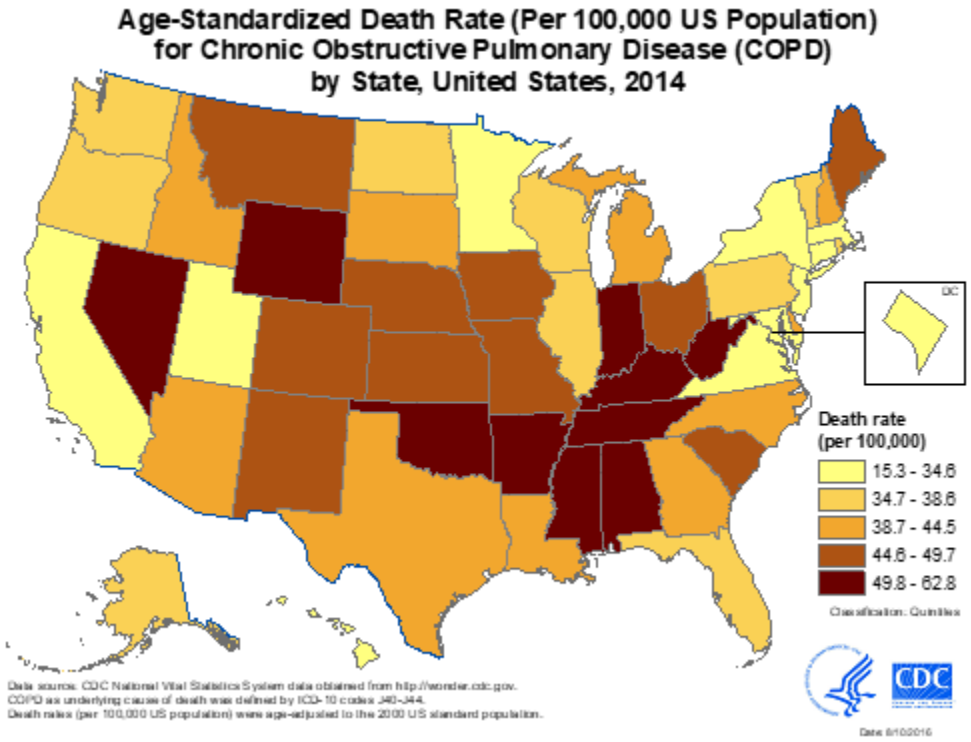
CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) TREATMENT PATTERNS AND GOLD GUIDELINES

BACKGROUND

Chronic obstructive pulmonary disease (COPD) is a major contributor to morbidity and mortality in the United States and around the world. According to the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics, chronic lower respiratory disease, primarily COPD, was the 3rd leading cause of death in the United States in 2016.[1] An estimated 15.7 million adults (6.4%) in the US reported that they have been diagnosed by a health professional as having COPD.[2] In 2014, Mississippi was in the top 10 states having the highest age-adjusted death rate for COPD. (Figure 1)

FIGURE 1: Age-standardized Death Rate for COPD United States 2014[3]



[1] National Center for Health Statistics. *Health, United States 2017 with Special Feature on Mortality.* Hyattsville, MD: US Dept Health and Human Services; 2018

[2] Wheaton AG, Cunningham TJ, Ford ES, Croft JB. Employment and activity limitations among adults with chronic obstructive pulmonary disease — United States, 2013. *MMWR Morb Mortal Wkly Rep.* 2015:64 (11):290–295.

