Hospital Procalcitonin Testing and Antibiotic Treatment of Patients Admitted for Chronic Obstructive Pulmonary Disease Exacerbation

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Abstract

Rationale: Randomized trials suggest that assessment of serum procalcitonin (PCT) levels can be used to safely limit antibiotic use among patients hospitalized for exacerbations of chronic obstructive pulmonary disease (COPD).

Objectives: To determine the impact of PCT testing on antibiotic treatment of patients hospitalized for exacerbations of COPD in routine practice.

Methods: We conducted a series of cross-sectional and longitudinal multivariable analyses using data from 2009 to 2011 and 2013 to 2014 from a sample of 505 U.S. hospitals.

Results: Of 203,177 patients hospitalized for COPD exacerbation in 2013 to 2014, nearly 9 out of 10 were treated with antibiotics. Hospital PCT testing rates ranged from 0 to 83%. In cross-sectional analysis, there was a weak negative association between the rate of PCT testing and risk-adjusted rates of antibiotic initiation (Spearman correlation,

−0.12; $P = 0.005$); each 10-point increase in the percentage of patients undergoing PCT testing was associated with a 0.7% decline in risk-adjusted antibiotic use ($P = 0.001$). There was no association between hospital rates of PCT testing and duration of antibiotic treatment. In a longitudinal analysis, comparing treatment patterns in 2009 to 2011 and 2013 to 2014, we did not observe a significant difference in the change in antibiotic treatment rates or duration of therapy between hospitals that had adopted PCT testing compared with those that had not.

Conclusions: As currently implemented, PCT testing appears to have had little impact on decisions to initiate antibiotic therapy or on duration of treatment for COPD exacerbations. Implementation research is necessary to translate the promising outcomes from PCT testing observed in randomized trials into clinical practice.

Keywords: chronic obstructive pulmonary disease; health care outcome assessment; health services research

(Received in original form February 13, 2017; accepted in final form August 8, 2017)

Supported by National Heart, Lung, and Blood Institute grants 1R18HL108810-01, K24-HL132008 (P.K.L.), K01-HL114631-011 (M.-S.S.), and K01-HL116768 (A.J.W.); and Agency for Healthcare Research and Quality grant K08-HS024596 (K.A.F.). The funders had no role in data collection, management, analysis; study design, conduct, or interpretation of study findings; or the preparation, review, or approval of the manuscript submitted for publication.

Author Contributions: P.K.L. and A.J.W. conceived of the study. M.-S.S. and P.S.P. analyzed the data. All authors contributed to the interpretations of the results. P.K.L. drafted the manuscript, had full access to all the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to revising the manuscript critically for important intellectual content. All authors give final approval of the version to be published. All authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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This article has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org

Ann Am Thorac Soc Vol 14, No 12, pp 1779–1785, Dec 2017

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DOI: 10.1513/AnnalsATS.201702-133OC

Internet address: www.atsjournals.org

Chronic obstructive pulmonary disease (COPD) affects at least 15 million individuals in the United States, millions more worldwide, and is the nation's third leading cause of death (1, 2). Exacerbations of COPD result in more than 1.5 million emergency department visits and close to 700,000 hospital admissions annually (3). Standard treatment for patients requiring hospitalization consists of supplemental oxygen, short-acting bronchodilators, and systemic corticosteroids (4, 5). In addition, nearly 9 out of 10 patients are treated with broad-spectrum antibiotics (6), despite the fact that only half to three-fourths of all exacerbations are believed to be caused by infections, and most infections are viral and not bacterial (7–11).

