Adherence to Maintenance Medications among Older Adults with Chronic Obstructive Pulmonary Disease

The Role of Depression

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Abstract

Rationale: Among individuals with chronic obstructive pulmonary disease (COPD), depression is one of the most common yet underrecognized and undertreated comorbidities. Although depression has been associated with reduced adherence to maintenance medications used in other conditions, such as diabetes, little research has assessed the role of depression in COPD medication use and adherence.

Objectives: The objective of this study was to assess the impact of depression on COPD maintenance medication adherence among a nationally representative sample of Medicare beneficiaries newly diagnosed with COPD.

Methods: We used a 5% random sample of Medicare administrative claims data to identify beneficiaries diagnosed with COPD between 2006 and 2010. We included beneficiaries with 2 years of continuous Medicare Parts A, B, and D coverage and at least two prescription fills for COPD maintenance medications after COPD diagnosis. We searched for prescription fills for inhaled corticosteroids, long-acting β-agonists, and long-acting anticholinergics and calculated adherence starting at the first fill. We modeled adherence to COPD maintenance medications as a function of new episodes of depression, using generalized estimated equations.

Measurements and Main Results: Our primary outcome was adherence to COPD maintenance medications, measured as proportion of days covered. The exposure measure was depression. Both COPD and depression were assessed using diagnostic codes in Part A and B data. Covariates included sociodemographics, as well as clinical markers, including comorbidities, COPD severity, and depression severity. Of 31,033 beneficiaries meeting inclusion criteria, 6,227 (20%) were diagnosed with depression after COPD diagnosis. Average monthly adherence to COPD maintenance medications was low, peaking at 57% in the month after first fill and decreasing to 35% within 6 months. In our adjusted regression model, depression was associated with decreased adherence to COPD maintenance medications (odds ratio, 0.93; 95% confidence interval, 0.89–0.98).

Conclusions: New episodes of depression decreased adherence to maintenance medications used to manage COPD among older adults. Clinicians who treat older adults with COPD should be aware of the development of depression, especially during the first 6 months after COPD diagnosis, and monitor patients' adherence to prescribed COPD medications to ensure best clinical outcomes.

Keywords: chronic obstructive pulmonary disease; depression; adherence

(Received in original form February 22, 2016; accepted in final form May 19, 2016)

Supported by National Institutes of Health grant R21AG045573-02 (Simoni-Wastila, PI). J.S.A. is supported by National Institutes of Health grant K12HD43489-13 (Tracey, PI). B.K. is supported by National Institutes of Health grant T32AG000262-14 (Magaziner, PI).

Author Contributions: J.S.A. takes responsibility for the content of the manuscript, including the data and analysis. L.S.-W. assumes full responsibility for the integrity of the submission as a whole, from inception to published article. Y.P., P.H., T.-Y.H., I.H., G.N., S.W.L., P.L., B.K., Y.-J.W., and P.M. contributed substantially to the study design, data analysis and interpretation, and writing of the manuscript.

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Ann Am Thorac Soc Vol 13, No 9, pp 1497–1504, Sep 2016
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DOI: 10.1513/AnnalsATS.201602-136OC
Internet address: www.atsjournals.org

Chronic obstructive pulmonary disease (COPD) is a chronic lower respiratory disease characterized by obstruction of airflow. COPD is a leading cause of morbidity and mortality worldwide, and the third leading cause of death in the United States (1, 2). Although smoking is the most common risk factor for the development of COPD in the United States, environmental exposures and genetics also play a role (1, 3). In 2010, medical costs of COPD in the United States were estimated at $36 billion and projected to reach $49 billion by 2020 (4).

Clinicians select pharmacologic strategies used for the management of COPD based on COPD severity to reduce symptoms and prevent COPD exacerbations (1). Maintenance medications, including inhaled corticosteroids, long-acting β-agonists, and long-acting anticholinergics, have been shown to reduce exacerbations and improve lung function and health-related quality of life among patients with moderate to severe disease (5–7). Nonetheless, use of and adherence to COPD maintenance medications remain low, ranging from 29 to 56%, and contribute to increased hospitalization, health care costs, and mortality (8–20).

