

The 2021 Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) guidelines and the outpatient management: Examining physician adherence and its effects on patient outcome

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a common preventable illness that carries a large global economic and social burden. The global initiative for chronic obstructive lung disease (GOLD) guidelines has been utilized as a global strategy for the continued COPD diagnosis, assessment, and treatment. We aimed to determine if the adherence to the 2021 GOLD guideline directed management influenced outcomes. **Materials and Methods:** Retrospective medical records review of adult patients with COPD, who received care in our office during the entire year of 2021. Patients managed as per the 2021 GOLD guidelines were compared with those who received usual care. **Results:** Among 242 patients, 171 (70.7%) were GOLD management adherent (GA) and 71 (29.3%) were GOLD non-adherent (GNA). Certain comorbidities were associated with higher frequencies in the GA group, such as allergic rhinitis (63.2 vs. 18.3%; $P < 0.001$), coronary artery disease (55.9 vs. 38.0%; $P = 0.011$), GERD (63.2 vs. 32.4%; $P < 0.001$), anemia (38.6 vs. 19.7%; $P = 0.004$), malignancy (34.5 vs. 19.7%; $P = 0.023$), and immunodeficiency (12.3 vs. 1.4%; $P = 0.007$). There was no significant difference in the mortality between the GA and GNA groups (5.3 vs. 9.9%; $P = 0.254$). Although the frequency of number of exacerbations was greater in the GA group, the difference in the mean number of exacerbations was not statistically significant (0.39 ± 1.08 vs. 0.39 ± 1.14 ; $P = 0.984$). **Conclusion:** We found no significant difference in the patient outcomes, such as number of exacerbations of COPD and mortality, when comparing the 2021 GOLD guideline adherent versus GOLD guideline non-adherent management of COPD.

Keywords: Chronic obstructive pulmonary disease, COPD management, GOLD guidelines

Introduction

Chronic obstructive pulmonary disease (COPD) is a common and preventable illness that carries a large global economic

and social burden. COPD stands among the top three leading causes of death worldwide. Approximately 90% of the deaths associated with COPD happen in the low to middle income countries.^[1] According to the burden of obstructive lung disease program (BOLD), the global prevalence of COPD happens to be 11.7%.^[2] Globally, there are approximately three million deaths annually.^[3] The burden of COPD is estimated to grow in the next decades given the aging population and continued rise of

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cigarette smoking around the world with a projected 5.4 million annual death rate by 2060.^[4] Aside from the social burden, COPD imposes a significant economic burden. In the United States, the estimated direct cost of COPD is approximately \$32 billion with another \$20.4 billion involving indirect costs.^[5] The most well-studied risk factor is cigarette smoking; however, environmental factors, such as occupational, outdoor, and indoor air pollution, are known contributors, as well.^[6] The American Thoracic Society estimates that 10–20% of symptoms and functional impairment consistent with COPD can be attributed to occupational exposures.^[7]

COPD is characterized by persistent respiratory symptoms and airflow limitations due to airway and alveolar abnormalities, mostly caused by significant exposure to noxious particles, or gases.^[8] These noxious particles and gases are responsible for chronic airway inflammation which may induce parenchymal tissue destruction, and disruption of normal repair and defense mechanisms. The mechanism of this inflammatory process has not been entirely well understood, but important contributing factors include oxidative stress, inflammatory cells' mediators, and protease antiprotease imbalances.^[9] The extent of inflammation, fibrosis, and luminal exudates in the small airways corresponds with the reduction in the forced expiratory volume in the first one second (FEV1) and the ratio of the FEV1 to the forced vital capacity of the lungs (FEV1/FVC), which results into progressive decline in FEV1, which is characteristic of COPD.^[10] These complications lead to abnormalities in gas exchange leading to hypoxemia, hypercapnia, mucus hypersecretion, and pulmonary hypertension.^[11]

While presenting with many clinical diagnostic indicators of COPD, a spirometry is necessary to establish the diagnosis of COPD. The presence of a post-bronchodilator FEV1/FVC <0.7 confirms the presence of COPD.^[12] Patients who present with dyspnea, chronic cough, sputum production, and recurrent lower respiratory tract infections, with or without a history of exposure to risk factors, should be evaluated for COPD. COPD assessment utilizes the severity of findings in the spirometry, severity of symptoms, number of exacerbations, and additional comorbidities. COPD assessment is eventually utilized to help guide therapy. In 1997, the National Heart, Lung, and Blood Institute (NHLBI), the National Institutes of Health (NIH), and the World Health Organization (WHO) started the global initiative for chronic obstructive lung disease (GOLD) guidelines with aims to raise awareness of COPD and to guide clinicians and other healthcare experts to design better ways to prevent and treat COPD. The GOLD guideline has been widely utilized as a global strategy for the continued COPD diagnosis, assessment, and treatment recommendations.