Widespread concern over increasing rates of antibiotic resistance, complications of antibiotic therapy, and the high cost of pharmaceuticals has galvanized national interest in improving antimicrobial stewardship (12–16). Procalcitonin (PCT) is a peptide precursor of calcitonin that is released in response to bacterial toxins and is down-regulated in the setting of viral infections (17, 18). Small, unblinded randomized trials among patients with COPD and larger multicenter trials among patients with lower respiratory tract infections that included subgroups with COPD have shown that measurement of serum PCT can be used to identify a subset of patients in whom antibiotics can be safely withheld (19–23). Furthermore, metaanalysis of randomized trials demonstrated that serial measurement of PCT can be used to determine when antibiotics can be discontinued during COPD exacerbation, resulting in reductions in antibiotic duration by approximately 4 days without evidence of adverse events (23). Although PCT testing has been available in the United States for several years, little is known about its diffusion into practice or whether the antimicrobial stewardship benefits achieved in the setting of randomized trials have been achieved in routine clinical settings. The objective of this study was to determine the impact of PCT testing on the decision to initiate antibiotics and on antibiotic treatment duration for patients hospitalized with exacerbations of COPD.

Methods

Design, Setting, and Patients

We performed a series of cross-sectional and longitudinal (difference-in-difference)

analyses using data from the Premier healthcare alliance, a geographically and structurally diverse consortium of hospitals committed to sharing detailed administrative and clinical data for the purposes of benchmarking and quality improvement. Premier data contain a nonrepresentative sample (with overrepresentation of hospitals in the southern United States) of approximately 20% of hospitalizations in the United States and undergo iterative validation and audit process, resulting in minimal missing data (24). In addition to the information contained in the standard hospital discharge abstract (i.e., Uniform Billing form 04), the Premier database contains a date-indexed log of all items and services charged to the patient or their insurer, including laboratory and radiologic tests, medications, and therapeutic services.

In the primary cross-sectional analysis, patients were included if they were 40 years or older, were hospitalized (as either an inpatient or observation case) between 2013 and 2014, and were discharged with a principal diagnosis of COPD or a principal diagnosis of acute respiratory failure with a secondary diagnosis of COPD with acute exacerbation. Patients were excluded if they were not treated with short-acting bronchodilators and systemic steroids on the first hospital day. We further limited the analysis to patients treated at hospitals that cared for at least 25 cases during the study period to ensure stability in our estimates of hospital PCT rates (25). Full inclusion and exclusion criteria are presented in Table E1 in the online supplement. In a secondary, longitudinal analysis, we also included patients hospitalized between July 2009 and June 2011, using the same inclusion and exclusion criteria. We then limited the sample to patients who had been treated at hospitals that contributed data in both the 2009 to 2011 and 2013 to 2014 periods.

Receipt of PCT Testing and Other Patient and Hospital Characteristics

For each patient, we analyzed laboratory charges to determine whether and when PCT testing was performed as well as the total number of PCT tests drawn during the hospital encounter. Patient characteristics included age, sex, race and ethnicity, marital status, and primary insurance provider. We used software from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project to

identify individual comorbidities, which were then summarized into a score using methods developed by Elixhauser and Gagne (26, 27). To characterize disease severity, we identified whether the patient had been hospitalized for COPD in the year before the index admission, whether they had a history of exposure to invasive or noninvasive ventilation, and whether they required treatment with invasive or noninvasive ventilation during the index admission. Because of its potential to impact decision-making surrounding antibiotic use, we also identified whether the patient received a secondary diagnosis of pneumonia that was noted to be present on admission. Hospital characteristics included number of beds, teaching status, census region, and whether it served an urban or rural population.

Outcomes

The primary study outcome was the hospital risk-adjusted percentage of patients receiving antibiotic therapy. Antibiotic administration was obtained from pharmacy charge files. Our secondary outcome was risk-adjusted duration of antibiotic therapy while in the hospital.