Among patients with COPD, depression remains one of the most common, yet least recognized and undertreated, comorbidities, with a prevalence of 17–44% (21–27). Depression has been associated with decreased adherence to maintenance medications used in chronic conditions such as diabetes (28, 29). Few studies have assessed the association between depression and adherence to COPD medications, and these were limited by a cross-sectional study design (30, 31). The objective of this study was to assess the impact of depression on COPD maintenance medication adherence among a nationally representative sample of Medicare beneficiaries newly diagnosed with COPD. We hypothesize that new episodes of depression will result in decreased adherence to COPD maintenance medications.

Methods

Study Population

We obtained Medicare administrative claims data from the Centers for Medicare and Medicaid Services (CMS) Chronic Condition Data Warehouse (CCW) for a 5% random sample of Medicare beneficiaries from 2006 to 2012. We identified beneficiaries with at least one inpatient or outpatient claim containing the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) for COPD (code 490, 491.x, 492.x, 494.x, or 496), and excluded beneficiaries with a history of respiratory cancer, tuberculosis, asbestosis, and sarcoidosis because their medication use may differ from that of other individuals with COPD. These ICD-9-CM codes are used by the CMS to identify beneficiaries with COPD and have a positive predictive value of 73% (32). We required continuous Medicare Parts A, B, D, and no Part C coverage for 24 months after initial diagnosis of COPD (index date) during the study period to ensure adequate follow-up. All Medicare beneficiaries who met criteria for COPD since 1999 have the date of first diagnosis of COPD reported in the CMS Master Beneficiary Summary File. We used this date to exclude beneficiaries whose first diagnosis of COPD occurred before the study period (2006–2012). We required that study participants have at least two prescription fills of a maintenance medication during the 24-month follow-up period.

Exposure

We used ICD-9-CM codes 296.2x, 296.3x, and 311.xx to define depression. These codes have been used previously and exclude bipolar disorder, schizoaffective disorder, and dysthymic disorder (33–35). Presence of depression was defined as at least one diagnosis code on at least one inpatient claim or at least two outpatient claims during the study period. To increase identification of beneficiaries with depression, we also accepted evidence of at least one antidepressant prescription fill in conjunction with diagnosis of depression on one outpatient claim. Information on antidepressant fills was collected from Part D prescription drug event files.

Depression is a chronic disorder that occurs as one or more unique episodes and could be diagnosed at any time during the study period (36, 37). We were interested in how new episodes of depression impacted adherence to COPD maintenance medications. Therefore, among individuals with depression episodes both before and after COPD diagnosis, we defined a new episode of depression after COPD diagnosis as one occurring more than 5 months after the depression episode before COPD diagnosis.

Outcome

The primary outcome of this study was adherence to inhaled COPD maintenance medications. We searched for all inhaled maintenance medications (inhaled corticosteroids, long-acting β-agonists, long-acting anticholinergics) in the Part D prescription drug events file. We excluded oral methylxanthines because they can be used as either acute or maintenance medications and are limited to severe COPD (37). We divided follow-up time after the COPD index date into 30-day months, and measured adherence using proportion of days covered (PDC) (number of daily doses in the prescription/30 d) for all maintenance medications per month. The PDC ranges from 0 to 1. The PDC is a widely used measure of medication adherence in administrative claims data (38, 39). Adherence was measured monthly from the date of the first fill of a COPD maintenance medication after COPD diagnosis through the end of the study period. We created a rolling 3-month average adherence to reduce variability in monthly adherence measures. Because distribution of this variable was highly skewed, we created adherence categories: <0.2, $\geqslant 0.2$ to <0.4, $\geqslant 0.4$ to <0.6, $\geqslant 0.6$ to <0.8, and $\geqslant 0.8$.

