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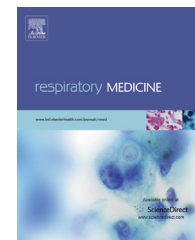
Guideline adherence in management of stable chronic obstructive pulmonary disease☆

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Summary

Background: Chronic obstructive pulmonary disease (COPD) is the only leading cause of death with rising morbidity and mortality. Clinical practice guidelines (CPGs) to optimize pharmaco-therapy for patients with COPD have been updated based on promising results of randomized clinical trials. We examined the frequency of and factors associated with guideline adherence by physicians in clinical practice at an academic medical center.

Methods: Patients with a clinical diagnosis of COPD, confirmed by spirometry, who presented to the ambulatory clinics, were enrolled. The primary outcome was provider's adherence to the 2007 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. Subjects were categorized as guideline-concordant who received a rescue inhaler (all patients), or at least one long-acting bronchodilator (stage II), or at least one long-acting bronchodilator plus an inhaled corticosteroid (stage III—IV). Demographics, clinical information and type of pro-vider were recorded. Provider type was classified as primary care physician (PCP), pulmonol-ogist, or co-management by both.

Results: Among 450 subjects who met study criteria, 246 (54.7%) received guideline-concordant treatment. Age, sex, race, disease severity, and co-morbidities were not associated with guide-line adherence. Multivariate analysis showed that patients co-managed by a PCP and pulmonol-ogist had a higher likelihood of receiving guideline-concordant treatment than those managed by one or the other (Odds Ratio: 4.59; 95% Confidence Interval: 2.92, 7.22, $p < 0.001$).

Conclusions: Just over half of stable COPD patients receive guideline-concordant care. Co-management by a PCP and pulmonologist increases the likelihood of receiving guideline-concordant inhaler therapy.

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by chronic inflammation and a slowly progressive persistent airflow obstruction.[1] COPD affects more than 5% of adults in the United States. Based on the most recent data, COPD is the 3rd most common cause of death[2] and the only leading cause of death with rising morbidity and mortality.[3,4]

High prevalence, complexity of clinical presentations, high mortality and morbidity,[5] and the substantial economic burden of COPD[6] prompt the need for clinical practice guidelines (CPGs) to further optimize its management. CPGs were developed to define standards of care and to focus efforts on improving quality.[7] Previous studies have demonstrated the impact of CPGs in improving the quality of care among patients with such conditions as community acquired pneumonia (CAP),[8,9] acute myocardial infarction,[10,11] and congestive heart failure (CHF).[12] Despite these, accumulating evidence in the literature suggests underutilization of pharmacotherapy in similar conditions.[13]

The first CPG for the diagnosis and management of patients with stable COPD was established more than a decade ago.[14] Since then, tremendous advances in pharmaceutical treatment for COPD[15–19] have improved the long-term prognosis and quality of life for COPD patients[15,20,21] while simultaneously lowering the overall cost of care.[19] The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline[22] provides stage-based recommendations for optimized pharmacotherapy for stable COPD patients.

The impact of patients' adherence to pharmacotherapy on exacerbation, quality of life, and mortality has been studied.[23] In this study, we aimed to investigate clinicians' adherence to pharmacotherapy recommendations in patients with COPD seen at the ambulatory clinics of an academic medical center. We also examined factors associated with adherence to these guidelines.

Patients and methods

Study design and population

In a retrospective study, we reviewed the electronic medical records of all 1234 patients who had at least one visit to the University of Texas Medical Branch (UTMB) ambulatory clinics with a clinical diagnosis of COPD, between January 1, 2010 and December 31, 2010. Of these, spirometry data were available for 657 (52.4%) cases. We included all 450 (35.9%) patients who met the clinical diagnosis of COPD confirmed by spirometry, i.e., ratio of forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) < 0.70.[23,25] Patients in acute exacerbation were excluded from further analysis. The

institutional review board approved the study protocol. Written informed consent was not required due to the nature of the study.

