Published in final edited form as:

Int J Geriatr Psychiatry. 2018 February ; 33(2): e212–e220. doi:10.1002/gps.4772.

The association of antidepressant treatment with COPD maintenance medication use and adherence in a comorbid Medicare population: A longitudinal cohort study

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Abstract

Background—The effect of treating comorbid depression to achieve optimal management of chronic obstructive pulmonary disease (COPD) has not yet empirically tested. We examined the association between antidepressant treatment and use of and adherence to COPD maintenance medications among patients with new-onset COPD and comorbid depression.

Methods: Using 2006–2012 Medicare data, this retrospective cohort study identified patients with newly diagnosed COPD and new-onset major depression. Two exposures—antidepressant use (versus non-use) and adherence measured by proportion of days covered (PDC) (PDC ≥ 0.8 versus <0.8)—were assessed quarterly. We used marginal structural models to estimate the effects of

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CONFLICT OF INTEREST

All authors have no conflict of interest.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

PREVIOUS PRESENTATION

32nd International Conference on Pharmacoepidemiology and Therapeutic Risk Management, Dublin, Ireland. August 2016.

prior antidepressant use and adherence on subsequent COPD maintenance inhaler use and adherence outcomes, accounting for time-varying confounders.

Results: A total of 25 458 COPD-depression patients, 82% with antidepressant treatment, were followed for a median of 2.5 years. Nearly half (48%) used at least 1 COPD maintenance inhaler in any given quarter; among users, 3 in 5 (61%) had a PDC of <0.8. Compared to patients with no antidepressant treatment, those with antidepressant use were more likely to use (relative ratio [RR] = 1.15, 95% confidence interval [CI] = 1.12-1.17) and adhere to (RR = 1.08, 95% = 1.03-1.14) their COPD maintenance inhalers. Patients who adhered to antidepressant treatment were more likely to use and adhere to COPD maintenance inhalers.

Conclusion: Regularly treated depression may increase use of and adherence to necessary maintenance medications for COPD. Antidepressant treatment may be a key determinant to improving medication-taking behaviors among COPD patients comorbid with depression.

Keywords

adherence; COPD; depression; multiple conditions

1 | INTRODUCTION

Chronic obstructive pulmonary disease (COPD), a progressive and irreversible chronic disorder, is the third leading cause of death in the United States¹ and exerts deleterious impacts on quality of life and morbidity.^{2,3} In addition to difficulty in breathing, many patients living with COPD also have mental health issues, such as depression.^{4,5} Up to 42% of COPD patients have depression; among those with severe COPD symptoms, up to 60% have depression diagnoses.⁴ The figure for COPD patients with comorbid depression is expected to rise and so are associated societal burdens and medical costs.⁶

Despite available, effective COPD medications and widely accepted medical guidelines for medication use,^{7,8} COPD remains undertreated.^{9,10} An estimated 60-70% of community-dwelling Medicare beneficiaries with COPD do not use any maintenance medications, regardless of disease severity^{10,11}; among those who do use COPD medications, treatment adherence remains low.^{3,11} Underlying reasons for suboptimal medication treatment of COPD are complex and include patient-related (eg, patients' perception of the disease), treatment-related (eg, complex regimens), and social/environmental (eg, patient-prescriber relationship) factors.¹² Understanding optimal clinical management of multimorbid individuals is further complicated by the current guidelines and clinical practice, which tend to focus on management of single conditions rather than multiple conditions faced by over half of adults with COPD.^{13,14}

Recognizing the need for better management of patients with COPD and comorbid depression, in 2008, the American College of Chest Physicians and the National Institute of Mental Health jointly noted the importance of understanding how depression and its treatment may affect clinical outcomes of COPD, including treatment adherence in COPD patients.⁴ Since then, much attention has focused on the role of adequate depression treatment, as evidence suggests persistent use of antidepressants is associated with improved

adherence to medications used to treat chronic comorbid conditions, such as heart failure,¹⁵ diabetes,^{15,16} and multiple sclerosis.¹⁷ Despite these findings, it remains unclear whether treated depression exerts similar benefits to COPD medication use and adherence. Thus, understanding the effects of treating depression may prove critical to improving COPD management, reducing COPD symptoms, and preventing acute exacerbations and adverse outcomes (eg, hospitalization) for patients who suffer from COPD and comorbid depression.
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This study aimed to examine whether use of and adherence to antidepressant treatment were associated with use of and adherence to COPD maintenance medications among Medicare beneficiaries with COPD and comorbid depression.

