Adherence to Oral Medications for Hypertension and Diabetes in Veterans with Comorbid Airflow Limitation

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Abstract

Rationale: Diabetes and hypertension are common among patients with airflow limitation and contribute to cardiovascular (CV) mortality, one of the leading causes of death among patients with airflow limitation.

Objectives: Our goal was to examine the association of severity of airflow limitation with adherence to medications for hypertension and diabetes.

Methods: We identified 7,359 veterans with hypertension and/or diabetes in the Veterans Integrated Service Network-20. Entry date into the cohort was defined as the date of a patient's first pulmonary function testing (PFT). Diagnostic codes (ICD-9), PFT, and pharmacy data were available via the electronic medical record or via direct interrogation of PFT equipment. Our primary exposure was airflow limitation defined as $FEV_1 \geq 80\%$ predicted (normal), $80 > FEV_1 \geq 50\%$ predicted (mild/moderate), $50 > FEV_1 \geq 30\%$ predicted (severe), and $FEV_1 < 30\%$ predicted (very severe). We assessed adherence using a validated method based on electronic pharmacy refill data and defined adherence as ⩾80% medication possession for the period 6–12 months after enrollment. Medications of interest included β-blockers, calcium channel blockers, thiazides, and angiotensin-converting-enzyme inhibitors for patients with hypertension, and metformin and sulfonylureas for patients with diabetes. We used logistic regression models to assess the association between severity of airflow limitation and adherence, adjusted for demographics, health behaviors, and comorbidities.

Measurements and Main Results: Overall adherence was poor (44.6–55.1%). Among patients with hypertension, when compared with subjects with normal FEV_1, subjects with each category lower of FEV_1 were less adherent to β-blockers, with an odds ratio (OR) of 0.87 (95% confidence interval [CI], 0.80–0.95); calcium channel blockers, with an OR of 0.83 (95% CI, 0.74–0.93); and angiotensin-converting-enzyme inhibitors with an OR of 0.91 (95% CI, 0.84–0.99). Airflow limitation was not associated with adherence to thiazides. Among patients with diabetes, we found no significant association of FEV_1 with adherence, although a similar lower trend with increasing airflow limitation. In a sensitivity analysis limited to patients with chronic obstructive pulmonary disease, we found a nonstatistically significant trend for decreased adherence to β-blockers, calcium channel blockers, and angiotensin-converting-enzyme inhibitors in subjects with higher GOLD (Global Initiative for Chronic Obstructive Lung Disease) stage.

Conclusions: Severity of airflow limitation is associated with decreased adherence to β-blockers, calcium channel blockers, and angiotensin-converting-enzyme inhibitors. The decreased adherence to these medications may be related to adverse effects on symptoms in patients with lung disease, and may partially explain excess CV mortality in these patients.

Keywords: adherence; pulmonary function tests; comorbidity

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Patients with respiratory disorders, often defined by a diminished FEV_1, commonly suffer from multiple chronic conditions such as hypertension, diabetes, and cardiovascular disease (1–3). These conditions complicate patients' pharmacy regimens, cause additional symptoms, and may lower adherence to treatments that are known to improve outcomes. Attenuation of risk for many of these chronic conditions is available only through intense lifestyle modification, and potentially through the use of pharmaceutical therapies. Poor medication adherence for chronic conditions is common among patients with respiratory diseases (4, 5) and may have important implications for outcomes for these patients.

How airflow limitation affects adherence to medications for hypertension and diabetes is unknown. In this study, we sought to examine the association between airflow limitation as measured by FEV_1 and adherence to oral medications for hypertension and diabetes. We hypothesized that increased airflow limitation would be associated with decreased adherence to oral medications for these conditions. Some of the results of this study have been previously reported in the form of an abstract (6).

Methods

Design, Setting, and Participants

We conducted a cohort study of patients who carried a diagnosis of hypertension and/or diabetes and were being treated with oral medications for these conditions among a larger cohort of patients who underwent spirometry within the Veterans Affairs (VA) Integrated Service Network (VISN)-20. This study was approved by the VA Puget Sound Health Care System Institutional Review Board as minimal risk under a waiver of informed consent.

Data Source

We used clinical information from the VISN-20 data warehouse that routinely collects data using the VA electronic medical record including demographics, prescription medications, office visits, hospital admissions, and hospital and outpatient diagnoses. Pulmonary function testing (PFT) data were available in the electronic medical record or via direct interrogation of pulmonary function testing equipment.