Variables

Demographic and access to healthcare
Age, sex and race (non-Hispanic white, black, other) were provided by patients during the clinical encounter. The patient's health insurance status (Medicare or other type of insurance) and type of healthcare provider were also recorded. Patients were categorized into three groups based on the type of provider: those seen by a primary care physician (PCP) only; those who had a regular PCP, but had at least one referral visit to a pulmonologist during the study period, 12 months before and after the date of spirometry (co-managed); and those seen by a pulmonologist for their COPD management. For the purpose of this study, an outpatient visit to an internist, family physician, or geriatrician established the presence of a PCP.

Clinical information
Body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) and history of co-morbid clinical conditions including hypertension (HTN) or other cardiovascular disease (coronary artery disease, CHF, ischemic or non-ischemic cardiomyopathy), diabetes mellitus, anxiety or depression, osteoporosis, or lung cancer were obtained. The number of comorbid conditions for each subject was calculated based on the number of above-mentioned clinical conditions. The type of inhalers prescribed within 90 days before and after the spirometry date was recorded for each patient.

All participants' spirometry data were reviewed. FEV_1, FEV_1 percent-predicted value, FVC, and FEV_1/FVC were recorded. Based on the GOLD criteria, severity of disease was categorized as mild, stage I ($FEV_1 \geq 80\%$), moderate, stage II ($50 \leq FEV_1 < 80\%$), severe, stage III ($30 \leq FEV_1 < 50\%$), or very severe, stage IV ($FEV_1 < 30\%$).

Exacerbation was defined as a worsening of symptoms or respiratory failure requiring a provider encounter (telephone, emergency room visit, office visit, or hospitalization) that resulted in a prescription of a steroid, antibiotic, or both. The number of exacerbations over 12 months before and after the time of spirometry was calculated.

Adherence to the guideline
The primary outcome was the provider's adherence to the 2007 GOLD guidelines[22] for the pharmacotherapeutic management of patients with stable COPD. Patients were categorized into guideline-concordant and guideline-discordant groups, based on the following criteria. According to the 2007 GOLD guidelines,[22] all stable COPD patients should have

at least one rescue inhaler. Patients with COPD GOLD stage I were categorized as guideline concordant if they received short acting bronchodilator as a rescue inhaler. Patients with COPD stage II were categorized as guideline concordant if they had at least one long-acting bronchodilator (long-acting beta agonist [LABA] or long-acting muscarinic antagonist [LAMA]) without an inhaled corticosteroid as part of their regimen. Patients with severe or very severe disease (COPD stage III and IV) were considered guideline concordant if they received at least one long-acting bronchodilator and an inhaled corticosteroid. Both under- and over-treated patients were categorized as guideline discordant.

Statistical analysis

Descriptive statistics are presented as proportions and percent. Provider adherence to guidelines for the 90 days before and after spirometry was compared, using the McNemar paired test. The student's t-test and χ^2 (chi-square) test were used for continuous and categorical variables, respectively, to compare all demographic variables, clinical variables, disease severity indices, and annual rates of exacerbation ± 12 months of spirometry time. Next, we used logistic regression for multivariable analysis with a forward hierarchical variable selection strategy to investigate the independent correlates of guideline-concordant management. We used SAS version 9.2 (SAS Institute Inc., Cary, NC) and STATA 11 (STATA Corp., College Station, TX) for all statistical analyses. All hypotheses testing were 2-sided with significance set at $p \leq 0.05$.

Results

Table 1 presents the baseline demographics of the patients who met the study criteria. Among 450 patients enrolled in the study, 208 (46.2%) were female. The mean age of the study population was 67.7 years, with sizable non- white (20.7%) and Medicare beneficiary (76%) populations. Overall, 32 patients (7.1%) were classed as GOLD Stage I, 210 (46.7%) as stage II, 150 (33.3%) as Stage III and the remaining 58 (12.9%) as Stage IV. The median (interquartile range [IQR]) FEV$_1$% was 51% (range, 39—64). Current tobacco use was reported in 182 patients (40.4%) in the cohort. A total of 213 patients (47.3%) were managed by their PCP, 185 (41.1%) were co-managed by both a PCP and a pulmonary physician, 44 (9.8%) were managed by a pulmonologist, and 8 (1.8%) had no assigned provider that could be determined.