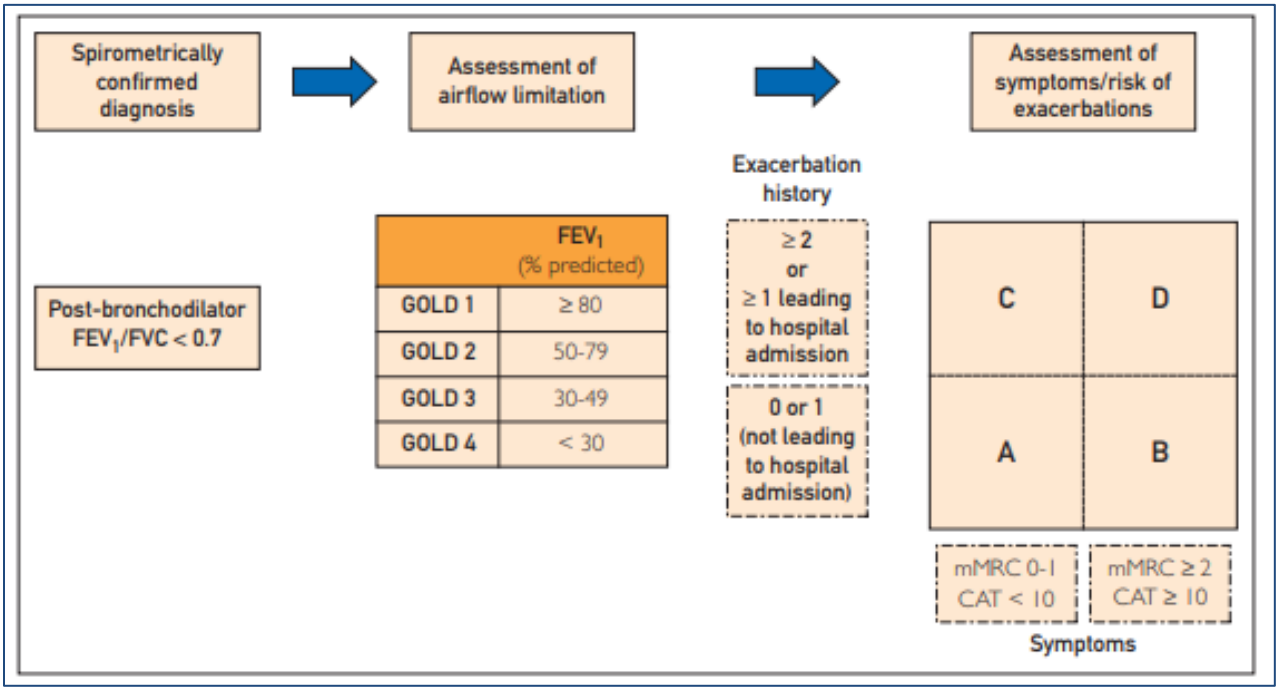
[3] Centers for Disease Control and Prevention: COPD Death Rates in the United States. https://www.cdc.gov/copd/data.htm
COPD as underlying cause of death was defined by ICD-10 codes J40-J44. Death rates (per 100,000 US population) were age-adjusted to the 2000 US standard population

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) was established with the purpose of focusing attention on the management and prevention of COPD. A diverse expert panel initially reviewed established guidelines and current evidence and presented the first consensus report in 2001. GOLD has since published major revisions to the original document in 2006, 2011, and 2017. Minor updates are published nearly annually.[4,5]

GOLD's treatment recommendations are based upon symptom burden and exacerbations. Patients are categorized into groups A to D correlating to exacerbation frequency and symptom severity. (Figure 2)

- Patients in groups A and C have lower symptom burden compared to groups B and D patients;
- Groups A and B include patients with ≤ 1 outpatient exacerbation annually;
- Groups C and D represent patients with ≥ 2 outpatient exacerbations annually or ≥ 1 exacerbation leading to hospitalization.

FIGURE 2: Refined ABCD Assessment Tool Recommended by GOLD 2017/2018



CAT = COPD Assessment Test; GOLD = Global Initiative for Chronic Obstructive Lung Disease; mMRC = modified Medical Research Council.