GOLD classifies airflow limitations based on the FEV1 values from a stage GOLD-1 (mild: FEV1 >80%), GOLD-2 (Moderate: FEV1 50% to <80% predicted), GOLD-3 (Severe: FEV1 30% to <50% predicted), to GOLD-4 (Very Severe: FEV1 <30% predicted). FEV1 severity alone is not a good prognostic indicator

of COPD severity;^[13] therefore, symptomatic assessment is also needed. In practice, there are two symptomatic assessment tools commonly utilized: COPD Assessment Test (CAT) and the modified Medical Research Council (mMRC) dyspnea scale. These tools along with the severity of exacerbations, including hospitalizations, help categorize a patient into the ABCD treatment groups. GOLD uses these COPD assessment tools with the severity of airflow limitation (spirometry grade 1 to 4) and the letters (group A to D) provide the necessary information related to symptom burden, and the risk of exacerbations to help guide medication management.^[8]

Treatment of COPD is guided by prevention and maintenance measures. Preventative measures have dealt greatly with smoking cessation, as it has shown to have the greatest impact on the development and/or worsening of COPD.^[14] Pharmacological therapy for stable COPD is geared toward reducing symptoms, reducing the frequency and severity of exacerbations, and improving quality of life. Pharmacologic modalities include bronchodilators: including short acting beta₂ agonists (SABA) and long acting beta₂ agonists (LABA), long-acting anti-muscarinic agents (LAMA), methylxanthines, inhaled corticosteroids (ICS) or oral corticosteroids, phosphodiesterase-4 inhibitors, and combination therapies. Non-pharmacologic modalities include pulmonary rehabilitation, oxygen therapy, and surgical interventions. Initial pharmacotherapy is based on the patient's GOLD group with follow-up recommendations based on the response to initial treatment.

Although the 2021 GOLD guidelines of COPD management are considered as the standard for diagnosis and treatment, strict adherence to the management recommendations varies among the clinical practices. There are a few studies that have examined the outcomes of morbidity and mortality in patients who were managed strictly by following the GOLD guidelines. One study examined the physicians' adherence or non-adherence to the 2017 GOLD management guidelines and outcomes in a single suburban clinic. They found that adherence to guidelines had no statistically significant difference in patient outcomes.^[15] Another retrospective cohort study looked at the effect of adherence to the 2017 GOLD treatment recommendations on COPD healthcare resource utilization, cost, and exacerbations among patients with COPD on maintenance therapy, and concluded that there was a trend toward a high prevalence of suboptimal prescriber compliance to GOLD treatment recommendations with 32.9% of patients in the GOLD A/B group and 58.9% of patients in the GOLD C/D group who were considered being on GOLD adherent regimens.^[16] In the GOLD adherent patients, there was an 8% reduction in exacerbation in GOLD A/B and another 12% reduction in GOLD C/D groups.^[16] Currently, there are no published studies that have described whether adherence to the 2021 GOLD guidelines improves outcomes. In this study, we aimed to examine whether adherence to the 2021 GOLD management guidelines affected patient outcomes in the form of reduced number of exacerbations, hospitalizations, and mortality, compared to non-adherence to the 2021 GOLD management guidelines.

Materials and Methods

Study design and setting

Our study was a retrospective cohort study of an entire population of the existing electronic medical records of patients with COPD or emphysema, who had an office visit in one of our internal medicine offices which serves the suburban population. Our internal medicine office is affiliated with a tertiary healthcare center.

Participants

We included adult patients who were 18 years of age, or older, with a diagnosis of COPD or emphysema as diagnosed by a post-bronchodilator FEV1/FVC <0.7 on spirometry, who were seen in our office between January 1 and December 31, 2021. We excluded patients under the age of 18, those without a documented diagnosis of COPD or emphysema, and patients with another underlying pulmonary disorder(s) other than COPD, such as patients with bronchial asthma as the only diagnosis, or who had hypersensitivity pneumonitis, interstitial lung disease, lung cancer, or severe restrictive lung disease due to chest wall disorders, such as kyphoscoliosis.

