Association between Depression and Maintenance Medication Adherence among Medicare Beneficiaries with COPD

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Abstract

Objective—Depression is a significant comorbidity in patients with chronic obstructive pulmonary disease (COPD). Although comorbid depression is associated with low use and poor adherence to medications treating other chronic conditions, evidence of the relationship between depression and COPD management is limited. This study estimated the association between depression and COPD maintenance medication (MM) adherence among patients with COPD.

Methods—This cross-sectional study used a 5% random sample of 2006–2007 Chronic Condition Warehouse data. Medicare beneficiaries enrolled in Parts A, B, and D plans with diagnosed COPD who survived through 2006 were included (n=74,863). COPD MM adherence was measured as medication discontinuation and Proportion of Days Covered (PDC). Depression was identified through ICD-9-CM diagnosis codes. Multivariable models with modified generalized estimating equations were used to estimate adjusted association between depression diagnosis and medication adherence, controlling for sociodemographics, comorbidities, and disease severity.

Results—Among the sample, about one-third (33.6%) had diagnosed depression. More than half (61.8%) of beneficiaries with COPD filled at least one COPD MM prescription. Depressed beneficiaries had a higher likelihood of using COPD MM than non-depressed beneficiaries (adjusted prevalence ratios (PR)=1.02; 95% confidence intervals (CI)=1.01, 1.03). Among COPD MM users, depressed beneficiaries were more likely to discontinue medications (PR=1.09; 95%

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CI=1.04, 1.14) and less likely to exhibit PDC 0.80 (PR=0.89; 95% CI=0.86, 0.92) than non-depressed beneficiaries.

Conclusions—Depression is prevalent in Medicare beneficiaries with COPD and independently associated with lower COPD MM adherence. Interventions to improve medication adherence for COPD patients may consider management of comorbidities such as depression.

Keywords

depression; chronic obstructive pulmonary disease; maintenance medication adherence; maintenance medication; Medicare beneficiaries

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a chronic condition associated with significant morbidity and mortality. It has become the third leading cause of death among U.S. adults (Centers for Disease Control and Prevention, 2008). Approximately 1 in 8 community-dwelling Medicare beneficiaries are diagnosed with COPD (Stuart et al., 2007). Preventing exacerbations is an important goal of COPD management. A cornerstone of COPD management is pharmacotherapy, which aims to reduce symptoms, decrease the frequency and severity of exacerbations, and improve health status and exercise tolerance (Global Initiative for Chronic Obstructive Pulmonary Disease, 2008, American Thoracic Society, 2004). However, COPD maintenance medication use among COPD patients remains low: only 40% of Medicare beneficiaries with COPD fill one or more COPD maintenance medications annually (Stuart et al., 2010).

Among individuals who take at least one COPD maintenance medication, many fail to adhere to prescribed therapy. In the literature, adherence to COPD medications ranges from 40%–60% (Rand, 2005, Restrepo et al., 2008, Charles et al., 2010). One observational study, using national Veteran's Affairs data, found only half of COPD patients used any maintenance medication. Among users, the overall medication adherence, measured by mean Medicare Possession Ratio (MPR [standard deviation]), was 0.44 [0.32] during the last year of life (Jung et al., 2009). Another observational study estimated adherence to inhalation medications through refill rates among stable COPD patients in Belgium. This study found almost half (48%) of COPD patients were under-adherent annually (Mehuys et al., 2010).

There is empirical evidence demonstrating the beneficial influence of good adherence on clinical outcomes among COPD patients (Vestbo et al., 2009, Toy et al., 2011). One study, using administrative claims data from U.S. employees and retirees and measuring Proportion of Days Covered (PDC) to assess COPD medication adherence, concluded that good adherence was associated with a lower annual rate of inpatient and emergency room visits (Toy et al., 2011). Another clinical study found association between good medication adherence and improved mortality and reduction in hospital admission among moderate and severe COPD patients (Vestbo et al., 2009). Despite the importance of adherence to maintenance medications in preventing COPD exacerbations, adherence to these medications remains a problematic area where improvements could result in significant benefits.

