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Commonly Prescribed Medications Among Patients in Hospice Care for Chronic Obstructive Pulmonary Disease

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Abstract

Purpose—End-stage chronic obstructive pulmonary disease (COPD) presents health care providers with challenges of providing optimal palliative care for patients who follow a less predictable trajectory. The objectives of this study were to evaluate medications being prescribed to patients with end-stage COPD, compared to recommendations made by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, and to determine which medications were provided by the hospice organization.

Methods—We retrospectively reviewed our database for medications pertaining to COPD management as stated in the GOLD criteria or those used for symptoms associated with end of life.

Results—A total of 745 patients met inclusion criteria, and approximately 63% were prescribed opioids. Prescribing rates for oxygen, short-acting β_2-agonists, and short-acting anticholinergics were 37%, 33%, and 31%, respectively. Systemic and inhaled corticosteroids were prescribed at higher rates of 20% and 18% compared to long-acting bronchodilators.

Discussion—Medications used for COPD exacerbation management were prescribed at higher rate than those used for maintenance treatment.

Keywords

chronic obstructive pulmonary disease; palliative care; hospice care; end of life; bronchodilators; opioids

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Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder defined as irreversible obstruction of the airways. Smoking is a primary risk factor for COPD that contributes to lung hyperinflation and increased sputum production. As of 2002, COPD was estimated by the World Health Organization to be the fifth leading cause of mortality worldwide and is projected to be the third leading cause of mortality by 2030. In the United States, COPD is the third leading cause of mortality with 134 676 deaths in 2010.[,] Chronic obstructive pulmonary disease is characterized by dyspnea, weakness, fatigue, and chronic increased mucus production. In advanced COPD, there is a severe reduction in quality of life and social functioning as well as an increased burden for caregivers. Terminally ill patients with COPD experience an increased level of psychological stress, anxiety, fatigue, and depression. Compared to patients with end-stage lung cancer, COPD is associated with lower quality of life.[,] An estimated 1.6 million people received hospice services in 2012, and lung disease was the fourth most common noncancer primary diagnosis for hospice admission accounting for 8.2% of total admissions. In the United Sates, patients with COPD are eligible for hospice admission under Medicare if they meet criteria for terminal stage of pulmonary disease (life expectancy of ≤6 months) listed in Table 1.[,]

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines (revised 2011) group patients with COPD into 4 categories based on symptoms, exacerbation, and spirometric classifications. Hospice patients most likely fit the profile of group D, characterized by severe or very severe airflow limitations, more symptoms, and high risk of exacerbations. Recommendations for initial pharmacologic management of COPD are summarized in Table 2. For patients with mild or moderate COPD in groups A and B, the first choice recommendation is to use bronchodilators as monotherapy. An alternative is to use a combination of 2 bronchodilators or add theophylline. For patients with severe or very severe COPD in groups C and D, the first choice recommendation is to use inhaled corticosteroids (ICSs) in combination with a long-acting B_2 agonist (LABA) or monotherapy with a long-acting anticholinergic (LAAC). As patients in group D experience more symptoms, a combination of 3 medications may be used as an alternative choice. There is a third-line recommendation for group D patients, which include a mucolytic, such as carbocysteine or N-acetylcysteine.

The sensation of breathlessness is the most troublesome symptom experienced by 90% of terminally ill patients with COPD. Patients are often afraid to sleep due to the fear that they will suffocate to death. Nonpharmacologic therapies for dyspnea symptom management such as supplemental oxygen help improve exercise tolerance and daily activity.[,] The GOLD guidelines also recommend opioids such as morphine for relief of dyspnea symptoms. Psychiatric symptoms such as depression and anxiety are also common in patients with advanced COPD. A 2006 systematic review showed that 51% to 75% patients with end-stage COPD experienced anxiety and 37% to 71% experienced depression. Thus, recognition and appropriate management of psychiatric symptoms are essential components of the comprehensive care of these patients. To the best of our knowledge, this is the first study to evaluate prescribing practices based on published practice guidelines for hospice patients with COPD.

