b>Do you see patients for COPD symptoms via telemedicine?, n (%)</b>						
Yes	730 (73.0)	243 (79.4)	126 (76.4)	361 (68.2)	7.4	25.6
No	270 (27.0)	63 (20.6)	39 (23.6)	168 (31.8)	–7.4	–25.6
<b>Does your practice utilize a medical records system that provides prompts to assist in diagnosing and/or treating patients with COPD?, n (%)</b>						
Yes	470 (47.0)	130 (42.5)	56 (33.9)	284 (53.7)	17.7	–22.6
No	530 (53.0)	176 (57.5)	109 (66.1)	245 (46.3)	–17.7	22.6
<b>Geographic location, n (%)</b>						
Northeast	225 (22.5)	74 (24.2)	39 (23.6)	112 (21.2)	1.3	7.2
Midwest	255 (25.5)	74 (24.2)	35 (21.2)	146 (27.6)	7.1	–7.8
South	330 (33.0)	107 (35.0)	58 (35.2)	165 (31.2)	–0.4	8.0
West	190 (19.0)	51 (16.7)	33 (20.0)	106 (20.0)	–8.6	–8.7
Other	0 (0)	0 (0)	0 (0)	0 (0)	–	–
<b>Urbanicity, n (%)</b>						
Urban	400 (40.0)	127 (41.5)	73 (44.2)	200 (37.8)	–5.5	7.6
Suburban	500 (50.0)	145 (47.4)	78 (47.3)	277 (52.4)	0.2	–10.0
Rural	100 (10.0)	34 (11.1)	14 (8.5)	52 (9.8)	8.8	4.2

(Continued)



Table 2 (Continued).

Physician Characteristics	Total (N=1000)	Triple Therapy Maintenance Inhaler (n=306)	Other Maintenance Inhaler Therapy (n=165)	No Change to Maintenance Inhaler Therapy (n=529)	Triple Therapy vs Other Standardized Difference, %	Triple Therapy vs No Standardized Difference, %
For how many years have you been managing patients with COPD? Mean (median)	20.5 (21.0)	22.5 (22.0)	19.7 (20.0)	19.7 (20.0)	34.0	35.5
Current mean (SD) age, years	53.1 (9.4)	54.7 (8.9)	52.5 (9.8)	52.3 (9.5)	24.3	27.0
Gender, n (%)						
Female	225 (22.5)	44 (14.4)	55 (33.3)	126 (23.8)	-45.6	-24.2
Male	730 (73.0)	250 (81.7)	101 (61.2)	379 (71.6)	46.6	23.9
Nonbinary	0 (0)	0 (0)	0 (0)	0 (0)	-	-
Another gender	0 (0)	0 (0)	0 (0)	0 (0)	-	-
Prefer not to say	45 (4.5)	12 (3.9)	9 (5.5)	24 (4.5)	-7.3	-3.1

**Notes:** <sup>a</sup>Calculated as the year of the survey (2022) minus self-reported year of training completion. <sup>b</sup>During cross-frequency analysis of physician specialty by practice setting, 18.0% were primary care specialty in a primary/ambulatory care practice setting, 13.5% were internal medicine specialty in primary/ambulatory care practice setting, 50.0% were pulmonologists in a primary/ambulatory care practice setting, and 12.5% were pulmonologists in an inpatient practice setting. Responses over all vignettes were aggregated for these analyses. The N of 1000 is calculated as 200 responses each, from vignettes 1, 2, 3, 4a, and 4b (5 vignettes x 200 respondents).

**Abbreviation:** COPD, chronic obstructive pulmonary disease.

### Treatment Preferences by Treatment Choice

When considering the role of comorbidities in their treatment decisions, physicians were less likely to change to triple therapy versus no change to maintenance inhaler if the patient had been diagnosed with hypertension, diabetes, emphysema/bronchitis, or lung cancer (Table 3).

