

# Procalcitonin-Guided Antibiotic Prescribing for Acute Exacerbations of Chronic Obstructive Pulmonary Disease in the Emergency Department

Leah J. Nguyen, PharmD, BCPS; Andrew Varker, PharmD, BCPS; Pamela Slaughter, PharmD, BCPS; Daniel Boyle, PharmD, BCOP; and Negin Nekahi, MD, PhD

**Purpose:** Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) can be caused by viral, bacterial, or environmental factors. Recent studies have suggested that procalcitonin serum levels may help reduce unnecessary antibiotic use without statistically significant differences in rates of treatment failure for AECOPD. The purpose of this quality improvement project was to create a procalcitonin-based algorithm to aid emergency department (ED) clinicians in the management of patients with AECOPD who do not require hospitalization and to evaluate its efficacy and practicality. The primary outcome of this project was the rate of antibiotic prescriptions before and after the initiation of the algorithm.

**Methods:** This study used an observational, retrospective, pre- and posteducation/intervention design. Clinicians were educated individually on the use of procalcitonin, and a copy of the algorithm was made available to each clinician and posted in the ED. Patients who were discharged from the ED with a diagnosis of an AECOPD were identified using *International Classification of Diseases, Tenth Revision* codes. Patient charts were reviewed from November 2018 to March 2019 for the preimplementation period and November 2019 to March 2020 for the postimplementation period. The rate of antibiotic prescriptions and the number of procalcitonin tests ordered before and after the introduction of the algorithm were analyzed. In addition, information on COPD Global Initiative for Chronic Obstructive Lung Disease (GOLD) grouping and 30-, 60-, and 90-day reexacerbation rates were collected. It was estimated that a sample size of 146 pa-

tients (73 patients/group) would provide 80% power to detect a between-group difference of 10% in the percentage of patients who were prescribed antibiotics. Categorical variables were expressed using estimates of their frequency and percentages. Percentages were compared using Fisher exact tests. For all tests, the significance level was set at 0.05.

**Results:** Seventy-three patients were included in the preintervention group, and 77 patients were included in the postintervention group. Patients in the preintervention and postintervention groups had similar representation in GOLD categories: 52% and 51% for D, 17.8% and 23.4% for C, 21.9% and 16.8% for B, and 8.2% and 7.8% for A, respectively. The rate of antibiotic prescriptions decreased by 20% after implementation from 83.6% before to 63.6% after implementation ( $P = .01$ ). The differences in reexacerbation rates between the preintervention and postintervention groups were similar: 19.2% vs 23.4% at 30 days, 12.3% vs 11.7% at 60 days, and 4.1% vs 9.1% at 90 days, respectively. Prior to education and introduction of the procalcitonin algorithm, procalcitonin was ordered for 1.4% of AECOPD cases. Postimplementation, procalcitonin was ordered for 28.6% of AECOPD cases and used in clinical decision making 81.8% of the time.

**Conclusions:** In this study of the implementation of a treatment algorithm for patients with mild and moderate AECOPD who present to the ED, procalcitonin was shown to reduce the rate of antibiotic prescriptions without an observable difference in reexacerbation rates 30, 60, and 90 days after presentation.

Author affiliations can be found at the end of the article.

**Correspondence:**

Leah Nguyen  
(leah.nguyen1@va.gov)

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The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines define acute exacerbations of chronic obstructive pulmonary disease (AECOPD) as a sudden worsening of respiratory symptoms that require additional interventions. Exacerbations are classified as mild (treated with short-acting bronchodilators only), moderate (treated with antibiotics and/or oral corticosteroids), or severe (treatment requiring hospitalization). Exacerbations must include increased dyspnea, and other symptoms may involve increased sputum volume and purulence, cough, and a change in sputum color. These symptoms can be due to viral, bacterial, or environmental causes, with viral respiratory infections being the

most common cause.<sup>1-4</sup> However, determining the etiology of an exacerbation can be difficult based on symptoms alone and can lead to an excessive and unnecessary use of antibiotics. Only the change in sputum color is considered highly sensitive and specific for bacterial causes.<sup>1</sup> As a result, there has been an increased interest in the use of acute biomarkers to determine whether antibiotics are necessary.