Overall, 196 (43.6%) patients were not receiving treatment in concordance with GOLD guideline pharmacotherapy recommendations. Of these, 15 (7.6%) were over-treated (all had GOLD stage I). As shown in Table 2, univariable analysis of the demographic and clinical variables of guideline-concordant and discordant groups indicated no significant difference in age, gender, race, number of co-morbid medical conditions, or type of insurance between the two groups. History of tobacco use (former or current smoker) was not associated with a higher likelihood of receiving guideline-concordant treatment compared to never having smoked. There was no difference between two groups in the use of short acting anticholinergic inhalers ($p = 0.7364$) and nearly half of the patients in each

Table 1 Baseline characteristics of patients with stable COPD seen in outpatient clinics between January 2010 and December 2010.

Variable	$N = 450$
Age, years (SD[a])	67.7 (9.9)
Gender, n (%)	
Male	242 (53.8)
Female	208 (46.2)
Race, n (%)	
Non-hispanic whites	357 (79.3)
Black	70 (15.6)
Other	23 (5.1)
Body mass index (kg/m^2), mean (SD)	28.5 (7.4)
Comorbidities, n (%)	
0	86 (19.1)
1	177 (39.3)
2	157 (34.9)
3 or more	30 (6.7)
Insurance, n (%)	
Medicare	355 (78.9)
Private insurance	94 (20.8)
Spirometry findings, mean (SD)	
Forced expiratory volume-1 (FEV$_1$, L)	1.5 (0.6)
FEV$_1$ (% predicted value)	51.7 (18.5)
Forced vital capacity (FVC, L)	2.8 (1.0)
FEV$_1$/FVC	52.5 (11.5)
Current smokers, n (%)	182 (40.4)
On supplemental oxygen, n (%)	71 (15.8)
Pulmonary rehabilitation, n (%)	43 (9.5)
Inhaler therapy, n (%)	
Short acting beta agonist	365 (81.1)
Short acting anticholinergic	237 (52.7)
Inhaled corticosteroid	245 (54.4)
Long acting beta agonist	202 (44.9)
Long acting muscarinic antagonist	143 (31.8)
Type of provider, n (%)	
Seen by PCP alone	213 (47.3)
Co-managed by PCP and pulmonary physician	185 (41.1)
No PCP and seen by pulmonary physician	44 (9.8)
No specific provider for COPD care	8 (1.8)
GOLD Stage, n (%)	
Mild (stage I)	32 (7.1)
Moderate (stage II)	210 (46.7)
Severe (stage III)	150 (33.3)
Very severe (stage IV)	58 (12.9)
Adherence to guidelines, n (%)	
Guideline-concordant therapy[b]	254 (56.4)
Guideline-disconcordant therapy	196 (43.6)

[a] SD: standard deviation; GOLD.
[b] Patients were categorized as guideline-concordant if they were receiving at least one rescue inhaler, or at least one long-acting bronchodilator (long-acting beta agonist or long-acting muscarinic antagonist) for stage II or they were receiving at least one long-acting bronchodilator and an inhaled corticosteroid for stage III and IV patients.

Table 2 Comparison of clinical and provider characteristics of patients with stable COPD receiving guideline-concordant or guideline-discordant treatment.