Covariates

Baseline comorbidities at COPD diagnosis were determined using the CCW 27 flagged comorbid conditions (40). If the date of first diagnosis of a chronic condition was before the date of COPD diagnosis, the patient was considered to have that chronic condition at baseline. We controlled for diagnosis of asthma (ICD-9-CM codes 493.xx on one or more inpatient claims or two or more outpatient claims). We summed indicator variables for chronic conditions including Alzheimer's disease and related dementias, atrial fibrillation, chronic kidney disease, heart failure, diabetes, ischemic heart disease, osteoarthritis, stroke, and asthma to create a comorbidity measure. Our measure had a range of 0–9 and was categorized as fewer than two, two or three, and more than three chronic conditions, based on its distribution. We created time-varying comorbidity diagnoses for use in

our regression model by comparing the first date of diagnosis with the first day of each month after diagnosis of COPD.

Depression is one of the CCW 27 flagged comorbid conditions. The CCW algorithm differs from our definition by including ICD-9-CM codes 296.5x, 296.6x, 296.89, 298.0, 300.4, and 309.1. We used the CCW depression algorithm to capture individuals with a history of depression before 2006.

To assess severity of depression, we created a variable comprising a count of three measures obtained from inpatient and outpatient claims: the presence of a "4" in the fifth place of an ICD-9-CM code for depression, evidence of psychotherapy or other nonpharmacological treatment, and psychiatric hospitalization with a primary diagnosis of depression. This variable had a range of 0–3 and was dichotomized at 1.

We created a variable indicating any use of short-acting β-agonists and short-acting anticholinergics (COPD acute medications) during the month. We searched for the presence of any nursing home claim on any inpatient stay, or health care common procedure coding system or place of service codes on a skilled nursing facility claim during the month to indicate nursing home stay within the month.

Characteristics suggestive of COPD severity included supplemental oxygen use, COPD-related hospitalization (dichotomized at ⩾1 COPD hospital days/mo), and monthly COPD-related emergency department visits (dichotomized at ⩾1 emergency department visit/mo) (30, 41, 42). We searched carrier and durable medical equipment claims for the following preventive health services use measures: influenza vaccination, colorectal cancer screening, prostate cancer screening, and mammography and Papanicolaou smears (43). An annual count of preventive health services use measures (including mammography or Papanicolaou test) was created as an indicator of healthy behavior. This variable had a range of 0–3 and, based on its distribution, was dichotomized at 1 or more.

We linked our Medicare cohort to county-level data from the Area Health Resource File. The Area Health Resource File contains health resources and socioeconomic indicators from multiple sources. We abstracted variables representing median household income, percentage of persons aged 25 and older with four or more years of college, percentage of persons aged 25 and older with less than a high school education, and number of primary care providers per 100,000 population.

Data Analysis

Distributions of variables were examined overall and by depression status. For descriptive purposes, we made comparisons between beneficiaries diagnosed with depression at any time during the 24-month follow-up and those who were not, using a χ^2 or Student t test as appropriate. We plotted the average 3-month adherence to COPD maintenance medications over time.

We used generalized estimating equations with a multinomial distribution and a cumulative logit link to model the odds of being in a higher adherence category (greater adherence) as a function of our time-varying depression variable and assumed a compound symmetry covariance matrix to estimate the correlations among measurements within an individual. The analyses were conducted at the person-month level. We tested interactions with sex, age, and low-income subsidy *a priori*. Covariates associated with depression or adherence were considered for inclusion in our model. Comorbidities, acute inhaler use, COPD severity variables, our preventive health measure, and nursing home residence were allowed to vary with time. Covariates resulting in a greater than 10% change to the effect estimate or whose type III P value was less than 0.001 were included in the final model. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported.

To test the assumption of proportionality in our multinomial model, we conducted sensitivity analyses. We created dichotomous variables representing 3-month average adherence at each decile between 0 and 1. We used generalized estimating equations with a binomial distribution and a logit link to model the odds of an observation falling into the higher adherence category and assumed a compound symmetry covariance matrix to estimate the correlations among measurements within an individual. We ran separate models for each decile. Sensitivity analyses included all variables from the final regression model of the main analysis.

This study was approved by the Institutional Review Board at the University of Maryland, Baltimore (Baltimore, MD), which waived the requirement for written informed consent. All analyses were conducted with SAS version 9.3 (SAS Institute, Cary, NC). Because of our large sample size, a P value less than 0.001 was considered statistically significant in bivariate analysis.