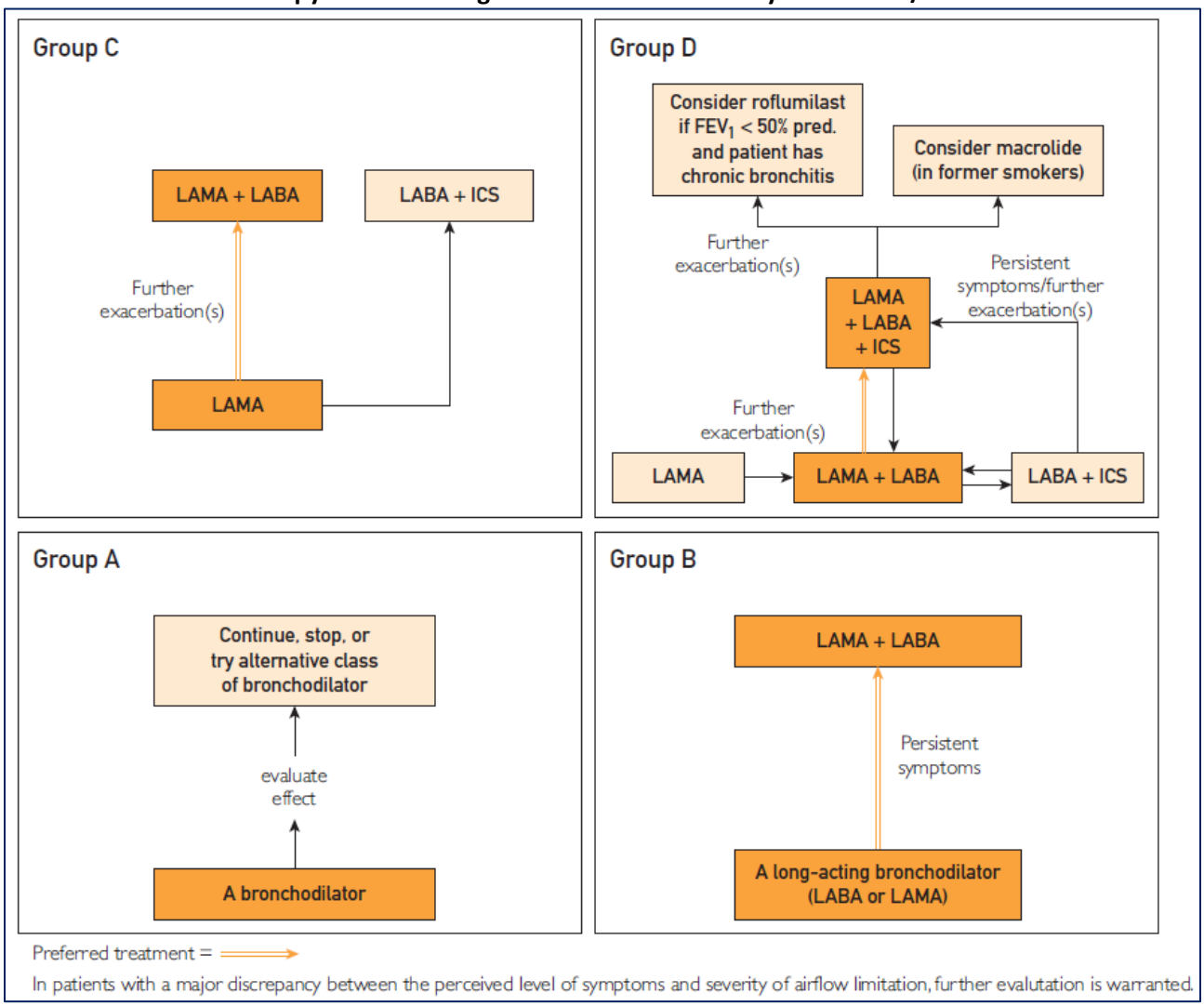
Source: Mirza S, Clay RD, Koslow MA, Scanlon PD. COPD Guidelines: A Review of the 2018 GOLD Report. Mayo Clin Proc. October 2018;93(10):1488-1502. https://doi.org/10.1016/j.mayocp.2018.05.026

[4] GOLD. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2018. 2018. https://goldcoped.org/. Accessed November 2018.

[5] *Mirza S, Clay RD, Koslow MA, Scanlon PD. COPD Guidelines: A Review of the 2018 GOLD Report. Mayo Clin Proc. October 2018;93(10):1488-1502. https://doi.org/10.1016/j.mayocp.2018.05.026*

Pharmacotherapy treatment recommendations for patients are based upon symptom burden and exacerbations as defined by group assignment. (Figure 3)

FIGURE 3: Pharmacotherapy Treatment Algorithm Recommended by GOLD 2017/ 2018



ICS = inhaled corticosteroid; LABA = long-acting beta agonist; LAMA = long-acting muscarinic antagonist

Source: Mirza S, Clay RD, Koslow MA, Scanlon PD. COPD Guidelines: A Review of the 2018 GOLD Report. Mayo Clin Proc. October 2018;93(10):1488-1502. https://doi.org/10.1016/j.mayocp.2018.05.026

A summary of key recommendations for each group based on the current model are as follows:

Group A:

- Trial of short-acting bronchodilator for intermittent symptoms
    - Short-acting beta agonist (SABA), short-acting muscarinic antagonist (SAMA), or combination SABA/SAMA
- Long-acting bronchodilator for low-grade persistent symptoms

Group B:

- Long-acting bronchodilator monotherapy
    - Long-acting beta agonist (LABA) or long-acting muscarinic antagonist (LAMA)
- Escalation to dual therapy with persistent symptoms (LABA/LAMA)

Group C:

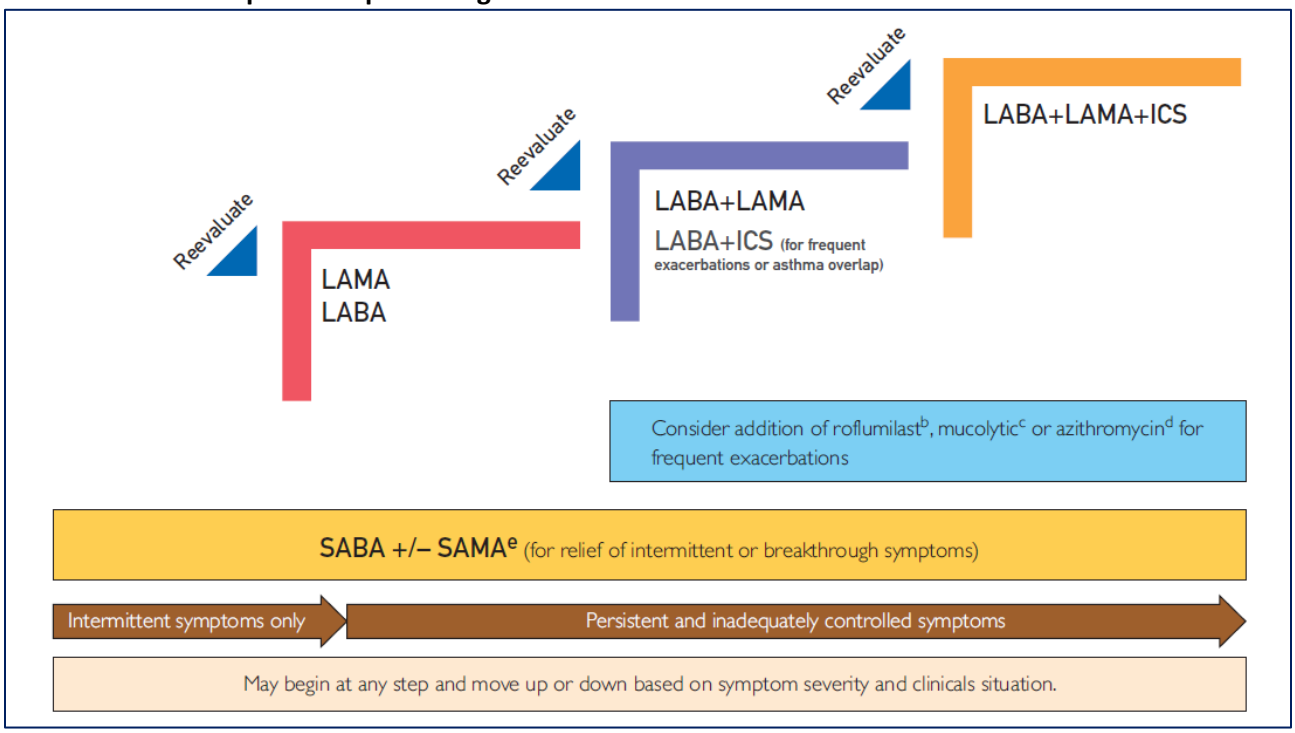
- LAMA monotherapy may be utilized for frequent exacerbations with low symptom burden
- For further exacerbations, LABA/LAMA combination or LABA/ inhaled corticosteroid (ICS) combination

Group D:

- Baseline therapy may include a LAMA, LABA/LAMA, or LABA/ICS
- Escalate to triple therapy with LABA/LAMA/ICS or phosphodiesterase 4 (PDE4) inhibitor or macrolide based on indications

A step-wise algorithm based on guideline recommendations is displayed below. (Figure 4)

FIGURE 4: GOLD Proposed Step-wise Algorithm Based on Usual Clinical Practice



[a] ICS = inhaled corticosteroid; LABA = long-acting beta agonist; LAMA = long-acting muscarinic antagonist; SABA = short-acting beta agonist; SAMA = short-acting muscarinic antagonist.