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Methods

This study retrospectively evaluated medications prescribed to hospice patients with a primary admission diagnosis of COPD. Data for this study were provided by Seasons Hospice & Palliative Care, a national hospice organization with locations in 15 states. We used a clinical database of patient demographic and medication information gathered from patients' electronic medical records. Patients were included in the study if they were admitted to hospice on or after January 1, 2013, and if they were discharged by death on or before December 31, 2013. Patients were excluded if they had admitting diagnoses other than COPD. The Institutional Review Board at the University of Maryland approved this study.

Medications prescribed at any time during a patient's hospice admission related to COPD management were included in this study. Therapeutic classes of medications or specific medications recommended in the GOLD guidelines for management of stable COPD or exacerbations pertaining to group D patients were counted as medications related to COPD. The electronic medical record contained information on drug name, dosage, formulation, strength, route and frequency of administration, and discontinuation date if applicable. In addition, information on the medication provider (hospice or patient) was also obtained. Combination formulations (eg, albuterol plus ipratropium) were evaluated as 2 separate medications. Different dosage formulations were considered to be the same drug (eg, albuterol metered dose inhalers and albuterol nebulizers). Demographic information extracted for analysis included age, sex, race, and length of stay. We determined the percentage of patients prescribed medications commonly used in the management of COPD and associated end-of-life symptoms as well as the percentage of medications for COPD treatment that were provided by the hospice organization. Our database was collected in the year 2013; therefore, in our analysis, we utilized the 2011 revised GOLD criteria, which was the most current version during the period of our data collection. We used Microsoft Excel for all analyses.

Results

A total of 8557 patients were screened, with 745 meeting the inclusion criteria. Patients included in this study were prescribed a total of 9980 medications, medical devices (ie, inhaler companions and masks), and nutritional supplements. The average age was 79.9 years (standard deviation 10.4 years), and the majority (55%) of patients were females. The average number of days spent in hospice was 28.9, with a range of 0 to 307 days. Patient demographics are summarized in Table 3.

Medications prescribed during hospice were analyzed according to their therapeutic class. The percentage of patients prescribed the various classes of medications analyzed is shown in Figure 1. Opioids were the most commonly prescribed COPD-related medication; notably morphine was prescribed for 54.1% of patients, hydromorphone for 5.5%, and codeine for 3.4%. The SABA was commonly prescribed, and albuterol and levalbuterol were prescribed for 29.3% and 2.0% of the patients, respectively. Most of the LABA prescribed were part of a combination with corticosteroids. Of the 109 (14.6%) patients prescribed LABA, 94

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(12.6%) patients received a combined LABA and ICS medication. Aformoterol, formoterol, and salmeterol were each prescribed for less than 1% of the patients. Comparatively, for the anticholinergic medications, SAAC (ipratropium) was prescribed more often than LAAC (tiotropium) at 30.6% versus 9.1%, respectively. Oral and inhaled corticosteroids were modestly prescribed for 20.3% and 17.9% of the patients. Codeine was the most prescribed antitussive. Twenty-five (3.4%) patients, were prescribed codeine, whereas nonnarcotic cough suppressants, such as benzonatate, were prescribed for less than 1% of the patients. Expectorants were prescribed at low rate, for 8.3% of the patients. Methylxanthines (theophylline) were prescribed for only 1.1% of the patients. Only 3 (0.4%) patients were prescribed a mucolytic medication (N-acetylcysteine). Although carbocysteine is in the GOLD guidelines, it is not an available medication in the United States, therefore N-acetylcyteine was evaluated. For COPD medications with multiple formulations, the solution for nebulizer was more prescribed compared to the metered-dose inhalers (MDIs) or dry powder inhalers (PDIs; Table 4).

The hospice organization provided the majority of COPD-related medications (Figure 2). Medications provided by hospice over 80% of the time included opioids, oxygen, SABA, SAAC, inhaled and oral corticosteroids, LABA, and antitussives. Medications with hospice coverage of 40% or less included LAAC, leukotriene receptor antagonist (LTRA), phosphodiesterase 4 inhibitor (PDE4-I), and mucolytics. Expectorants and methylxanthines were moderately covered by hospice. Overall, there was a low rate of medication discontinuation prior to discharge.