2 | METHODS

2.1 | Study design and source

This retrospective, longitudinal cohort study used a 5% random sample of Medicare fee-for-service beneficiaries' administrative claims data from 2006 to 2012. Medicare administrative data include claims for Parts A (inpatient), B (physician/supplier), and D (prescription drug) services. The University of Maryland Baltimore Institutional Review Board (HP-00055737) approved this study on 05/10/2013.

2.2 | Study sample

The study sample consists of all beneficiaries with newly diagnosed COPD and new-onset major depression following their COPD diagnosis during 2006 and 2011. New COPD cases were identified based on the date of the first occurrence of a COPD diagnosis (*International Classification of Disease, Ninth Revision, Clinical Modification* [ICD-9-CM] codes 490, 491.x, 492.x, 494.x, 496) in inpatient or outpatient claims.²¹ Incident depression cases were defined as those having no depression in the 6 months before the first COPD diagnosis. We measured depression using relevant ICD-9-CM codes (296.2x, 296.3x, and 311.xx) and identified cases using a diagnosis-based algorithm that includes 1 inpatient or 2 outpatient claims for depression diagnosis or 1 outpatient depression claim plus 1 antidepressant prescription fill.¹⁷ This depression algorithm has been validated against medical charts and shown good to excellent agreement.²² To ensure the presence of active major depression, we required beneficiaries to have evidence of depression after their first depression diagnosis. We assigned a depression index date as the time of the first major depression claim after COPD diagnosis and considered 6 months before the index date as a baseline.

Patients were excluded if, at baseline, they had (1) discontinuous Medicare Parts A, B, and D enrollment, or Medicare Advantage insurance; (2) diagnoses of respiratory tract cancer, tuberculosis, asbestosis, and sarcoidosis (because these conditions are also treated by COPD maintenance medications); or (3) diagnoses of schizophrenia and bipolar disorder (because these conditions are commonly treated with antidepressants). Beneficiaries with 1-year survival after the index date were excluded to avoid an insufficient period for observing antidepressant exposures and COPD medication use outcomes.

Follow-up started from the depression index date for analysis with antidepressant use as the main exposure and the date of the first antidepressant prescription fill for analysis with antidepressant adherence exposure. Follow-up ended at death or 12/31/2012 for the outcome of COPD maintenance inhaler use, while for the COPD maintenance medication adherence outcome, additional censoring was performed when patients discontinued their COPD maintenance treatment, defined as no additional refill for >90 days after the prior prescription claim.²³

2.3 | Antidepressant treatment exposure

Using National Drug Codes, we captured 29 antidepressants approved for treatment of clinical depression and severe depression symptoms (Supplementary Table 1) through the Part D prescription file. We measured the use of and adherence to antidepressant treatment quarterly. Patients who had 1 prescription fill of the studied antidepressants for their depression comorbidity were defined as antidepressant users or non-users, otherwise. Among users, adherence to antidepressants was defined as the extent to which patients take antidepressants as prescribed.²⁴ Medication adherence was measured using proportion of days covered (PDC), calculated as the number of days with available medications divided by the number of days at quarterly intervals.²⁵ We categorized PDC values as adherent or non-adherent using a commonly used, clinically relevant cutoff of PDC 0.8. For any medication use and PDC, we adjusted for Part A-covered skill nursing facility or hospitalization days, as drug payment for these days is bundled under Part A and unavailable for measurement.²⁶

2.4 | COPD maintenance medication use and adherence

COPD maintenance inhaler use and adherence were measured quarterly, starting the second quarter of the follow-ups. The outcome was dichotomized as use versus non-use and PDC of 0.8 versus <0.8, respectively. COPD maintenance medications included long-acting beta-agonists (LABAs), long-acting anticholinergics (LAACs), and inhaled corticosteroids (ICSs), alone or in combination with each other (eg, LABA + LAAC). We also included short-acting anticholinergics (SAACs) and short-acting beta-agonists (SABAs), used in combination with the abovementioned COPD maintenance medications (eg, SABA + ICS) because the combinations are recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines as maintenance therapy options for COPD patients⁷ (Supplementary Table 1). We refrained from including COPD rescue/acute medications because these medications are used *pro re nata* (PRN) or “as needed” and use and adherence cannot be adequately assessed for PRN medications.