Table 3 Treatment Preferences by Treatment Choice

	Total (N=1000), n (%)	Triple Therapy Maintenance Inhaler (n=306), n (%)	Other Maintenance Inhaler Therapy (n=165), n (%)	No Change to Maintenance Inhaler Therapy (n=529), n (%)	Triple Therapy vs Other Standardized Difference, %	Triple Therapy vs No Standardized Difference, %
How often do you consider treatment guidelines (GOLD, etc.) when making prescribing decisions for your patients with recurrent COPD exacerbations?						
Always	220 (22.0)	71 (23.2)	44 (26.7)	105 (19.8)	-8.0	8.2
Often	430 (43.0)	120 (39.2)	79 (47.9)	231 (43.7)	-17.5	-9.1
Sometimes	295 (29.5)	92 (30.1)	35 (21.2)	168 (31.8)	20.4	-3.7
Rarely	40 (4.0)	22 (7.2)	3 (1.8)	15 (2.8)	26.1	20.1
Never	15 (1.5)	1 (0.3)	4 (2.4)	10 (1.9)	-18.1	-15.0
I am not familiar with guidelines	0 (0)	0 (0)	0 (0)	0 (0)	-	-
Mean, median item response <sup>a,b</sup>	2.8, 3.0	2.8, 3.0	3.0, 3.0	2.8, 3.0	-18.9	1.2
Knowing that your patient has a diagnosis of which of the following comorbidities would impact your treatment decisions? (Select all that apply)						
Hypertension	335 (33.5)	86 (28.1)	49 (29.7)	200 (37.8)	-3.5	-20.8

(Continued)

Table 3 (Continued).

	Total (N=1000), n (%)	Triple Therapy Maintenance Inhaler (n=306), n (%)	Other Maintenance Inhaler Therapy (n=165), n (%)	No Change to Maintenance Inhaler Therapy (n=529), n (%)	Triple Therapy vs Other Standardized Difference, %	Triple Therapy vs No Standardized Difference, %
Heart failure	525 (52.5)	158 (51.6)	79 (47.9)	288 (54.4)	7.5	-5.6
Diabetes	430 (43.0)	88 (28.8)	62 (37.6)	280 (52.9)	-18.8	-50.7
Emphysema/chronic bronchitis	620 (62.0)	166 (54.2)	101 (61.2)	353 (66.7)	-14.1	-25.7
Lung cancer	335 (33.5)	76 (24.8)	47 (28.5)	212 (40.1)	-8.3	-33.0
Other	80 (8.0)	30 (9.8)	19 (11.5)	31 (5.9)	-5.6	14.7
Comorbidities do not impact my treatment decision(s)	150 (15.0)	62 (20.3)	37 (22.4)	51 (9.6)	-5.3	30.1
<b>Which of the following are reasons you might switch a patient's maintenance inhaler? (Select all that apply)</b>						
Access: difficult to find a pharmacy that carries desired device	445 (44.5)	156 (51.0)	77 (46.7)	212 (40.1)	8.6	22.0
Drug is no longer effective	665 (66.5)	211 (69.0)	114 (69.1)	340 (64.3)	-0.3	9.9
Concerns about long-term steroid side effects	380 (38.0)	116 (37.9)	59 (35.8)	205 (38.8)	4.5	-1.7
Insurance coverage	765 (76.5)	257 (84.0)	138 (83.6)	370 (69.9)	1.0	33.8
Complexity: two inhalers are too many	505 (50.5)	181 (59.2)	86 (52.1)	238 (45.0)	14.2	28.6
Patient adherence	540 (54.0)	182 (59.5)	105 (63.6)	253 (47.8)	-8.6	23.5
Other	30 (3.0)	17 (5.6)	6 (3.6)	7 (1.3)	9.2	23.4
None of the above	30 (3.0)	4 (1.3)	4 (2.4)	22 (4.2)	-8.3	-17.6
<b>Which of the following reasons for non-adherence do you see most often in your practice? (Select all that apply)</b>						
Patient age	130 (13.0)	40 (13.1)	18 (10.9)	72 (13.6)	6.7	-1.6
Patient access	280 (28.0)	87 (28.4)	39 (23.6)	154 (29.1)	10.9	-1.5
Cost to patient	770 (77.0)	252 (82.4)	145 (87.9)	373 (70.5)	-15.6	28.2
Difficulty self-administering treatment	415 (41.5)	143 (46.7)	62 (37.6)	210 (39.7)	18.6	14.2
Patient perception of treatment need	485 (48.5)	176 (57.5)	87 (52.7)	222 (42.0)	9.6	31.5
Other (please specify)	30 (3.0)	10 (3.3)	7 (4.2)	13 (2.5)	-5.1	4.9
None of the above	30 (3.0)	3 (1.0)	2 (1.2)	25 (4.7)	-2.2	-22.6
<b>Frequency physician administers the mMRC questionnaire, or the CAT? (Select one)</b>						
At every visit, with every patient diagnosed with COPD	140 (14.0)	48 (15.7)	32 (19.4)	60 (11.3)	-9.8	12.7
At every visit, with patients with severe/very severe COPD	105 (10.5)	26 (8.5)	13 (7.9)	66 (12.5)	2.3	-13.0
Occasionally, with every patient diagnosed with COPD	230 (23.0)	66 (21.6)	25 (15.2)	139 (26.3)	16.6	-11.1