Psychotropic medications used for management of symptoms associated with end-of-life illness such as anxiety, delirium, depression, and sleep dysfunction were analyzed. As shown in Figure 3, anxiolytic medications, which included mostly benzodiazepines, were prescribed for 58.5% of the patients followed by antipsychotics at 42.4%. Antidepressants (ie, serotonin and norepinephrine reuptake inhibitors [SNRIs]) and nonbenzodiazepine hypnotics (zolpidem) were prescribed at 19.1% and 3.1%, respectively. The hospice organization provided the majority of these medications (Figure 4).

Discussion

The GOLD criteria (2011) recommend LAAC or ICS plus LABA as the first-line options for end-stage COPD. In our analysis of hospice patients, approximately 1 in 5 patients were prescribed a combined ICS/LABA agent, and 1 in 10 patients were prescribed a noncombination LAAC agent. A second-line recommendation is the addition of PDE4-I to the chosen first-line treatment. We found that PDE4-I was not commonly prescribed. A third-line option for hospice patients with COPD is to add a mucolytic agent as it is speculated that the antioxidant properties of N-acetylcysteine offer benefit for patients with recurrent exacerbation. The use of mucolytics is not presently recommended by the GOLD guidelines due to inconclusive results on the benefits of these agents. Not surprisingly, less than 1% of this study population received a mucolytic medication. For COPD exacerbations, the preferred treatment is SABA with or without SAAC, and oral corticosteroids may be added. Medications used for the treatment of exacerbations such as albuterol, ipratropium, and oral corticosteroids were prescribed for a higher percentage of our patient population

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than first-line maintenance medications, that is, tiotropium and ICS/LABA combinations. First-line agents prescribed for this patient population were ordered mostly as MDI and DPI formulations. In end-stage COPD, where functional capacity is limited, inhalers, that is, DPIs, which require high inspiratory rate to actuate the inhaler, can be difficult for patients to use correctly. Previous studies have suggested that inhaler technique errors increase with severity of airflow limitation and number of different types of inhalers used.[9]

Therapies commonly prescribed for controlling dyspnea were opioids and oxygen. Opioids have been the mainstay treatment for end-of-life dyspnea.[10] We found a low use of cough-specific medications. This observation most likely suggests that in this patient population where the majority of patients were prescribed opioids, additional cough-specific preparations are not needed, given the cough suppressive effects of opioids. Antitussives are not recommended by the GOLD guidelines for routine use in stable COPD due to the protective role of productive cough in early disease; however, in severe COPD where cough is distressing, it is acceptable to use antitussives to relieve patients of symptoms.

Management of psychiatric symptoms that present themselves in end-stage COPD is essential. We found that 40% to 60% of the study population were prescribed anxiolytics and antipsychotics. Medications for depression and anxiety have to be used cautiously, as these drugs present increased adverse risk to the frail and elderly population. Anxiolytics such as lorazepam can cause delirium in elderly patients. Given the fact that there are risks associated with the use of psychotropic medications, nonpharmacologic therapies such as cognitive/behavioral modification with music therapy, guided imagery, and bedside relaxation techniques are great alternatives that can be employed to reduce anxiety and depression in the end-of-life care. Comparatively, antidepressants and nonbenzodiazepine hypnotics were prescribed at much lower rates.

The primary strength of this analysis is that the data source included a diverse group of patients from 15 states in the United States in various hospice settings. Another strength is the detailed prescription information such as medication formulation, dosage, strength, and route of administration that were provided in the patient database set. Limitations of this study include the lack of information on medication indication and actual administration, for instance, it is not clear if or how frequently patients actually used prescribed medications. Additionally, the database did not contain information on comorbidities, therefore an evaluation of the appropriateness of prescribed medications in the presence of comorbidities was not possible. Because some medications (eg, opioids and corticosteroids) have multiple indications, medications that we considered to be used for COPD-related symptoms may not have been prescribed for that purpose.

Since the collection of our database in 2013, there have been updates made to the GOLD guidelines. The 2011 version of the GOLD guidelines was the most current vision in 2013, thus we utilized the 2011 version in our analysis instead of the newer 2015 version. There were no significant differences in regard to treatment recommendations between the older and the newer version of guidelines. Therefore, our study conclusions are still relevant in face of the newer guideline version.