[b] Roflumilast (Daliresp) may be considered for patients with severe-very severe obstruction with chronic bronchitis and frequent exacerbations.

[c] Mucolytics may be considered in patients with chronic bronchitis and frequent exacerbations.

[d] Azithromycin may be considered for reduction of exacerbations in former smokers over age 65 and mild airflow obstruction.

[e] Avoid routine concomitant SAMA use when on LAMA.

Source: Mirza S, Clay RD, Koslow MA, Scanlon PD. COPD Guidelines: A Review of the 2018 GOLD Report. Mayo Clin Proc. October 2018;93(10):1488-1502. https://doi.org/10.1016/j.mayocp.2018.05.026

METHODS

A retrospective analysis was conducted using Mississippi Medicaid pharmacy and medical claims data from January 1, 2017 to June 30, 2018. The sample included beneficiaries enrolled in Medicaid fee-for-service (FFS) and coordinated care organizations (CCOs). Beneficiaries were classified as having COPD if they had a medical claim for a physician visit, emergency department (ED) visit, or hospitalization containing a COPD diagnoses code (J41, J43.9, J44) during the study period. Treatment patterns were evaluated for compliance with the GOLD guidelines following exacerbation events occurring for "stable" COPD patients.

- Patients were considered to be stable on therapy if they had gone at least six months without an exacerbation event.
    - Exacerbation events included any ED visit or hospitalization with a primary diagnosis of COPD.

Post-exacerbation treatment was examined for agreement with the GOLD guidelines. Pre-exacerbation treatment included all prescriptions filled within 45 days of the exacerbation event and post-exacerbation treatment included all prescriptions filled within 45 days after discharge for the exacerbation event. Three criteria were evaluated with respect to agreement with GOLD guidelines for treatment post-exacerbation.

1. Regardless of the COPD maintenance medication used by stable patients prior to an exacerbation event, post-event regimens should include a long-acting bronchodilator to prevent further exacerbations. Any regimen containing a long-acting bronchodilator was considered as appropriate treatment (LABA, LAMA, LABA/LAMA, LABA/ICS, LABA/LAMA/ICS).
2. If a patient had been on a single long-acting bronchodilator prior to an exacerbation event, the GOLD guidelines recommend a combination inhaler should be provided after further exacerbations occur (e.g. prior regimen was LABA or LAMA change to LABA/LAMA or LABA/ICS).
3. When further exacerbations occur for patients already on a combination inhaler regimen, the GOLD guidelines recommend triple therapy be provided (e.g. prior regimen was LABA/LAMA or LABA/ICS change to LABA/LAMA/ICS).

RESULTS

Table 1 summarizes the COPD population in Mississippi Medicaid. A total of 23,365 beneficiaries were identified as having COPD during the observation period. Of these, 22,171 (95%) were stable (exacerbation free) on therapy for 6 months or more. Of the patients who had a stable period of therapy, 2,915 (13%) had one or more exacerbation during the observation year. Patients who did not remain stable for the entire observation year had an average of 1.8 exacerbation events during the observation year. A total of 5,269 exacerbation events were identified among the patients classified as stable for at least 6 months. The vast majority (86%) of these events were ED visits. Only 21% of the COPD exacerbations were preceded by a doctor's visit within 6 months for managing COPD.

TABLE 1: Summary of Medicaid COPD Population
(FFS and CCOs, January 1, 2017 to June 30, 2018)

Total number of beneficiaries with COPD	**23,365**
Beneficiaries with stable COPD during observation period	22,171 (94.9%)
Beneficiaries having 1 or more exacerbations	2,915 (12.5%)
Total number of exacerbation events	5,269
ED visits	4,518
Hospitalizations	751
Average number of exacerbation events for beneficiaries experiencing exacerbations	1.8
Exacerbation events where patient had COPD related physician visit within 6 months	1,101 (20.9%)
Mean time to last physician visit when one occurred before an exacerbation event	69.8 days

Table 2 shows the pre-exacerbation regimen and post-exacerbation regimen for patients who were classified as stable before having a COPD exacerbation event. The pre-event regimen was determined by prescription fills 45 days prior to the event and the post-event regimen was determined by prescription fills 45 days following the event.