(Continued)

**Table 3** (Continued).

	Total (N=1000), n (%)	Triple Therapy Maintenance Inhaler (n=306), n (%)	Other Maintenance Inhaler Therapy (n=165), n (%)	No Change to Maintenance Inhaler Therapy (n=529), n (%)	Triple Therapy vs Other Standardized Difference, %	Triple Therapy vs No Standardized Difference, %
Occasionally, with patients with severe/very severe COPD	185 (18.5)	54 (17.6)	30 (18.2)	101 (19.1)	-1.4	-3.7
Never, but I am familiar with at least one of the questionnaires	250 (25.0)	88 (28.8)	50 (30.3)	112 (21.2)	-3.4	17.6
I do not know what either the mMRC or the CAT is	90 (9.0)	24 (7.8)	15 (9.1)	51 (9.6)	-4.5	-6.4
<b>If you use the mMRC or the CAT in your practice, does your patient's score impact your treatment decisions?</b>						
Yes	445 (44.5)	145 (47.4)	71 (43.0)	229 (43.3)	8.8	8.2
No	165 (16.5)	34 (11.1)	22 (13.3)	109 (20.6)	-6.8	-26.2
N/A, I do not use the mMRC or the CAT with my patients	390 (39.0)	127 (41.5)	72 (43.6)	191 (36.1)	-4.3	11.1

**Notes:** Responses over all vignettes were aggregated for these analyses. The N of 1000 is calculated as 200 responses each, from vignettes 1, 2, 3, 4a, and 4b (5 vignettes x 200 respondents). \*Higher score means more likely. <sup>a</sup>Excludes "I am not familiar with the guidelines".

**Abbreviations:** CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified Medical Research Council.

## Multivariable Analysis

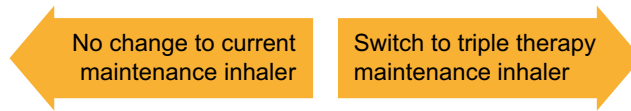
The final multivariable model included a total of 14 predictors ([Table S3](#)), and comprised 1000 responses (200 physicians selecting one choice for each of the five vignettes). For the response options for the outcome variable, almost half of all physicians' responses (n=442; 44.2%) were to not change maintenance inhaler, while 30.6% (n=306) changed to triple therapy. Additionally, 8.7% (n=87) of physicians responded that they would escalate the current maintenance inhaler therapy, and 16.5% (n=165) responded that they would switch to another maintenance inhaler. [Figure 4](#) summarizes the results from the final multivariable model examining triple therapy prescribing patterns.

### Physician Decision-Making Factors

Physicians who ranked cost of alternative treatments as one of the most important details considered when making treatment decisions were more likely to switch to triple therapy versus switching to a single- or dual-agent maintenance inhaler. Physicians who included history of new symptoms, clinical guidelines, or patient insurance status in their top three most important factors when making treatment decisions were more likely to switch to triple therapy versus no change or escalating current maintenance inhaler dose.