Variables	Guideline concordant[a] (n = 254)	Guideline discordant (n = 196)	p-Value
Age, mean ($\pm$SD[b]) years	68.14 (9.53)	67.31 (10.22)	0.381
Gender, female, n (%)	125 (49.2)	83 (42.3)	0.148
Ethnic background, non-hispanic whites, n (%)	203 (80.6)	154 (79)	0.679
No. of comorbid conditions, n (%)			
0	50 (19.7)	36 (18.4)	0.871
1	95 (37.4)	82 (41.8)	
2	90 (35.4)	67 (34.2)	
3 or more	19 (7.5)	11 (5.6)	
Type of insurance, medicare, n (%)	194 (76.4)	161 (82.1)	0.137
Long volumes			
FEV_1, mean ($\pm$SD), liter	1.47 (0.66)	1.47 (0.66)	0.816
FEV_1 % predicted value, mean ($\pm$SD)	51.71 (18.87)	51.71 (18.87)	
FVC, mean ($\pm$SD), liter	2.74 (1.04)	2.74 (1.04)	
FEV_1/FVC, mean ($\pm$SD)	53.17 (11.74)	53.17 (11.74)	
Current smokers, n (%)	97 (38.2)	85 (43.4)	0.267
Inhaled therapy, n (%)			
Short acting beta agonist	223 (87.8)	142 (72.4)	< 0.001
Short acting anticholinergic	132 (52.0)	105 (53.6)	0.736
Inhaled corticosteroid	214 (84.3)	31 (15.8)	< 0.001
Long acting beta agonist	193 (76)	9 (4.6)	< 0.001
Long acting muscarinic antagonist	118 (46.5)	25 (12.8)	< 0.001
Type of provider, n (%)			
PCP only	91 (36.0)	122 (64.6)	<0.001
Co-management by PCP and pulmonologist	138 (54.5)	47 (24.9)	
Pulmonologist only	25 (9.5)	37 (10.5)	
GOLD stage, n (%)			
Mild (stage I)	17 (6.7)	15 (7.7)	0.663
Moderate (stage II)	125 (49.2)	85 (43.4)	
Severe (stage III)	80 (31.5)	70 (35.7)	
Very severe (stage IV)	32 (12.6)	26 (13.3)	

[a] Patients were categorized as guideline-concordant if they were receiving at least one rescue inhaler, or at least one long-acting bronchodilator for stage II or they were receiving at least one long-acting bronchodilator and an inhaled corticosteroid for stage III and IV patients.
[b] SD: standard deviation.

group were on a short acting anticholinergic. The rate of adherence to pharmacotherapy guidelines for management of stable COPD was higher after spirometry (56.1% versus 51.7%); however, this difference did not attain statistical significance ($p = 0.068$).

As illustrated in Fig. 1, patients co-managed by both a PCP and a pulmonologist were more likely to receive guideline-concordant pharmacotherapy than those managed by a PCP alone.

Table 3 presents the results of multivariate analysis adjusted for the potential confounders of age, sex, smoking history, BMI, number of comorbid conditions, and type of insurance. Patients co-managed by a PCP and a pulmonologist had significantly higher odds of receiving guideline-concordant therapy (Odds Ratio [OR]: 4.59, 95% Confidence Interval [CI]: 2.92-7.22, $p < 0.0001$) than those managed by a PCP alone. Similar results were observed for co-managed patients compared with those managed by a pulmonologist alone (Odds Ratio [OR]: 2.23, 95% CI: 1.46−4.75, $p < 0.0001$).

Finally, we examined the effect of guideline-concordant therapy on the risk of exacerbations. Patients managed according to the 2007 GOLD guidelines had significantly fewer exacerbations per year than those managed not according to guidelines (1.10 versus 1.56, $p = 0.0012$). However, the total number of exacerbation was not statistically significant between the two groups for the 12 months prior to spirometry ($p = 0.2353$). Nevertheless, patients in the guideline-concordant group had almost half as many exacerbations over the one-year period after spirometry (0.78 versus 1.45, $p < 0.0001$), suggesting a beneficial effect of spirometry in the management of COPD.

Discussion

Our study demonstrated that patients with stable COPD are undertreated (43.6% not receiving guideline-concordant therapy) and co-management is an independent correlate
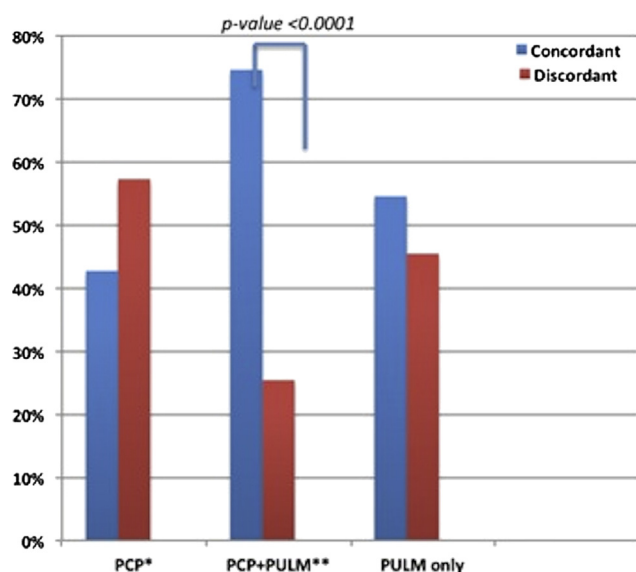
*PCP: primary care physician; **PULM: pulmonologist.