Results

There were 129,606 Medicare beneficiaries diagnosed with COPD between 2006 and 2010. Of these, 80,487 (62%) had 24 months of continuous coverage of Medicare Parts A, B, D, and no Part C after COPD diagnosis. Of these, 31,033 (39%) had at least two fills of a COPD maintenance medication, and this group formed our sample population. The average age was 68.4 (SD, 12.2) years (Table 1). The study sample was primarily female (64.8%) and white (83.2%).

During the 24-month follow-up period, 6,227 (20.1%) beneficiaries were diagnosed with depression (Table 1). Individuals diagnosed with depression were younger than those who were not diagnosed with depression (66.9 [SD, 14.0] yr vs. 68.8 [SD, 11.7] yr; $P < 0.001$). Depressed beneficiaries were more likely to be female (74.4 vs. 62.4%; $P < 0.001$), to have more than three comorbid conditions (32.6 vs. 22.6%; $P < 0.001$), and to have evidence of a nursing home stay (12.1 vs. 4.8%; $P < 0.001$). Beneficiaries with depression had more severe COPD symptoms in the month of depression diagnosis as evidenced by higher rates of oxygen use (9.7 vs. 8.2%; $P < 0.001$).

Average monthly adherence to COPD maintenance medications was low, with a peak of 0.57 in the month after the first fill and decreasing rapidly before plateauing at 0.35 by the seventh month (Figure 1). Individuals with depression had lower adherence throughout the study period compared with those without depression. Only 20% of depressed individuals and 22% of nondepressed individuals fell into the highest (>80%) adherence category.

Our adjusted multinomial regression model contained terms for new episode depression, time, COPD index year, age, sex, race, region, percentage of county-level population without a high school diploma, original reason for Medicare entitlement, low-income subsidy, comorbid conditions, acute inhaler use, COPD severity variables, preventive health measures, nursing home residence within the month, and polypharmacy. There was no effect

Table 1. Baseline characteristics of Medicare beneficiaries diagnosed with chronic obstructive pulmonary disease (COPD) between 2006 and 2010 and receiving at least two fills of COPD maintenance medication, by depression status at 24 months of follow-up