2.5 | Time-dependent and time-independent covariates

Time-independent covariates measured at baseline included: socio-demographics, reason for Medicare entitlement, low-income subsidy status, and geographically based income and education level. Regional data for each patient were obtained from the Area Health Resources Files linked to CCW Medicare beneficiary summary files through county codes.²⁷ The calendar year of the first COPD diagnosis, the depression index date, and baseline COPD maintenance medication use and adherence also were included in analyses.

Time-dependent confounders measured at baseline and quarterly during the follow-up included the following: health behaviors, comorbidity, COPD severity, depression severity, number of unique medications (excluding COPD and depression medications), and nursing home stay (yes/no). We measured health behaviors using the presence or absence of utilization of 3 preventive health services: pneumococcal and influenza vaccinations, colorectal cancer screening, prostate cancer screening (males), and mammography screening and/or pap smears (females) in Part B claims data.^{28,29} This measure, which ranged from 0 (unhealthy behavior) to 3 (healthier behavior), was analyzed as a categorical variable (0, 1, 2) due to its skewed distribution. Overall comorbidity was measured with the Charlson Comorbidity Index (CCI) score, calculated as the weighted count of 17 chronic conditions, excluding COPD, identified by ICD-9-CM diagnoses codes.³⁰ For analyses, patients were grouped into 1 of the 3 groups: CCI = 0, 1, or 2 chronic comorbid conditions.

COPD severity was assessed quarterly in 4 ways: rescue medication use (yes/no), supplemental oxygen use (yes/no), and utilization of COPD-related ED visits (yes/no), and COPD-related hospitalizations (yes/no).^{3,7,11} Depression severity was measured based on the presence of severe depression with mention of psychosis (ICD-9-CM 5th digit code = “4”) or psychiatric hospitalizations in Medicare claims data.^{31–33} Finally, we measured whether residents resided in a long-term care facility using Part A skill nursing facility admission and discharge dates and Part B Claims.

2.6 | Statistical analysis

To account for time-varying confounders that also are intermediates between antidepressant treatment (exposures) and COPD maintenance medication use and adherence (outcomes), we adopted marginal structural models (MSMs) that use weighting strategies for balancing covariates between exposure and non-exposure.³⁴ MSM analysis involves 2 steps. The first step is to estimate a stabilized weight for an individual in each quarter based on inverse probability of treatment weighting (IPTW) and inverse probability of censoring weighting (IPCW). To estimate IPTW and IPCW, we fitted 2 multivariate logistic regression models, using antidepressant exposure and death as the outcome, respectively, and observed time-dependent and time-independent variables as covariates (Supplementary Table 2). In the second step, we incorporated the estimated stabilized weights into generalized linear models (GLMs) with a Poisson distribution and log link to estimate the effects of current quarterly antidepressant exposure on the subsequent quarter of COPD medication outcomes.³⁵ Generalized estimating equations (GEE) was also included in the GLMs to account for clustering of quarterly repeated measures of antidepressant exposures.³⁶ We reported relative ratios (RRs) and corresponding 95% confidence intervals (CIs) derived from the GLMs. To further understand what other factors, in addition to antidepressant treatment, may contribute to COPD maintenance medication use and adherence, we conducted additional analyses by including baseline characteristics in the final weighted models as covariates.

To test the robustness of the associations, we performed 3 sets of sensitivity analyses. First, to compare estimates from MSMs (with stabilized weights) and conventional methods (without weights), we constructed multivariate unweighted regression models with the time-dependent and time-independent variables as covariates. Second, to analyze antidepressant

treatment effect in a homogeneous group, we repeated the MSM analysis among a subgroup of patients with their first depression diagnosed within 12 months of the newly diagnosed COPD. Three, to address missing data on the COPD adherence outcome ($n = 4267$ had missing adherence due to no use of COPD maintenance medications until months after the depression index date), we used complete case analysis that included COPD-depression patients who had received COPD maintenance medication treatment since the beginning of and throughout the follow-up period. All analyses were performed using SAS® 9.4 (SAS Institute, Cary, NC).