Procalcitonin (PCT) is an acute phase reactant that increases in response to inflammation, especially inflammation caused by a bacterial infection. Recent studies have suggested that PCT may be used in patients experiencing an AECOPD to reduce antibiotic use without impacting rates of treatment

failure.<sup>5-9</sup> A majority of these studies have been in the inpatient setting or a combination of inpatient and outpatient settings.

The purpose of this study was to create and to evaluate the efficacy and practicality of a PCT-based algorithm to aid emergency department (ED) clinicians in the evaluation of patients with AECOPD who do not require hospitalization. The primary outcome of this project was the rate of antibiotic prescriptions before and after the initiation of the algorithm.

### Methods

This was an observational, retrospective, pre/post assessment at the Phoenix Veterans Affairs Health Care System (PVAHCS) in Arizona. Patients who were discharged from the ED with a diagnosis of an AECOPD were identified using *International Classification of Diseases, Tenth Revision* (ICD-10) codes. Patient charts were reviewed from November 2018 to March 2019 for the preimplementation group and from November 2019 for March 2020 in the postimplementation group. The periods were chosen to reflect similar seasons for both the pre- and postimplementation interventions. Patients were excluded from analysis if they required hospital admission, were immunocompromised, on chronic antimicrobial therapy, had no documented medical history of COPD, or if they were presenting primarily for medication refills. Information collected included the rate of antibiotic prescriptions, procalcitonin test orders, COPD GOLD classification, and 30-, 60-, and 90-day re-exacerbation rates.

A PCT-based algorithm (Figure 1) was developed and approved by the PVAHCS Antimicrobial Stewardship Program, the Pharmacy and Therapeutics committee, and ED leadership. PCT threshold values were based on values approved by the US Food and Drug Administration and previous studies—antibiotics were discouraged for PCT levels  $\leq 0.25$  ng/mL but could be considered for PCT levels  $> 0.25$  ng/mL.<sup>5,8,9</sup> Clinicians were not required to use the algorithm, and the use of clinical judgement was encouraged. The recommended antibiotic therapies were based on previously approved PVAHCS antimicrobial stewardship guidance. To pro-

**TABLE 1** GOLD Classification of Patients

GOLD Classifications <sup>a</sup>	Preintervention, % (n = 73)	Postintervention, % (n = 77)
A	8.2	7.8
B	21.9	16.8
C	17.8	23.4
D	52	51

Abbreviation: GOLD, Global Initiative for Chronic Obstructive Lung Disease.

<sup>a</sup>A, low risk for an exacerbation, fewer symptoms; B, low risk for an exacerbation, more symptoms; C, high risk of an exacerbation, fewer symptoms; D, high risk for an exacerbation, more symptoms.

mote utilization, a PCT quick order option was added to the ED laboratory order menu.

ED clinicians were individually educated by the antimicrobial stewardship and emergency medicine pharmacists, an infectious disease physician champion, and the pharmacy resident. Clinicians were educated about PCT and its use in the setting of AECOPD to aid in the determination of bacterial infections. Each clinician received an electronic copy the algorithm and summary of the study protocol before implementation and 3 months after implementation for follow-up education. In addition, a printed copy of the algorithm was posted in multiple clinician workstations within the ED. For the first month of implementation, the project lead was available full-time in the ED to encourage algorithm use and to field questions or concerns from clinicians.

### Outcome Measures

The primary outcome was the rate of antibiotic prescriptions pre- and postintervention. The safety endpoints were 30-, 60-, and 90-day reexacerbation rates. Reexacerbation rates were defined by ICD-10 codes and documentation from a primary care visit or subsequent ED visit. The secondary outcomes were the rate of PCT tests ordered and used for treatment decisions. Other areas of interest were antibiotic prescribing trends, duration of therapy, and patient COPD GOLD classification.

