Title

Prevalence of Discordant Procalcitonin Use at an Academic Medical Center

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Authors

Seymann, Gregory B

Bevins, Nicholas

Wu, Christina

et al.

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Title Page

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ABSTRACT

Objectives: Despite multiple trials demonstrating procalcitonin is an effective tool for antibiotic stewardship, , inconsistent application in real-world settings continues to fuel controversy regarding its clinical utility . We sought to determine rates of concordance between procalcitonin results and antibiotic prescribing in hospitalized patients.

Methods: We performed a retrospective review of all inpatient encounters at an academic tertiary care health system with a procalcitonin result between February 2017 and October 2019. Concordant prescribing was defined as starting or continuing antibiotics following an elevated procalcitonin (>0.5 ng/ml), and withholding or stopping antibiotics following a low procalcitonin (< 0.1 ng/ml).

Results: Antibiotic prescribing decisions were discordant from the procalcitonin level in 32.5% of our sample. Among patients not receiving antibiotics at the time of testing, 25.9% (430 of 1662) were prescribed antibiotics despite a low procalcitonin. Among patients already on antibiotics, treatment was continued despite a low procalcitonin in 80.4% (728 of 906) of cases. Enhanced decision support tools introduced during the study period had no impact on procalcitonin utilization for antibiotic decisions.

Conclusions: Overall concordance between procalcitonin results and antibiotic use is relatively low in a real-world setting. The potential value of procalcitonin for antibiotic stewardship may not be fully realized.

KEY POINTS

Question: How often do providers who order procalcitonin assays use the result for antibiotic stewardship?

Findings: In this single-center review of 9,385 encounters encompassing 15,229 procalcitonin assays performed at a tertiary-care university health system, 32.5% of the antibiotic decisions were not aligned with the procalcitonin value. Passive clinical decision support interventions were not effective in changing behavior.

Meaning: Given the frequency with which providers ignored the test result, targeting overutilization of procalcitonin represents an opportunity to improve high-value laboratory utilization. More rational clinical testing may strengthen its impact as a tool for stewardship.

INTRODUCTION

The Centers for Disease Control estimates that 30% of antibiotic prescriptions in US hospitals are inappropriate or altogether unnecessary;[1,2] such overprescribing contributes to increasing rates of multidrug resistant bacterial and *Clostridioides difficile* infections. Antibiotic stewardship programs are currently required for hospital accreditation by The Joint Commission.

Procalcitonin (PCT) is a biomarker that has been shown in multiple studies to be a safe and effective tool to reduce antibiotic exposure in patients with respiratory infections and sepsis.[3,4] In 2017 the Federal Drug Administration approved its use to guide antibiotic stewardship efforts in patients with these conditions.[5]

Although PCT usage has steadily increased,[6] professional societies have been cautious about supporting its use.[7] In addition, several high-profile clinical trials concluded that PCT-guided protocols did not effectively reduce antibiotic duration.[8–10] Despite methodologic weaknesses limiting the generalizability of these studies,[11,12] acceptance of PCT as a tool for antibiotic stewardship remains controversial.

The most well-established protocols recommend withholding antibiotics for patients with low PCT values[11] barring overriding clinical concerns. Major barriers to assessing the effectiveness of PCT-guided antibiotic stewardship involve a failure to apply the PCT result to clinical decision making; in the trials noted above, deviation from the study protocol for antibiotic prescribing was as high as 60%.[8] Clearly, it is difficult to demonstrate efficacy of PCT guided antibiotic stewardship when prescribing decisions are so frequently discordant. The American Society for Clinical Pathology underscores this concern with its "Choosing Wisely" recommendation to avoid performing procalcitonin testing without an established, evidence-based protocol.[13] They note "procalcitonin is often either misused (i.e. not used in the appropriate setting) or established algorithms are not followed," and call on local leaders to create clinical guidelines and monitor use.

To inform such improvement efforts, we aimed to define and quantify the prevalence of low-value PCT testing in a real-world practice setting by assessing the extent to which antibiotic prescribing behavior correlated with the test result.

METHODS

We performed a retrospective analysis of all adults admitted to our large University teaching hospitals between February 2017 and October 2019 who had at least 1 PCT assay performed. Data was extracted from the electronic medical record using an automated query. Antibiotic start and stop times used to calculate duration of therapy were based on time-stamped entries recorded on the Medication Administration Record (MAR). We excluded antibiotics which do not primarily target systemic bacterial infections (i.e. antiprotozoal agents, antimycobacterial agents), antibiotics specifically targeting C. difficile (oral vancomycin, fidaxamicin, but NOT oral flagyl), antibiotics administered by routes other than oral or intravenous (i.e. inhaled, topical or ocular), and antibiotics used specifically as part of a desensitization protocol.

Procalcitonin was measured using the Elecsys BRAHMS PCT assay on e-601 or e-602 COBAS analyzers (Roche Diagnostics, Indianapolis, IN, USA). The validated analytical measurement range was 0.02-100 ng/mL and the clinical reportable range was 0.02 – 400 ng/mL.