Analyses

We calculated summary statistics using frequencies and proportions for categorical data and means, medians, and interquartile ranges for continuous variables. We compared the characteristics of patients who underwent PCT testing with those who did not using standardized differences, χ^2 , or Kruskal-Wallis tests. To examine how PCT has diffused into practice, in our primary analysis, using data from 2013 to 2014, we calculated hospital-specific PCT testing rates, defined as the number of admissions for COPD receiving PCT testing at each hospital divided by the hospital's number of admissions for COPD. For each hospital, we then calculated a risk-adjusted rate of antibiotic prescribing, using multivariable hierarchical logistic regression models (with hospital random effects) that took into account patient characteristics including age, other demographic characteristics, comorbidities, measures of COPD severity, the presence or absence of pneumonia, and available hospital characteristics (which may serve as proxies for unmeasured differences between patients). Using similar methods, we also computed a

hospital-specific risk-adjusted duration of antibiotic therapy.

We used Spearman correlation to explore the association between hospital PCT testing rates and risk-adjusted antibiotic prescribing rates and between risk-adjusted duration of antibiotic therapy. We used linear regression to estimate the impact of increasing hospital rates of PCT testing on risk-adjusted hospital antibiotic initiation and duration of therapy. Because we were unable to ascertain antibiotic duration after hospital discharge, and antibiotic durations were similar to hospital length of stay, we performed an additional analysis evaluating the association between hospital PCT rate and the proportion of hospital days during which a patient received an antibiotic.

In the secondary, longitudinal, difference-in-difference analysis, we grouped hospitals on the basis of their rates of PCT testing in 2013 to 2014 as (<5, 5–20, 21–40, >40%) (28). We then compared the four groups of hospitals, contrasting changes in antibiotic prescribing that occurred between 2009 to 2011 and 2013 to 2014 at hospitals that showed the greatest level of PCT adoption to the changes at hospitals that had little to no use of PCT testing in either period, adjusted for observed differences in patient and hospital characteristics. These analyses were motivated by the hypothesis that hospitals that embraced PCT testing would demonstrate greater reductions in antibiotic use over time than would occur at hospitals that had not adopted PCT and by the ability of within-hospital, difference-in-difference designs to mitigate unmeasured confounding by indication and differential misclassification of International Classification of Diseases, Ninth Revision (ICD-9) codes between centers.

In the first of several sensitivity analyses, we repeated our cross-sectional and longitudinal analyses after excluding patients who were initially treated with mechanical ventilation, a high-risk patient population in whom guidelines recommend antibiotic therapy unconditionally. In a second analysis, we repeated the cross-sectional analyses after excluding patients with a secondary diagnosis of pneumonia that was present on admission as well as other potential indications for antibiotic therapy, including sinusitis, urinary tract infections, and skin and soft tissue infections. In a third analysis, we restricted our analysis of PCT testing and

antibiotic use to the first or second hospital day, to focus exclusively on treatment decisions influenced by diagnostic testing early in the hospitalizations. Finally, we repeated the longitudinal analysis comparing changes in antibiotic use and duration at hospitals in the top two categories of PCT use to those in the bottom category.

All analyses were performed using the Statistical Analysis System (version 9.4; SAS Institute Inc., Cary, NC). The institutional review board at Baystate Medical Center approved the study.

Results

A total of 203,177 patients hospitalized with COPD in 2013 to 2014 at 505 U.S. hospitals were included in the primary analysis (Figure 1). The median age was 67 years (interquartile range, 58–75 years), 59.1% were female, and 73.0% identified as white (Table 1). Diabetes, heart failure, and obesity were the most commonly recorded comorbidities. Slightly more than one-third of patients (35.7%) had been hospitalized for COPD in the year before the index admission, and pneumonia was present on admission in 16.2% of cases. A total of 180,958 patients (89.1%) were treated with antibiotics during the hospitalization, including 86.7% on the first or second

hospital day. The most commonly prescribed antibiotics were fluoroquinolones, third-generation cephalosporins, and macrolides. The median duration of antibiotic therapy was 4 days, similar to the 4-day median of hospital length of stay. In-hospital mortality was 1.5%, and 21.6% of patients were rehospitalized within 30 days of discharge. Most admissions were to urban (79.4%) nonteaching (66.8%) hospitals and were distributed across small- (26.6%), medium- (38.2%), and large- (35.3%) sized institutions. Although care was provided in all census regions, 55.6% of admissions were to hospitals located in the South.