Cohort Development

We identified 14,541 veterans who underwent pulmonary function testing as part of routine care at one of three VISN-20 medical centers located throughout the Pacific Northwest, between January 2003 and December 2007. We defined an index date as the date spirometry was performed. The presence of hypertension or diabetes was determined administratively via ICD.9 diagnostic codes (ICD.9 code 401.X or ICD.9 diagnostic code 250.0x–250.3x) assessed in the year before the index date. Disease categories were not mutually exclusive. Patients were excluded if they lacked a value for FEV_1 or were not prescribed any study medications of interest during the assessment period.

Outcome Assessment

The outcome of interest was adherence to oral medications for hypertension and diabetes. Medication adherence was assessed using ReComp, a previously validated method for assessing adherence on the basis of electronic pharmacy data, validated with clinical outcomes (7). Over longer time windows, ReComp reflects the proportion of time a subject is in possession of medication and is equivalent to a medication possession ratio. Adherence to medication was defined as having a score equal to or greater than 80% in the 6–12 months after the index date. This threshold was selected because of previous studies demonstrating clinically meaningful benefit (8, 9). We examined the use of β-blockers, calcium channel blockers, thiazides, and angiotensin-converting enzyme inhibitors (ACEIs) in the subjects with hypertension. Medications of interest were sulfonylureas and metformin in the subjects with diabetes.

Predictors of Adherence

Our primary exposure was the severity of airflow limitation as measured by pulmonary function testing (PFT). Categories of airflow limitation (AFL) were defined as $FEV_1 \geq 80\%$ predicted (normal), $80 > FEV_1 \geq 50\%$ predicted (mild to moderate limitation), $50 > FEV_1 \geq 30\%$ predicted (severe limitation), and $FEV_1 <$ 30% predicted (very severe limitation). As a secondary predictor, we examined the presence or absence of airflow obstruction.

Confounders

Potential confounders known or expected to be associated with adherence were assessed administratively in the 1 year before index date. We collected patient information that we conceptually grouped into one of three categories: (*1*) demographics and health behaviors (age, body mass index, race, sex, smoking status within the past year); (*2*) additional comorbid conditions by ICD.9 diagnostic code (congestive heart failure, acute coronary syndrome, lung cancer, depression, obstructive sleep apnea, schizophrenia) and complexity of medication regimen as described by a count of medication classes both oral and inhaled (including all study medications, statins, long-acting β-agonists, short-acting β-agonists, tiotroprium, and ipratropium); and (*3*) markers of lung disease severity (history of chronic obstructive pulmonary disease [COPD] exacerbation within the past year, presence of airflow obstruction on pulmonary function testing). Presence of a COPD exacerbation was defined administratively, either by a primary discharge diagnosis code of COPD, or by an outpatient visit for COPD accompanied within 48 hours by a prescription for an oral steroid or antibiotic, a previously validated method (10). Airflow obstruction was defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria as an FEV_1/FVC ratio less than 0.70. These categories were chosen because of previous studies indicating that demographics, psychiatric conditions, health behaviors such as smoking, severity of pulmonary disease, and complexity of medication regimens were conceptually associated with medication adherence.

Statistical Analysis

Using STATA 12 (StataCorp, College Station, TX) and SAS (2011; SAS Institute Inc., Cary, NC) software, we performed logistic regression to assess the effects of AFL on medication adherence. We developed multivariable logistic regression models to adjust for potential confounding variables. We created separate models for each group of potential confounders as described previously, with each model containing our primary exposure, degree of airflow limitation. To create a parsimonious final adjusted model, variables that achieved $P \leq 0.1$ in the preliminary models were included in the final model, with the exception of age, sex, and race, which were

included in each final model. Test of linear trend was performed to assess the significance of advancing category of airflow limitation, our primary exposure, on medication adherence. An α level less than 0.05 was considered significant.

Sensitivity Analysis

We were interested to determine whether patients with obstructive lung disease had a different adherence pattern when compared with patients with diminished FEV_1 as a whole. We performed a sensitivity analysis restricted to patients with a post-bronchodilator FEV_1/FVC ratio less than 0.70. Patients having no airflow obstruction and/or an FEV1 equal to or greater than 80% predicted served as the referent group for advancing GOLD stage. We used the same blocks of variables, outcomes, exposures, and methods as described previously.