Figure 1 Number of stable COPD patients receiving guideline-concordant versus discordant therapy by provider type.

of adherence to optimized pharmacotherapy. In the current study, we focused on the healthcare provider's adherence rates to available CPGs for optimal pharmacotherapy among patients with stable COPD.

Clinical decision-making is a process that involves an interplay between the complexity of a patient's medical condition, the provider's knowledge and experience, and the availability of resources. CPGs are systematically developed statements based on robust clinical evidence to help the practitioner and patient decide on the appropriate healthcare for specific conditions.[25] The caveat is that clinicians face the intimidating task of managing information to meet each patient's condition and individual expectations. Guidelines help refine clinical questions so practitioners can balance the demands of the clinical

situation with the reality of health economics. The explicit recommendations of guidelines help define standards of care while they focus effort on improved quality of care.[7] The majority of CPGs address a particular disease, based on the most recent clinical evidence,[26] such as CAP,[8,9] acute myocardial infarction,[10,11] and CHF.[12] Studies have shown that how implementing guideline based tools may facilitate quality improvement across a variety of institutions, patients, and caregivers.

Since the introduction of the first GOLD guidelines for management of COPD more than a decade ago,[14] there have been worldwide efforts to implement as well as periodically improve these guidelines.[27-29] Despite these efforts, COPD patients, especially those at early stages, remain undiagnosed.[30,31] Our findings further demonstrated that adherence to the guidelines is low. Similarly, Boyd et al. used the 5% Standard Analytic File from the Medicare beneficiaries to review quality of care across 15 common chronic conditions. They, too, found undesirable adherence rates.[13,32] A recent survey of more than 26,000 COPD patients in North Carolina showed that many patients who might benefit from daily medications such as long-acting bronchodilators and inhaled corticosteroids were not receiving them.[33]

The impact of provider adherence to guidelines has been reported for other common conditions. In a survey of 2250 general physicians, internists, and cardiologists, Edep et al found cardiologists much more likely than other types of physicians to provide guideline-concordant management for patients with CHF.[34] Similarly, Roche et al showed that the use of inhaled corticosteroids in patients with COPD increases after a visit to respiratory physicians.[35] The results of the current study indicated that patients co-managed by both a PCP and a specialist were more likely to receive guideline-concordant therapy. PCPs are usually at the frontline of the diagnosis and care for patients with COPD.[36] As such, they are uniquely positioned to make early diagnoses and provide optimal management of COPD. A recent worldwide survey found that many PCPs have limited knowledge of COPD and its management.[37] These results indicated that PCPs and specialists need to

Table 3 Multivariable analysis of independent correlates of guideline-concordant treatment for patients with stable COPD managed in ambulatory clinics of a tertiary medical center.

Variable	OR	95% CI		P Value
Age	0.993	0.967	1.021	0.6242
BMI	1.012	0.982	1.043	0.4420
Sex, male versus female	0.647	0.414	1.010	0.0553
GOLD stage (3,4) versus (1,2)	0.694	0.446	1.079	0.1050
Insurance medicare versus other	0.576	0.310	1.069	0.0805
Non-hispanic white versus others	1.032	0.598	1.781	0.9109
Current smoker versus not current smoker	0.778	0.480	1.262	0.3088
Number of comorbid conditions				
One comorbid condition versus none	0.872	0.460	1.653	0.7918
Two comorbid conditions versus none	0.822	0.423	1.597	
≥3 comorbid conditions versus none	1.260	0.461	3.440	
Type of provider				
PCP and pulmonologist versus PCP	4.593	2.923	7.218	<0.0001
Pulmonologist versus PCP and pulmonologist	2.148	1.364	2.741	<0.0001

establish better communication to ensure regular follow up for COPD patients and increase the likelihood of adherence to guidelines. The spread of health information technology can facilitate greater provision of evidence-based care.