A total of 10,377 (5.1%) cases underwent PCT testing during the hospitalization, including 8,388 (4.1%) who were tested once and 1,989 (1.0% of total, 24% of patients with one PCT test) who were tested two or more times. Approximately 85% of all PCT testing occurred on the first or second hospital day. Compared with patients who did not undergo PCT testing, those who were tested were marginally older, were more likely to be white, and had a greater comorbidity burden, higher severity of illness, and higher in-hospital mortality (Table 1). Patients who underwent PCT testing were more likely to receive care at larger hospitals and those located in the South.

Figure 1. Derivation of study cohort. COPD = chronic obstructive pulmonary disease; DRG = Diagnosis Related Group; ICD-9 = *International Classification of Diseases, Ninth Revision*.

Table 1. Characteristics of patients included in the study

	All Patients (N = 203,177)	PCT (n = 10,377)	No PCT (n = 192,800)	Absolute Standardized Difference*
Age, mean (median, IQR)	66.6 (67, 58–75)	67.2 (67, 58–76)	66.6 (66, 58–75)	0.05
Sex				
Female	120,055 (59.1)	6,016 (58.0)	114,039 (59.2)	0.001
Male	83,122 (40.9)	4,361 (42.0)	78,761 (40.9)	
Race				
White	148,225 (73.0)	8,053 (77.6)	140,172 (72.7)	0.12
Black	26,889 (13.2)	1,141 (11.0)	25,748 (13.4)	
Hispanic	8,813 (4.3)	439 (4.2)	8,374 (4.3)	
Other	19,250 (9.5)	744 (7.2)	18,506 (9.6)	
Payer				
Medicare	137,681 (67.8)	7,189 (69.3)	130,492 (67.7)	0.08
Medicaid	26,846 (13.2)	1,166 (11.2)	25,680 (13.3)	
Private	24,652 (12.1)	1,240 (12.0)	23,412 (12.1)	
Uninsured	9,581 (4.7)	473 (4.6)	9,108 (4.7)	
Other/unknown	4,417 (2.2)	309 (3.0)	4,108 (2.1)	
Marital status				
Married	69,319 (34.1)	3,671 (35.4)	65,648 (34.1)	0.08
Single	115,547 (56.9)	5,987 (57.7)	109,560 (56.8)	
Other/missing	18,311 (9.0)	719 (6.9)	17,592 (9.1)	
Comorbidities				
Diabetes	67,159 (33.1)	3,527 (34.0)	63,632 (33.0)	0.02
Congestive heart failure	53,839 (26.5)	3,271 (31.5)	50,568 (26.2)	0.12
Obesity	42,206 (20.8)	2,375 (22.9)	39,831 (20.7)	0.05
Depression	38,396 (18.9)	2,112 (20.4)	36,284 (18.8)	0.04
Deficiency anemias	33,131 (16.3)	2,127 (20.5)	31,004 (16.1)	0.11
Comorbidity score, mean (median, IQR)	2.5 (2, 1–4)	2.9 (2, 1–4)	2.5 (2, 1–4)	0.17
Concurrent pneumonia	32,967 (16.2)	2,664 (25.7)	30,303 (15.7)	0.25
Markers of disease severity				
Prior admission for COPD	72,573 (35.7)	3,566 (34.4)	69,007 (35.8)	0.03
Prior receipt NIV	34,755 (17.1)	2,063 (19.9)	32,692 (17.0)	0.08
Prior receipt IMV	15,426 (7.6)	959 (9.2)	14,467 (7.5)	0.06
NIV at admission	35,400 (17.4)	2,421 (23.3)	32,979 (17.1)	0.16
IMV at admission	12,674 (6.2)	1,247 (12.0)	11,427 (5.9)	0.21
Outcomes				
Antibiotic use (any)	180,958 (89.1)	9,511 (91.7)	171,447 (88.9)	0.09
Antibiotic use (Day 1, 2)	176,045 (86.7)	9,189 (88.6)	166,856 (86.5)	0.06
Duration of antibiotic, mean d (median, IQR)	4.3 (4, 2–5)	5.2 (4, 3–6)	4.4 (4, 2–6)	0.23
30-d all-cause readmission	43,826 (21.6)	2,234 (21.5)	41,592 (21.6)	0.001
In-hospital mortality	2,974 (1.5)	345 (3.3)	2,629 (1.4)	0.13
Length of stay, [†] mean (median, IQR)	5.4 (4, 3–6)	6.7 (5, 4–8)	5.3 (3, 2–5)	0.27