Results

A total of 7,359 unique individuals were available for analysis. This resulted in 6,851 subjects with hypertension and 2,117 subjects with diabetes (Figure 1). Individuals were predominantly older white males. There were a number of significant differences observed between patients with and without airflow limitation. Among individuals with diabetes and individuals with hypertension, patients with airflow limitation were significantly older. A higher proportion of female patients with diabetes and with hypertension had no airflow limitation. Histories of congestive heart failure and lung cancer were both more common in patients with airflow limitation. A history of recent tobacco use was associated with airflow limitation among subjects with hypertension only. Subjects without airflow limitation were more likely to have a history of depression, but no difference was observed for a history of schizophrenia. We observed a high proportion of obesity among all patients, particularly in those with diabetes. Patients were taking a significant number of medications, averaging between three and four oral medications and one and two inhaled medications (Table 1).

Adherence to Medications

The proportions of patients adherent to medications for hypertension were low, ranging from 44.6 to 55.15%. Across a number of antihypertensive medications, adherence was lower as severity of AFL increased (Table 2). For example, among patients prescribed β-blockers, 54.5% of patients with mild to moderate airflow limitation were adherent, versus 50.0% of subjects with severe limitation, and 45.7% of patients with very severe limitation. Similarly, among those with mild to moderate airflow limitation who were prescribed calcium channel blockers, 55.1% of patients were adherent versus only 48.0% with severe limitation and 44.9% with very severe limitation. Likewise, patients with mild to moderate airflow limitation had a higher proportion of adherence to ACEIs when compared with those with severe limitation (53.6 vs. 47.5%). In contrast, adherence to thiazides did not vary by severity of AFL (47.9% mild to moderate vs. 45.6% very severe limitation).

Similar to antihypertensive medications, adherence to antihyperglycemic medications was also low, ranging from 42.5 to 54.1%. There appeared to be a trend for decreased adherence in subjects with very severe limitation, although adherence overall was not associated with airflow limitation (Tables 2 and 3).

Association of Airflow Limitation with Adherence

In the adjusted models, test of linear trend indicated decreased odds of adherence with increasing severity of airflow limitation for β-blockers (odds ratio [OR], 0.92; 95% confidence interval [CI], 0.85–0.99), calcium channel blockers (OR, 0.84; 95% CI, 0.76–0.94), and ACEIs (OR, 0.91; 95% CI, 0.84–0.99). This association was not observed in thiazides (Table 3).

Among patients with diabetes, the presence or degree of airflow limitation was not predictive of a linear trend in adherence to metformin or sulfonylureas. However, when analyzed by each individual category of severity in comparison with the referent group, there was a nonsignificant trend for decreased adherence among subjects with more severe airflow limitation, with significantly decreased adherence among patients with very severe airflow limitation who were taking sulfonylureas (Table 4).

Association of Airflow Obstruction with Adherence

In a sensitivity analysis, we identified 3,281 patients with hypertension, and 1,059 patients with diabetes with airflow obstruction on PFTs, who qualified for a diagnosis of COPD. We examined the odds of adherence for each antihypertensive and diabetes medication. In the adjusted models, there was a similar but not statistically significant linear trend of association between severity of airflow obstruction and adherence for β-blockers (OR, 0.92; 95% CI, 0.83–1.01), calcium channel blockers (OR, 0.93;

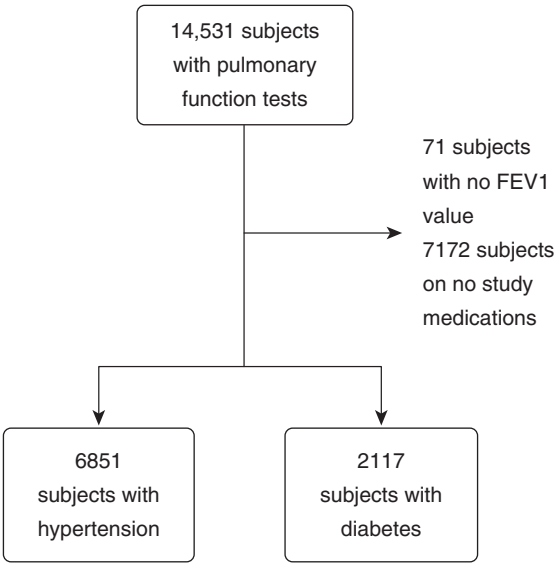

Figure 1. Results of cohort selection. All patients undergoing pulmonary function testing were screened for history of hypertension and diabetes, and use of study medications.