### Statistical analysis

It was estimated that a sample size of 146 patients (73 patients/group) would

**TABLE 2** Pre- and Postintervention Outcomes

Outcomes	Preintervention (n = 73)	Postintervention (n = 77)	P value
Antibiotic prescribed, No. (%)	61 (83.6)	49 (63.6)	.01
Azithromycin	27 (37.0)	21 (27.3)	-
Doxycycline	24 (32.9)	0 (0)	-
Levofloxacin	8 (11.0)	2 (2.6)	-
Other	2 (3.3)	9 (18.4)	-
Duration of therapy, d	6.8	6.2	-
Reexacerbation rates, No. (%)			
30 d	14 (19.2)	18 (23.4)	-
60 d	9 (12.3)	9 (11.7)	-
90 d	3 (4.1)	7 (9.1)	-
Procalcitonin tests, No. (%)			
Ordered	1 (1.4)	22 (28.6)	-
Used	0 (0)	18 (81.8)	-
Documented change in sputum color, No. (%)	13 (17.8)	13 (16.9)	-

provide 80% power to detect a between-group difference of 10% in the percentage of patients who were prescribed antibiotics. Categorical variables were expressed using estimates of frequency and percentages. Percentages were compared using Fisher exact tests. For all tests, the significance level was set at 0.05.

## RESULTS

Seventy-three patients were included in the preintervention group and 77 in the postintervention group. The GOLD classification rates were similar between the groups (Table 1). In addition, > 90% of patients were White males and all patients were aged  $\geq$  50 years, which is characteristic of the US Department of Veterans Affairs (VA) population.

The percentage of antibiotic prescriptions decreased by 20% after implementation, falling from 83.6% before to 63.6% after the implementation ( $P = .01$ ). The documented change in sputum color remained low compared with antibiotic prescriptions: 17.8% preimplementation and 16.9% postimplementation. The reduction in antibiotic prescriptions was associated with limited differences observed in 30-, 60-, and 90-day reexacerbation rates pre- and postintervention: 19.2% vs 23.4%, 12.3% vs 11.7%, and 4.1% vs 9.1%, respectively.

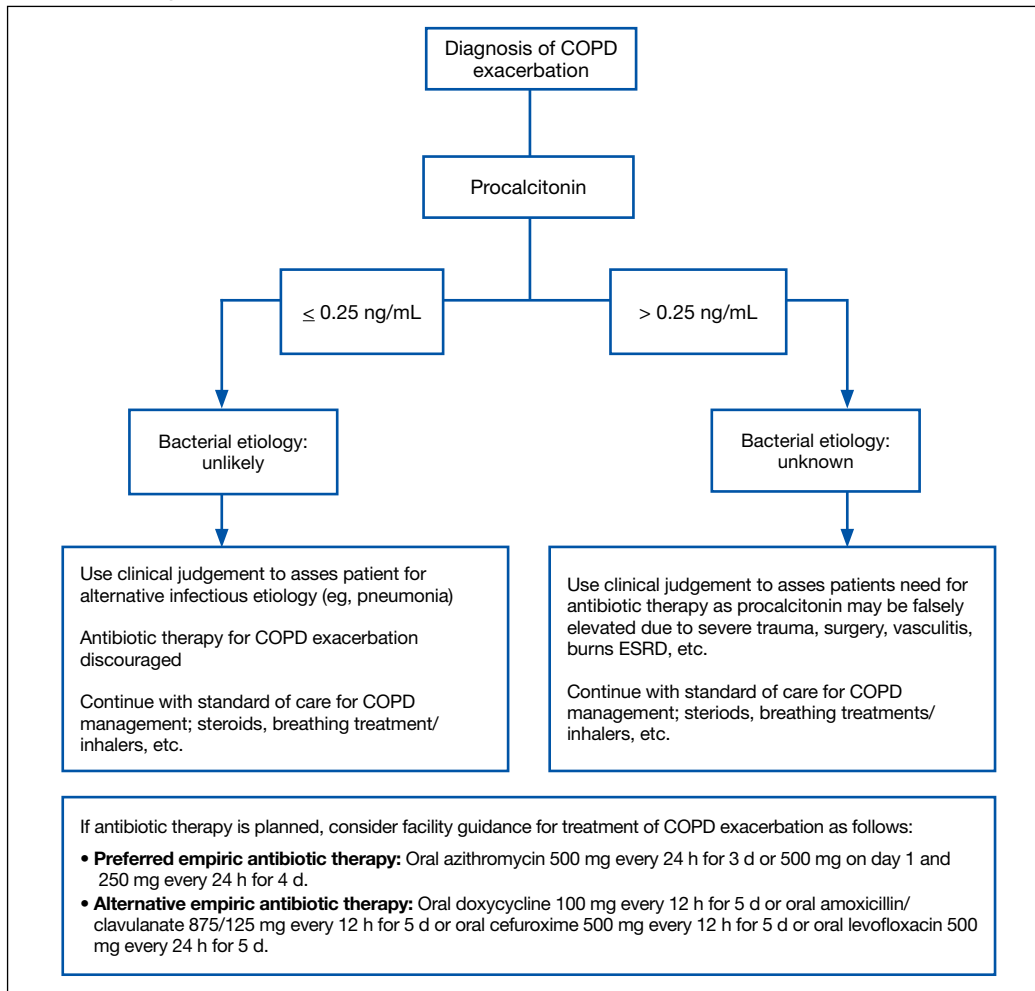
Prior to the education, introduction of the algorithm, and implementation of the PCT quick-order menu, PCT was ordered