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; IMV = invasive mechanical ventilation; IQR = interquartile range; NIV = noninvasive ventilation; PCT = procalcitonin.

Data presented as n (%) unless otherwise noted.

*Absolute standardized difference > 0.10 considered to be a meaningful difference.

[†]Length of stay = number of calendar days in hospital.

Rates of PCT testing varied widely between hospitals, ranging from 0 to 83%, with more than half of all hospitals not doing any PCT testing in patients with COPD (Figure E1). We found a weak negative correlation between hospital rates of PCT testing and risk-adjusted hospital rates of antibiotic initiation (Spearman coefficient, -0.12 ; $P = 0.005$; Figure 2A). When hospital risk-adjusted rates of antibiotic use were regressed on PCT testing rates, each 10% increase in the

percentage of patients undergoing PCT testing was associated with a 0.7% lower rate of antibiotic use ($P = 0.001$). PCT testing rates were not correlated with risk-adjusted duration of antibiotic therapy (Spearman coefficient, -0.05 ; $P = 0.23$; Figure 2B). Excluding patients who never received an antibiotic, patients at lowest PCT use (<5% of patients) hospitals received antibiotics during 81.4% of hospital days, compared with 78.3% of hospital days exposed to antibiotics for

patients at highest PCT use hospitals (>40% of patients), $P < 0.001$.

In a secondary analysis, we compared changes in rates of antibiotic treatment and antibiotic duration at hospitals that showed the highest levels of PCT adoption to those that rarely or never used the test in either period (Table 2). Between 2009 to 2011 and 2013 to 2014, PCT testing increased from 4.5 to 45.2% of patients at the 10 hospitals with the highest PCT testing rates. In contrast, rates of PCT testing increased

Figure 2. (A) Risk-adjusted rate of antibiotic use among 505 hospitals according to the percentage of patients with chronic obstructive pulmonary disease (COPD) receiving serum procalcitonin testing. (B) Risk-adjusted duration of antibiotic administration (mean days) among 505 U.S. hospitals according to the percentage of patients with COPD receiving serum procalcitonin (PCT) testing.

from 0 to 0.4% of patients among the 281 hospitals in the lowest category of PCT use. We observed little or no change over time in either adjusted rates or duration of antibiotic treatment in both the non-PCT-adopting and high-PCT-adopting hospitals (Table 2). Consequently, the difference-in-difference analysis suggested that there was no effect of PCT testing on antibiotic initiation (estimate, -0.1% ; $P = 0.99$) or duration.