The results of the third National Health and Nutrition Examination Survey (NHANES III) confirmed that COPD patients had higher mortality than those with other chronic conditions.[5] Despite therapeutic advancements for patients with COPD, their overall survival rate has not significantly changed in 20 years.[38] However, promising results of recent well-designed clinical trials of pharmacotherapeutic management of COPD[15,18] and studies confirming the survival benefit of guideline concordant therapy in other conditions like myocardial infarction, CHF, and CAP[9–11] hold out hope for future improvement in survival rates for those with COPD.

Comorbidities are common and associated with significant morbidity and mortality in patients with COPD. Recent 2011 GOLD guidelines[45] recommend evaluation and management of common comorbidities such as cardiovascular disorders, depression/anxiety, osteoporosis, and lung cancer. Future studies need to address the benefit of screening for these comorbidities and the effect of pharmacotherapy in patients with multiple comorbidites.

A low rate of CPG adherence to pharmacologic management of stable COPD patients could be attributed to the complexity of clinical conditions or guidelines, the quality of the level of evidence, and the source of evidence. Most CPGs and standards of care address the benefits of adherence based on discrete outcomes such as death[39]; however, practical management of complex disease such as COPD must take into account the interplay of clinical severity, patient's overall well-being, physician experience, and system based resources. In addition, the majority of randomized clinical trials of COPD management have been sponsored by pharmaceutical companies, which may affect the clinician's judgment of the validity of the data.[15,17,18,21] Although results have been robust and several professional societies have made strong recommendations based on these results,[24] the level of evidence has been evaluated as moderate. Several strategies have been suggested to improve physician adherence to CPGs, from checklists and monthly reports[40] to automated tools[41] including best practice advisers (BPA) to improve adherence to guidelines or standard care.[42–44]

This study had several limitations. The study population was enrolled from a single academic tertiary medical center; such patients are usually sicker than COPD patients in the community. Adherence to non-pharmacologic interventions, including reduction of exposure to risk factors (tobacco use), promotion of exercise (referral to pulmonary rehabilitation), appropriate use of long-term oxygen therapy and immunization were not assessed. In addition, the confirmation of the diagnosis of COPD requires persistent post-bronchodilator airflow limitation; however this information was not available on all patients. This gap in information may have resulted in some asthmatic patients misclassified as COPD. In addition, almost all of our patients had health insurance, which overlooks the sizeable portion of uninsured COPD patients whose access to healthcare may be more limited. Recently, GOLD guidelines were updated to incorporate clinical presentation, including dyspnea as measured by COPD Assessment Test (CAT) and the modified British Medical Research Council (mMRC). The updated version of the guidelines incorporates clinical presentation with spirometry findings.[45] In the current study, we did not have the comprehensive clinical information on all patients by which to calculate CAT and mMRC; therefore, compliance with the new 2011 GOLD guidelines could not be accurately assessed.

In conclusion, guideline-concordant management of patients with stable COPD is low. Further system-level efforts need to be undertaken to improve compliance with CPGs. Additional studies are needed to identify factors important in physician compliance to CPGs.

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Disclosure

All authors had access to the data and contributed to writing the manuscript.

Conflict of interest

Authors of this research article have no affiliation with any organization with a financial interest (including consultancies, employment, expert testimony, honoraria, retainers, or stock), direct or indirect, in the subject matter or materials discussed in the manuscript that may affect the conduct or reporting of the work submitted.