Variables

The data collected for each patient included their age, gender, race, body mass index (BMI), history of cigarette smoking, spirometry parameters, pulmonologist evaluation and follow-up; comorbid medical conditions, such as hypertension, hyperlipidemia, atherosclerotic cardiovascular disease (ASCVD), diabetes mellitus, allergic and immunological disorders, immunodeficiency, thyroid disorder, malignancy, gastrointestinal disorder, polycythemia, other hematological illnesses, obstructive sleep apnea, central nervous system disorders, and chronic kidney disease. We also collected data on the number of exacerbations in a year (defined as episodes of increasing respiratory symptoms, such as cough, dyspnea, sputum production, and increased sputum purulence, which resulted in sustained worsening of symptoms from a stable state necessitating office evaluation, emergency room visit, or hospitalization for a change in regular medication, additional medication management, and/or mechanical ventilator support), Modified Medical Research Council (mMRC) dyspnea score; management, such as SABA, LABA, short acting antimuscarinic agent (SAMA), LAMA, ICS, long-term oral antibiotic, roflumilast, oral corticosteroid, home oxygen therapy, pulmonary rehabilitation; 2021 GOLD assessment and management group (A/B/C/D), adherence to GOLD recommendations, hospitalization for COPD exacerbation, and mortality.

Data source and access

The Institutional Review Board (IRB) of our institution reviewed and approved this study (IRB: 22-078). The IRB granted permission to collect data and other materials solely for the purpose of research as permitted by the Health Insurance Portability and Accountability Act (HIPAA), and informed

consent waivers were granted. The study was also compliant with the IRB ethical standards. We used the EPIC electronic medical records (Epic Systems Corporation, Verona, Wisconsin, USA) that are used by our institution for the electronic medical record keeping of our patients. There was no built-in clinical decision support program to assess the GOLD treatment groups; hence, each medical record was individually reviewed for data collection. Full access to data recorded in the electronic medical records was granted to all the investigators only for the list of patients approved by the medical informatics who fitted into the inclusion criteria of our study.

Bias

To address the potential for inaccurate or inconsistent diagnosis of COPD, we carefully reviewed each progress note and excluded patients with bronchial asthma as the only diagnosis, or who had hypersensitivity pneumonitis, interstitial lung disease, lung cancer, or severe restrictive lung disease due to chest wall disorders, such as kyphoscoliosis. We also excluded patients who had FEV1/FVC value of 0.7 or greater.

Study size

The entire population of our 242 adult patients who had a diagnosis of COPD received care in our office during the entire year of 2021. This sample size was able to provide 80% power and 5% alpha error.

Quantitative variables

The most recent data of the quantitative variables were selected, which include age, BMI, FEV1, FEV1/FVC ratio, and DLCO.

Statistical methods

We used Microsoft Excel (2016, Redmond, Washington, USA) spreadsheet for data entry, and we used SPSS (Statistical Package for the Social Sciences, version 15.01, IBM, Armonk, New York, USA) software for data analysis. We grouped our patients into two groups: the first represented the group of patients who received management as per the 2021 GOLD guidelines (GOLD adherent group, or GA), and the second included the group of patients who received management that did not align with the 2021 GOLD guidelines (GOLD non-adherent group, or GNA). To determine the alignment of management of as per the 2021 GOLD assessment and management guidelines, the management groups (A/B/C/D) were individually assessed based on the documentation of FEV1, mMRC score, and the number of exacerbations in a year.^[8] We analyzed the categorical data as frequencies using percentages and the continuous data as means with standard deviations, or medians and interquartile ranges. We applied Chi-Square and Fisher's exact tests to compare the proportions. To determine whether the variables had a significant relationship with mortality, exacerbations, and disease progression, we used logistic regression models. It was also determined by the distribution of the data for several exacerbations. We interpreted a *P* value of < 0.05 as the definition of statistical significance.