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Conclusion

Our study illustrates that, like other advanced diseases, end-of-life COPD care is more focused on palliative therapy and acute symptom management as evident by the lower prescribing rates of first- and second-line long-term maintenance medications compared to therapies for acute exacerbation. Although it may be practical for health care providers to adhere to recommendation guidelines for patients in stable COPD, the recommendations have to be more flexible in end-stage disease. Thus, individualization of therapy in hospice is important as patients with COPD do not follow a predictable trajectory in end of life. In cases where providers are not familiar with the patient's COPD history and management, it might be expected of the provider to adhere to guideline recommendations initially; however, as patient–provider relationship become established, management can be modified with the primary goal of meeting individual comfort and maintaining quality of life without strict adherence to guidelines. This study will hopefully serve as a starting point for further research into optimal treatment of patients with end-stage COPD and may help hospice organizations develop educational materials for hospice staff and patients.

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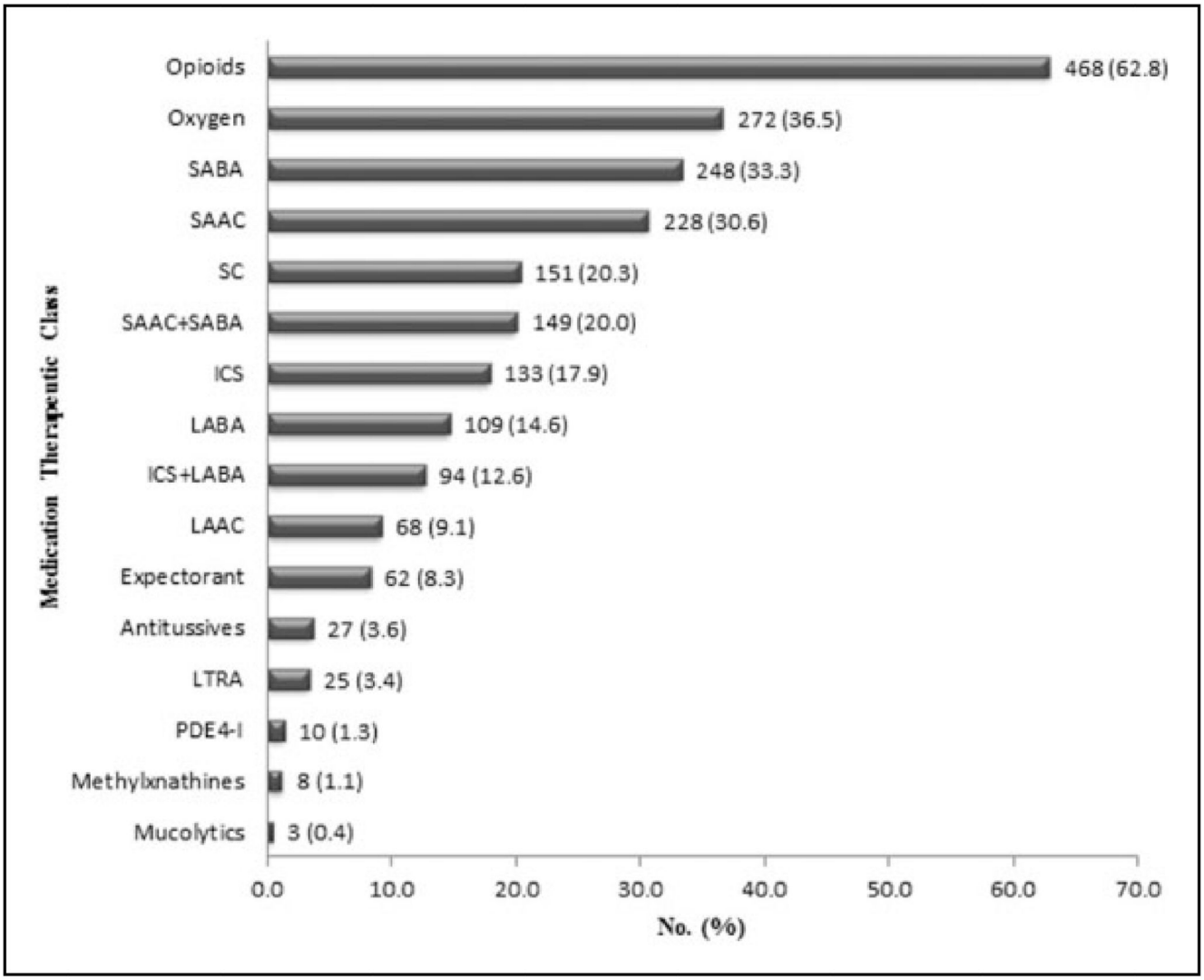

Figure 1.