	Study Population (*n* = 31,033)	Depression (*n* = 9,593)	No Depression (*n* = 21,440)	*P* Value*
Age (yr), mean (SD)	68.4 (12.2)	66.9 (14.0)	68.8 (11.7)	<0.001
Age (yr) categories, n (%)				<0.001
<65	8,469 (27.3)	2,358 (37.9)	6,111 (24.6)	
65–74	13,128 (42.3)	1,927 (30.9)	11,201 (45.2)	
75–84	6,545 (21.1)	1,187 (19.1)	5,358 (21.6)	
>84	2,891 (9.3)	755 (12.1)	2,136 (8.6)	
Female, n (%)	20,122 (64.8)	4,654 (74.7)	15,468 (62.4)	<0.001
Race/ethnicity, n (%)				<0.001
White	25,819 (83.2)	5,266 (84.6)	20,553 (82.9)	
Black	3,120 (10.1)	573 (9.2)	2,547 (10.3)	
Hispanic	881 (2.8)	229 (3.7)	652 (2.6)	
Other	1,213 (3.9)	159 (2.6)	1,054 (4.2)	
COPD index year, n (%)				<0.001
2006	5,155 (16.6)	939 (15.1)	4,216 (17.0)	
2007	6,035 (19.4)	1,097 (17.6)	4,938 (19.9)	
2008	6,354 (20.5)	1,263 (20.3)	5,091 (20.5)	
2009	6,615 (21.3)	1,328 (21.3)	5,287 (21.3)	
2010	6,874 (22.2)	1,600 (25.7)	5,274 (21.3)	
Region, n (%)				<0.001
Northeast	7,979 (25.7)	1,716 (27.6)	6,263 (25.2)	
Midwest	5,539 (17.8)	1,151 (18.5)	4,388 (17.7)	
South	12,528 (40.4)	2,513 (40.4)	10,015 (40.4)	
West	4,958 (16.0)	839 (13.5)	4,119 (16.6)	
Median household income				<0.001
<$39,000	6,657 (21.5)	1,289 (20.7)	5,368 (21.6)	
⩾$39,000 to <$53,000	13,836 (44.6)	3,522 (56.6)	13,346 (53.8)	
⩾$53,000	6,238 (20.1)	1,399 (22.5)	6,053 (24.4)	
Primary care providers per 100,000				0.262
<49	7,420 (23.9)	1,458 (23.4)	5,962 (24.0)	
⩾49 to <84	15,351 (49.5)	3,061 (49.2)	12,290 (49.5)	
⩾84	8,229 (26.5)	1,699 (27.3)	6,530 (26.3)	
Percentage without a high school diploma				0.584
<11%	8,297 (26.7)	1,695 (27.2)	6,602 (26.6)	
11–18%	15,108 (48.7)	3,019 (48.5)	12,089 (48.7)	
>18%	7,595 (24.5)	1,504 (24.2)	6,091 (24.6)	
Percentage with ⩾4 yr of college				0.005
<17%	7,624 (24.6)	1,445 (23.2)	6,179 (24.9)	
⩾17% to <31%	15,395 (49.6)	3,192 (51.3)	12,203 (49.2)	
⩾31%	7,981 (25.7)	1,581 (25.4)	6,400 (25.8)	
Original reason for Medicare entitlement, n (%)				<0.001
Age	20,552 (66.2)	3,444 (55.3)	17,108 (69.0)	
Disability (receipt of SSDI)	10,140 (32.7)	2,714 (43.6)	7,426 (29.9)	
ESRD†	341 (1.1)	69 (1.1)	272 (1.1)	
Low-income subsidy, n (%)	16,951 (54.6)	4,194 (67.4)	12,757 (51.4)	<0.001
Nursing home residence in month of diagnosis, n (%)	1,942 (6.3)	756 (12.1)	1,186 (4.8)	<0.001
Comorbid medical conditions, n (%)				
Acute myocardial infarction	969 (3.1)	228 (3.7)	741 (3.0)	0.006
Alzheimer's disease and related disorders	2,811 (9.1)	990 (15.9)	1,821 (7.3)	<0.001
Asthma	10,677 (34.4)	2,055 (33.0)	8,622 (34.8)	0.009
Chronic kidney disease	4,644 (15.0)	1,134 (18.2)	3,510 (14.1)	<0.001
History of depression before 2006	7,280 (23.5)	3,206 (51.5)	4,074 (16.4)	<0.001
Diabetes	9,415 (30.3)	2,121 (34.1)	7,294 (29.4)	<0.001
Heart failure	8,409 (27.1)	1,950 (31.3)	6,459 (26.0)	<0.001
Hip fracture	678 (2.2)	212 (3.4)	466 (1.9)	<0.001
Ischemic heart disease	13,034 (42.0)	2,756 (44.3)	10,278 (41.4)	0.027
Rheumatoid arthritis/osteoarthritis	12,937 (41.7)	3,046 (48.9)	9,891 (39.9)	<0.001
Stroke/transient ischemic attack	3,555 (11.5)	956 (15.4)	2,599 (10.5)	<0.001
Comorbid conditions,‡ n (%)				<0.001
<2	13,094 (42.2)	2,205 (35.4)	10,889 (43.9)	
2 or 3	10,295 (33.2)	1,993 (32.0)	8,302 (33.5)	
>3	7,644 (24.6)	2,029 (32.6)	5,615 (22.6)	
⩾1 Preventive health measures, n (%)	3,052 (9.8)	493 (7.9)	2,559 (10.3)	<0.001

(Continued)

Table 1. (*Continued*)

