

# Antibiotic Practice Patterns With Procalcitonin Levels in Patients With Acute Lower Respiratory Tract Infection

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Unnecessary use of antibiotics has major short- and long-term consequences, including antibiotic resistance, adverse drug reactions, *Clostridioides difficile* infections, and high health care costs.<sup>1-5</sup> In a 2017 report on antibiotic use in the United States, the CDC estimated that unnecessary antibiotic prescriptions for respiratory infections occur at least 50% of the time in ambulatory settings.<sup>1</sup> The overuse of antibiotics is particularly common in patients with suspected lower respiratory tract infections (LRTIs) because of the difficulty in distinguishing bacterial and viral etiologies of infection.<sup>6-8</sup>

Procalcitonin (PCT) is a biomarker released in response to bacterial infection and is downregulated in viral infections.<sup>7</sup> Baseline PCT level is low (< 0.05 mcg/L) in healthy patients. In the setting of bacterial infection, PCT is produced either by direct stimulation from lipopolysaccharides and other microbial metabolites or indirectly from inflammatory mediators such as interleukin 6 and tumor necrosis factor  $\alpha$ . Levels increase with severity of infection and decrease by approximately 50% with control of infection by effective antibiotics.<sup>9-14</sup>

PCT testing is approved by the FDA to guide antibiotic therapy in patients with LRTI with the intent of improving antibiotic stewardship. Several randomized controlled clinical trials (RCTs) have investigated the use of PCT-based algorithms to guide initiation and duration of therapy in LRTIs.<sup>15-20</sup> A meta-analysis of 18 RCTs by Schuetz et al found that there was lower mortality, a 2.4-day reduction in antibiotic exposure, and lower risk of antibiotic-related adverse effects in PCT-guided trial participants compared with those receiving standard treatment.<sup>19</sup> However, there were also low adherence rates to the algorithms within these trials (41%-72% in the emergency department/hospital-based setting).<sup>21</sup> In the real-world clinical setting, PCT testing is ordered in patients admitted with respiratory conditions, such as suspected LRTIs. To date, clinical practice guidelines have been inconsistent and the majority have not recommended PCT-guided management in respiratory infections due to uncertain benefit.<sup>22</sup> Thus, understanding the rate of PCT testing and the effect that PCT levels have on antibiotic prescribing behavior would provide

## ABSTRACT

**OBJECTIVES:** Procalcitonin (PCT) testing is FDA approved to guide antibiotic therapy in patients with lower respiratory tract infection (LRTI). However, its utilization and impact on real-world antibiotic prescribing behavior are unknown. We investigated the rate of PCT testing to evaluate an association between initial PCT level and antibiotic prescription patterns for patients with suspected LRTI within a large integrated health system.

**STUDY DESIGN:** Retrospective cohort study.

**METHODS:** A retrospective cohort study (January 1, 2016, through December 31, 2017) was performed in patients 18 years and older who were hospitalized with LRTI and had a PCT measurement. Antibiotic changes were noted before and 36 hours after initial PCT results. Antibiotic concordance was determined using a PCT cutoff value of 0.25 mcg/L. Concordance was defined as (1) patients received antibiotics after a PCT of at least 0.25 mcg/L resulted or (2) antibiotics were withheld after a PCT less than 0.25 mcg/L resulted.

**RESULTS:** PCT testing occurred in 18% of hospitalized patients with LRTI. Among 1606 patients, antibiotic concordance with PCT results was 55%. Among the discordant population, 77% of patients received antibiotics in the setting of a low PCT level compared with 23% who did not receive antibiotics at a high PCT level. There were no statistical differences between LRTI types between patients with PCT-discordant and PCT-concordant care.

**CONCLUSIONS:** Within a real-world environment of patients hospitalized with LRTI, PCT testing was low and the PCT levels did not appear to influence antibiotic prescribing behavior. Our findings suggest that clinicians continue to prioritize clinical judgment over initial PCT levels when prescribing antibiotics for suspected LRTIs.

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## TAKEAWAY POINTS

- ▶ Understanding procalcitonin (PCT) testing rates and their impact on real-world antibiotic prescribing behavior would provide further insights into the utility of PCT testing and may help management strategies.
- ▶ In a real-world environment, we observed that 18% of patients hospitalized with lower respiratory tract infection (LRTI) had PCT levels tested and among these 1606 patients, antibiotic use concordant with PCT results was only 55%.
- ▶ Our findings suggest that clinicians continue to prioritize clinical judgment over PCT testing when prescribing antibiotics for suspected LRTI.

insights into the utility of PCT testing and may shape future management strategies.

Using a real-world clinical practice environment, we sought to investigate PCT testing rates among patients hospitalized with suspected acute LRTIs. We also evaluated the association between PCT levels and provider antibiotic prescribing patterns and whether that led to changes in outcomes.