Depression remains an important and overlooked risk factor for medication non-adherence. In other chronic conditions, including diabetes and heart failure, comorbid depression has been found to be associated with lower medication use and adherence (Ciechanowski et al., 2000, DiMatteo et al., 2000, Hansen et al., 2009, Lin et al., 2004, Morgan et al., 2006). Depression occurs commonly in COPD patients. Prevalence estimates of comorbid

depression range between 10% and 42% in stable COPD patients (Maurer et al., 2008, Yohannes et al., 2010, Kunik et al., 2005, van Manen et al., 2002, Lacasse et al., 2001, Yohannes et al., 2000). The wide range of estimates is due to differences in study populations, depression assessment measures, and illness severity. Increased evidence has shown depression places COPD patients at higher risks for hospitalizations, readmissions, and increased hospital days (Almagro et al., 2002, Stuart et al., 2010, Xu et al., 2008, Ng et al., 2007). However, despite the high prevalence of comorbid depression in COPD patients, little is known about the role of depression on COPD maintenance medication use or adherence.

The objective of this study is to estimate the association between comorbid depression diagnosis and COPD maintenance medication adherence among a nationally representative sample of Medicare beneficiaries with COPD. This study is among the first to date to explore the relationships among diagnosed depression and COPD maintenance medication use and adherence in Medicare beneficiaries with COPD.

METHODS

Data Source

This retrospective cross-sectional study used a random 5% sample of 2006–2007 Centers for Medicare and Medicaid Services Chronic Condition Warehouse (CCW) data. The CCW files include Medicare Parts A (inpatient), B (outpatient), and D (prescription) claims data plus 27 chronic condition flags (including COPD and depression). These flags are operationalized based on the relevant International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes associated with Medicare claims from 1999 forward (Chronic Condition Data Warehouse, 2012). Personal identifying information (such as name, address, and Medicare claim number) has been stripped and replaced with encrypted beneficiary IDs. The researchers had no access to the encryption links or to personal identifying information of beneficiaries.

Study Population

Medicare beneficiaries in stand-alone Part D plans (PDPs) through the two-year study period with a COPD diagnosis between July 1, 2005 and June 30, 2006 were identified. Individuals with a COPD diagnosis were identified using the CCW COPD algorithm (Chronic Condition Data Warehouse, 2012), which uses at least one inpatient, skilled nursing home (SNF), home health (HHA), or two hospital outpatient (HOP) or carrier claims with any of the following ICD-9-CM codes: 491.xx, 492.xx, or 496.xx. The study sample was further restricted to those enrolled in PDPs between January 1, 2006 and June 30, 2006. Subjects were required to be continuously enrolled in Medicare Parts A, B, and stand-alone PDPs through the two-year study period in order to observe all medical and prescription events.

Individuals enrolled in Medicare Advantage plans or Health Maintenance Organizations (HMO) were excluded due to inability to elucidate diagnoses (n=10,447), as were those who died prior to January 1, 2007 (all beneficiaries were required to live through 2006 to have one year observation window for baseline sociodemographic and clinical factors). Beneficiaries with selected respiratory conditions (cystic fibrosis, alpha-1 antitrypsin, respiratory cancer, fibrosis due to tuberculosis, bronchiecstasis, pneumoconiosis, pulmonary fibrosis, pulmonary tuberculosis, and sarcoidosis) were also excluded as their use of COPD maintenance medications is markedly different from those with COPD (n=9,412). After applying inclusion and exclusion criteria, the study cohort included a total of 74,863 Medicare beneficiaries. The conduct of this study was approved by the institutional review

board (IRB) of the University of Maryland Baltimore, Maryland, and the requirement for written informed consent was waived.

Measures

Depression status—Individuals with depression were identified using the CCW depression algorithm, which included the following ICD-9-CM codes for depression (ICD-9-CM codes: 296.20–296.26, 296.30–296.36, 296.50–296.56, 296.60–296.66, 296.89, 298.0, 300.4, 309.1, and 311.x) in at least one inpatient, SNF, HHA, HOP or carrier claim (Chronic Condition Data Warehouse, 2012). Since the CCW depression definition includes a broad array of conditions with a depression component, such as bipolar, schizophrenia, and other psychotic disorders, sensitivity analyses excluding beneficiaries with these comorbid conditions were performed to test the robustness of study results. Depression diagnoses were assessed during the two-year study period.