Results of sensitivity analyses were similar to primary analyses. For example,

analyses excluding patients treated with either noninvasive ventilation or invasive mechanical ventilation at the time of hospital admission found weak inverse correlations between PCT testing rate and the percentage of patients treated with antibiotics (-0.13 ; $P = 0.003$; Figure E2A) and duration of antibiotic therapy (-0.09 ; $P = 0.05$; Figure E2B). A difference-in-difference analysis using this more restricted cohort yielded results similar to the primary analysis (Table E2). A second sensitivity analysis excluding patients with

pneumonia or other infectious diagnoses also yielded similar results (correlation between PCT testing and risk-adjusted rates of antibiotic administration, -0.13 ; $P = 0.005$; association between PCT testing and antibiotic duration, -0.07 ; $P = 0.14$; Figures E3A and E3B). A third sensitivity analysis restricted to PCT testing and antibiotic administration occurring at the time of admission showed consistent findings with regard to antibiotic initiation (-0.10 ; $P = 0.02$) and duration (-0.05 ; $P = 0.30$) (Figures E4A and E4B). A fourth sensitivity

Table 2. Changes in risk-adjusted rates of antibiotic administration and risk-adjusted duration of antibiotic treatment between 2009 to 2011 and 2013 to 2014 at hospitals demonstrating the highest and lowest level of procalcitonin adoption

	Non-PCT-Adopting Hospitals 2009–2011 ($n = 281$)	Non-PCT-Adopting Hospitals 2013–2014 ($n = 281$)	Difference between 2009–2011 and 2013–2014	High-PCT-Adopting Hospitals 2009–2011 ($n = 10$)	High-PCT-Adopting Hospitals 2013–2014 ($n = 10$)	Difference between 2009–2011 and 2013–2014	High vs. Low, Difference in Difference	<i>P</i> Value
Patients undergoing PCT testing, %	0	0.4	0.4	4.5	45.2	40.7	40.3	
Risk-adjusted antibiotic treatment rate	89.0	89.0	0.0	86.1	86.0	-0.1	-0.1	0.99
Risk-adjusted mean duration of antibiotic treatment, d	4.7	4.7	0.0	4.3	4.2	-0.1	-0.1	0.96

Definition of abbreviation: PCT = procalcitonin.

analysis comparing hospitals in the two highest PCT rate categories (those 20–40% and >40%) to those in the lowest rate category (Table E3) also demonstrated no association between rates of PCT testing and antibiotic treatment outcomes.

Discussion

In this study of more than 200,000 patients hospitalized for exacerbations of COPD at more than 500 U.S. hospitals, nearly 9 out of 10 were treated with antibiotics. Rates of PCT testing were low, as were rates of serial PCT testing necessary to guide decisions on antibiotic duration, and testing rates varied markedly between institutions. Contrary to results from clinical trials, more PCT testing was associated with only modestly lower risk-adjusted rates of antibiotic prescribing, and PCT testing was not associated with shorter duration of antibiotic treatment. These findings were corroborated in multiple sensitivity analyses, including a difference-in-differences approach showing that antibiotic prescribing rates remained stable regardless of whether hospitals had, or had not, adopted PCT testing. Taken together, these findings suggest that, as currently implemented in routine clinical practice, PCT has yet to fulfill the promise of improved antimicrobial stewardship suggested by earlier randomized trials.

A number of randomized trials have demonstrated efficacy of PCT to reduce antibiotics use without affecting clinical outcomes in the setting of COPD exacerbations. In a single-center Swiss trial, Stolz and colleagues reported that 40% of patients randomized to PCT were treated with antibiotics compared with 72% in the control group (20). Among the subset of patients with COPD enrolled in the multicenter Pro-HOSP trial, PCT testing was associated with a reduction in the mean duration of antibiotic treatment from 5.1 to 2.5 days (21). Finally, recent metaanalyses of 14 trials in acute respiratory tract infections and 8 trials specifically investigating patients with COPD (23) found that PCT testing reduced antibiotic exposure by approximately 50%, while achieving similar rates of treatment failure and death (29).

Although our findings demonstrate that PCT began diffusing into practice by 2013 to 2014, rates of use remained low. More disappointing was the fact that each

10% increase in the hospital rate of PCT testing was associated with only a 0.7% lower risk-adjusted rate of antibiotic administration and no change in antibiotic duration. Extrapolating these results suggests that PCT testing of all patients at the time of admission would lead to a reduction in antibiotic use from 90 to 83% of cases, far less than the 32% absolute reduction reported in prior trials.