Results

We included 242 adult patients. One hundred seventy-one (70.7%) were in the GOLD adherent (GA) group, and 71 (29.3%) were in the GOLD non-adherent (GNA) group. We found no significant difference in the mean ages of patients in the GA group (72.9 years) compared to the GNA group (72.9 years) ($P=0.999$) [Table 1]. Among the frequencies of males and females, there were no statistically significant differences between the two groups. Race distribution showed that the majority of the patients in both groups identified as White, followed by Black, Hispanic, and other races; however, we

found no significant difference between the two groups in the race distribution [Table 1]. In both groups, tobacco use was high; we found no significant difference between the GA and GNA groups (86.9% vs. 87.3%, respectively). We found no significant difference in the mean BMI between the two groups, which indicated that the patients were in the overweight category in both groups ($GA = 27.9 \pm 7.0 \text{ kg/m}^2$ vs. $GNA = 28.9 \pm 7.6 \text{ kg/m}^2$) [Table 1]. Similarly, spirometry indices showed no significant difference [Table 1].

Analysis of comorbidities revealed that certain comorbidities had higher frequencies of association in the GA group compared

Table 1: Baseline characteristics

Variable	Variable	GOLD not adherent (n=71)	GOLD adherent (n=171)	P
Age	Years, mean (SD)	72.9 (10.2)	72.9 (11.1)	0.999
Sex	Male, n (%)	36 (50.7)	81 (47.4)	0.636
	Female, n (%)	35 (49.3)	90 (55.6)	
Race	White, n (%)	51 (71.8)	125 (73.1)	0.792
	Black, n (%)	11 (15.5)	27 (15.8)	
	Hispanic, n (%)	4 (5.6)	12 (7.0)	
	Other, n (%)	5 (7.0)	7 (4.1)	
Social	Tobacco use, n (%)	62 (87.3)	146 (86.9)	0.930
Weight	BMI (kg/m ²), mean (SD)	28.9 (7.6)	27.9 (7.0)	0.338
Spirometry	FEV ₁ /FVC ratio, mean (SD)	61.6 (15.1)	61.9 (19.7)	0.936
	FEV ₁ %, mean (SD)	77.3 (26.1)	73.6 (35.1)	0.436
	DLCO, mean (SD)	67.9 (22.1)	70.5 (21.8)	0.580
Comorbidities	Hypertension, n (%)	56 (78.9)	135 (78.9)	0.990
	DM, n (%)	22 (31.0)	59 (34.5)	0.659
	CVA, n (%)	8 (11.3)	23 (13.5)	0.644
	Hyperlipidemia, n (%)	51 (71.8)	130 (76.0)	0.494
	Allergic Rhinitis, n (%)	13 (18.3)	108 (63.2)	<0.001
	CAD, n (%)	27 (38.0)	95 (55.9)	0.011
	CHF, n (%)	5 (7.3)	10 (6.1)	0.478
	OSA, n (%)	13 (18.3)	49 (28.7)	0.093
	GERD, n (%)	23 (32.4)	108 (63.2)	<0.001
	CKD, n (%)	15 (10.7)	28 (16.4)	0.379
	Anemia, n (%)	14 (19.7)	66 (38.6)	0.004
	Malignancy, n (%)	14 (19.7)	59 (34.5)	0.023
	Hypothyroidism, n (%)	13 (18.3)	37 (21.6)	0.560
	Immunodeficiency, n (%)	1 (1.4)	21 (12.3)	0.007
Medications	Polycythemia, n (%)	1 (1.4)	2 (1.2)	1.000
	SABA, n (%)	44 (47.9)	118 (69.0)	0.290
	LAMA-LABA, n (%)	34 (52.1)	61 (35.7)	0.076
	ICS, n (%)	37 (61.1)	84 (49.1)	0.672
	Roflumilast, n (%)	2 (5.6)	0 (0.0)	0.085
	Oral Corticosteroid, n (%)	4 (2.8)	17 (9.9)	0.278
	Home Oxygen, n (%)	2 (1.4)	14 (8.2)	0.161
	Oral Antibiotic, n (%)	0 (0.0)	26 (15.2)	<0.001
	Pulmonary Rehab, n (%)	3 (4.2)	2 (1.2)	0.128
	GOLD Class	A	47 (66.2)	117 (68.4)
B		15 (21.1)	9 (5.3)	<0.001
C		3 (4.2)	28 (16.4)	<0.001
D		6 (8.5)	17 (9.9)	<0.001
Subspecialty	Pulmonologist follow-up	48 (67.6)	108 (63.5)	0.546
Exacerbations	1 or more per year	9 (12.7)	29 (17.0)	0.404
Mortality	Dead, n (%)	7 (9.9)	9 (5.3)	0.254