COPD maintenance medications use and adherence—Based on the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) guidelines, the following therapeutic classes were included as COPD maintenance medications: inhaled corticosteroids [ICS] (alone or in combination with long-acting β_2–agonists [LABA]), LABA, anticholinergics, and methylxanthines. Use of any of these medications was measured as a binary variable based on one or more prescription claims in the two-year study period. Adherence measures included medication discontinuation (defined as a binary variable of medication stopped three months or more prior to the end of the observation period or death, whichever came first) and PDC. PDC values range from 0–1 and are calculated as the number of days with any COPD maintenance medication divided by duration of therapy with these agents. PDC has been widely used to measure adherence to medication in observational studies (Choudhry et al., 2009, Toy et al., 2011) and it was calculated for COPD maintenance medications prescribed to each beneficiary from the date of the first to the last prescription during the follow up period. PDC was calculated at the therapeutic class level (ICS, LABA, ICS/LABA combination, anticholinergics, and methylxanthines) and combined across classes. In this study, the cut point for PDC was 0.80, considered 'good' adherence (Choudhry et al., 2009, Zeng et al., 2010). Measurement of adherence was limited to those beneficiaries who had evidence of any COPD maintenance medication prescriptions with at least two Medicare Part D claims in order to calculate medication adherence (Peterson et al., 2007, Karve et al., 2008).

Covariates—All covariates were measured in baseline year 2006. Demographic characteristics included age, gender, race, and geographic region. Medicare coverage variables included original social security disability insurance [SSDI] Medicare entitlement and low-income subsidy (LIS) status. General health indicators included evidence of specific comorbid conditions. Among those, the CCW condition flags were used to identify some comorbidities (diabetes, ischemic heart disease, congestive heart failure, and Alzheimer's disease and related dementias); other conditions of interest without CCW condition flags (asthma, hypertension, other cardiovascular diseases, and anxiety) were identified by the presence of any claim in 2006 with relevant ICD-9-CM codes. Any all-cause hospitalization was identified as a general health status measure. Two other indicators in claims data were used to assess COPD severity – any evidence of supplemental oxygen use and COPD rescue medication use (short-acting β_2–agonists [SABA]) (Yohannes et al., 2002).

Statistical Analyses

Univariable and bivariable analyses were conducted to describe COPD cohort characteristics and COPD maintenance medication use and adherence. Chi-square tests (for differences in

distribution of categorical variables) and t-tests (for differences in values of continuous variables) were used to estimate the unadjusted relationships between depression status and medication use and adherence. Multivariable models using modified Poisson regression and log link with generalized estimating equations (GEE) were applied to estimate the association between depression and COPD maintenance medication use and adherence, controlling for covariates (Spiegelman and Hertzmark, 2005). All multivariable analyses reported adjusted prevalence ratios (PR) with 95% confidence intervals (CI) to reflect the marginal differences. Significance was set *a priori* at p < 0.05. All analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, NC).

In order to test the robustness of findings and to identify possible disease misclassification bias, a series of sensitivity analyses were performed: (1) exclusion of beneficiaries with evidence of both COPD and asthma (ICD-9-CM codes 493.xx) to examine potential respiratory disease misclassification bias; (2) exclusion of beneficiaries with evidence of bipolar (ICD-9-CM codes 296.5x, 296.6x, 296.7x, 296.8x, 296.9x) and/or psychotic disorders (ICD-9-CM codes 293.81, 293.82, 295.xx, 297.1x-297.3x, 297.8x, 297.9x, and 298.x) to study potential psychiatric disease misclassification bias; (3) comparison of different PDC cut points (e.g. PDC=0.90, and 0.70 relative to PDC 0.80); and (4) exclusion of beneficiaries who died in 2007 to examine potential bias on medication adherence measures before death.