	Study Population (*n* = 31,033)	Depression (*n* = 9,593)	No Depression (*n* = 21,440)	*P* Value*
Depression severity count ⩾ 1, n (%)	1,071 (3.3)	715 (11.1)	356 (1.4)	<0.001
COPD severity measures, n (%)				
Use of acute COPD medication in month	11,061 (35.6)	2,310 (37.1)	8,751 (35.3)	0.007
Oxygen use in month of diagnosis	2,633 (8.5)	607 (9.7)	2,026 (8.2)	<0.001
⩾1 COPD-related emergency department visit in month of diagnosis	1,589 (5.1)	370 (5.9)	1,219 (4.9)	0.001
⩾1 COPD-related hospitalization in month of diagnosis	1,271 (4.1)	298 (4.8)	973 (3.9)	0.002
Number of COPD maintenance medication fills, mean (SD)	11.0 (7.8)	10.5 (7.5)	11.1 (7.9)	<0.001

Definition of abbreviation: ESRD = end-stage renal disease; SSDI = Social Security disability insurance.
**P* value from Student *t* test for age, Wilcoxon rank-sum test for number of medication fills, and χ^2 test for categorical variables and reflects differences between depression and no depression.
†End-stage renal disease ± disability.
‡Includes Alzheimer's disease and related dementias, atrial fibrillation, chronic kidney disease, heart failure, diabetes, ischemic heart disease, osteoarthritis, stroke, and asthma.

modification by sex, age, or low-income subsidy.

In our adjusted model, a new episode of depression was associated with decreased odds of greater adherence to COPD maintenance medications (OR, 0.93; 95% CI, 0.89–0.98) (Table 2). Acute inhaler use (OR, 2.08; 95% CI, 2.02–2.15), supplemental oxygen use (OR, 1.43; 95% CI, 1.36–1.51), nursing home residence (OR, 1.20; 95% CI, 1.11–1.230), and low-income subsidy (OR, 1.31; 95% CI, 1.27–1.37) were associated with increased adherence to COPD maintenance medications. Our assumption of proportionality was supported.

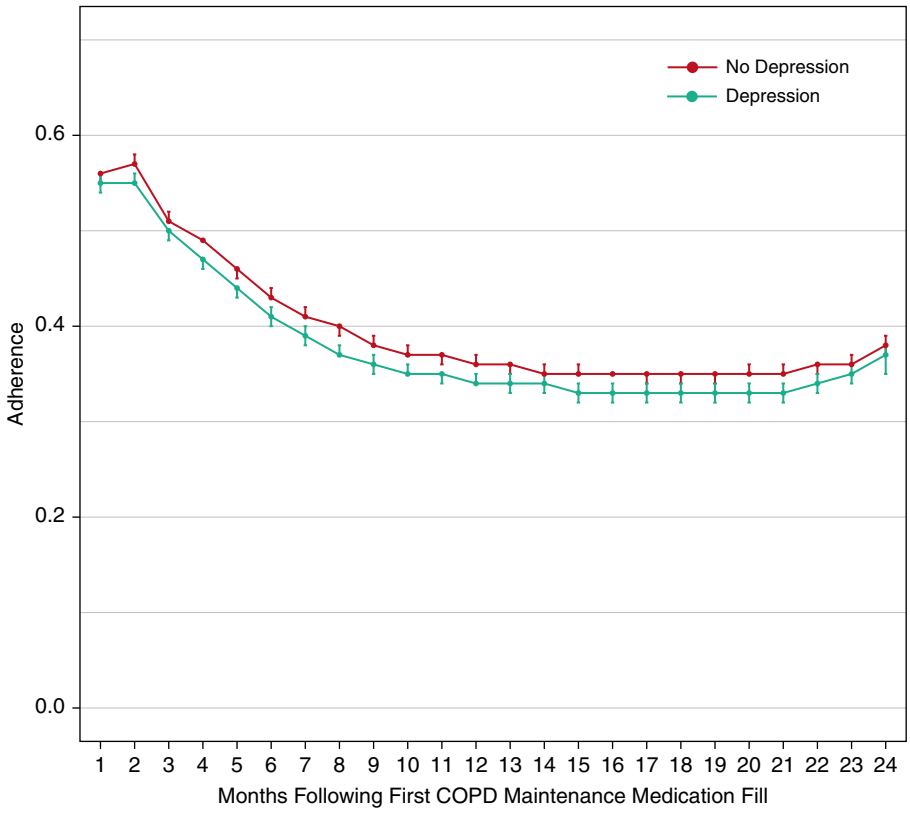

Figure 1. Average 3-month rolling adherence to chronic obstructive pulmonary disease (COPD) maintenance medications over time by depression status.