Percentage of patients prescribed medications commonly used in chronic obstructive pulmonary disease (COPD) grouped by therapeutic class. ICS indicates inhaled corticosteroid; LAAC, long-acting anticholinergic; LABA, long-acting β_2-agonist; LTRA, leukotriene receptor antagonist; PDE4-I, phosphodiesterase-4 inhibitor; SAAC, short-acting anticholinergic; SABA, short-acting β_2-agonist; SC, systemic corticosteroid.

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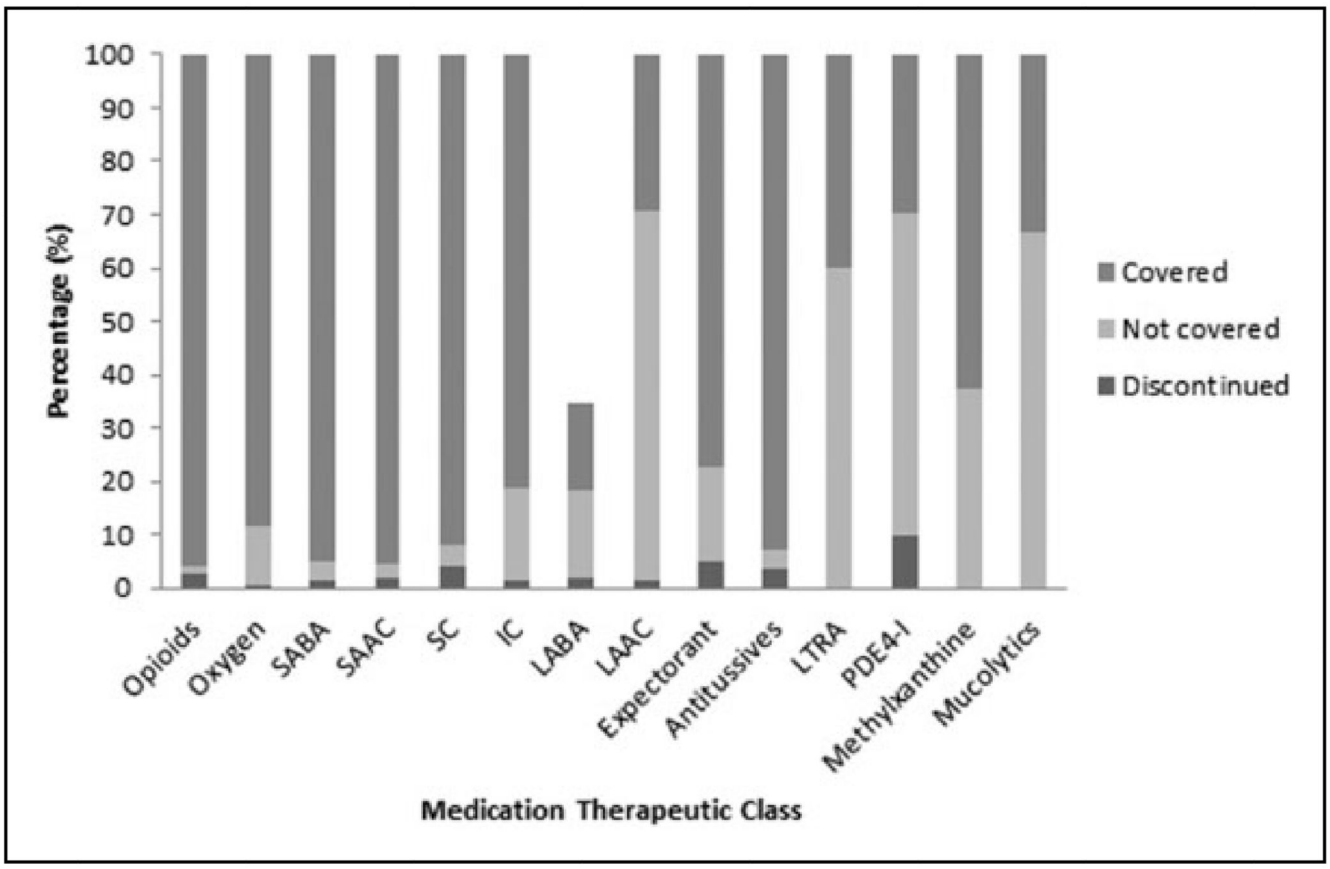

Figure 2.