n=Number of patients, SD=Standard deviation, BMI=Body mass index, FEV₁/FVC=Forced expiratory volume in the first one second to the Forced vital capacity ratio, FEV₁=Forced expiratory volume in the first one second, DLCO=Diffusing capacity of the lungs for carbon monoxide, DM=Diabetes mellitus, CVA=Cerebrovascular accident, CAD=Coronary artery disease, CHF=Congestive heart failure, OSA=Obstructive sleep apnea, GERD=Gastroesophageal reflux disorder, CKD=Chronic kidney disease, SABA=Short-acting beta2 agent, LAMA=Long-acting muscarinic antagonist, LABA=Long-acting beta2 agonist, ICS=Inhaled corticosteroid

to the GNA group, such as allergic rhinitis (63.2 vs. 18.3%; $P < 0.001$), GERD (63.2 vs. 32.4%; $P < 0.001$), coronary artery disease (55.9 vs. 38.0%; $P = 0.011$), anemia (38.6 vs. 19.7%; $P = 0.004$), malignancy (34.5 vs. 19.7%; $P = 0.023$), and immunodeficiency (12.3 vs. 1.4%; $P = 0.007$) [Table 1].

We found that although there were more patients in the GNA group who were on LABA-LAMA and ICS compared to the GA group, nonetheless the differences in the frequencies were not statistically significant (52.1 vs. 35.7%; $P = 0.076$, and 61.1 vs. 49.1%; $P = 0.672$, respectively). Similarly, there were no differences in the use of SABA, Roflumilast, oral corticosteroid, home oxygen use, and pulmonary rehabilitation, between the two groups [Table 1]. The patients in the GA group had a significantly higher frequency of use of long-term oral antibiotics compared to GNA group [Table 1].

Most of the patients in both groups were categorized as in the 2021 GOLD management group A (GA = 68.4% vs. GNA = 66.2%). However, there were significantly more patients in the GA group who belonged to the GOLD management group A, C, and D; and significantly lesser patients who were in the group B management group compared to the GNA group. About two-thirds of the patients in each group received outpatient pulmonologist care [Table 1]. Although the mean frequency of number of exacerbations per year was higher in GA group, the difference was not statistically significant ($0.39 + 1.08$ vs. $0.39 + 1.14$; $P = 0.984$) [Figure 1]. We found that the patients in the GA group had a mortality rate of 5.3%, while those in the GNA group had a mortality rate of 9.9%; however, the difference was not statistically significant ($P = 0.254$).

Logistic regression revealed that for each unit increase in FEV1%, there was 0.94 times decrease in the odds of exacerbations (95% CI 0.91–0.97, $P = 0.001$) [Table 2]. We also found that there were increased odds of mortality in patients who were on home oxygen therapy (OR 8.77, 95% CI 1.93–39.72, $P = 0.041$), and for each unit increase in BMI (OR 1.083, 95% CI 1–1.17, $P = 0.041$) [Table 3].

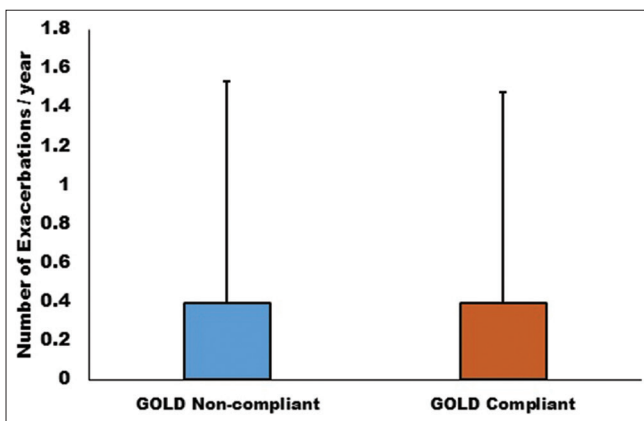


Figure 1: Mean number of symptom exacerbations in patients treated as per the GOLD guidelines compared to those who were not

Discussion

The majority of our patients with COPD (70.7%) received management as per the 2021 GOLD management guidelines, which happens to be far greater than the GOLD adherent COPD management reported in various studies as per the various editions of GOLD guidelines, which range from only one-third to half of the cases in similar settings.^[17-21] However, 29.3% of our patients received management that did not align with the 2021 GOLD management guidelines.