Discussion

Beneficiaries with evidence of depression were less likely to adhere to COPD maintenance medications compared with their nondepressed peers. Adherence to COPD maintenance medications falls precipitously within the first 6 months of use, regardless of depression status. Our study results highlight the importance of evaluation and monitoring of depression, as well as the importance of regular follow-up and counseling on medication adherence, to maximize well-being of individuals with COPD. Although our study findings suggest that the first 6 months after COPD diagnosis is a critical time period for medication monitoring, given the chronic and progressive nature of COPD, close attention throughout the disease trajectory may be important.

The association between depression and decreased adherence to COPD medications has been previously reported (31, 41, 42, 44); however, only a single study quantified the effect (30). Qian and colleagues analyzed maintenance medication adherence, using a cross-sectional study design, among Medicare beneficiaries with COPD and reported that individuals with depression were 11% less likely to have high adherence (30). Our study overcame the limitations of the cross-sectional study design by examining the longitudinal association between depression and medication adherence, yet reported results consistent with those of the study by Qian and colleagues (9% less likely to have greater adherence).

Comorbid depression in COPD resulted in decreased adherence, as did the presence of any other comorbid condition

Table 2. Adjusted and unadjusted odds of greater adherence to chronic obstructive pulmonary disease (COPD) maintenance medications among Medicare beneficiaries diagnosed with COPD between 2006 and 2010 and receiving at least two fills of COPD maintenance medication over 24 months of follow-up

	Odds Ratio (95% Confidence Interval)
Unadjusted Results	
New episode depression	0.86 (0.83–0.90)
Adjusted Results	
New episode depression	0.93 (0.89–0.98)
Time, mo	0.97 (0.97–0.97)
COPD index year	
2006	Reference
2007	1.15 (1.09–1.22)
2008	1.16 (1.10–1.23)
2009	1.24 (1.17–1.31)
2010	1.30 (1.23–1.37)
Age, yr	1.00 (1.00– 1.00)
Sex	
Male	Reference
Female	0.94 (0.91–0.98)
Race/ethnicity	
White	Reference
Black	0.80 (0.76–0.85)
Hispanic	0.68 (0.62–0.76)
Other	0.88 (0.91–0.96)
Region	
Midwest	Reference
Northeast	1.10 (1.05–1.16)
South	0.89 (0.85–0.93)
West	0.95 (0.90–1.01)
Percentage of census tract without a high school diploma	
<11%	Reference
11–18%	0.92 (0.88–0.96)
>18%	0.84 (0.80–0.88)
Original reason for Medicare entitlement	
Age	Reference
Disability	0.85 (0.81–0.90)
ESRD*	0.63 (0.53–0.74)
Comorbid medical conditions	
Acute myocardial infarction	0.84 (0.78–0.91)
Asthma	1.35 (1.30–1.40)
History of depression	0.81 (0.78–0.85)
Diabetes	0.91 (0.87–0.95)
Ischemic heart disease	0.93 (0.89–0.97)
Rheumatoid arthritis/osteoarthritis	0.76 (0.74–0.79)
Stroke/transient ischemic attack	0.84 (0.79–0.88)
Comorbid conditions†	
<2	Reference
2 or 3	0.77 (0.74–0.81)
>3	0.68 (0.64–0.73)
Acute inhaler use	2.08 (2.02–2.15
COPD severity variables	
Oxygen use in month of diagnosis	1.43 (1.36–1.51)
⩾1 COPD-related ED visit	1.00 (0.93–1.07)
⩾1 COPD-related hospitalization	1.33 (1.23–1.44)
⩾1 Preventive health measures	1.05 (1.03–1.07)
Nursing home residence	1.20 (1.11–1.30)
Polypharmacy (per medication)	1.01 (1.01–1.01)
Low-income subsidy	1.32 (1.27–1.37)

Definition of abbreviation: ED = emergency department; ESRD = end-stage renal disease.
Study population: n = 31,033.
*End-stage renal disease ± disability.
†Includes Alzheimer's disease and related dementias, atrial fibrillation, chronic kidney disease, heart failure, diabetes, ischemic heart disease, osteoarthritis, stroke, and asthma.