### Practice- and Physician-Related Factors

Physicians who saw a higher weekly volume of patients with COPD and physicians who reported seeing patients for COPD symptoms in a telemedicine setting (independent of the setting where they reported seeing most of their patients with COPD) were more likely to switch to triple therapy versus no change or escalating current maintenance inhaler dose. Physicians who primarily worked in an urgent care setting were less likely to switch to triple therapy versus no change to maintenance inhaler or escalating current maintenance inhaler dose versus physicians working in primary/ambulatory care practice settings. Physicians with more experience treating patients with COPD were more likely to switch to triple therapy versus no change to maintenance inhaler, or switching to single- or dual-agent maintenance inhalers versus physicians with less experience.



**Provider-Level Factors**

**Respondent's speciality**

- Primary care (ref.)
- Internal medicine
- Pulmonology

**Years managing patients with COPD?**

- Less than 10 (ref.)
- 10–14
- 15–19
- 20–24
- At least 25

**Gender**

- Female (ref.)
- Male
- Prefer not to say

**Decision-Making Factors (Yes vs No)**

- Guidelines such as GOLD
- Cost of alternative treatments
- History of new symptoms
- Patient insurance status
- Clinical guidelines

**Practice-Related Factors**

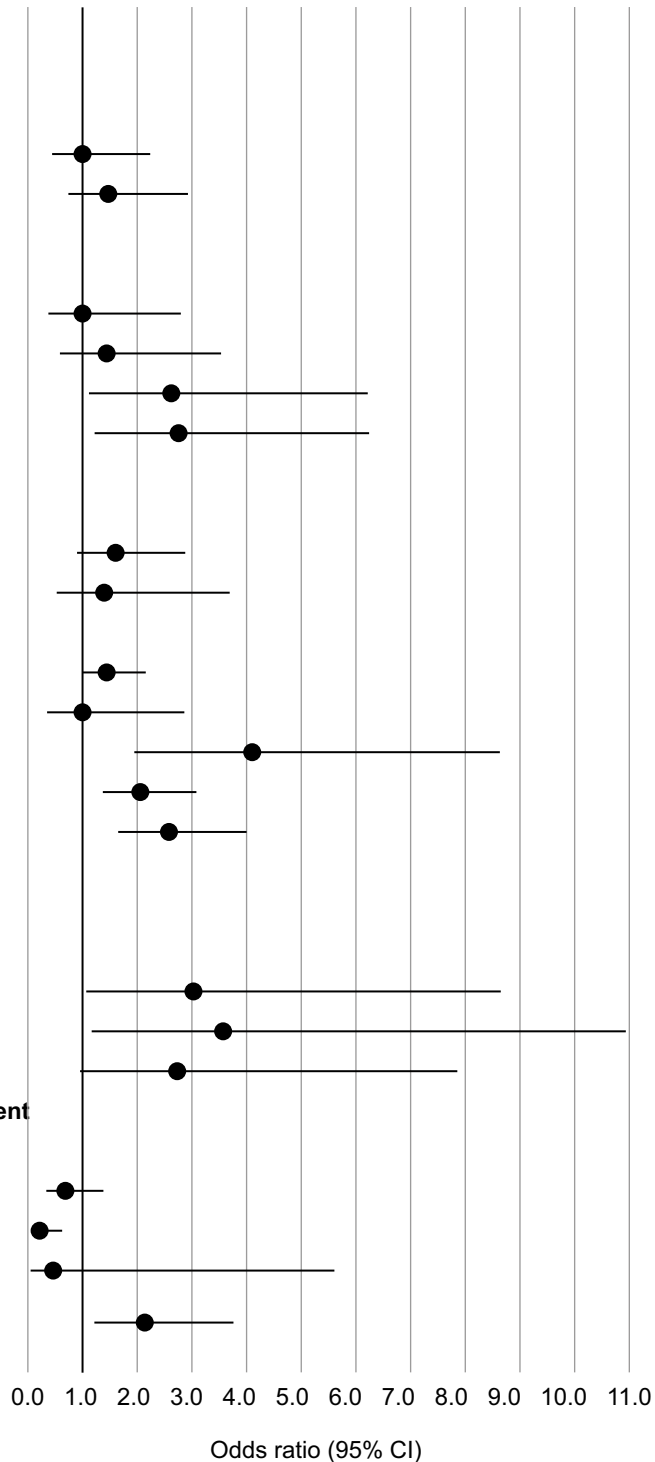
**Patients with COPD managed per week**

- 1–5 (ref.)
- 6–10
- 11–15
- At least 16

**Primary setting where you see your patient**

- Primary/ambulatory care setting (ref.)
- Inpatient setting
- Urgent care
- Telemedicine

**Do you see patients for COPD symptoms via telemedicine? (Yes vs No)**



**Figure 4** Forest plot of multivariable results demonstrating triple therapy maintenance inhaler prescription patterns.

**Notes:** Observations read = 1000, Observations used = 748. Likelihood ratio: chi-square = 194.751, *DF* = 30, *p*-value < 0.001. Hosmer and Lemeshow: chi-square = 10.112, *DF* = 8, *p*-value = 0.257. *c* statistic = 0.781. Robust standard errors. Removed from final model for lack of contribution: patient age, smoking history, and medication adherence as most important detail(s); cost of alternative treatments; single- vs multispecialty group as practice setting; and provider's current age in years. Removed from the forest plot due to lack of space: which of the following best describes your practice setting? (urban, suburban, or rural); medical records system provides prompts to assist in diagnosing/treating patients with COPD? (Yes vs No); and geographic location (Northeast, Midwest, South, or West). Removed for collinearity: years since training. **Abbreviations:** CI, confidence interval; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ref., reference.