## METHODS

### Source Cohort

We performed a retrospective cohort study of members within Kaiser Permanente Southern California (KPSC) between January 1, 2016, and December 31, 2017. KPSC is an integrated health system providing comprehensive care to more than 4.7 million members at 15 medical centers and more than 200 satellite clinics throughout Southern California. The patient population is racially, ethnically, and socioeconomically diverse, reflecting the general population of Southern California. All KPSC members have similar benefits, co-pays for medications, and access to health care services, clinic visits, and procedures. Health care encounters are tracked using an electronic health record from which all study information was extracted.<sup>23</sup> The KPSC pharmacy analytic database captures all information on inpatient and outpatient medication fills and refills. All data for this study were collected as part of routine clinical encounters in which health care providers determined the need for laboratory measurements, procedures, and medications.<sup>23,24</sup> KPSC has standardized approaches to management of chronic conditions and disease processes whereby heterogeneity of practice patterns is minimized.<sup>25,26</sup> However, KPSC does *not* have a specific guideline or endorsement for PCT testing. PCT testing is performed based upon the discretion of each provider if they feel that it may be clinically indicated for patient care. The study protocol was reviewed and approved by the KPSC Institutional Review Board.

### Study Population

Patients 18 years and older admitted to the hospital with a primary admission diagnosis of an acute LRTI with at least 1 PCT measurement during the hospitalization were included in the study population. Exclusion criteria included patients receiving oral, intravenous, or

intramuscular antibiotics within 30 days prior to admission; patients who had concurrent conditions during hospitalization that can affect PCT level, including chronic kidney disease stage 5 or end-stage kidney disease requiring dialysis, neutropenia, sepsis, tuberculosis, pregnancy, cardiogenic shock, and burns over greater than 10% of body surface area; and patients with a chronic medical history of HIV/AIDS, bone marrow transplant, congenital and acquired immunodeficiencies, or cystic fibrosis. Patients who were discharged before a PCT level was obtained were also excluded.

### Study Covariates

Information on demographics (including age, sex, and race/ethnicity), comorbidities, type of respiratory infection, length of stay, intensive care unit (ICU) level of care, PCT level, and antibiotic prescriptions was extracted. Disease conditions were identified using *International Classification of Diseases, Tenth Revision* diagnosis codes. Acute LRTIs were defined as pneumonia (community acquired, hospital acquired, health care acquired), acute bronchitis, acute exacerbation of chronic obstructive pulmonary disease (AECOPD), influenza, and other unspecified LRTI (**eAppendix Table 1** [eAppendix available at [ajmc.com](http://ajmc.com)]).

### Exposure Ascertainment

PCT was measured using an enzyme-linked fluorescent assay with fluorescence detection (VIDAS B.R.A.H.M.S. PCT assay; BioMérieux). Using PCT cutoffs from clinical trial data studying the use of PCT algorithms in LRTIs, we defined a low PCT level as less than 0.25 mcg/L and a high level as at least 0.25 mcg/L. If multiple PCT measurements were available, the first value was used in the analysis.

Antibiotic information was retrieved from the KPSC pharmacy analytic database. Only antibiotics administered via oral, intravenous, injection, and intramuscular routes were included in the study (**eAppendix Table 2**). Antibiotic practice patterns were evaluated using pharmacy analytic information and antibiotic status to note antibiotic prescriptions and changes that occurred within 36 hours of the PCT result.

### Main Measures

Our primary measure was to evaluate overall concordance/discordance of antibiotic prescriptions with the PCT results. A PCT cutoff of 0.25 mcg/L was used based on clinical trials of PCT testing utilization among patients with LRTIs.<sup>16,27</sup> Concordance was defined as (1) antibiotic initiation or continuation if a high PCT level resulted (PCT  $\geq$  0.25 mcg/L) or (2) antibiotic discontinuation or no initiation if a low PCT level resulted (PCT  $<$  0.25 mcg/L). Discordance was defined as (1) antibiotic initiation or continuation if a low PCT level resulted (PCT  $<$  0.25 mcg/L) or (2) antibiotic discontinuation or no initiation if a high PCT level resulted (PCT  $\geq$  0.25 mcg/L).

As a secondary analysis, we stratified patients based on concordance categories to compare the baseline characteristics and analyze hospital outcomes such as length of stay.

**Statistical Analysis**

Age, Charlson Comorbidity Index (CCI) score, length of hospital stay, and PCT level were reported as means with SDs. Sex, race/ethnicity, type of respiratory infection, and ICU level of care were reported as absolute numbers and percentages. The CCI was based on the Deyo adaptation.<sup>28</sup>

The Kruskal-Wallis test was used for comparison of continuous variables, and  $\chi^2$  or Fisher's exact test was used for categorical variables. Cramer's V was used for strength of association. All analyses were 2-sided and performed using SAS version 9.4 (SAS Institute). P values less than .05 were deemed statistically significant.