Table 1. Characteristics of patients with hypertension and diabetes, by the presence or absence of airflow limitation

Variable*	Hypertension			Diabetes		
	$FEV_1 \geq 80\%$ (*n = 2,026*)	$FEV_1 < 80\%$ (*n = 4,825*)	*P* Value	$FEV_1 \geq 80\%$ (*n = 571*)	$FEV_1 < 80\%$ (*n = 1,546*)	*P* Value
Age, yr	63.0 ± 10.8	66.9 ± 10.2	<0.001	63.1 ± 9.7	65.5 ± 9.8	<0.001
Male	1,887 (93.2%)	4,688 (97.2%)	<0.001	531 (93.0%)	1503 (97.2%)	<0.001
History of diabetes	570 (28.1%)	1,634 (33.8%)	<0.001	—	—	
History of hypertension	—	—		451 (79.0%)	1,222 (79.0%)	0.977
Smoker in the past year	629 (31.0%)	1,708 (35.4%)	0.001	149 (26.1%)	465 (30.1%)	0.073
CHF	191 (8.9%)	1,002 (20.7%)	<0.001	75 (13.1%)	382 (24.7%)	<0.001
History of lung cancer	18 (0.9%)	158 (3.2%)	<0.001	2 (0.35%)	48 (3.1%)	<0.001
History of ACS	62 (3.1%)	220 (4.6%)	0.004	20 (3.5%)	62 (4.0%)	0.591
History of OSA	238 (11.7%)	535 (11.1%)	0.431	101 (17.7%)	256 (16.6%)	0.538
History of depression	605 (29.9%)	1,080 (22.4%)	<0.001	165 (28.7%)	369 (23.9%)	0.022
History of schizophrenia	32 (1.6%)	95 (1.9%)	0.275	11 (1.9%)	33 (2.1%)	0.766
Airflow obstruction on PFT	348 (17.2%)	2,630 (54.5%)	<0.001	64 (11.2%)	656 (42.4%)	<0.001
FEV_1						
$50\% \leq FEV_1 < 80\%$	—	3,393 (70.3%)		—	1,129 (73.0%)	
$30\% \leq FEV_1 < 50\%$ predicted	—	1,120 (23.2%)		—	337 (21.8%)	
$FEV_1 < 30\%$ predicted	—	312 (6.5%)		—	80 (5.2%)	
History of COPD exacerbation in past year	60 (3.0%)	619 (12.8%)	<0.001	12 (2.1%)	158 (10.2%)	<0.001
BMI†			<0.001			0.407
25–30	656 (32.4%)	1,475 (30.6%)		145 (25.4%)	367 (23.7%)	
>30	1,118 (55.2%)	2,380 (49.3%)		387 (67.8%)	1,023 (66.2%)	
Race			<0.001			0.003
White	1,443 (71.2%)	3,529 (73.1%)		408 (71.5%)	1,099 (71.1%)	
Nonwhite	125 (6.2%)	451 (9.3%)		39 (6.8%)	174 (11.3%)	
Unknown	458 (22.6%)	845 (17.5%)		124 (21.7%)	273 (17.7%)	
Number of oral medications	3.01 ± 1.34	3.12 ± 1.37	0.002	4.19 ± 1.25	4.12 ± 1.31	0.844
Number of respiratory medications	0.87 ± 1.10	1.67 ± 1.40	<0.001	0.84 ± 1.09	1.54 ± 1.37	<0.001

Definition of abbreviations: ACS = acute coronary syndrome; BMI = body mass index; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; OSA = obstructive sleep apnea; PFT = pulmonary function testing.
*Values represent n (percent) with the exception of age (mean, SD).
†Sixty subjects were missing BMI values.

95% CI, 0.83–1.05), thiazides (OR, 1.1; 95% CI, 0.99–1.23), ACEIs (OR, 0.94; 95% CI, 0.86–1.03), metformin (OR, 0.89; 95% CI, 0.76–1.05), or sulfonylureas (OR, 0.88; 95% CI, 0.76–1.03).

We found a similar but not statistically significant pattern of lower odds of adherence with very severe airflow limitation, which was observed for β-blockers (OR for adherence in GOLD stage IV, 0.71; 95% CI, 0.48–1.04) and ACEIs (OR for adherence in GOLD stage IV, 0.77; 95% CI, 0.55–1.08). GOLD stage IV disease was associated with increased adherence for thiazides (OR, 1.55; 95% CI, 1.00–2.53).