## Discussion

This study aimed to explore how physicians make treatment decisions regarding COPD, and how they utilize combination therapies. In this study, physicians who had more experience treating patients with COPD and/or who considered patient's history of new symptoms were more likely to switch to triple therapy versus no change to maintenance inhaler or switch to another maintenance inhaler. Cost to the patient was considered the most common reason for non-adherence and was considered the most common barrier to prescribing rescue inhalers, and single- or dual-agent maintenance inhalers.

Few studies have previously used a survey with real-world patient vignettes to describe the prescribing patterns and behaviors of physicians managing patients with COPD. A 2007 study used vignettes describing patients with COPD followed by multiple choice questions to determine physicians' treatment decisions.<sup>13</sup> However, triple therapy would not have been recommended as a maintenance option in clinical guidelines at the time.<sup>14</sup> A recent survey including a case vignette determined that medical specialty influenced treatment decisions in patients with end-stage COPD and acute respiratory failure.<sup>15</sup>

The results of this current study demonstrate that clinical considerations, including patient's current treatment no longer being effective due to worsening symptoms and recurrent exacerbations, were general acknowledgments among physicians when switching a patient's maintenance inhaler. Cost to the patient was perceived by physicians to be a main reason for patient non-adherence in their own clinical practice, and was one of the most common barriers physicians considered in their general treatment decisions. This reflects real-world physician considerations and highlights ongoing gaps in the healthcare system.<sup>16,17</sup> However, physicians in this study still prioritized the clinical characteristics of the patients over cost when making specific decisions in response to the vignettes. This suggests that physicians may have prescribing preferences that are not always aligned to reimbursement realities. The results of this study show similar barriers to COPD treatment as described in a recent review article, such as patient's age and healthcare system barriers (cost and availability of treatment).<sup>16,17</sup> The findings of our study also show that changes in a patient's treatment plan were most likely a result of a change in patient symptomology. Similarly, in a recent study examining treatment patterns for COPD in the US via a cross-sectional physician and patient survey, the most common reason given by physicians for prescribing a patient's current treatment was 24-hour symptom relief, and the most common reason given to change a patient's current treatment was lack of control of shortness of breath.<sup>18</sup> Other patient characteristics that were not included in our study, but which may have influenced physicians' decision-making include patient's psychological well-being and self-efficacy.