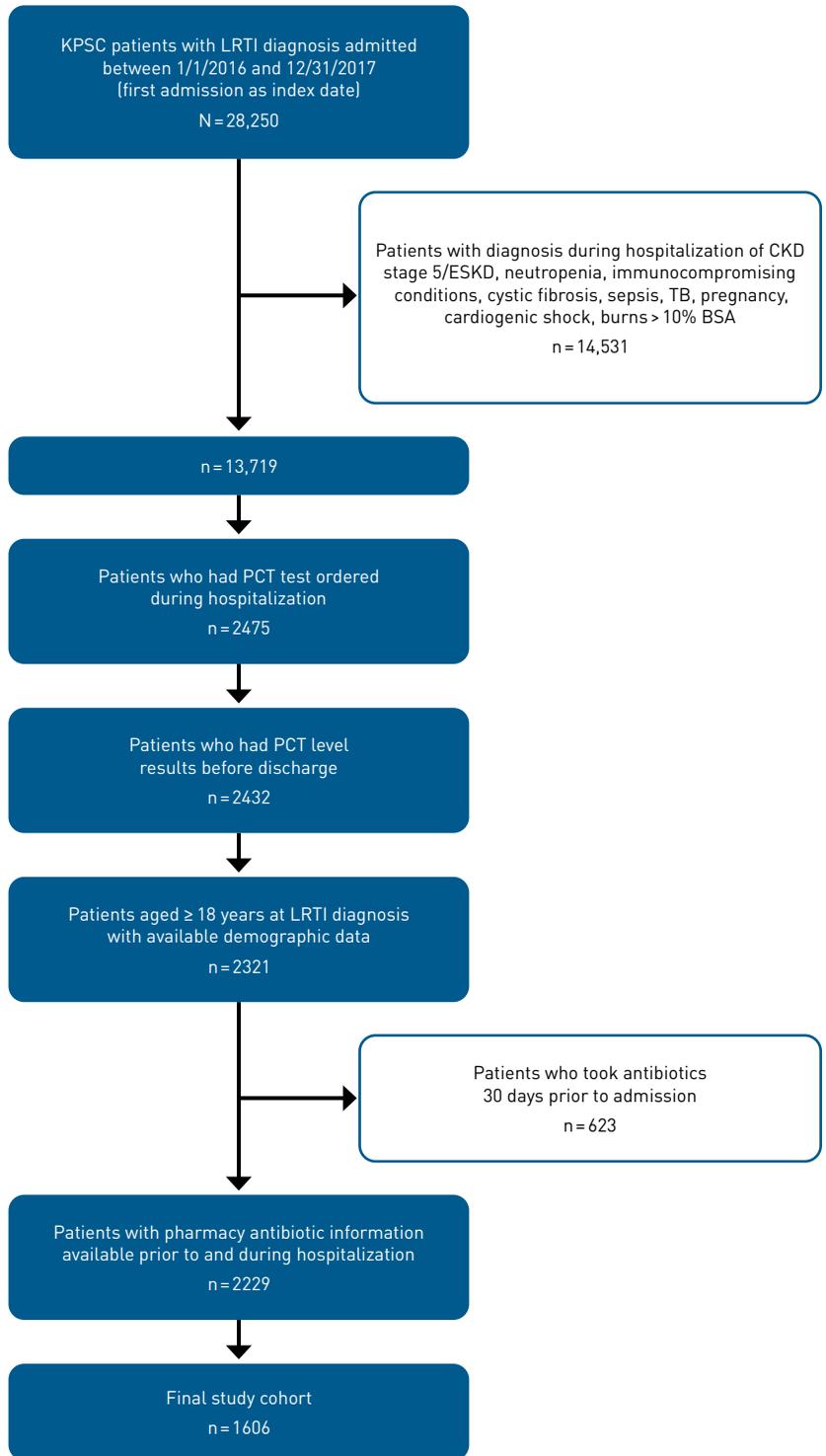
**RESULTS**

**Study Population**

A total of 28,250 patients admitted with a diagnosis of LRTI between January 1, 2016, and December 31, 2017, were identified. After exclusion due to comorbidities, only 2475 (18%) of 14,719 patients had PCT levels tested during the hospitalization. Among this population, a total of 1606 patients met inclusion criteria for our study (Figure). The mean (SD) age of the cohort was 73.0 (15.05) years and 50.2% were male. White, Hispanic, Black, and Asian patients and those of other races/ethnicities comprised 56.5%, 22.2%, 10.1%, 9.0%, and 2.2% of the study population, respectively. With respect to type of respiratory infection, most patients had a diagnosis of pneumonia (76.5%), followed by influenza (11.5%), AECOPD (11.5%), acute bronchitis (0.4%), and other unspecified acute LRTI (0.4%). The mean CCI score was 3.9 and mean length of hospital stay was 9.3 days (Table 1).

Among the study population, 63.4% of patients had a low PCT level and 36.6% had a high PCT level. The mean CCI score was higher in patients with high PCT levels than in patients with low PCT levels (4.3 vs 3.8;  $P < .0001$ ). Length of stay was longer in patients with high PCT levels compared with patients with low PCT levels (9.5 vs 9.2 days;  $P = .0014$ ).