Percentage of medications that were either provided by the hospice organization (covered) or by the patient (not covered) and any that were discontinued while on hospice.

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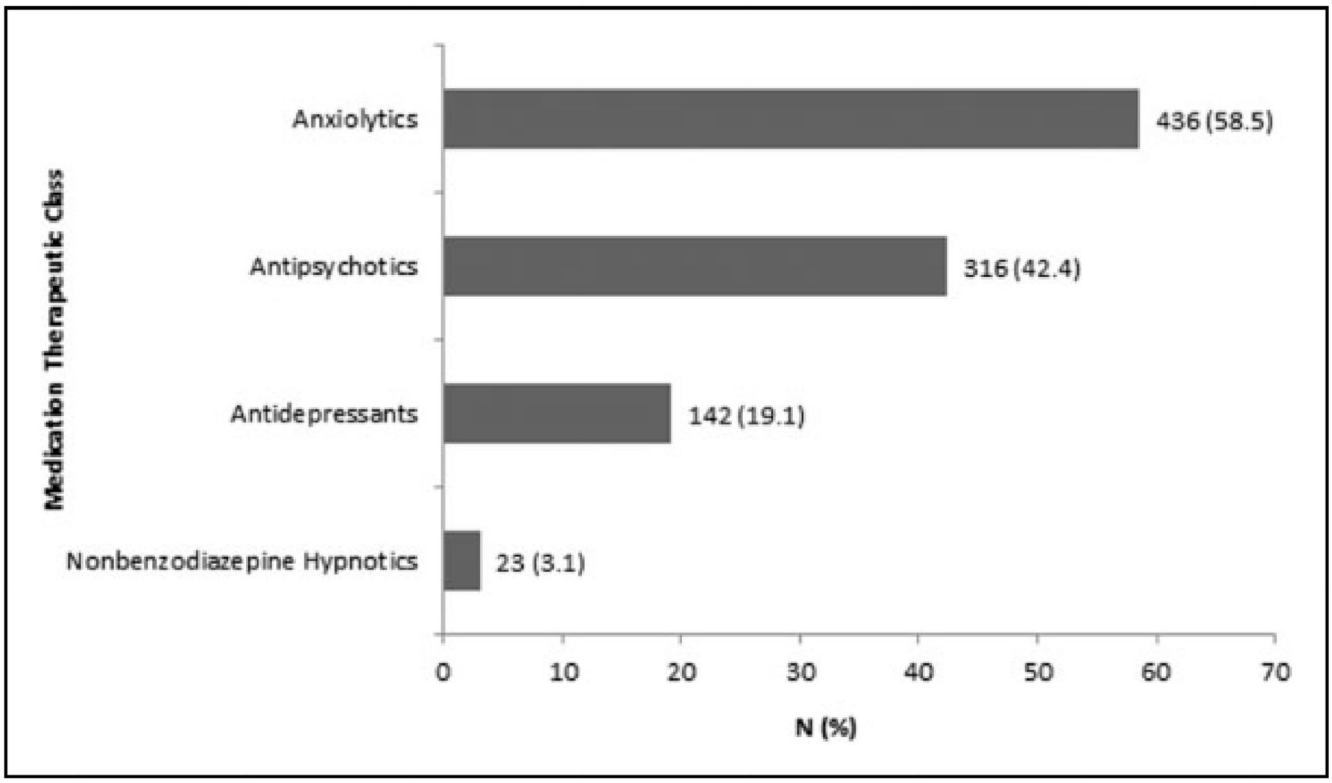

Figure 3.

Percentage of patients prescribed medications belonging to the therapeutic classes of anxiolytics, antipsychotics, antidepressants, and nonbenzodiazepine hypnotics.