RESULTS

Among the COPD cohort (n=74,863), 33.6% had diagnosed depression. The mean age within the cohort was 72 years and almost two-thirds (63.2%) were female (Table 1). Over 85% of the sample was identified as white and over three-fifths (61.0%) were LIS-eligible for Part D benefits. Relative to non-depressed COPD beneficiaries, depressed beneficiaries were younger, more likely to be female and white, and more likely to be LIS-eligible (all p<0.0001). A higher proportion of those with depression had other conditions, including asthma, diabetes, ischemic heart disease, congestive heart failure, hypertension, Alzheimer's disease and related dementias, and anxiety (all p<0.0001). Compared to non-depressed COPD beneficiaries, those with diagnosed depression had a higher proportion of baseline all-cause hospitalization and rescue medication use (all p<0.0001) but similar supplemental oxygen use (p=0.4492).

Overall, more than three-fifths (61.8%) of the cohort received at least one COPD maintenance medication prescription during the two-year study period (Table 2). The proportion of COPD maintenance medication use was higher in depressed than in non-depressed beneficiaries (64.1% vs. 60.6%). Among COPD maintenance medication users with at least two Part D prescription claims (n=35,985), depressed patients were more likely to discontinue (23.9% vs. 20.6%) and were less likely to exhibit PDC 0.80 (31.4% vs. 38.5%) than non-depressed patients (all p<0.0001).

In multivariable models, depression was associated with a higher likelihood of COPD maintenance medication use (adjusted PR=1.02; 95% CI=1.01, 1.03) (Table 3). However, among users with one or more Part D claims, depressed patients were 9% more likely to discontinue medication (PR=1.09; 95% CI=1.04, 1.14) and 11% less likely to exhibit PDC 0.80 (PR=0.89; 95% CI=0.86, 0.92) than non-depressed patients, controlling for all covariates.

In addition, differences in COPD maintenance medication use and adherence also were found by covariates (Table 3). For example, compared to beneficiaries less than 65 years old, those 65 years and older (except for the subgroup of 85 years and older) were more

likely to fill a COPD maintenance medication and less likely to discontinue their treatment. Females were less likely to exhibit PDC 0.80 (PR=0.93; 95% CI=0.90, 0.96) than males. Compared to whites, blacks were less likely to fill a COPD maintenance medication (PR=0.90; 95% CI=0.88, 0.91), more likely to discontinue their treatment (PR=1.19; 95% CI=1.12, 1.28), and less likely to exhibit PDC 0.80 (PR=0.79; 95% CI=0.75, 0.84). Geographically, beneficiaries residing in north central, south and west regions were less likely to fill a COPD maintenance medication and adhere to treatment than those in northeast region. Beneficiaries who were eligible for LIS were more likely to fill a COPD maintenance medication and less likely to discontinue treatment than non-LIS beneficiaries. Further, beneficiaries with worse health status (having any all-cause hospitalization at baseline) and selected comorbidities (including diabetes, ischemic heart disease, and Alzheimer's disease) were less likely to fill a COPD maintenance medication and adhere to treatment. However, beneficiaries with severe COPD were more likely to use COPD maintenance medication and adhere to treatment.

Sensitivity analyses confirmed the robustness of study results (Table 4). First, after restricting the sample to beneficiaries without comorbid asthma (excluding 28.7% of study sample with both COPD and asthma), depression diagnosis was still associated with a 7% higher likelihood of discontinuation (PR=1.07; 95% CI=1.01, 1.14) and 9% lower likelihood of PDC 0.80 (PR=0.91; 95% CI=0.87, 0.95). Second, after excluding beneficiaries with comorbid bipolar and/or schizophrenia (n=2,919), depressed beneficiaries still were 8% more likely to discontinue medication (PR=1.08; 95% CI=1.03, 1.13) and 10% less likely to exhibit PDC 0.80 (PR=0.90; 95% CI=0.87; 0.93). Third, using different PDC cut points (e.g. 0.90, and 0.70) to define "good" adherence did not affect the findings – those with depression were less likely to exhibit good adherence. Finally, after excluding beneficiaries who died in 2007 (n=9,287) to avoid bias on medication adherence measures before death, depression was still independently associated with 10% higher likelihood of discontinuation (PR=1.10; 95% CI=1.05, 1.16) and 13% lower likelihood of PDC 0.80 (PR=0.87; 95% CI=0.84, 0.91).