Procalcitonin values were categorized into 4 quartiles to correspond with the majority of published protocols for procalcitonin-guided antibiotic therapy[12] as follows: > 0.5 ng/ml = high, 0.25 – 0.5 ng/ml = intermediate high, 0.1 – 0.24 ng/ml = intermediate low, < 0.1 ng/ml low. The PCT value was compared with antibiotic use patterns, and antibiotic use was classified as concordant or discordant with the PCT.

Antibiotic start or stop timing relative to the PCT value was calculated by subtracting the PCT result posting time from the administration or discontinuation time of any antibiotic on the MAR. Using this methodology, we stratified all PCT results into 2 separate cohorts to discern the impact of the test. For

PCT results from patients not on antibiotics prior to the PCT result, we defined concordant antibiotic use as patients with a high PCT value started on antibiotics within 24 hours of the result, and discordant use as patients with a low PCT started on antibiotics within 24 hours of the result. Similarly, we evaluated PCT results from patients already on antibiotics at the time of the PCT result; concordant antibiotic use was defined as patients whose antibiotics were stopped within 24 hours of a low PCT value, and discordant use was defined as patients with a high PCT whose antibiotics were stopped within 24 hours of the result.

Given the differing thresholds used for PCT-guided antibiotic stewardship studies in sepsis and lower respiratory infections, we limited our analysis to the most conservative definitions of "high" (>0.5 ng/mL) and "low"(<0.1 ng/mL) when determining concordance between the PCT value and the antibiotic decisionmaking. Intermediate values were excluded from the analysis of concordance.

To estimate cost of PCT, we used the Center for Medicare and Medicaid Services Clinical Lab Fee schedule reimbursement rate as of October 2019, which was $29.77. Although hospital payments are made through the diagnostic related group (DRG) system for inpatients, we felt this surrogate estimate reflected a well recognized standard.

We tracked the impact of various improvements in clinical decision support implemented during the course of the study period on usage patterns. The first intervention involved the clarification of the language available in the detail screen of the EMR that offered evidence-based guidance on cutoff points for antibiotic usage (Figure 2A and 2B). Second, alert flags on the EMR result display that triggered for mildly elevated PCT values were modified with the intent of better aligning alerts to clinically significant abnormalities (Figure 3); alerts characterizing elevated PCT as an "alarm" value (which looked like "!!") were modified to characterize it simply as "elevated" (which looked like "^"). The 3rd event on the timeline connotes the FDA's formal approval of the PCT assay for use as an antimicrobial stewardship tool. Although this was not tied to a specific local intervention, we tracked it as a potential influencer of

clinician behavior. Finally, the 4th intervention involved further clarification of the decision support language contained on the detail screen in the EMR for ease of use (Figure 2C).

Statistical significance testing reports the results of the Chi Squared Test as available in the R programming language with the function 'chisq.test()'. Significance testing was performed by comparing the Start/Hold or Stop/Continue decision within each procalcitonin result segment with the overall distribution of Start/Hold or Stop/Contine decisions, as appropriate. Graphs were created using the ggplot function within the tidyverse package (cran.r-project.org/web/packages/tidyverse).

The project was reviewed and approved by the local Institutional Review Board.

RESULTS

Overview

At least 1 PCT was ordered in 9,385 unique hospital encounters during the study period. Among these encounters, 87.5% (n = 8,215) of patients received an antibiotic during their stay and 82.8% of all patients (n= 7,772) received IV antibiotics. Median duration of treatment with any antibiotics was 4.3 days.

A total of 15,229 PCT were resulted during the study period. Within the study sample, 69% (n=6,429) of patients had only a single PCT checked and 97% (n=9,095) of the samples had 4 or fewer assays. Mean PCT was 3.65 ng/mL, median 0.28 ng/mL, with a range of 0.02- 400 ng/mL. PCT ordering location varied, with 32% of orders initiated in the emergency department, 39% in the critical care units, 24% in medical-surgical wards, and 4.6% in outpatient or other locations. .

Procalcitonin-guided Antibiotic Start

To assess the impact of PCT on antibiotic initiation, we reviewed the subset of 4,510 PCT results from patients not receiving antibiotic therapy at the time of testing. As illustrated in Figure 1A, we defined a discordant antibiotic start as a patient with a PCT < 0.1 administered an antibiotic within 24 hours of the low result. Conversely, discordant antibiotic hold was defined as a patient with a PCT > 0.5 who did not

receive an antibiotic in the 24 hours following the test result. Figure 4A and 4B illustrate discordant antibiotic prescribing rates over time in this population. Overall we found prescribing was discordant from the PCT value 40.1% of the time in this group. Discordant prescribing rates in the setting of low PCT were 25.9%, and discordant withholding of antibiotics in the setting of a high PCT were 55.8%. (Table 1). For patients not already on antibiotics at the time of the PCT assay, antibiotics were withheld from patients with a high PCT (discordant use) more often than they were prescribed to patients with high PCT ($p<0.001$). Our concordant use was better for the low PCT group with a higher proportion of patients with low PCT not being prescribed antibiotics.