Several studies have attempted to address the barriers to the implementation of GOLD guidelines in managing patients with COPD, such as insufficient familiarity with the evolving guidelines among the physicians, as well as the inadequacy of the implementation programs.^[22,23] A study examining the management of COPD by 593 primary care general practitioners found that about 8% of the subjects received management based on their GOLD severity staging.^[24] Certain factors, such as lack of familiarity with GOLD management guidelines, decreased self-efficacy, and severe time constraints were identified as barriers.^[25]

A study of 15 hospitals and 340 privately practicing pulmonologists examined their management of COPD as per the GOLD guidelines. The study concluded that the compliance was problematic and showed a significant discrepancy between the complex ABCD group system of GOLD management categorization and real-life COPD management in their clinical practice.^[26] The more recent 2023 GOLD COPD guidelines regarding medication management of COPD based on the assessment of individual patients’ symptoms and exacerbation

Table 2: Logistic regression: Outcome exacerbations

Variable	B	P	Exp (B)	95% C.I. for Exp (B)	
				Lower	Upper
Age	0.046	0.236	1.047	0.970	1.131
Body mass index	-0.034	0.463	0.966	0.882	1.059
Sex Male	-1.122	0.104	0.326	0.084	1.257
Race White	-0.971	0.191	0.379	0.088	1.625
FEV1%	0.060	0.001	0.942	0.910	0.974
DLCO	0.012	0.511	1.012	0.976	1.050
GOLD Class	0.331	0.648	1.392	0.336	5.764

Table 3: Logistic regression: Outcome mortality

Variable	B	P	Exp (B)	95% C.I. for Exp (B)	
				Lower	Upper
Age	0.031	0.349	1.032	0.966	1.101
Body mass index	0.080	0.041	1.083	1.003	1.170
Sex Male	0.477	0.413	1.612	0.514	5.054
Race White	-0.440	0.550	0.644	0.152	2.724
Malignancy	0.837	0.194	2.309	0.654	8.156
Chronic kidney disease	1.310	0.050	3.705	0.998	13.757
Home Oxygen	2.171	0.005	8.766	1.934	39.721
GOLD Class	-0.888	0.159	0.411	0.120	1.416

risk follow the ABE assessment categories, which essentially combines groups C and D into group E (patients with a rate of ≥ 1 severe or ≥ 2 moderate exacerbations per year, irrespective of their symptoms degree), indicating no difference in the management between the groups C and D.^[27] The 2023 GOLD guidelines highlight the fact that there are no randomized controlled trials or other high-quality meaningful research studies that support initial medication management strategy in newly diagnosed COPD patients.^[27] Additionally, there are studies that also indicate patient related barriers in adherence to GOLD management guidelines as well, such as accurately reporting symptoms or exacerbation rate, in contrast to objective spirometry findings.^[17,28]

Our study showed no significant difference in the mean frequency of number of exacerbations per year or mortality between the GA and GNA groups. Although certain comorbidities were greater in the GA group compared to the GNA group, such as allergic rhinitis, coronary artery disease, GERD, anemia, malignancy, and immunodeficiency; nevertheless, we found no significant differences in the number of exacerbations, or mortality. In our study, although not statistically significant, nonetheless more patients in the GNA group received triple therapy with LABA, LAMA, and ICS compared to the GA group based on their clinical presentation, regardless of symptoms degree or the number of exacerbations; which is likely supported by the findings of the studies which concluded that triple therapy was associated with lower rates of exacerbations, better health related quality of life, better lung functions, and fewer hospitalizations compared to dual therapy (LABA and LABA, or LABA and ICS), or monotherapy with only LAMA or only LABA.^[29,30] We believe that it is important to recognize the potential harms of possible overtreatment with triple therapy in the form of increasing management cost or increasing the incidence of pneumonia.