for 1.4% of AECOPD cases. Postintervention, PCT was ordered for 28.6% of mild-to-moderate AECOPD cases and used in clinical decision making per clinical documentation 81.8% of the time. PCT was used in 5 GOLD group B patients, 5 GOLD group C patients, and 7 GOLD group D patients. In all cases, PCT was  $< 0.25$  ng/mL. In 4 cases PCT was ordered but not used: 1 GOLD group D patient refused traditional treatment with oral corticosteroids, which resulted in the clinician prescribing antibiotics, and the other 3 cases did not use PCT based on clinical decision making. The rate of PCT tests ordered for mild-to-moderate AECOPD over time is depicted in Figure 2.

The average duration of antibiotic therapy was about 6 days pre- and postintervention. This is longer than the PVAHCS recommended duration of 5 days but is consistent with the GOLD guidelines recommended duration of 5 to 7 days.<sup>1</sup> Azithromycin is recommended as a first-line treatment option at the PVAHCS based on the local antibiogram, and it remained the most commonly prescribed antibiotic pre- and postintervention. Outcomes of interest are detailed in Table 2.

## DISCUSSION

The implementation of PCT-guided antibiotic prescribing for patients with mild and

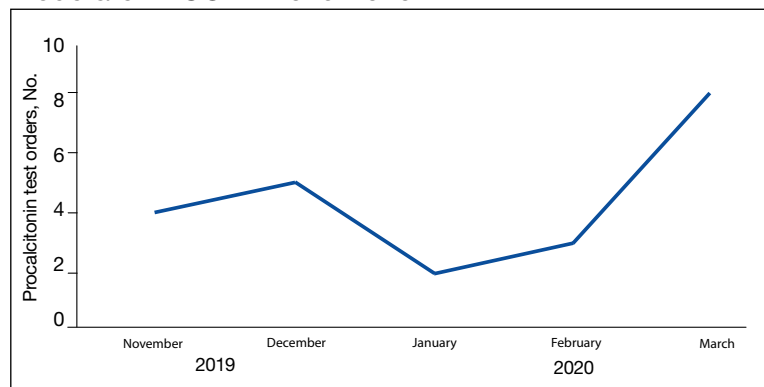
**FIGURE 1** Algorithm Used to Aid Interpretation of Procalcitonin Results

Abbreviations: COPD, chronic obstructive pulmonary disease; ESRD, end stage renal disease.

moderate AECOPD who presented to the ED resulted in a 20% reduction in antibiotic prescriptions, falling from 83.6% before the intervention to 63.6% afterward ( $P = .01$ ). The measured decrease in antibiotic prescriptions is consistent with other studies evaluating the use of acute phase reactants to guide antibiotic prescribing for AECOPD.<sup>10,11</sup> In addition, there was no observed difference in reexacerbation rates. This adds to the increasing body of evidence that antibiotics are overprescribed in mild and moderate AECOPD.<sup>12</sup> This is exemplified in our data by the low percentage of patients who had a documented change in sputum color; symptoms that are well known to be highly specific and sensitive for a bacterial infection in AECOPD.