3 | RESULTS

We identified a cohort of 25 458 eligible new-onset COPD patients with newly diagnosed comorbid depression, contributing 290 630 person-quarters of observations. The sample was predominately female (72.3%), white (85.6%), over 64 years old (70.1%), and low-income subsidy recipients (55.2%), with most (98.4%) entitled to Medicare due to old age or disability (Table 1). At baseline, 22.8% of the COPD sample had multiple CCI conditions, and 30% used more than 9 medications. Two-thirds (65.5%) did not utilize preventive health services, and approximately 1 in 7 (14.4%) had a nursing home stay. Few used oxygen (6.5%) or experienced COPD-related hospitalizations (2.3%) or emergency room visits (4.0%) at baseline; however, 21.9% used rescue/acute respiratory medications as initial treatment for COPD in the 6 months before the time they developed depression.

During follow-up, 82% of patients with COPD and depression received at least 1 antidepressant and nearly half (48%) used at least 1 COPD maintenance inhaler in any given quarter (Table 1). Among users of COPD maintenance medications, 2 in 5 (39%) had a PDC of ≥ 0.8 (data not shown). Overall, we observed an increasing proportion of patients who had a PDC of ≥ 0.8 for COPD maintenance medications over time. The proportions were higher among antidepressant users than among non-users (Figure 1).

Table 2 shows the effect of antidepressant-treated depression on COPD maintenance medication outcomes. Without covariate adjustment, patients who used antidepressants were more likely to use COPD maintenance inhalers (RR = 1.36, 95% CI = 1.34-1.38) and adhere to these medications (RR = 1.10, 95% CI = 1.05-1.16). After adjustment for baseline and time-dependent variables in unweighted models, the RR estimates decreased but remained statistically significant (adjusted RR = 1.18, 95% CI = 1.15-1.20 for any use; adjusted RR = 1.09, 95% CI = 1.01-1.15 for adherence outcome). Compared to the multivariate unweighted models, the MSM analysis with stabilized weights yielded smaller, conservative RR estimates for any use (adjusted RR = 1.15, 95% CI = 1.12-1.17) and adherence (adjusted RR = 1.08, 95% CI = 1.03-1.14) outcomes. Similar antidepressant exposure effect estimates were observed in subgroup analyses (Table 2).

The probability of using any COPD maintenance medication was higher among beneficiaries who were white, female, younger than 65 years old, entitled to Medicare due to elderly, or low-income subsidy recipients (Table 3). The same characteristics, except gender, also were observed as significant factors for predicting adherence to COPD maintenance medication treatment in COPD patients with depression comorbidity.

Table 4 shows the effect of adherence to antidepressants on COPD maintenance medication outcomes. Both MSM (with weights) and adjustment regression (without weights) analysis showed similar results—that is, patients who adhered to antidepressants were significantly more likely to use and adhere their COPD maintenance medications.

4 | DISCUSSION

Utilizing nationally representative data of Medicare beneficiaries, this study provides real-world evidence of the positive influence of antidepressant treatment in promoting the use of and adherence to necessary COPD maintenance medications in a COPD-depression population. Our results indicate that COPD patients with treated comorbid depression have a 15% higher probability of any use and 8% higher probability of regular use of their COPD maintenance medications compared to peers untreated with antidepressants. Furthermore, COPD-depression patients who adhered to their antidepressant treatment were more likely to use and adhere to their COPD maintenance medications. Our study demonstrates the importance of regularly treating depression in initiating and maintaining COPD medication use, 2 key factors in preventing COPD exacerbations and other adverse health outcomes, including hospitalization³ and death.³⁷

Our study, which repeatedly measured antidepressant treatment exposure over a maximum of 7 years, found the majority (82%) of newly diagnosed COPD-depression patients used antidepressants at least once over 7 years. Our findings from administrative data are similar to those of previous studies on antidepressant use in a prevalent and incident cohort of COPD-depression patients (81% and 70%, respectively).^{32,38} Our data, however, are higher than those of prior clinical trials^{39,40} and observational studies of COPD patients with comorbid depression.⁴¹ These previous studies were cross sectional with small sample sizes and short follow-up times, and relied on self-report for evidence of antidepressant use, reasons that may explain the observed discrepancy.