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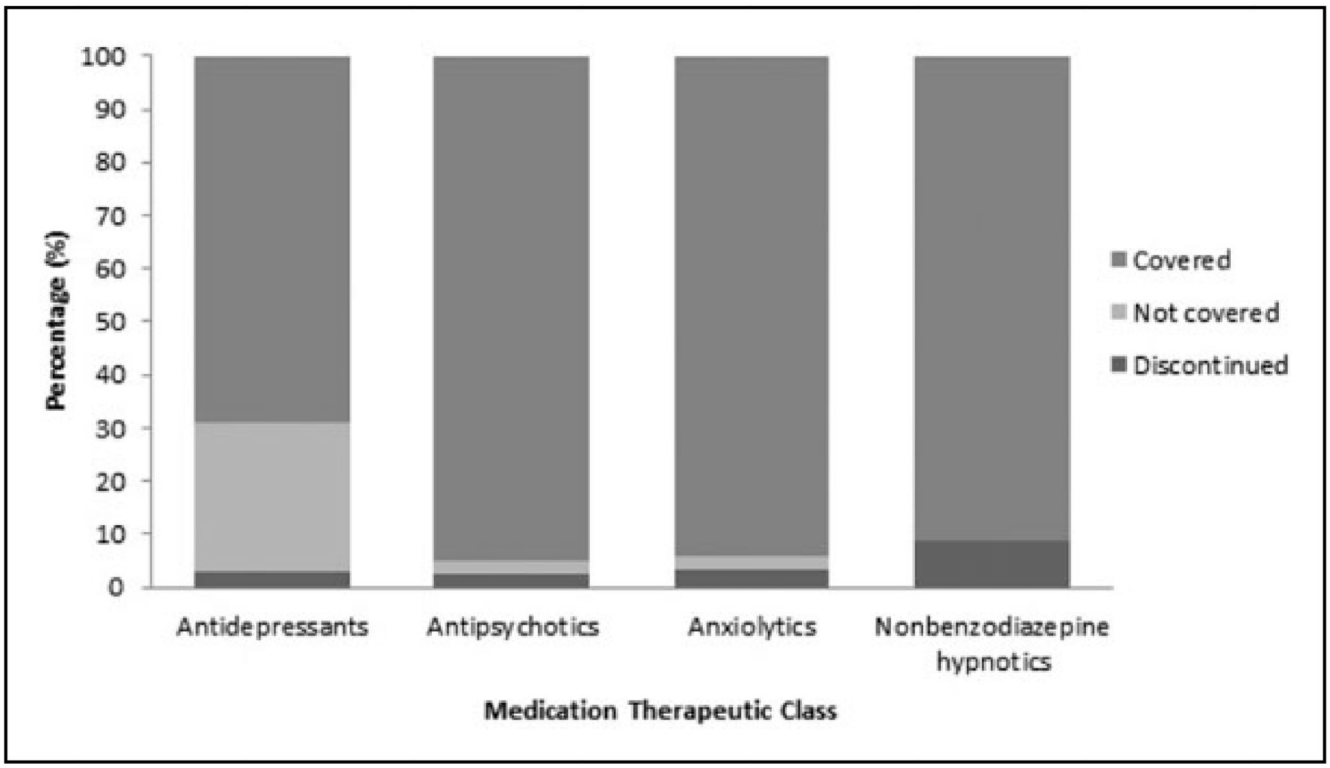

Figure 4.

Percentage of psychotropic medications that were either provided by hospice (covered) or the patient (not covered) as well as those discontinued during hospice stay.

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Table 1

Criteria for Terminal Stage of Pulmonary Disease.