Many health care providers (HCPs) in the ED were unfamiliar with PCT prior to implementation. A primary concern with this study was its impact on diagnostic stewardship. Preimplementation, ED clinicians ordered PCT 8 times for any cause. Postintervention, ED clinicians ordered PCT 180 times for any cause: 36% of these orders were for patients with AECOPD who were discharged from the ED or who required hospital admission. The other orders were for other respiratory conditions, including asthma exacerbations, pneumonia, bronchitis, sinusitis, pharyngitis, nonspecific respiratory infections, and respiratory failure.

The early phase of the COVID-19 pandemic coincided with the postintervention phase of this project. PVAHCS started

**FIGURE 2** Procalcitonin Tests Ordered for Mild and Moderate AECOPD 2019-2020

Abbreviation: AECOPD, acute exacerbations of chronic obstructive pulmonary disease.

preparing for the pandemic in March 2020, and the first confirmed diagnosis at the facility occurred mid-March. COVID-19 may have contributed to the sharp increase in PCT tests. There is currently no well-defined role for PCT in the diagnosis or management of COVID-19, but ED clinicians may have increased their use of PCT tests to help characterize the etiology of the large influx of patients presenting with respiratory symptoms.<sup>13</sup>

### Strengths

Strengths of this project include its multimodal implementation and overall pragmatic design, which reflects real-world utilization of procalcitonin by ED HCPs. The HCPs were not mandated to follow the procalcitonin algorithm, and the use of clinical judgment was strongly encouraged. This project occurred concomitantly with the VA Infectious Disease Academic Detailing education program. The program focused on clinician education for the proper diagnosis and treatment of respiratory tract infections. In addition, viral illness packs were introduced as part of this initiative to reduce unnecessary antibiotic prescribing. The viral illness pack included standard items for symptom relief, such as saline nasal spray, cough drops, and hand sanitizer, as well as an explanation card of why the patient was not receiving antibiotics. Several studies have suggested that patients expect a prescription for an antibiotic when they present with respiratory tract symptoms, and HCPs often are com-

pelled to maintain patient satisfaction, thus leading to unnecessary antibiotic prescriptions.<sup>14</sup> The viral illness pack helped fulfill the patient's expectation to receive treatment after seeking care. In addition, the project lead was available full time during the first month of PCT algorithm implementation to address questions and concerns, which may have improved HCPs overall confidence in using PCT.

### Limitations

Limitations of this project include its population and its retrospective nature. The PVAHCS patient population is predominantly older, more White, and more male compared with the general civilian population, and results may not be generalizable to other populations. Data were limited to documentation in the electronic health record. The population was based on data extraction by the ICD-10 code, which may not be an accurate capture of the total population as HCPs may not select the most accurate ICD-10 code on documentation. Another potential limitation was the COVID-19 pandemic which may have resulted in HCPs ordering PCT more frequently as more patients presented to the ED with undifferentiated respiratory symptoms. Finally, there were minimal differences observed in reexacerbation rates; however, although the sample size was powered to detect a difference in antibiotic prescriptions, the sample size was not powered to detect a statistically significant difference in the primary safety outcome.

### CONCLUSIONS

PCT-guided antibiotic prescribing significantly reduced the number of antibiotic prescriptions without an observable increase in reexacerbation rates for patients with mild and moderate AECOPD in the ED. This study provides a pragmatic evaluation of PCT-guided antibiotic prescribing for patients with AECOPD solely in the outpatient setting. Acute phase reactants like PCT can play a role in the management of AECOPD to reduce unnecessary antibiotic prescriptions.

### Author affiliations

**Leah Nguyen** is an Emergency Medicine Clinical Pharmacy Specialist at the Portland Veterans Affairs Health Care

System in Oregon; **Andrew Varker** is an Infectious Disease Clinical Pharmacy Specialist; **Pamela Slaughter** and **Daniel Boyle** are Emergency Medicine Clinical Pharmacy Specialists; **Negin Nekahi** is an Infectious Disease Specialist; Leah Nguyen was a Pharmacy Resident at the time this article was written; all at Phoenix Veterans Affairs Health Care System in Arizona.

### Author disclosures

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### Disclaimer

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