**FIGURE. Study Population\***



BSA, body surface area; CKD, chronic kidney disease; ESKD, end-stage kidney disease; KPSC, Kaiser Permanente Southern California; LRTI, lower respiratory tract infection; PCT, procalcitonin; TB, tuberculosis.

\*A total of 28,250 patients admitted with a diagnosis of LRTI were identified. After 15,154 patients were excluded based on exclusion criteria, a total of 1606 patients were included in our study population.

## CLINICAL

**TABLE 1.** Characteristics of KPSC Patients With Acute LRTI Diagnoses Admitted Between 1/1/2016 and 12/31/2017 Categorized by PCT Level

Characteristic	PCT Level		Total (N = 1606)	P
	< 0.25 mcg/L (n = 1019)	≥ 0.25 mcg/L (n = 587)		
Age in years				.1150 <sup>a</sup>
Mean (SD)	73.4 (14.91)	72.2 (15.26)	73.0 (15.05)	
Median	75.0	75.0	75.0	
Q1, Q3	65.0, 85.0	63.0, 84.0	64.0, 84.0	
Range	19.0-104.0	21.0-104.0	19.0-104.0	
Gender, n (%)				.0114 <sup>b</sup>
Female	532 (52.2%)	268 (45.7%)	800 (49.8%)	
Male	487 (47.8%)	319 (54.3%)	806 (50.2%)	
Race/ethnicity, n (%)				.0608 <sup>b</sup>
White	601 (59%)	306 (52.1%)	907 (56.5%)	
Hispanic	212 (20.8%)	144 (24.5%)	356 (22.2%)	
Black	93 (9.1%)	69 (11.8%)	162 (10.1%)	
Asian	88 (8.6%)	57 (9.7%)	145 (9.0%)	
Other/unknown	25 (2.5%)	11 (1.9%)	36 (2.2%)	
CCI score				.0028 <sup>a</sup>
Mean (SD)	3.8 (2.68)	4.3 (3.05)	3.9 (2.83)	
Median	3.0	4.0	4.0	
Q1, Q3	2.0, 6.0	2.0, 6.0	2.0, 6.0	
Range	0.0-15.0	0.0-17.0	0.0-17.0	
CCI score categories, n (%)				.0064 <sup>b</sup>
0	115 (11.3%)	76 (12.9%)	191 (11.9%)	
1-2	269 (26.4%)	114 (19.4%)	383 (23.8%)	
≥ 3	635 (62.3%)	397 (67.6%)	1032 (64.3%)	
Type of LRTI, n (%)				<.0001 <sup>c</sup>
Acute bronchitis	7 (0.7%)	0 (0%)	7 (0.4%)	
Acute exacerbation of COPD	157 (15.4%)	27 (4.6%)	184 (11.5%)	
Influenza	131 (12.9%)	55 (9.4%)	186 (11.6%)	
Pneumonia	723 (71%)	505 (86%)	1228 (76.5%)	
Other unspecified acute LRTI	1 (0.1%)	0 (0%)	1 (0.1%)	
Length of hospital stay in days				.0014 <sup>a</sup>
Mean (SD)	9.2 (10.67)	9.5 (8.20)	9.3 (9.84)	
Median	6.0	7.0	6.0	
Q1, Q3	4.0, 10.0	4.0, 11.0	4.0, 10.0	
Range	2.0-131.0	2.0-65.0	2.0-131.0	
30-day mortality, n (%)				<.0001 <sup>b</sup>
No	938 (92.1)	485 (82.6)	1423 (88.6)	
Yes	81 (7.9)	102 (17.4)	183 (11.4)	
PCT level in mcg/L				<.0001 <sup>a</sup>
Mean (SD)	0.1 (0.06)	2.5 (5.99)	1.0 (3.80)	
Median	0.1	0.7	0.1	
Q1, Q3	0.0, 0.1	0.4, 1.8	0.0, 0.4	
Range	0.0-0.2	0.3-59.7	0.0-59.7	

CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; KPSC, Kaiser Permanente Southern California; LRTI, lower respiratory tract infection; PCT, procalcitonin; Q, quartile.

<sup>a</sup>Kruskal Wallis test.

<sup>b</sup>Chi-square test.

<sup>c</sup>Fisher's exact test.

(Table 1). Only 242 (15%) patients had serial PCT levels measured during hospitalization.

### Rates of Discordance

The overall antibiotic discordance rate was 45%. Among the discordant population, 77% of discordance occurred in patients receiving antibiotics in the setting of a low PCT level compared with 23% in the withholding of antibiotics at a high PCT level (Table 2). The patients who received antibiotics discordant to PCT had a lower mean PCT level of 0.7 mcg/L compared with those who received antibiotics concordant to PCT (1.2 mcg/L) (Table 3). Characteristics of the discordant population based on PCT are shown in Table 4.