Discussion

In this cohort of patients who underwent pulmonary function testing, we found that both hypertension and diabetes were common, but that overall adherence to antihypertensive or hypoglycemic medications was low. Previous studies of

Table 2. Adherence by severity of airflow limitation (unadjusted)

Medication	$FEV_1 \geq 80\%$		$50\% \leq FEV_1 < 80\%$		$30\% \leq FEV_1 < 50\%$		$FEV_1 < 30\%$	
	n	% Adherent	n	% Adherent	n	% Adherent	n	% Adherent
Antihypertensives								
β-Blockers	1,592	50.4%	2,818	54.5%	938	50.0%	234	45.7%
Calcium channel blockers	869	52.8%	1,632	55.1%	592	48.0%	176	44.9%
Thiazides	1,159	48.0%	1,777	46.9%	547	43.0%	158	45.6%
ACEIs	1,621	54.7%	2,775	53.6%	939	52.1%	265	47.5%
Diabetes medications								
Sulfonylureas	453	51.9%	911	54.1%	296	49.3%	73	42.5%
Metformin	471	50.5%	848	48.9%	209	45.0%	54	42.6%

Definition of abbreviation: ACEIs = angiotensin-converting enzyme inhibitors.

Table 3. Odds ratios of adherence by severity of airflow limitation in subjects with hypertension (adjusted)*

Medication	n	Overall Test of Trend		50% ⩽ FEV_1 < 80%†		30% ⩽ FEV_1 < 50%†		FEV_1 < 30%†	
		OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
β-Blockers	4,141	**0.87 (0.80, 0.95)**	**0.002**	1.06 (0.91,1.23)	0.439	**0.78 (0.64, 0.95)**	0.016	**0.61 (0.43, 0.86)**	**0.005**
Calcium channel blockers	2,717	**0.83 (0.74, 0.93)**	**0.001**	1.01 (0.83, 1.22)	0.955	**0.65 (0.50, 0.84)**	**0.001**	**0.64 (0.42, 0.96)**	**0.033**
Thiazides	3,017	1.04 (0.94, 1.15)	0.421	1.03 (0.87, 1.22)	0.698	0.97 (0.76, 1.24)	0.823	1.45 (0.95, 2.21)	0.086
ACE inhibitors	4,449	**0.91 (0.94, 0.99)**	**0.025**	0.92 (0.80, 1.06)	0.251	0.88 (0.72, 1.07)	0.195	**0.68 (0.50, 0.94)**	**0.019**

Definition of abbreviations: ACE = angiotensin-converting enzyme; CI = confidence interval; OR = odds ratio.
Bold typeface indicates statistical significance.
*Referent group is subjects with FEV_1 ⩾ 80% predicted.
†FEV_1 values are expressed as a percentage of the predicted value.

adherence to antihypertensive medications in the overall VA population have shown proportions of adherence to be notably higher that what we describe (11). Our cohort differs from previous VA cohorts assessed for adherence to chronic medications in that PFTs were ordered as part of clinical care, suggesting that these patients were symptomatic with dyspnea or other respiratory complaint. The low rates of adherence in our cohort in comparison with others suggest that patients with airflow limitation represent an important group to target for improved adherence, and may differ in important ways from patients with chronic conditions who are asymptomatic. Our primary predictor, severity of airflow limitation, was associated with lower adherence to several important medications including β-blockers, calcium channel blockers, and ACEIs. Although we were unable to examine the reasons behind lower adherence to β-blockers, calcium channel blockers, and ACEIs, our results suggest that poor patient adherence may partially account for the worse cardiovascular outcomes associated with airflow limitation.

The lower adherence seen with β-blockers, calcium channel blockers, and ACEIs among subjects with increasing severity of airflow limitation may be due to several reasons, both biological and behavioral. Nonadherence may be related to side effects associated with these medications. For example, although the likelihood of worsening bronchospasm may be low, β-blockers may predispose patients to fatigue as a side effect (12). β-Blockers may also contribute to an inadequate heart rate response during exercise, which again may further limit exercise capacity in a patient already limited by lung disease. Patients suffering from fatigue or dyspnea related to pulmonary disease may be particularly intolerant of this side effect, and may choose not to be adherent despite documented benefits on morbidity and mortality. Similarly, calcium channel blockers and ACEIs are generally well-tolerated classes of medications for hypertension. However, they too can contribute to dizziness and fatigue. Calcium channel blockers can cause bothersome leg swelling (13). For patients with severe lung diseases who rely on hypoxic pulmonary vasoconstriction to maintain ventilation and perfusion matching, use of calcium channel blockers may in fact worsen hypoxemia, which may be more apparent with exercise, and which may lead patients to adhere to medications less often. ACE inhibitors cause cough in up to 10% of patients (14), which may be more bothersome to patients with preexisting airflow limitation.