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References

1. Decramer M, Janssens W, Miravitlles M. Chronic obstructive pulmonary disease. *Lancet* 2012;**379**:1341–51.
2. Deaths from chronic obstructive pulmonary disease—United States, 2000–2005. *MMWR Morb Mortal Wkly Rep* 2008;**57**:1229–32.
3. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet* 1997;**349**:1498–504.
4. Gershon AS, Wang C, Wilton AS, Raut R, To T. Trends in chronic obstructive pulmonary disease prevalence, incidence, and mortality in ontario, Canada, 1996 to 2007: a population-based study. *Arch Intern Med* 2010;**170**:560–5.
5. Shavelle RM, Paculdo DR, Kush SJ, Mannino DM, Strauss DJ. Life expectancy and years of life lost in chronic obstructive pulmonary disease: findings from the NHANES III Follow-up Study. *Int J Chron Obstruct Pulmon Dis* 2009;**4**:137–48.
6. National Heart LaBI. *The morbidity & mortality: the 2009 chart book on cardiovascular, lung, and blood disease*. Bethesda, MD: National Heart, Lung, and Blood Institute; 2009.
7. Garber AM. Evidence-based guidelines as a foundation for performance incentives. *Health Aff (Millwood)* 2005;**24**:174–9.
8. Asadi L, Eurich DT, Gamble JM, Minhas-Sandhu JK, Marrie TJ, Majumdar SR. Impact of guideline-concordant antibiotics and

macrolide/beta-lactam combinations in 3203 patients hospitalized with pneumonia: prospective cohort study. *Clin Microbiol Infect* 2012.

9. Asadi L, Eurich DT, Gamble JM, Minhas-Sandhu JK, Marrie TJ, Majumdar SR. Guideline adherence and macrolides reduced mortality in outpatients with pneumonia. *Respir Med* 2012; **106**:451–8.

10. Eagle KA, Montoye CK, Riba AL, et al. Guideline-based standardized care is associated with substantially lower mortality in medicare patients with acute myocardial infarction: the American College of Cardiology's Guidelines Applied in Practice (GAP) Projects in Michigan. *J Am Coll Cardiol* 2005;**46**:1242–8.

11. Mehta RH, Montoye CK, Gallogly M, et al. Improving quality of care for acute myocardial infarction: the Guidelines Applied in Practice (GAP) Initiative. *JAMA* 2002;**287**:1269–76.

12. Stork S, Hense HW, Zentgraf C, et al. Pharmacotherapy according to treatment guidelines is associated with lower mortality in a community-based sample of patients with chronic heart failure: a prospective cohort study. *Eur J Heart Fail* 2008;**10**:1236–45.

13. Calvin JE, Shanbhag S, Avery E, Kane J, Richardson D, Powell L. Adherence to evidence-based guidelines for heart failure in physicians and their patients: lessons from the Heart Failure Adherence Retention Trial (HART). *Congest Heart Fail* 2012;**18**: 73–8.

14. Pauwels RA, Buist AS, Ma P, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: National Heart, Lung, and Blood Institute and World Health Organization Global Initiative for Chronic Obstructive Lung Disease (GOLD): executive summary. *Respir Care* 2001;**46**:798–825.

15. Tashkin DP, Celli B, Senn S, et al. a 4-year trial of tiotropium in chronic obstructive pulmonary disease. *N Engl J Med* 2008; **359**(15):1543–54.

16. Decramer M, Celli B, Tashkin DP, et al. Clinical trial design considerations in assessing long-term functional impacts of tiotropium in COPD: the UPLIFT trial. *COPD* 2004;**1**:303–12.

17. Decramer M, Celli B, Kesten S, Lystig T, Mehra S, Tashkin DP. Effect of tiotropium on outcomes in patients with moderate chronic obstructive pulmonary disease (UPLIFT): a prespecified subgroup analysis of a randomised controlled trial. *Lancet* 2009;**374**:1171–8.

18. Tashkin DP, Celli B, Senn S, et al. A 4-year trial of tiotropium in chronic obstructive pulmonary disease. *N Engl J Med* 2008;**359**: 1543–54.

19. Mapel DW, Roberts MH. New clinical insights into chronic obstructive pulmonary disease and their implications for pharmacoeconomic analyses. *Pharmacoeconomics* 2012;**30**:869–85.

20. Calverley PM, Anderson JA, Celli B, et al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. *N Engl J Med* 2007;**356**:775–89.