There were no differences in age, sex, race/ethnicity, CCI score, ICU admission, or type of respiratory diagnosis between the patients receiving PCT-discordant and PCT-concordant care.

Additional sensitivity analysis using the B.R.A.H.M.S. PCT assay cutoff values revealed that concordance rates were 41%, 70%, 47%, and 73% for PCT values of less than 0.1, 0.1 to 0.25, 0.25 to 0.5, and greater than 0.5 mcg/L, respectively (eAppendix Table 3).

### Outcomes

Patients in the discordant group had a longer mean length of hospital stay than those who received antibiotics concordant with PCT levels (10.4 days vs 8.4 days;  $P < .0005$ ). The 30-day mortality rate was 10.4% in the concordant population compared with 12.5% in the discordant population ( $P = .1856$ ) (Table 3).

## DISCUSSION

In this study of adult patients hospitalized with acute LRTI, we observed a PCT testing rate of only 18%. Among those who had PCT level results, we found an overall high rate of discordance (45%) between antibiotic prescriptions and initial PCT levels. Thus, only about 9% to 10% of overall hospitalized patients with acute LRTI would have been managed concordantly with their PCT values. Our findings from a real-world environment suggest that clinicians did not routinely order PCT tests. Even when PCT levels were obtained, clinical judgment appeared to supersede what was suggested

by initial PCT levels when antibiotics were prescribed in patients with suspected LRTI. Our findings may indicate that there may be opportunities to improve antibiotic stewardship in patients who are less ill by greater adoption of a PCT-based approach.

The majority of discordance observed in our study occurred among patients with low PCT (77%) compared with those with high PCT (23%). This was further captured by our noting that patients who received discordant antibiotics had a lower mean PCT value (0.7 mcg/L) vs patients who received concordant antibiotics (1.2 mcg/L). Taken together, our findings suggest that providers were more likely to continue antibiotics with a high PCT level than to discontinue antibiotics when there was a low PCT level.

**Limitations and Strengths**

Our study has several potential limitations that may confound the interpretation of our findings. First, antibiotic changes were assessed within the time period of up to 36 hours after the PCT level results. During this time period, there may have been a variety of other factors leading to a change in antibiotic use during the hospitalization, and therefore we cannot fully account for PCT level as the sole factor driving antibiotic prescription patterns. Secondly, our study was limited to inpatient hospitalizations only; thus, we cannot generalize our findings to outpatient use of PCT. Patients treated in concordance with their PCT values had fewer hospitalization days and a trend for lower mortality. This is likely more reflective of the fact that the discordant population was sicker and that clinical judgment superseded PCT results, leading to more antibiotic use. Another important consideration is the impact from the heterogeneity in management strategies based on the different decisions of individual providers. We did not have specific information on the characteristics of the providers who ordered PCT testing and made decisions on antibiotics. Only 242 patients (15%) had a serial measurement in our study population, suggesting that PCT testing may not be ordered in the manner that would have the best utility for interpretation and implementation. Lastly, it should be noted that our study cohort and observation window did not include patients with an LRTI caused by SARS-CoV-2.

**TABLE 2.** Concordant and Discordant Antibiotic Use Stratified by Low vs High PCT Level

Antibiotic use	PCT level		Total
	<0.25 mcg/L	≥ 0.25 mcg/L	
Concordant			
n (%)	461 (52.3%)	420 (47.7%)	881 (100%)
Discordant			
n (%)	558 (77.0%)	167 (23.0%)	725 (100%)

PCT, procalcitonin.