(Criteria 1 and 2 must be present; 3, 4, or 5 are supporting documentation)	
1	Severe chronic lung disease as documented by both A and B;
	A. Disabling dyspnea at rest, poorly or unresponsive to bronchodilators, resulting in decreased functional capacity, for example, bed to chair existence, fatigue, and cough (documentation of forced expiratory volume in 1 second [FEV1], after bronchodilator, <30% of predicated is objective evidence for disabling dyspnea but is not necessary to obtain)
	B. Progression of end-stage pulmonary disease as evidenced by prior increasing visits to the emergency department or prior hospitalizations for pulmonary infections and/or respiratory failure (documentation of serial decrease of FEV1 > 40 mL/year is objective evidence for disease progression but is not necessary to obtain)
2	Hypoxemia at rest on room air, as evidenced by pO_2 < 55 mm Hg or oxygen saturation <88% on supplemental oxygen or hypercapnia, as evidenced by pCo_2 > 50 mm Hg
3	Cor pulmonale and right heart failure (RHF) secondary to pulmonary disease (eg, not secondary to left heart disease or valvulopathy)
4	Unintentional progressive weight loss >10% of body weight over the preceding 6 months
5	Resting tachycardia >100 beats/min

[a]Modified from references.›

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Table 2

Initial Pharmacologic Management of COPD.[a]

Patient Category	Recommended first choice	Alternative choice	Other possible treatment
A • Few symptoms • Low Risk of exacerbations • GOLD 1-2	SAAC prn or SABA prn	LAAC or LABA or SABA and SAAC	Theophylline
B • More symptoms • Low Risk of exacerbations • GOLD 1-2	LAAC or LABA	LAAC and LABA	SABA and/or SAAC Theophylline
C • Few symptoms • High risk of exacerbations • GOLD 3-4	ICS + LABA or LAAC	LAAC and LABA or LAAC and PDE4-I	SABA and/or SAAC Theophylline
D • More symptoms • High risk of exacerbations • GOLD 3-4	ICS + LABA or LAAC	ICS + LABA and LAAC or ICS + LABA and PDE4-I or LAAC and LABA or LAAC and PDE4-I	Carbocysteine[b] SABA and/or SAAC Theophylline

Abbreviations: CPOD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LAAC, long-acting anticholinergic; LABA, long-acting β_2-agonist; PDE4-I, phosphodiesterase 4 inhibitor; SAAC, short-acting anticholinergic; SABA, short-acting β_2-agonist.

[a] Modified from reference.

[b] Carbocysteine is not available in the United States and thus, N-acetylcysteine use was evaluated.

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Table 3

Patient Demographics.

Characteristic	N (%)
Total no. patients	745
Age, mean years + SD	79.9 (10.4)
Male	333 (44.1)
Female	410 (55.0)
Unknown sex	2 (0.3)
Race	
Caucasian	556 (74.6)
African American	82 (11)
Hispanic	79 (10.6)
Asian	7 (0.9)
Other	3 (0.4)
Unknown	18 (2.4)
Length of stay on hospice, days	
<8	365 (49.0)
8-30	211 (28.3)
31-90	96 (12.9)
>90	73 (9.8)
Average	28.9 days
Range	0-307 days

Abbreviation: SD, standard deviation.

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Table 4

Formulations and Routes for Prescribed COPD-Related Medications According to Therapeutic Class.

Medication and/or therapeutic class, [N][a]	Inhalation route, N (%)			Oral, N (%)
	Metered dose inhaler	Dry powder inhaler	Solution for nebulizer	
N-acetylcysteine 20% solution, [3]			3 (100)	
SABA: single agent product (albuterol, levalbuterol) [261]	64 (24.5)		197 (75.5)	
SAAC: single agent product (ipratropium) [68]	18 (26.5)		50 (73.5)	
SABA/SAAC: combination product [176]	22 (12.5)		154 (87.5)	
LABA: single agent product (formoterol, salmeterol) [12]		4 (33.3)	8 (66.7)	
LABA/ICS: combination product [102]	35 (34.3)	67 (65.7)		
LAAC (tiotropium) [68]		68 (100)		
PDE4-I (roflumilast) [10]				Tablet-10 (100)
Theophylline [8]				Tablet-7 (87.5), Elixir-1 (12.5)

Abbreviations: COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LAAC, long-acting anticholinergic; LABA, long-acting β_2-agonist; PDE4-I, phosphodiesterase 4 inhibitor; SAAC, short-acting anticholinergic; SABA: short-acting β_2-agonist.

[a] N is the total count of unique formulations prescribed per patients; total counts may be higher than the actual number of patients prescribed specific agents in Figure 1 due to different formulations being prescribed for a single patient. For example, a patient may have been prescribed an SABA aerosol and solution for nebulizer during their time in hospice.