(except asthma), suggesting that multimorbidity decreases adherence, possibly through complex medication regimens or patient prioritization of one comorbid illness over another (45). Our results suggest that individuals with more than three chronic conditions are at highest risk of poor adherence. This effect was mitigated by increased severity of COPD symptoms, evidenced by acute inhaler use, oxygen use, and COPD-related hospitalizations, and is consistent with a prior report (30).

Historically, use of and adherence to COPD maintenance medications has been suboptimal, with many individuals with COPD not receiving any maintenance medications (14, 15, 17). Among individuals who use COPD medications, adherence is low, which poses difficulties in medication management (8–18). In this study, we found that only 22% of the sample achieved adherence of at least 80%, regardless of depression status. Our study was conducted among beneficiaries with at least two medication fills over the 24 months after COPD diagnosis, representing those most likely to adhere to COPD medications, as they have documented primary adherence by picking up their COPD medication prescriptions. Nonetheless, the observed drop in adherence after first COPD maintenance medication fill suggests most individuals with COPD are not using medications as prescribed. Although a prior study by Qian and colleagues reported adherence of at least 80% in 36% of Medicare beneficiaries with COPD, it did not assess adherence among patients newly diagnosed with COPD and evaluated adherence from first-filled to last-filled prescription, differences that could account for our lower adherence rate (30). Women were less likely to be adherent to COPD maintenance medications compared with men, which is consistent with two prior studies conducted among individuals with COPD (30, 46). Other studies have not reported a significant association between sex and adherence to COPD medications or medications generally (11, 20, 44, 47). In our study, women composed 65% of the study sample, and 75% of those with depression; hence, residual confounding by depression status is possible. Race was associated with decreased adherence to COPD medications, which is consistent with the study by Qian and colleagues

conducted among Medicare beneficiaries with COPD (30).

Limitations and Strengths

As with any study, ours has limitations that should be noted. Our study includes Medicare beneficiaries diagnosed with depression; however, depression is underdiagnosed in administrative claims data (48). This potential misclassification of exposure would cause our results to be biased toward the null. In addition, we likely underestimated the burden of depression in COPD by excluding dysthymic disorder and depression found in bipolar and schizoaffective disorder from our depression definition. Furthermore, our adherence measure was based on prescription fills and does not measure actual use of inhaled medications. Finally, we could not control for all confounding or direct influences of medication adherence. For example, future work may consider evaluating the impact of other medications, such as oral corticosteroids, which can mimic psychiatric side effects.

As well, this study has notable strengths. This study is the first to assess adherence to COPD maintenance medications among Medicare beneficiaries newly diagnosed with COPD. In addition, we used a longitudinal study design to capture episodes of diagnosed depression, calculated a rolling monthly adherence value to reduce variance between monthly observations, and treated depression and other covariates as time-varying. Although our data did not include FEV values, a common COPD severity measure, the proxy measures we used for COPD severity (oxygen use, acute inhaler use, hospitalizations) have been used in other studies and correlated with medication adherence in the expected direction (30, 41, 42, 49–51).

Conclusions

Our study found that new episodes of depression have a negative influence on adherence to maintenance medications used to manage COPD among older adults. Clinicians who treat older adults newly diagnosed with COPD should be aware of the development of depression, especially during the first 6 months. As such, clinicians should consider the need to monitor their patients with COPD for need for treatment of depression, as well as use of and adherence to prescribed COPD medications. Close management of these and other aspects of newly diagnosed older adults with COPD will help to ensure optimal clinical outcomes. This study provides foundational work elucidating the association between depression and adherence in older adults with COPD. Future research should consider prospective, longitudinal studies to replicate our findings as well as to further explore the relationship of these comorbid conditions. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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