**TABLE 3.** Characteristics of Patients by Concordant and Discordant Antibiotic Use

Characteristic	Concordant (n = 881)	Discordant (n = 725)	Total (N = 1606)	P
Age in years				.2478 <sup>a</sup>
Mean (SD)	73.4 (14.82)	72.5 (15.31)	73.0 (15.05)	
Median	76.0	75.0	75.0	
Q1, Q3	65.0, 85.0	64.0, 84.0	64.0, 84.0	
Range	19.0-104.0	21.0-104.0	19.0-104.0	
Sex, n (%)				.3230 <sup>b</sup>
Female	429 (48.7%)	371 (51.2%)	800 (49.8%)	
Male	452 (51.3%)	354 (48.8%)	806 (50.2%)	
Race/ethnicity, n (%)				.5316 <sup>b</sup>
Asian	79 (9%)	66 (9.1%)	145 (9%)	
Black	99 (11.2%)	63 (8.7%)	162 (10.1%)	
Hispanic	197 (22.4%)	159 (21.9%)	356 (22.2%)	
Other/unknown	19 (2.2%)	17 (2.3%)	36 (2.2%)	
White	487 (55.3%)	420 (57.9%)	907 (56.5%)	
CCI score				.0048 <sup>a</sup>
Mean (SD)	4.1 (2.90)	3.7 (2.72)	3.9 (2.83)	
Median	4.0	3.0	4.0	
Q1, Q3	2.0, 6.0	2.0, 6.0	2.0, 6.0	
Range	0.0-17.0	0.0-15.0	0.0-17.0	
CCI score categories, n (%)				.1416 <sup>b</sup>
0	99 (11.2%)	92 (12.7%)	191 (11.9%)	
1-2	197 (22.4%)	186 (25.7%)	383 (23.8%)	
≥ 3	585 (66.4%)	447 (61.7%)	1032 (64.3%)	
Length of hospital stay in days				.0005 <sup>a</sup>
Mean (SD)	8.4 (7.47)	10.4 (12.02)	9.3 (9.84)	
Median	6.0	6.0	6.0	
Q1, Q3	4.0, 10.0	4.0, 11.0	4.0, 10.0	
Range	2.0-65.0	2.0-131.0	2.0-131.0	
30-day mortality, n (%)				.1856 <sup>b</sup>
No	789 (89.6)	634 (87.5)	1423 (88.6)	
Yes	92 (10.4)	91 (12.5)	183 (11.4)	
PCT level in mcg/L				<.0001 <sup>a</sup>
Mean (SD)	1.2 (3.89)	0.7 (3.67)	1.0 (3.80)	
Median	0.2	0.1	0.1	
Q1, Q3	0.1, 0.7	0.0, 0.2	0.0, 0.4	
Range	0.0-48.0	0.0-59.7	0.0-59.7	

(continued)

## CLINICAL

**TABLE 3.** (Continued) Characteristics of Patients by Concordant and Discordant Antibiotic Use

Characteristic	Concordant (n = 881)	Discordant (n = 725)	Total (N = 1606)	P
ICU, n (%)				.9393 <sup>b</sup>
No	751 (85.2%)	619 (85.4%)	1370 (85.3%)	
Yes	130 (14.8%)	106 (14.6%)	236 (14.7%)	
Type of LRTI, n (%)				.2386 <sup>b</sup>
Acute bronchitis	5 (0.6%)	2 (0.3%)	7 (0.4%)	
Acute exacerbation of COPD	91 (10.3%)	93 (12.8%)	184 (11.5%)	
Influenza	111 (12.6%)	75 (10.3%)	186 (11.6%)	
Other unspecified acute LRTI	1 (0.1%)	0 (0%)	1 (0.1%)	
Pneumonia	673 (76.4%)	555 (76.6%)	1228 (76.5%)	

CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; LRTI, lower respiratory tract infection; PCT, procalcitonin; Q, quartile.

<sup>a</sup>Kruskal-Wallis test.

<sup>b</sup>Chi-square test.

**TABLE 4.** Characteristics of Discordant Population Based on PCT Levels

Discordant population	PCT level		Total (n = 725)	P
	<0.25 mcg/L (n = 558)	≥0.25 mcg/L (n = 167)		
Age in years				.2391 <sup>a</sup>
Mean (SD)	72.7 (15.66)	71.9 (14.10)	72.5 (15.31)	
Median	75.0	73.0	75.0	
Q1, Q3	65.0, 84.0	63.0, 84.0	64.0, 84.0	
Range	21.0-104.0	33.0-96.0	21.0-104.0	
Sex, n (%)				.0951 <sup>b</sup>
Female	295 (52.9%)	76 (45.5%)	371 (51.2%)	
Male	263 (47.1%)	91 (54.5%)	354 (48.8%)	
Race/ethnicity, n (%)				.0951 <sup>b</sup>
White	326 (58.4%)	94 (56.3%)	420 (57.9%)	
Asian	54 (9.7%)	12 (7.2%)	66 (9.1%)	
Black	54 (9.7%)	9 (5.4%)	63 (8.7%)	
Hispanic	112 (20.1%)	47 (28.1%)	159 (21.9%)	
Other/unknown	12 (2.2%)	5 (3%)	17 (2.3%)	
CCI score				.1203 <sup>a</sup>
Mean (SD)	3.6 (2.61)	4.1 (3.04)	3.7 (2.72)	
Median	3.0	4.0	3.0	
Q1, Q3	2.0, 5.0	1.0, 6.0	2.0, 6.0	
Range	0.0-15.0	0.0-13.0	0.0-15.0	
CCI score categories, n (%)				.0213 <sup>b</sup>
0	65 (11.6%)	27 (16.2%)	92 (12.7%)	
1-2	156 (28%)	30 (18%)	186 (25.7%)	
≥3	337 (60.4%)	110 (65.9%)	447 (61.7%)	
Length of hospital stay in days				<.0001 <sup>a</sup>
Mean (SD)	12.0 (13.17)	5.1 (3.54)	10.4 (12.02)	
Median	7.0	4.0	6.0	
Q1, Q3	5.0, 13.0	3.0, 6.0	4.0, 11.0	
Range	3.0-131.0	2.0-27.0	2.0-131.0	

(continued)