DISCUSSION

Findings from this study demonstrate COPD maintenance medication use is low in Medicare beneficiaries with COPD, regardless of the presence of depression. However, among those COPD patients who filled COPD maintenance medications, depression diagnosis is associated with lower COPD maintenance medication adherence. This study is among the first to date to explore the relationships among diagnosed depression and COPD maintenance medication use and adherence in Medicare beneficiaries with COPD. Findings indicate that interventions to improve medication adherence for COPD patients may consider management of comorbidities such as depression.

Indeed, the finding that 40% of Medicare beneficiaries diagnosed with COPD failed to use any COPD maintenance medication in two years indicates the challenges clinicians face in managing the care of their COPD patients. Our finding is consistent with previous studies demonstrating that less than half of COPD patients were prescribed maintenance medication (Stuart et al., 2010, Jung et al., 2009). Sub-analyses from the Understanding Potential Long-term Impacts on Function with Tiotropium (UPLIFT) trial indicated that initiating maintenance treatment at early stages of COPD can alter progression of the disease and maximize patient benefit at later stages of the disease (Troosters et al., 2010). Therefore, clinicians might focus on improving maintenance medication use to reduce symptoms.

Consistent with studies demonstrating depression as an independent risk factor for reduced adherence to treatments for other chronic conditions (Ciechanowski et al., 2000, DiMatteo et

al., 2000, Lin et al., 2004) this study found that depression is associated with lower COPD maintenance medication adherence. Depression may cause patients to neglect medical care and their prescribed regimens so that, in turn, being non-adherent may increase respiratory symptoms (Restrepo et al., 2008). In addition, COPD patients who report poor quality of life are more likely to be depressed, feel unsupported by clinic staff and be poorly adherent to treatment (Bosley et al., 1996). One study investigating psychosocial factors on medication adherence among COPD patients in outpatient clinics also found that the presence of depressed mood was associated with medication non-adherence (Khdour et al., 2012). Future research is warranted to investigate causal inferences and explore mechanisms to explain this relationship.

Limited evidence has demonstrated that patients who are most severely ill with chronic conditions may be at greatest risk for treatment non-adherence (DiMatteo et al., 2007). However, in this study, COPD severity indicators (supplemental oxygen use and COPD rescue medication use) were associated with better adherence to COPD maintenance medications. In sensitivity analyses estimating adherence among beneficiaries requiring supplemental oxygen (considered the most severe stage of COPD), the association between depression diagnosis and lower medication adherence still presented (data not shown but available from the authors).

The independent association between comorbid depression and COPD maintenance medication adherence has implications for both research and practice. It suggests that interventions to improve COPD medication use and adherence are needed for this particular population. Growing evidence suggests antidepressant medications may be effective in treating depression and depressive symptoms in COPD patients (Borson et al., 1992, Lacasse et al., 2004, Smoller et al., 1998, Yohannes et al., 2001). Thus, interventions to better manage depression in COPD population are needed.

This study has several limitations. First, as in all analyses conducted using administrative claims data, measurements and disease ascertainment are limited to information available in such data. Thus, it was unable to ascertain the severity of COPD or depression afforded from laboratory data and other clinical measures (e.g., forced expiratory volume in one second [FEV_1] measures, clinical depression scales). Although we controlled COPD severity in multivariable analysis and conducted a series of sensitivity analyses to examine potential disease misclassification (e.g., COPD and asthma, depression and schizophrenia/bipolar disorders), the unobservable variation in depression severity and potential duration may affect study outcomes. In addition, depression diagnosis regardless of treatment effects on depression was assessed. Beneficiaries with evidence of treatment for depression might exhibit improved COPD maintenance medication adherence. Future investigations on the relationships between treatment effects for depression on COPD medication adherence and clinical outcomes are needed.