While this study considered several potential barriers that may influence patients' adherence to treatment, smoking was not included as a potential barrier. Several studies have shown that the stigmatization that surrounds smoking-related illnesses, such as COPD, can negatively affect patients' inclination to seek effective treatments to manage COPD.<sup>19,20</sup> Future studies should therefore investigate the impact of smoking as a potential barrier physicians consider when making treatment decisions for patients with COPD.

We found that physicians who would change a patient's treatment in response to the vignettes were more likely to report that comorbidities do not impact their decision. Conversely, physicians who said they considered comorbidities in their decision-making were less likely to decide to change a patient's treatment in the vignettes, possibly due to long-term considerations of drug use or concerns of how step-ups in treatment may impact comorbidities.

Results of the multivariable modelling suggest that physicians who highly ranked history of new symptoms, patient insurance status, and clinical guidelines in their considerations were more likely to switch to triple therapy versus no change to treatment or escalating current maintenance inhaler dose. In addition, physicians who most often see their patients with COPD in a primary/ambulatory care practice setting also appeared more likely to switch to triple therapy compared with physicians who worked in other practice settings. This is as expected, as physicians who see patients in an inpatient or urgent care setting do not manage these patients in the long term and may be more likely to defer to the patients' usual physician to initiate a change in therapy. Notably, we found that physicians with more experience managing patients with COPD were more likely to switch to triple therapy than those with less experience.

More recently, recommendations regarding the use of ICS as part of dual or triple therapy have been evolving. ICS should only be added in COPD for patients with a history of asthma, eosinophilia, or those who exacerbate on dual bronchodilators.<sup>21</sup> The addition of triple therapy as an option for initial maintenance therapy is a new recommendation in the GOLD 2023 strategy document, which has been published since completion of this study.<sup>6</sup> Therefore, the number of physicians who would switch to triple therapy may now be higher since the publication of the 2023 guidelines.<sup>3</sup> Previous studies have shown that there is significant variability in adherence to GOLD recommendations, and have identified barriers to the implementation of COPD guidelines, including lack of clarity and familiarity with guidelines among clinicians, and inadequate implementation programs.<sup>22,23</sup>

The GOLD 2023 recommendations include evidence to suggest that blood eosinophil counts may be a prognostic factor for risk of exacerbations and response to ICS in patients with COPD.<sup>3</sup> In the current study, white blood cell/eosinophil count was one of the most selected additional clinical assessments that a physician would request to assess the need for a treatment change. However, eosinophil count was not included in the patient vignettes, and it is possible that physicians made more conservative treatment suggestions in the absence of this information. Inclusion of eosinophil counts in future studies using patient vignettes would be useful.

This study has some limitations, which should be considered. Physicians who agreed to be a part of the panel may differ from the general practicing clinical community, which may have introduced selection bias into the study. However, this is a common limitation among exploratory studies, which are often subjected to bias due to small sample sizes, and every effort was made to report any observable selection or response bias.<sup>24</sup> The number of physicians who reported that they regularly use the mMRC or CAT when making decisions about a patient's treatment was higher than expected, particularly as findings from a recent study found that the CAT was only used with approximately 7% of pulmonary patients in real-world practice.<sup>25</sup> While this may be the result of the sample intentionally including mainly pulmonologists, who are more likely to be familiar with, and use, these tools regularly in practice, other factors may have influenced these results. Some physicians may not use these tests consistently for all patients, or physicians may intend to use these tests but do not actually end up using them in practice. This study may have also been limited by the potential implicit bias of healthcare professionals in relation to patient characteristics, such as age and gender. This study used a non-validated survey instrument; however, the survey was developed with clinical input and received a critical clinical review prior to survey fielding (including a review from at least one pulmonologist). Survey responses could not be linked directly with data to confirm if physician-reported treatment patterns match the observable data, such as claims or electronic records. Furthermore, vignettes do not capture all the nuances of patient care, including variability in which treatments are covered by patients' insurance. Subsequently, important details could have been missed. Ambiguity in survey questions and/or lack of granularity in responses are also possible limitations. Questions regarding specialty and practice setting may have been answered differently by the physicians based on their own interpretation and/or perception of what the questions were asking, and there may have been some overlap/uncertainty in the responses. For example, it is likely that "primary care" settings may also incorporate physicians who work in ambulatory care practice settings, but this was not offered as a separate option on the survey. Notably, physicians' responses may have been impacted by the coronavirus disease 2019 (COVID-19) pandemic. For example, healthcare workers have experienced a heightened psychological burden as a result of the pandemic, which may have influenced their results. However, as COVID-19 was considered endemic at the time of this study, these findings are expected to still be relevant in future contexts.