21. Celli BR, Thomas NE, Anderson JA, et al. Effect of pharmacotherapy on rate of decline of lung function in chronic obstructive pulmonary disease: results from the TORCH study. *Am J Respir Crit Care Med* 2008;**178**:332–8.

22. Gold PM. The 2007 GOLD Guidelines: a comprehensive care framework. *Respir Care* 2009;**54**:1040–9.

23. Vestbo J, Anderson JA, Calverley PM, et al. Adherence to inhaled therapy, mortality and hospital admission in COPD. *Thorax* 2009;**64**:939–43.

24. Qaseem A, Wilt TJ, Weinberger SE, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann Intern Med* 2011;**155**:179–91.

25. Eddy DM. The challenge. *JAMA* 1990;**263**:287–90.

26. Tinetti ME, Fried T. The end of the disease era. *Am J Med* 2004; **116**:179–85.

27. Fabbri L, Pauwels RA, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary updated 2003. *COPD* 2004;**1**:105–41.

28. Rabe KF, Hurd S, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007;**176**:532–55.

29. Rodriguez-Roisin R, Agusti A. The GOLD Initiative 2011: a change of paradigm? *Arch Bronconeumol* 2012.

30. Bourbeau J, Sebaldt RJ, Day A, et al. Practice patterns in the management of chronic obstructive pulmonary disease in primary practice: the CAGE study. *Can Respir J* 2008;**15**:13–9.

31. Soriano JB, Zielinski J, Price D. Screening for and early detection of chronic obstructive pulmonary disease. *Lancet* 2009;**374**:721–32.

32. Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *JAMA* 2005;**294**:716–24.

33. Chronic obstructive pulmonary disease and associated health-care resource use - North Carolina, 2007 and 2009. *MMWR Morb Mortal Wkly Rep* 2012;**61**:143–6.

34. Edep ME, Shah NB, Tateo IM, Massie BM. Differences between primary care physicians and cardiologists in management of congestive heart failure: relation to practice guidelines. *J Am Coll Cardiol* 1997;**30**:518–26.

35. Roche N, Lepage T, Bourcereau J, Terrioux P. Guidelines versus clinical practice in the treatment of chronic obstructive pulmonary disease. *Eur Respir J* 2001;**18**:903–8.

36. Belfer MH. Office management of COPD in primary care: a 2009 clinical update. *Postgrad Med* 2009;**121**:82–90.

37. Aisanov Z, Bai C, Bauerle O, et al. Primary care physician perceptions on the diagnosis and management of chronic obstructive pulmonary disease in diverse regions of the world. *Int J Chron Obstruct Pulmon Dis* 2012;**7**:271–82.

38. Fremault A, Janssens W, Beaucage F, Celis G, Perez-Bogerd S, Decramer M. Modification of COPD presentation during the last 25 years. *COPD* 2010;**7**:345–51.

39. Hartzband P, Groopman J. There is more to life than death. *N Engl J Med* 2012;**367**:987–9.

40. Yinnon AM, Wiener-Well Y, Jerassy Z, et al. Improving implementation of infection control guidelines to reduce nosocomial infection rates: pioneering the report card. *J Hosp Infect* 2012; **81**:169–76.

41. Schiro TA, Sakowski J, Romanelli RJ, et al. Improving adherence to best-practice guidelines for venous thromboembolism risk assessment and prevention. *Am J Health Syst Pharm* 2011; **68**:2184–9.

42. Ledwich LJ, Harrington TM, Ayoub WT, Sartorius JA, Newman ED. Improved influenza and pneumococcal vaccination in rheumatology patients taking immunosuppressants using an electronic health record best practice alert. *Arthritis Rheum* 2009;**61**:1505–10.

43. Fricton J, Rindal DB, Rush W, et al. The effect of electronic health records on the use of clinical care guidelines for patients with medically complex conditions. *J Am Dent Assoc* 2011;**142**:1133–42.

44. Sikka R, Sweis R, Kaucky C, Kulstad E. Automated dispensing cabin et alert improves compliance with obtaining blood cultures before antibiotic administration for patients admitted with pneumonia. *Jt Comm J Qual Patient Saf* 2012;**38**:224–8.

45. UpdateGlobal strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2011. 2–1–2012.