Second, measures were determined by refill patterns available in prescription drug event claims data and do not reflect actual patient consumption. However, adherence measured by prescription refill patterns in administrative claims data is widely accepted and shown to be valid in observational studies (Choudhry et al., 2009, Toy et al., 2011). Different from two other studies examining COPD medication adherence in one year,(Jung et al., 2009, Toy et al., 2011) this study assessed COPD maintenance medication adherence over two years, which achieves more stable adherence measurements. Furthermore, since COPD patients can be on multiple inhalation medications concurrently, PDC was used instead of MPR to avoid overestimation of adherence behaviors (Choudhry et al., 2009). Sensitivity analyses using varying PDC levels other than 0.80 obtained similar results on the associations among depression diagnosis and COPD maintenance medication adherence. However, reasons for

medication discontinuation such as intolerance or inadequate response to the regimens were not taken into account in the multivariate analysis due to the lack of information used to identify reasons of discontinuation in claims data.

Third, since both depression diagnosis and COPD maintenance medication adherence were measured during the same two-year study period, findings are associational rather than causal. At the time of this analysis, only 2006–2007 CCW data were available. Future research incorporating additional years of data will allow construction of longitudinal analytic files and time-to-event analyses to confirm the associations reported in this study. Additionally, study results might not be generalizable to newly approved COPD maintenance medications after 2007.

Finally, even though a wide range of potential confounders were controlled, unobservable factors were not. Findings therefore may not be generalizable to Medicare MA-PD and/or HMO enrollees and those with characteristics excluded from the study sample and other non-Medicare population.

CONCLUSION

In conclusion, findings demonstrate Medicare beneficiaries with COPD and comorbid depression have lower COPD maintenance medication use and adherence. An implication of the findings of this study is that health care providers should focus on improving maintenance medication use and adherence, especially for patients with chronic comorbidities such as depression. Depression should be screened among COPD population and considered as a potential risk factor for low COPD maintenance medication adherence. Further research evaluating whether interventions treating depression improve COPD maintenance medication use, adherence and/or outcomes is warranted.

Acknowledgments

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Key points

- COPD maintenance medication use is low in Medicare beneficiaries with COPD, regardless of the presence of comorbid depression

- Among COPD patients who filled COPD maintenance medications, depression diagnosis is associated with lower COPD maintenance medication adherence

- Health care providers should focus on improving maintenance medication use and adherence, as well as consider the presence of comorbid depression in their COPD patients as a potential risk factor for low COPD maintenance medication adherence

Table 1

Characteristics of Beneficiaries with COPD Enrolled in Medicare Part D PDP Plans, Stratified by Depression Status (n=74,863)

Characteristics	All COPD Beneficiaries		Depression[a]			
			Yes		No	
	N	%	N	%	N	%
Sample size	74,863	100.0	25,130	100	49,733	100
Age[†]						
Mean (SD)	72.2	12.0	70.0	13.6	73.4	10.9
< 65	15,175	20.3	7,426	29.6	7,749	15.6
65 – 74	24,950	33.3	7,170	28.5	17,780	35.8
75 – 84	24,163	32.3	7,067	28.1	17,096	34.4
85 +	10,575	14.1	3,467	13.8	7,108	14.3
65 were SSDI[b] eligible	10,286	13.7	3,686	14.7	6,600	13.3
Sex[†]						
Female	47,337	63.2	17,652	70.2	29,685	59.7
Male	27,526	36.8	7,478	29.8	20,048	40.3
Race[†]						
White	64,283	85.9	21,938	87.3	42,345	85.1
Black	6,590	8.8	1,941	7.7	4,649	9.4
Hispanic	1,953	2.6	803	3.2	1,150	2.3
Asian	1,071	1.4	142	0.6	929	1.9
Other	966	1.3	306	1.2	660	1.3
Region[†]						
Northeast	12,835	17.1	4,347	17.3	8,488	17.0
North Central	18,390	24.6	6,354	25.3	12,036	24.2
West	10,600	14.2	3,223	12.8	7,377	14.8
South	32,937	44.0	11,206	44.6	21,832	43.9