Despite these limitations, our study includes one of the largest diverse populations examining the relationship between initial PCT level and antibiotic prescribing behavior in LRTIs within a real-world clinical environment. Findings from our study showed that initial PCT level did not significantly alter antibiotic prescribing practices in patients with acute LRTI and there was a paucity of serial PCT values taken during admission to potentially aid in antibiotic guidance in LRTIs. Notably, this study was performed prior to the updated 2019 Clinical Practice Guidelines of the American Thoracic Society and Infectious Diseases Society of America on the diagnosis and management of community-acquired pneumonia. These guidelines state that clinical judgment alone should be used to guide the use of empiric antibiotic therapy regardless of initial PCT level in adults with suspected community-acquired pneumonia.<sup>29</sup> Given these guidelines, and our study noting that initial PCT level did not alter prescribing behavior, clinicians should reevaluate ordering a *single* PCT measurement to delineate between bacterial and viral LRTIs. Rather, using serial PCT levels to guide antibiotic use in LRTIs may be of more utility in guiding antibiotic use than a single level, but further studies are needed.

## Conclusions

Our findings from a large diverse population in the United States demonstrate that the rate of PCT testing in hospitalized patients with LRTI is only 18%. Among those who were tested, the initial PCT levels did not significantly alter antibiotic prescribing practices, suggesting that providers were relying more on clinical judgment to guide empiric antibiotic therapy rather than initial PCT level. Our study findings highlight a potential opportunity to improve antibiotic stewardship and patient care with better utilization of a PCT-based approach for patients hospitalized with LRTI in real-world clinical practice. ■

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**TABLE 4.** (Continued) Characteristics of Discordant Population Based on PCT Levels

Discordant population	PCT level		Total (n = 725)	P
	<0.25 mcg/L (n = 558)	≥ 0.25 mcg/L (n = 167)		
30-day mortality, n (%)				<.0001 <sup>b</sup>
No	504 (90.3%)	130 (77.8%)	634 (87.4%)	
Yes	54 (9.7%)	37 (22.2%)	91 (12.6%)	
PCT level in mcg/L				<.0001 <sup>a</sup>
Mean (SD)	0.1 (0.06)	2.7 (7.31)	0.7 (3.67)	
Median	0.1	0.6	0.1	
Q1, Q3	0.0, 0.1	0.4, 1.9	0.0, 0.2	
Range	0.0-0.2	0.3-59.7	0.0-59.7	
ICU, n (%)				.0641 <sup>b</sup>
No	469 (84.1%)	150 (89.8%)	619 (85.4%)	
Yes	89 (15.9%)	17 (10.2%)	106 (14.6%)	
Type of LRTI, n (%)				.0700
Acute bronchitis	2 (0.4%)	0 (0%)	2 (0.3%)	
Acute exacerbation of COPD	81 (14.5%)	12 (7.2%)	93 (12.8%)	
Influenza	55 (9.9%)	20 (12%)	75 (10.3%)	
Other unspecified acute LRTI	0 (0%)	0 (0%)	0 (0%)	
Pneumonia	420 (75.3%)	135 (80.8%)	555 (76.6%)	

CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; LRTI, lower respiratory tract infection; PCT, procalcitonin; Q, quartile.

<sup>a</sup>Kruskal-Wallis test.

<sup>b</sup>Chi-square test.

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**eAppendix Table 1.** ICD-10 codes used to identify pneumonia, acute bronchitis, AECOPD, and influenza

<b>Pneumonia</b>	
<b>Diagnosis</b>	<b>Code</b>
Bacterial pneumonia, not elsewhere classified (includes bronchopneumonia due to bacteria other than <i>S. pneumonia</i> and <i>H. influenza</i> )	J15
Pneumonia due to <i>Hemophilus influenzae</i>	J14
Pneumonia due to other infectious organisms, not elsewhere classified	J16
Pneumonia due to <i>Streptococcus pneumoniae</i>	J13
Pneumonia, unspecified organism	J18
Legionnaire's disease	A48.1
<i>Mycoplasma pneumoniae</i>	B96
Respiratory syncytial virus pneumonia	J12
Ventilator-associated pneumonia	J95.851
<b>Acute bronchitis/AECOPD</b>	
<b>Diagnosis</b>	<b>Code</b>
Acute bronchitis	J20
Acute bronchiolitis	J21
Chronic obstructive pulmonary disease with (acute) lower respiratory infection	J44.0 and J44.1
<b>Other lower respiratory tract infection codes</b>	
<b>Diagnosis</b>	<b>Code</b>
Unspecified acute lower respiratory infection	J22
<b>Influenza</b>	
<b>Diagnosis</b>	<b>Code</b>
Influenza due to certain identified influenza viruses	J09
Influenza due to other identified influenza virus	J10
Influenza due to unidentified influenza virus	J11