From a behavioral standpoint, patients with increased airflow limitation may have other barriers that predispose to lower adherence. These patients may suffer from greater comorbidity, which carries with it higher symptom burden (15) and number

Table 4. Odds ratios of adherence by severity of airflow limitation in subjects with diabetes (adjusted)*

Medication	n	Overall Test of Trend		50% ⩽ FEV_1 < 80%†		30% ⩽ FEV_1 < 50%†		FEV_1 < 30%†	
		OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Metformin	1,440	0.87 (0.76, 1.01)	0.068	0.93 (0.73, 1.18)	0.544	0.77 (0.54, 1.09	0.143	0.64 (0.35, 1.16)	0.142
Sulfonylureas	1,554	0.88 (0.76, 1.01)	0.060	1.01 (0.79, 1.29)	0.951	0.86 (0.62, 1.20)	0.365	**0.52 (0.29, 0.92)**	**0.026**

Definition of abbreviations: CI = confidence interval; OR = odds ratio.
Bold typeface indicates statistical significance.
*Referent group is subjects with FEV_1 ⩾ 80% predicted.
†FEV_1 values are expressed as a percentage of the predicted value.

of prescribed medications. Complex medication regimens (4) and inadequate time for doctor–patient communication about chronic medical conditions (16, 17) are both associated with decreased adherence in some studies. Conversely, other studies have found that increased numbers of medications prescribed are associated with increased adherence (18–20). As airflow limitation becomes more severe, symptoms may worsen to the point that performing the tasks needed to obtain refills becomes more difficult. There was a significant finding of decreased adherence to sulfonylureas in the subjects with very severe airflow limitation. This may be explained by these complex behavioral interactions, rather than by symptomatic side effects. Poor lung function may be associated with other conditions such as lack of social support, homelessness, or alcohol use that may influence adherence, but were unmeasured in this study design. There was a suggestion of increased adherence to thiazides in the subjects with very severe airflow limitation, which may suggest a therapeutic benefit to diuretics for patients with lung disease as has been seen in other studies (21).

This study had several limitations. First, the data were obtained administratively and we did not know whether patients consumed the medications they received. The anticipated effect in this situation would be to overestimate adherence. Second, we may not have captured all medication refills if they were performed outside the VA system. We believe that subsequently refilling medications outside the system is unlikely to be common, as the majority of patients receiving care within the VA use it as their primary pharmacy resource because of financial incentives (22, 23). Third, data were collected within the VA system, which may limit some of the generalizability outside of an integrated health care system. Fourth, despite being representative of the veterans who seek care in the Pacific Northwest, there were relatively few women and minorities in our cohort, limiting the ability to generalize to these groups. Finally, if a patient was verbally instructed to discontinue a medication by their physician, without a change in the electronic order, we would not have been able to distinguish between nonuse and nonadherence.

Our study has several strengths. We were able to examine a large cohort of patients with a wide range in FEV_1 and a high prevalence of comorbid conditions and medication use. In addition, we included patients from a diverse set of VA settings including academically and nonacademically affiliated centers. We performed an unbiased collection of patients, including all patients who had pulmonary function testing. We had access to excellent completeness of medications prescribed and filled within the VA system. We maintained a clear and unbiased approach to the assessment of the exposure as well as the outcome.

In summary, we found that overall prevalence of adherence to chronic oral medications was low among this population of veterans with hypertension and/or diabetes, and airflow limitation. Although improved medication adherence will not prevent all of the consequences of chronic diseases, it is an important target for improving health and the delivery of quality care. Patients with diminished FEV_1 are at high risk of death from cardiovascular disease and stroke (24–26), independent of smoking history (2, 27), making this an important group to target for modification of cardiovascular risk. Our data suggest that several key classes of medications may be associated with decreased adherence in these subjects, a finding that has important implications for prescribing patterns and counseling in these patients. Data suggest that a better understanding of the expected function of chronic medications can encourage patients to maintain compliance over time (28). Focusing on the interplay between chronic diseases may be a target for improving adherence among patients with multiple conditions. ■

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

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