| Characteristics | All COPD Beneficiaries | | Depression[a] | | | |
| | | | Yes | | No | |
	N	%	N	%	N	%
Low-income subsidy status[†]						
Yes	45,679	61.0	18,471	73.5	27,208	54.7
No	29,184	39.0	6,659	26.5	22,525	45.3
Comorbid medical conditions[†]						
Asthma	21,466	28.7	8,244	32.8	13,222	26.6
Diabetes	26,636	35.6	9,937	39.5	16,699	33.6
Ischemic heart disease	41,481	55.4	14,686	58.4	26,795	53.9
Congestive heart failure	32,772	43.8	12,146	48.3	20,626	41.5
All other cardiovascular disease	51,708	69.1	17,124	68.1	34,584	69.5
Hypertension	60,713	81.1	20,935	83.3	39,778	80.0
Alzheimer's disease and related dementias	14,662	19.6	7,519	29.9	7,143	14.4
Anxiety	14,172	18.9	9,766	38.9	4,406	8.9
COPD severity indicators						
Had supplemental oxygen claims	14,699	19.6	4,973	19.8	9,726	19.6
Had any COPD rescue medication[†]	23,138	30.9	8,736	34.8	14,402	29.0
Hospitalization at baseline[†]						
Had any hospitalization	34,905	46.6	14,683	58.4	20,222	40.7
# of hospitalization (Mean, SD)	2.2	1.8	2.5	2.1	1.9	1.4

SD: standard deviation

[a]2006 and/or 2007 depression annual flag in the CCW data

[b]SSDI: Social security disability insurance

[†]P values < 0.0001 from Chi-square tests for categorical variables or t tests for continuous variables

Table 2

Two-year COPD Maintenance Medication Use and Adherence in Medicare Part D Beneficiaries with COPD, Stratified by Depression Status

Drug Use and Hospitalization Measures	All COPD Beneficiaries		Depression[a]			
			Yes		No	
	N	%	N	%	N	%
Sample size	74,863	100.0	25,130	100	49,733	100
Any COPD Maintenance Medication						
Any use[b†]	46,271	61.8	16,115	64.1	30,156	60.6
Sample size[c]	35,985		12,574		23,411	
Discontinuer[c†]	7,835	21.8	3,009	23.9	4,826	20.6
Proportion of days covered (PDC) 0.80[c†]	12,956	36.0	3,953	31.4	9,003	38.5

[a] 2006 and/or 2007 depression annual flag in the CCW data

[b] Among the total sample (n=74,863)

[c] Limited to who had any COPD maintenance medication use and at least two Part D claims (n=35,985)

[†] P values < 0.0001 from Chi-square tests or t tests

Table 3

Association between Depression Diagnosis and Two-year COPD Maintenance Medication Use and Adherence in Medicare Part D Beneficiaries with COPD

Predictors	Medication Use and Adherence								
	Any Use[a]			Discontinuation[b]			PDC (>=0.8)[b]		
	PR	Lower 95% CI	Upper 95% CI	PR	Lower 95% CI	Upper 95% CI	PR	Lower 95% CI	Upper 95% CI
Crude Depression	1.06	1.05	1.07	1.16	1.12	1.21	0.82	0.79	0.84
Adjusted Depression	1.02	1.01	1.03	1.09	1.04	1.14	0.89	0.86	0.92
Age									
< 65		reference			reference			reference	
65 – 74	1.08	1.06	1.09	0.82	0.77	0.87	1.09	1.04	1.13
75 – 84	1.06	1.04	1.08	0.81	0.76	0.86	1.04	0.99	1.08
85 +	0.97	0.95	0.99	0.83	0.77	0.89	1.00	0.95	1.06
65 were SSDI[c] eligible	0.99	0.97	1.00	1.06	1.00	1.13	1.01	0.97	1.05
Female	1.00	0.99	1.01	1.02	0.98	1.07	0.93	0.90	0.96
Race									
White		reference			reference			reference	
Black	0.90	0.88	0.91	1.19	1.12	1.28	0.79	0.75	0.84
Hispanic	1.01	0.98	1.05	1.23	1.09	1.40	0.93	0.83	1.03
Asian	0.88	0.83	0.92	1.45	1.25	1.68	0.97	0.86	1.10
Other	0.96	0.91	1.00	1.29	1.11	1.51	0.87	0.76	1.00
Region									
Northeast		reference			reference			reference	
North Central	0.97	0.96	0.99	1.07	1.01	1.14	0.97	0.93	1.01
West	0.92	0.90	0.94	1.13	1.06	1.21	0.95	0.90	0.99
South	0.97	0.96	0.99	1.14	1.08	1.20	0.93	0.90	0.97