Our study also identified several characteristics as significant factors in predicting untreated depression, including male sex, non-white race/ethnicity, older age, no use of studied preventive services, having multiple comorbid conditions in addition to depression and COPD, and higher COPD and depression severity (see Supplementary Table 2). In particular, racial/ethnic differences in receiving adequate depression treatment have been documented in the literature.^{42–44} Reasons responsible for such differences are multiple but include variation in access to mental health care, insurance coverage, and language and cultural background.⁴² After MSM weighting analysis, black race (vs white race) remains a significant predictor of both nonuse and nonadherence to COPD maintenance medications, consistent with a major study indicating the blacks are disproportionately not adherent to prescription medications in general.⁴³ Interventions targeted to patients with comorbid COPD and depression with these characteristics may be warranted to reduce inadequate depression and COPD treatment.

Of particular concern is the high level of undertreatment of COPD in our COPD-depression cohort. Over 1 in 4 (28.4%) of patients did not use any COPD medications, including acute or maintenance respiratory medications, after COPD diagnosis. Of those who used COPD

maintenance inhalers, 55.0% delayed treatment immediately after COPD diagnosis, and 40.0% initiated but later discontinued COPD medications (data not shown). Among those who used COPD maintenance medications, 3 in 5 (61%) evidenced had suboptimal adherence (ie, PDC <0.8). Our finding of low COPD treatment adherence is consistent with findings from previous population-based studies,^{45,46} but higher than the 10-30% demonstrated in clinical trials.³⁷ Differences in adherence likely are due to the attention clinical trial study patients receive, as well as to patient selection criteria required of clinical trial patients.

The presence of comorbid depression has a detrimental effect on treatment and management of many chronic conditions.^{47,48} For example, patients with diabetes and depression are more likely to discontinue medication treatment, compared to patients with diabetes alone.^{47,48} However, when adequately treated, comorbid depression is associated with improved adherence to medications used to treat coronary artery disease and/or dyslipidemia, diabetes,¹⁵ and multiple sclerosis.¹⁷ Our study adds to the current body of knowledge by showing that antidepressant treatment may improve use of and adherence to COPD maintenance medications. One potential mechanism is that the symptoms of depression, including apathy, hopelessness, and concomitant anxiety, may be alleviated after antidepressant treatment, and improvement in depressive symptoms enhances patients' adoption of healthy behaviors, including regularly taking COPD medications as prescribed. Taken together, these studies emphasize the importance of treating depression and the need to improve depression care in patients with multiple chronic conditions, including COPD.

This study has notable strengths. First, we followed patients' medication usage for symptom management of depression and COPD over time and analyzed use based on medications dispensed to patients. This approach, which considers treatment initiation, persistence, and discontinuation, provides results that more likely reflect "real-world" medication-taking behaviors than those witnessed in clinical trials. Second, we focused on patients with new-onset COPD and depression and used the MSM approach to account for available time-independent and time-dependent variables. The MSM uses weighting methods to balance observed confounders, some of which may act as intermediate variables and change over time between the antidepressant exposure and non-exposure groups. Thus, our MSM-derived estimates may be closer to actual causal effects than those offered by conventional multivariate adjustment models where confounders are included as regressors.³⁴

Our study has several limitations. Although substantial weighting adjustments were made for confounding variables through MSM analysis, unmeasured confounding may exist. For example, self-medication behaviors, such as cigarette smoking, alcohol, and substance use, cannot be measured with these data; as well, use of non-pharmacological interventions (eg, cognitive therapy for depression, herbal supplements), which may be associated with both antidepressant exposure and COPD medication treatment, also is not recorded in the data. The lack of measurement of non-pharmacological interventions hinders our complete understanding of depression treatment in this population. Potential residual confounding may persist due to the imperfect measures of depression severity that based on the presence of severe depression with mention of psychosis (ie, ICD-9-CM 5th digit code = "4") and psychiatric-related hospitalization.²³ Further studies that validate these depression severity

measures are needed. Also, our study is unable to distinguish whether patients received antidepressants for depression or other comorbid diseases (eg, anxiety, pain) because indications for the prescribed medication are not recorded in the data. Likewise, the absence of lung function data limits our ability to understand the role of antidepressant treatment in reducing the severity of respiratory symptoms. Finally, this study may not capture patients' medical and pharmacy services received at non-Medicare sites and/or reimbursed by non-Medicare payers (eg, the VA or out-of-pocket), as well as reflect changes in clinical practice due to the Affordable Care Act implemented in 2013.⁴⁹

In conclusion, in a Medicare COPD-depression cohort, treated depression increased use of and adherence to necessary maintenance medications for COPD. Antidepressant treatment is a key determinant that can be effectively intervened to improving COPD medication-taking behaviors among COPD patients comorbid with depression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENT

This research was supported by National Institute on Aging at NIH/Grant number: 21AG045573-02.