A study examining the GOLD recommendations on patient outcomes and cost-effectiveness revealed that redistributing patients from the usual COPD management strategy to medication management based on the GOLD recommendations resulted in reduced incidence of pneumonia across Belgium, Sweden, Germany, and the USA.^[31] Other significant findings included a decreased number of exacerbations in Belgium, Germany, and the USA; however, there was a small increase in Sweden. Results even demonstrated a reduction of up to 13% in estimated annual direct costs stemming from reduced hospitalizations, cost of treatment for pneumonia, and cost savings from long-acting inhaler therapy.^[31] On the contrary, there are studies that reported that adherence to COPD management as per the GOLD guidelines demonstrated no superiority in lung function, prevalence of symptom severity or annual number of exacerbations,^[32] and no significant difference in patient outcomes,^[15] which align with our findings. It is noteworthy that about two-thirds of the patients in each group belonged to GOLD management group A, indicating a well-functioning or less symptomatic population of patients in both groups. In our study, there were significantly more patients who belonged to

GOLD management group B in the GNA group as compared to the GA group indicating a relatively more symptomatic and advanced remaining population of COPD patients who likely required triple therapy.

We would like to emphasize that all the patients in our study were followed and treated by the physicians. No one received medical care from nurse practitioners (NP) or physician assistants (PA). Additionally, all the patients in our study had medical insurance (commercial, private, Medicare, and Medicaid) that covered the cost of their prescription medications.

There were several limitations to our study. Retrospective data collection limited our ability to rely solely on the available data entry by the patient care teams; hence, variables, such as socioeconomic status and other social determinants of health, could not be reliably ascertained, which could have influenced the medication affordability and compliance. We also acknowledge that our suburban office setting limits the patient population to a specific type based on their race distribution, which limits the generalizability. The major strength of our study was the entire population of patients who followed a single office and received care from their specific physicians in the practice over a long time period. It allowed them to document their degree of symptoms, exacerbations, spirometry values, associated comorbidities, and emerging disorders as they emerged over a long time period.

Conclusions

We found no significant difference in the patient outcomes, such as number of exacerbations of COPD and mortality, when comparing the 2021 GOLD guideline adherent versus GOLD guideline non-adherent management of COPD. Long-term studies in different settings are needed to further evaluate the guideline-based management of COPD.

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Conflicts of interest

There are no conflicts of interest.

References

1. Halpin DMG, Celli BR, Criner GJ, Frith P, López Varela MV, Salvi S, *et al.* The GOLD Summit on chronic obstructive pulmonary disease in low- and middle-income countries. *Int J Tuberc Lung Dis* 2019;23:1131-41.
2. Adeloye D, Chua S, Lee C, Basquill C, Papan A, Theodoratou E, *et al.* Global and regional estimates of COPD prevalence: Systematic review and meta-analysis. *J Glob Health* 2015;5:020415.

3. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;385:117-71.
4. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS, *et al.* Chronic obstructive pulmonary disease: Current burden and future projections. *Eur Respir J* 2006;27:397-412.
5. Guarascio AJ, Ray SM, Finch CK, Self TH. The clinical and economic burden of chronic obstructive pulmonary disease in the USA. *Clinicoecon Outcomes Res* 2013;5:235-45.
6. Eisner MD, Anthonisen N, Coultas D, Kuenzli N, Perez-Padilla R, Postma D, *et al.* An official American Thoracic Society public policy statement: Novel risk factors and the global burden of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2010;182:693-718.
7. Balmes J, Becklake M, Blanc P, Henneberger P, Kreiss K, Mapp C, *et al.* American Thoracic Society Statement: Occupational contribution to the burden of airway disease. *Am J Respir Crit Care Med* 2003;167:787-97.
8. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2021. Available from: https://goldcopd.org/gold-reports/gold-report-2021-v1-0-11nov20_wmv/. [Last accessed on 2023 June 28].
9. Barnes PJ. Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. *J Allergy Clin Immunol* 2016;138:16-27.
10. Hogg JC, Chu F, Utokaparch S, Woods R, Elliott WM, Buzatu L, *et al.* The nature of small-airway obstruction in chronic obstructive pulmonary disease. *N Engl J Med* 2004;350:2645-53.
11. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006;3:e442. doi: 10.1371/journal.pmed.0030442.
12. Buist AS, McBurnie MA, Vollmer WM, Gillespie S, Burney P, Mannino DM, *et al.* International variation in the prevalence of COPD (the BOLD Study): A population-based prevalence study. *Lancet* 2007;370:741-50.
13. Jones PW. Health status and the spiral of decline. *COPD* 2009;6:59-63.
14. van Eerd EA, van der Meer RM, van Schayck OC, Kotz D. Smoking cessation for people with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2016;2016:CD010744.
15. Chinai B, Hunter K, Roy S. Outpatient management of chronic obstructive pulmonary disease: Physician adherence to the 2017 global initiative for chronic obstructive lung disease guidelines and its effect on patient outcomes. *J Clin Med Res* 2019;11:556-62.
16. Palli SR, Zhou S, Shaikh A, Willey VJ. Effect of compliance with GOLD treatment recommendations on COPD health care resource utilization, cost, and exacerbations among patients with COPD on maintenance therapy. *J Manag Care Spec Pharm* 2021;27:625-37.
17. Mannino DM, Yu TC, Zhou H, Higuchi K. Effects of GOLD-adherent prescribing on COPD symptom burden, exacerbations, and health care utilization in a real-world setting. *Chronic Obstr Pulm Dis* 2015;2:223-35.
18. Mularski RA, Asch SM, Shrank WH, Kerr EA, Setodji CM, Adams JL, *et al.* The quality of obstructive lung disease care for adults in the United States as measured by adherence to recommended processes. *Chest* 2006;130:1844-50.
19. Koblizek V, Pecan L, Zatloukal J, Kocianova J, Plutinsky M, Kolek V, *et al.* Real-life GOLD 2011 implementation: The management of COPD lacks correct classification and adequate treatment. *PLoS One* 2014;9:e111078.
20. Sharif R, Cuevas CR, Wang Y, Arora M, Sharma G. Guideline adherence in management of stable chronic obstructive pulmonary disease. *Respir Med* 2013;107:1046-52.
21. Yawn BP, Wollan PC. Knowledge and attitudes of family physicians coming to COPD continuing medical education. *Int J Chron Obstruct Pulmon Dis* 2008;3:311-7.
22. Overington JD, Huang YC, Abramson MJ, Brown JL, Goddard JR, Bowman RV, *et al.* Implementing clinical guidelines for chronic obstructive pulmonary disease: Barriers and solutions. *J Thorac Dis* 2014;6:1586-96.
23. Rutschmann OT, Janssens JP, Vermeulen B, Sarasin FP. Knowledge of guidelines for the management of COPD: A survey of primary care physicians. *Respir Med* 2004;98:932-7.
24. Li F, Cai Y, Zhu Y, Chen X, Xu X, Zhang X, *et al.* The evaluation of general practitioners' awareness/knowledge and adherence to the GOLD guidelines in a Shanghai suburb. *Asia Pac J Public Health* 2015;27:NP2067-78.
25. Perez X, Wisnivesky JP, Lurshurchachai L, Kleinman LC, Kronish IM. Barriers to adherence to COPD guidelines among primary care providers. *Respir Med* 2012;106:374-81.
26. Tzanakis N, Koulouris N, Dimakou K, Gourgoulisanis K, Kosmas E, Chasapidou G, *et al.* Classification of COPD patients and compliance to recommended treatment in Greece according to GOLD 2017 report: The RELICO study. *BMC Pulm Med* 2021;21:216.
27. Global strategy for the diagnosis, management and prevention of COPD; 2023. Available from: <https://goldcopd.org/2023-gold-report-2/>. [Last accessed on 2023 June 28].
28. Foda HD, Brehm A, Goldstein K, Edelman NH. Inverse relationship between nonadherence to original GOLD treatment guidelines and exacerbations of COPD. *Int J Chron Obstruct Pulmon Dis* 2017;12:209-14.
29. Zheng Y, Zhu J, Liu Y, Lai W, Lin C, Qiu K, *et al.* Triple therapy in the management of chronic obstructive pulmonary disease: Systematic review and meta-analysis. *BMJ* 2018;363:k4388.
30. Lipson DA, Barnhart F, Brealey N, Brooks J, Criner GJ, Day NC, *et al.* Once-daily single-inhaler triple versus dual therapy in patients with COPD. *N Engl J Med* 2018;378:1671-80.
31. Sethi S, Wright A, Hartgers-Gubbels ES, Hechtner M, Clark B, Wright C, *et al.* Costs and clinical consequences of compliance with COPD GOLD recommendations or national guidelines compared with current clinical practice in Belgium, Germany, Sweden, and the United States. *Int J Chron Obstruct Pulmon Dis* 2022;17:2149-60.
32. Jochmann A, Scherr A, Jochmann DC, Miedinger D, Török SS, Chhajed PN, *et al.* Impact of adherence to the GOLD guidelines on symptom prevalence, lung function decline and exacerbation rate in the Swiss COPD cohort. *Swiss Med Wkly* 2012;142:w13567.