Predictors	Medication Use and Adherence								
	Any Use[a]			Discontinuation[b]			PDC (>=0.8)[b]		
	PR	Lower 95% CI	Upper 95% CI	PR	Lower 95% CI	Upper 95% CI	PR	Lower 95% CI	Upper 95% CI
Low-income subsidy status									
No	reference			reference			reference		
Yes	1.06	1.05	1.07	0.87	0.83	0.91	0.97	0.93	1.00
Comorbid medical conditions									
Asthma	1.39	1.38	1.41	0.92	0.88	0.96	1.01	0.98	1.04
Diabetes	0.98	0.97	0.99	1.12	1.07	1.17	0.95	0.92	0.98
Ischemic heart disease	0.97	0.96	0.99	1.13	1.08	1.18	0.92	0.89	0.95
Congestive heart failure	1.03	1.02	1.04	1.04	0.99	1.09	0.98	0.95	1.01
All other cardiovascular disease	1.00	0.98	1.01	1.07	1.02	1.12	0.97	0.94	1.00
Hypertension	0.99	0.98	1.01	1.04	0.98	1.10	0.96	0.93	1.00
Alzheimer's disease and related dementias	0.92	0.91	0.94	1.10	1.04	1.16	0.84	0.81	0.88
Anxiety	1.01	1.00	1.03	1.02	0.97	1.07	0.99	0.95	1.03
Had any baseline hospitalization	0.94	0.93	0.95	1.20	1.15	1.25	0.86	0.83	0.89
COPD severity indicators									
Had supplemental oxygen claims	1.39	1.38	1.41	0.76	0.73	0.80	1.33	1.30	1.37
Had any COPD rescue medication	1.44	1.43	1.46	0.93	0.89	0.97	1.10	1.07	1.13

PR: prevalence ratios; CI: confidence intervals. Multivariable models used modified Poisson regression and log link with generalized estimating equations. Bold numbers indicate P < 0.05

[a] Among the total sample (n=74,863)

[b] Limited to who had any COPD maintenance medication and had at least two Part D claims (n=35,985)

[c] SSDI: Social security disability insurance

Table 4

Influence of Depression on Two-year COPD Maintenance Medication Use and Adherence in Medicare Part D Beneficiaries with COPD – Sensitivity Analysis[a]

Models	Medication Adherence					
	Discontinuation			PDC (>=0.8)		
		Lower	Upper		Lower	Upper
	PR	95% CI	95% CI	PR	95% CI	95% CI
I: excluding asthma	**1.07**	**1.01**	**1.14**	**0.91**	**0.87**	**0.95**
II: excluding bipolar and/or other psychotic disorders	**1.08**	**1.03**	**1.13**	**0.90**	**0.87**	**0.93**
IIIa: using PDC cut point 0.90				**0.83**	**0.79**	**0.87**
IIIb: using PDC cut point 0.70				**0.92**	**0.89**	**0.94**
IV: excluding benes died in 2006	**1.10**	**1.05**	**1.16**	**0.87**	**0.84**	**0.91**

PR: prevalence ratios; CI: confidence intervals. Multivariable models used modified Poisson regression and log link with generalized estimating equations. Bold numbers indicate P < 0.05

[a]Limited to who had any COPD maintenance medication and had at least two Part D claims (n=35,985)