Funding information

National Institute on Aging at NIH, Grant/Award Number: 21AG045573-02

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Key points

- In a Medicare COPD-depression cohort, antidepressant-treated depression was associated with increased use and adherence to COPD maintenance medications, when compared with nontreated depression.
- A higher probability of COPD maintenance medication use and adherence also was observed among patients who adhered to their antidepressants than among nonadherent patients.
- Antidepressant treatment may be a key determinant to improving medication-taking behaviors among COPD patients comorbid with depression.

FIGURE 1.
COPD maintenance medication adherence, overall, and by antidepressant use

Table 1
 Characteristics of Medicare beneficiaries with newly diagnosed COPD and new-onset depression during 2006–2011

Characteristics ^a	COPD-depression sample <i>n</i> = 25 458 (100%)
Year of first COPD diagnosis	
2006	5303 (20.8)
2007	4989 (19.6)
2008	4668 (18.3)
2009	4178 (16.4)
2010	3727 (14.6)
2011	2593 (10.2)
Year of first depression diagnosis	
2006	1901 (7.5)
2007	3245 (12.7)
2008	4196 (16.5)
2009	4623 (18.2)
2010	5195 (20.4)
2011	6298 (24.7)
Age	
<65	7602 (29.9)
65–74	7793 (30.6)
75–84	6135 (24.1)
85	3928 (15.4)
Female	18 415 (72.3)
Race/ethnicities	
Whites	21 803 (85.6)
Blacks	2251 (8.9)
Others	1404 (5.5)
Low-income subsidy recipients	14 052 (55.2)
Original reason for Medicare entitlement	
Old age (≥ 65 years old)	15 797 (62.1)
Disability	9264 (36.4)

Characteristics ^a	COPD-depression sample n = 25 458 (100%)
End stage renal disease	397 (1.6)
Region	
Midwest	6715 (26.4)
Northeast	4444 (17.5)
South	10 862 (42.7)
West	3437 (13.5)
Regional median household income	
<\$39 000	5682 (22.3)
\$39 000 to <\$53 000	14 192 (55.8)
\$53 000	5584 (21.9)
Regional percentage with < high school diplomas	
<11%	6676 (26.2)
11%–18%	11 728 (46.1)
>18%	6954 (27.3)
Charlson Comorbidity Index	
0	14 475 (56.9)
1	5176 (20.3)
2–12	5807 (22.8)
Total number of medications used, excluding COPD medications and antidepressants	
0–1	3451 (13.6)
2–5	8714 (34.2)
6–9	5652 (22.2)
10+	7641 (30.0)
Utilization of select preventive health services	
0	16 687 (65.5)
1	8191 (32.2)
2–3	580 (2.3)
Any nursing home stay	3654 (14.4)
COPD severity measures	
Use of oxygen (yes/no)	1663 (6.5)
Use of COPD rescue/acute medications	5564 (21.9)

Characteristics ^a	COPD-depression sample <i>n</i> = 25 458 (100%)
Any COPD-related hospitalization	572 (2.2)
Any COPD-related emergency room visits	1005 (3.9)
Receiving 1 antidepressants during follow-up	20 876 (82.0)
Receiving 1 COPD maintenance medications during follow-up	12 220 (48.0)

^a Characteristics were measured at baseline, ie, 6 months prior to the depression index date, unless specified otherwise.