## Conclusions

This study demonstrates the complexity of factors that can influence physicians' decisions when prescribing treatments for patients with COPD. Physicians who considered patient's history of new symptoms were more likely to switch to triple therapy versus no change to maintenance inhaler or switch to another maintenance inhaler. This suggests that physicians are more likely to follow treatment guidelines as patients' symptoms become worse or their current maintenance therapy proves to be ineffective. In addition, physicians who had more experience treating patients with COPD were also more likely to switch to triple therapy versus no change to maintenance inhaler or switch to another maintenance inhaler, suggesting that physicians with less experience may choose to observe patients on their current

maintenance therapy before changing their treatment. This research helped generate several hypotheses that would benefit from further research, such as exploring the impact of factors like symptoms and physician years of experience in actual practice versus responding to vignettes. Further work might also address how best to support physicians in the decisions they make, to ensure patients receive appropriate treatment regimens in a timely manner. For example, repeating the survey may help evolve our understanding of how closely physicians follow guidelines. We could also consider tailoring the vignettes/questions more specifically to guideline recommendations.

## Abbreviations

CAT, COPD Assessment Test; CI, Confidence interval; COPD, Chronic obstructive pulmonary disease; COVID-19, Coronavirus disease 2019; ED, Emergency department; FEV<sub>1</sub>, Forced expiratory volume in one second; FVC, Forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, Inhaled corticosteroid; LABA, Long-acting  $\beta_2$ -agonist; LAMA, Long-acting muscarinic antagonist; mMRC, modified Medical Research Council; SABA, Short-acting  $\beta_2$ -agonist; SD, Standard deviation; SOB, Shortness of breath; TT, Triple therapy; US, United States.

## Data Sharing Statement

The datasets supporting the results in this manuscript are not publicly available and will not be provided upon request due to pre-existing data use agreements.

## Ethics Approval and Informed Consent

The study protocol and the survey were submitted to the WCG Institutional Review Board (IRB) for review. All regulatory, independent ethics, and any other review and approvals were obtained and maintained in the study file. The IRB submission package contained documents specified by the central IRB, which included the study protocol and the data collection survey. Study participant recruitment did not begin until IRB approval of all components of the study had been obtained. The study team communicated directly with the central IRB to address any questions and provided any additional information requested in connection with the central IRB's review. Study results were in tabular form, and aggregated analyses omitted subject identification. Study participants provided their consent online to the survey vendor and agreed to the processing and storage of their personal information by the survey vendor. They consented to the transfer of their personal information from relevant third parties (ie, the American Medical Association) and validated the accuracy of the information that they provided to the vendor.

## Consent for Publication

This manuscript does not contain any images, videos, or recordings that require consent for publication.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that was in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the manuscript; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.



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## Disclosure

KK-W is an employee of, and holds stocks/shares in, GSK. BKHB, KJM, MC, NSW, and CKM are employees of Optum, which received research funds from GSK to conduct this study, but not for manuscript development. JF was an employee of Optum, which received research funds from GSK to conduct this study, but not for manuscript development, at the time of this study. WDP and JMW are employees of DARTNet, which received funding from GSK to conduct this study. WDP also reports grants from Boehringer Ingelheim, AstraZeneca, Teva, and Circassia, outside the submitted work. The authors report no other conflicts of interest in this work.

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