**eAppendix Table 2.** Antibiotics included in analysis. Medication routes only IV, IM, PO.

Amoxicillin
Amoxicillin-clavulanate
Ampicillin (sodium)
Ampicillin-sulbactam
Azithromycin
Aztreonam
Cefazolin
Cefepime
Cefpodoxime
Ceftazidime
Ceftriaxone
Cefuroxime
Cephalexin
Ciprofloxacin
Clarithromycin
Clindamycin
Dicloxacillin
Doxycycline
Ertapenem
Gentamicin
Imipenem-cilastatin
Levofloxacin
Linezolid
Meropenem
Metronidazole
Moxifloxacin
Nfacillin
Oxacillin
Penicillin G
Piperacillin-tazobactam
Polymyxin B sulf-trimethoprim
Trimethoprim-sulfamethoxazole
Vancomycin

**eAppendix Table 3.** Characteristics of KPSC patients with ARI diagnosis admitted between 1/1/2016 and 12/31/2017

PCT level						
	<0.1 (N=698)	0.1-0.25 (N=321)	0.25-0.5 (N=225)	>0.5 (N=362)	Total (N=1606)	p-value
<b>Age</b>						0.2225 <sup>1</sup>
Mean (SD)	73.3 (15.43)	73.8 (13.75)	73.6 (14.05)	71.3 (15.92)	73.0 (15.05)	
Median	76.0	75.0	76.0	73.5	75.0	
Q1, Q3	66.0, 84.0	64.0, 85.0	66.0, 83.0	61.0, 84.0	64.0, 84.0	
Range	(19.0-103.0)	(30.0-104.0)	(21.0-101.0)	(22.0-104.0)	(19.0-104.0)	
<b>Gender</b>						0.0123 <sup>2</sup>
F	378 (54.2%)	154 (48%)	109 (48.4%)	159 (43.9%)	800 (49.8%)	
M	320 (45.8%)	167 (52%)	116 (51.6%)	203 (56.1%)	806 (50.2%)	
<b>Race/Ethnicity</b>						0.2073 <sup>2</sup>
White	419 (60%)	182 (56.7%)	123 (54.7%)	183 (50.6%)	907 (56.5%)	
Black	69 (9.9%)	24 (7.5%)	27 (12%)	42 (11.6%)	162 (10.1%)	
Hispanic	139 (19.9%)	73 (22.7%)	48 (21.3%)	96 (26.5%)	356 (22.2%)	
Asian	56 (8%)	32 (10%)	22 (9.8%)	35 (9.7%)	145 (9%)	
Other/Unknown	15 (2.1%)	10 (3.1%)	5 (2.2%)	6 (1.7%)	36 (2.2%)	
<b>Charlson Comorbidities Score</b>						0.0226 <sup>2</sup>
0	82 (11.7%)	33 (10.3%)	33 (14.7%)	43 (11.9%)	191 (11.9%)	
1-2	192 (27.5%)	77 (24%)	48 (21.3%)	66 (18.2%)	383 (23.8%)	
3+	424 (60.7%)	211 (65.7%)	144 (64%)	253 (69.9%)	1032 (64.3%)	
Mean (SD)	3.6 (2.66)	4.1 (2.71)	4.2 (3.21)	4.3 (2.94)	3.9 (2.83)	
Median	3.0	4.0	4.0	4.0	4.0	
Q1, Q3	2.0, 5.0	2.0, 6.0	2.0, 6.0	2.0, 6.0	2.0, 6.0	
Range	(0.0-15.0)	(0.0-13.0)	(0.0-17.0)	(0.0-14.0)	(0.0-17.0)	
<b>Year of ARI diagnosis</b>						0.6768 <sup>2</sup>
2016	363 (52%)	157 (48.9%)	110 (48.9%)	177 (48.9%)	807 (50.2%)	
2017	335 (48%)	164 (51.1%)	115 (51.1%)	185 (51.1%)	799 (49.8%)	
<b>Length of stay in day</b>						0.0022 <sup>1</sup>
Mean (SD)	8.9 (9.91)	9.9 (12.15)	9.6 (8.20)	9.4 (8.21)	9.3 (9.84)	
Median	6.0	6.0	7.0	6.0	6.0	
Q1, Q3	4.0, 9.0	4.0, 11.0	5.0, 12.0	4.0, 11.0	4.0, 10.0	
Range	(2.0-101.0)	(2.0-131.0)	(2.0-65.0)	(2.0-57.0)	(2.0-131.0)	
<b>PCT</b>						<0.0001 <sup>1</sup>

Mean (SD)	0.04(0.02)	0.2 (0.04)	0.4 (0.08)	3.8 (7.32)	1.0 (3.80)	
Median	0.04	0.2	0.4	1.3	0.13	
Q1, Q3	0.04, 0.1	0.1, 0.2	0.3, 0.4	0.8, 3.3	0.04, 0.4	
Range	(0.04-0.1)	(0.1-0.2)	(0.3-0.5)	(0.5-59.7)	(0.04-59.7)	
Concordance with PCT (%)	41	70	47	73	55	

<sup>1</sup> Kruskal Wallis <sup>2</sup>Chi-Square