Effect of antidepressant-treated depression on subsequent use of and adherence to COPD maintenance medications in the COPD-depression patients

Table 2

Independent variable	Outcomes	
	Any use (<i>n</i> = 12 220) vs no use (<i>n</i> = 13 238)	PDC 0.8 (<i>n</i> = 4513) vs PDC < 0.8 (<i>n</i> = 7059) ^a
Antidepressant-treated depression (vs untreated depression)	Relative ratio (95% CI)	Relative ratio (95% CI)
Unweighted models, no covariates	1.36 (1.34–1.38) ***	1.10 (1.05–1.16) ***
Unweighted models, baseline and time-dependent variables	1.18 (1.15–1.20) ***	1.09 (1.04–1.15) ***
MSM weighted models, baseline covariates	1.15 (1.12–1.17) ***	1.08 (1.03–1.14) ***
Subgroup analyses		
<i>Patients with depression within 1 year of COPD diagnosis</i>	(<i>n</i> = 16 462)	(<i>n</i> = 6942)
Unweighted models, no covariates	1.41 (1.38–1.43) ***	1.10 (1.04–1.17) ***
Unweighted models, baseline and time-dependent variables	1.18 (1.15–1.22) ***	1.09 (1.03–1.16) **
MSM weighted models, baseline covariates	1.15 (1.12–1.18) ***	1.08 (1.01–1.14) *
<i>Patients without delayed use of COPD maintenance medications</i>		(<i>n</i> = 6259)
Unweighted models, no covariates	-	1.09 (1.05–1.13) ***
Unweighted models, baseline and time-dependent variables	-	1.08 (1.04–1.12) ***
MSM weighted models, baseline covariates	-	1.07 (1.04–1.11) ***

^a Analyses were restricted to 11 572 COPD-depression patients who had at least 2 prescriptions for COPD maintenance inhalers to measure medication adherence.

*** <0.001.

** <0.01.

* <0.05.

Table 3

Baseline characteristics associated with use of and adherence to COPD maintenance medications in COPD patients with comorbid depression

Baseline time-independent factors	Any use (vs no use)	PDC 0.80 (vs <0.8)
	Weighted relative ratio (95% CI)	Weighted relative ratio (95% CI)
Total sample		
Age	25 458	11 572
<65 (reference)	1.0	1.0
65–74	0.90 (0.86–0.94) ***	0.87 (0.80–0.94) ***
75–84	0.63 (0.60–0.67) ***	0.73 (0.66–0.80) ***
85	0.59 (0.55–0.63) ***	0.66 (0.59–0.74) ***
Female vs male	1.13 (1.09–1.18) ***	0.95 (0.90–1.01)
Race/ethnicities		
Whites (reference)	1.0	1.0
Blacks	0.86 (0.81–0.92) ***	0.90 (0.82–0.98) ***
Others	0.96 (0.89–1.04)	0.94 (0.85–1.04)
Original reason for Medicare entitlement		
Old age (reference)	1.0	1.0
Disability	0.79 (0.74–0.85) ***	0.81 (0.75–0.88) ***
End stage renal disease	0.49 (0.41–0.59) ***	0.59 (0.45–0.78) ***
Low income subsidy (yes vs no)	1.23 (1.18–1.28) ***	1.24 (1.18–1.31) ***

<0.001.

**
<0.01.

*
<0.05.

Effect of adherence to antidepressants on subsequent use of and adherence to COPD maintenance medications in the COPD-depression patients who had 2 prescriptions for both medication classes (*n* = 6446)

Table 4

Independent variable	Outcomes		
	Any use (<i>n</i> = 10 684) vs no use (<i>n</i> = 11 575) ^{<i>a</i>}	PDC 0.8 (<i>n</i> = 2579) vs PDC < 0.8 (<i>n</i> = 3867) ^{<i>b</i>}	Relative ratio (95% CI)
Adherence to antidepressants (PDC of 0.8 vs <0.8)			
Unweighted models, no covariates	1.05 (1.03–1.07)***	1.39 (1.33–1.45)***	
Unweighted models, baseline and time-dependent variables	1.06 (1.04–1.09)***	1.13 (1.09–1.18)***	
MSM weighted models, baseline covariates	1.06 (1.04–1.08)***	1.13 (1.09–1.17)***	

^{*a*} Analyses were restricted to 22 259 COPD-depression patients who had at least 2 prescriptions for antidepressants.

^{*b*} Analyses were restricted to 6446 COPD-depression patients who had at least 2 antidepressant prescriptions and at least 2 prescriptions for COPD maintenance inhalers.

**
*
<0.001.
<0.01.
<0.05.