Given the encouraging results of randomized trials, what factors might explain the muted findings from clinical practice? Although our study was not designed to answer this question directly, our own clinical experience suggests several possibilities. First, our study represents an analysis of PCT testing relatively early in its adoption, and it is possible that with greater experience, and with active implementation efforts, physicians might become more comfortable withholding or curtailing antibiotic treatment on the basis of test results. Along these lines, it is only recently that the Infectious Disease Society of America antimicrobial stewardship guidelines have provided weak recommendations for use of PCT, whereas current Global Initiative for Chronic Obstructive Lung Disease COPD guidelines now state that PCT may reduce antibiotics exposure with similar clinical efficacy (30). Further studies will need to be done to evaluate whether cautious endorsement of PCT testing in clinical guidelines is associated with changing PCT practices. Second, we observed that very few patients underwent serial testing used in PCT algorithms from randomized trials during the hospitalization. Without repeat testing, it is impossible to identify patients in whom PCT levels have fallen below a safe threshold for antibiotic discontinuation. Finally, hospitals that send the test to an outside laboratory for processing could experience a delay in reporting of results that would largely negate PCT's ability to influence antibiotic decision-making.

Our study has a number of strengths. First, we included a large and diverse sample of hospitals, enhancing the generalizability of findings. Second, we conducted a secondary analysis using longitudinal data that corroborated the results of our cross-sectional analysis. Third, our findings were robust in a series of sensitivity analyses, including among patients who did not receive mechanical ventilation and after excluding patients with evidence of other types of

infections. Finally, we investigated the impact of PCT testing on the decision to initiate and the decision to continue antibiotic treatment, both of which have been shown to be influenced by use of PCT in trials enrolling patients with COPD.

Although the poor real-world effectiveness of PCT testing in COPD was striking, our results should be considered in light of several limitations. First, we used ICD-9 and billing codes to identify patients hospitalized for COPD and comorbidities for risk adjustment, which are neither perfectly sensitive nor specific (31) and may be subject to unmeasured confounding. However, within-hospital difference-in-difference analyses were performed to mitigate the potential for differential misclassification of ICD-9 codes across hospitals as well as unmeasured confounding by indication for PCT testing. In addition, to increase the likelihood that patients had been hospitalized for COPD, we took advantage of pharmacy data to limit the study to those who had received both short-acting bronchodilators and systemic corticosteroids at the time of admission. Second, we did not have access to the results of PCT tests. However, our primary outcomes of antibiotic initiation and duration were adjusted for numerous patient and hospital characteristics that might be associated with the risk of bacterial infection. Third, given the retrospective nature of our study, we did not have information about why treating physicians chose to initiate or continue antibiotics. Fourth, we did not know whether patients had been treated with antibiotics before admission. Although PCT testing might be particularly useful in this setting to assess the need for further antibiotic treatment, it is possible that physicians may have been reluctant to discontinue treatment initiated outside of the hospital. Fifth, we did not have information about antibiotic use after discharge; however, we performed a sensitivity analysis using proportion of hospital days exposed to antibiotics, with similar results to primary analyses. Furthermore, if PCT is going to have an impact on clinical decision-making, it should be evident before discharge. Finally, although our analyses of hospital antibiotic prescribing rates adjusted for numerous potential confounders, it is possible that we have underestimated the benefits of PCT testing

if patients treated at hospitals with higher rates of PCT testing had substantially higher rates of bacterial infection.

In conclusion, use of PCT testing was weakly associated with antibiotic initiation

and unassociated with duration of antibiotic treatment among patients hospitalized with exacerbations of COPD. Further research is needed to understand the barriers to achieving greater antimicrobial stewardship gains and to

develop strategies to bring the promising findings from randomized trials into clinical practice. ■

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

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