Of particular concern is the finding that following exacerbation events:

- 1,735 (48%) patients did not fill a prescription for any COPD treatment within 45 days, and
- 1,104 (31%) filled prescriptions for short acting bronchodilators products only.

Although these patients may have still been taking other COPD products, not having filled a controller medication within 45 days of an exacerbation could indicate poor medication adherence/ lack of persistency when prescribed COPD medication(s).

TABLE 2: COPD Regimen Pre- and Post-Exacerbation for Beneficiaries Stable for Six or More Months
(FFS and CCOs, January 1, 2017 to June 30, 2018)

Regimen Pre-exacerbation[a]	Regimen Post-exacerbation[b]													
	NONE	SA	LABA	LABA / ICS	LABA / ICS / SA	LABA / LAMA / SA	LABA /SA	LAMA	LAMA / ICS	LAMA / ICS / SA	LAMA / SA	TRIPLE	TRIPLE / SA	Total number on pre-exacerbation regimen
NONE	1,026	242	1	27	17	0	0	14	2	0	5	0	4	1,338
SA	482	657	1	60	74	1	4	11	1	0	29	2	20	1,342
LABA	1	1	0	0	0	0	0	0	0	0	0	0	0	2
LABA / ICS	94	89	0	83	43	0	0	4	2	0	4	2	2	323
LABA / ICS / SA	54	68	0	44	110	0	0	4	0	0	10	4	1	295
LABA / LAMA / SA	0	1	0	0	1	1	0	0	0	0	0	0	0	3
LABA /SA	2	7	0	0	1	0	0	0	0	0	0	0	0	10
LAMA	33	12	0	6	1	0	0	28	1	0	7	5	0	93
LAMA / ICS	5	0	0	0	0	0	0	0	0	0	0	0	0	5
LAMA / ICS / SA	0	0	0	0	0	0	0	0	0	2	0	0	0	2
LAMA / SA	16	16	0	1	3	3	0	3	1	0	22	2	1	68
TRIPLE	11	5	1	3	1	0	0	6	0	0	4	19	8	58
TRIPLE/ SA	11	6	0	1	7	0	0	9	0	0	8	13	23	78
Total number on post-excerbation regimen	1,735	1,104	3	225	258	5	4	79	7	2	89	47	59	3,617

ICS = inhaled corticosteroid; LABA = long-acting beta agonist; LAMA = long-acting muscarinic antagonist; SA = short-acting beta agonist, short-acting muscarinic antagonist and combinations of these; TRIPLE = Trelegy Ellipta, a combination LABA/LAMA/ICS.

[a] *Pre-exacerbation regimen included all prescriptions filled within 45 days of the exacerbation event.*

[b] *Post-exacerbation regimen included all prescriptions filled within 45 days of discharge from exacerbation event.*

Coding key: *post regimen not consistent with GOLD recommendations*

The following is an example of how to interpret table 2:

- See row 2 (SA): 1,342 beneficiaries were only taking SA products prior to having an exacerbation event. Of these, after the exacerbation 657 were only taking SA products, a total of 180 were taking regimens including LABA or LAMA, and 23 were taking regimens including both LABA and LAMA.

CONCLUSIONS AND RECOMMENDATIONS

During this measurement period, there is room for improvement in compliance with the GOLD guidelines for COPD in the treatment of Medicaid beneficiaries. Although minor changes in treatment recommendations were made in the 2018 guidelines, the vast majority of treatment recommendations evaluated in this study were included in the 2017 guidelines. Increasing compliance with the GOLD guidelines should help to maintain control of COPD and thus decrease the number of exacerbations resulting in ED visits and hospitalizations, as well as, a decrease in productivity, quality of life, and even death.

Recommendations

1. DOM and MS-DUR should undertake a provider educational initiative to promote greater adherence to the GOLD guidelines.
2. If possible, DOM and the CCOs should implement patient management programs to improve medication adherence and help assure appropriate treatment regimens among COPD patients following an exacerbation event.
3. CCOs are invited to present at the next DUR meeting their initiatives and related outcomes on improving treatment regimens for COPD beneficiaries.