Procalcitonin-guided Antibiotic Stop

To assess the impact of PCT on antibiotic stop, we analyzed the subset of PCT results from patients already receiving antibiotics at the time of the PCT result. We assumed that the intent of PCT measurement in this subgroup was to assist with decisions about cessation of therapy. To avoid overcounting errors, we limited our assessment to patients with a single PCT result (n =3,559). As illustrated in Figure 1B, we defined discordant stop as an antibiotic discontinuation within 24 hours of a PCT > 0.5, and a discordant continue as an antibiotic continuation 24 hours following a PCT < 0.1. Rates of discordant prescribing over time in this population are illustrated in Figure 5A and 5B. Decisions to continue antibiotics were discordant from the PCT value 35.3% of the time in this population. Antibiotics were frequently continued despite a low PCT, which was the predominant driver of discordance; 80.4% of patients with a PCT < 0.1 remained on antibiotics (Table 2, top).

Among patients on antibiotics who had multiple PCT results, we assessed whether a reduction of > 80% from peak PCT value drove cessation of antibiotics, consistent with the protocols from large clinical trials.[8,14] Table 2 (bottom) demonstrates that even large decreases in the PCT value rarely led antibiotic discontinuation (4.8%), with 90.5% of patients with a PCT < 0.1 OR > 80% reduction from peak remaining on antibiotics. Overall discordance rates in this group were 28% ([1,516+500]/7,161).

Systems Improvement Initiatives

Timing of the various systems improvement initiatives is noted on the trendlines for discordant use in Figures 4 and 5. Event 1 corresponds to the addition of specific cutoff values for antibiotic use to the detail screen for the PCT result in the EMR (Figure 2B). Event 2 was the modification of the alert flags for mildly elevated PCT values (Figure 3). Event 3 correlated with the FDA approval of the PCT test for antibiotic stewardship, and Event 4 involved further clarification of the decision support language on the EMR result screen (Figure 2C). No appreciable change in ordering or prescribing patterns was evident following any of the 4 interventions.

Financial Impact

Based on a Center for Medicare and Medicaid Services (CMS) reimbursement rate of $29.77 per result, estimated spending on the 15,229 PCT tests during the 2.5-year study period was $453,367.33. 32.5% of those assays were discordant with antibiotic prescribing behavior, indicating low-value expenditures of $47,344.38

For patients with a single PCT tested during the encounter and a result of < 0.1 ng/mL we found the median duration of discordant antibiotic usage to be 2.3 days. We did not assess the additional cost of care (e.g. hospital stay, antibiotic cost) or clinical risk (e.g. development of active *Clostridioides difficile* infection) for patients started on antibiotics despite a low PCT.

DISCUSSION

Although relatively straightforward guidelines exist around which conditions (lower respiratory tract infections, sepsis) and parameters are most appropriate for PCT-guided antibiotic stewardship,[15] our study suggests that despite high rates of testing, prescribing decisions were often inconsistent with the PCT results. These findings suggest test overutilization.

Antibiotic prescribing behavior was discordant from the PCT result 32.5% of the time at our academic medical center, representing > 7000 tests during the 2.5 year study period. Despite the fact that the current literature argues most strongly for the use of PCT as a tool to move us toward evidence-based rather than arbitrary antibiotic durations,[16–19] we found clinicians in our study rarely stopped antibiotics after a low PCT. A different pattern of discordance was observed for patients not on antibiotics prior to PCT testing; in that cohort, antibiotics were frequently withheld despite an elevated value. Both scenarios demonstrate clinical inertia; in other words, the existing treatment plan was not modified in the face of additional data. Although we were not able to assess the clinical factors driving prescribing decisions in this retrospective review, opportunities to reduce testing seem to exist.

Noncompliance with PCT guided antibiotic protocols is not unique to our study. In the largest US study to date,[8] providers deviated from the protocol to guide antibiotic decision making 60% of the time. Other studies found similar prescribing patterns; in the PRORATA study of patients with sepsis requiring ICU care, adherence was 40%,[20] and 55% in the similarly designed SAPS trial.[21] The HiTEMP study of ED patients with fever reported protocol noncompliance 44% of the time.[9] Clinicians will have fewer opportunities to build a positive clinical experience with PCT-guided antibiotic stewardship with such high rates of deviation.

Various factors impact appropriate testing practices. In our study, despite attempts to address any knowledge barriers by improving the quality and accessibility of real-time decision support, prescribing behavior remained static. This suggests cultural barriers to adopting shorter course antibiotic therapy exist, and despite mounting evidence to support it,[18] provider comfort levels with short-course therapy are low. The highest impact interventions have involved active management and oversight by dedicated pharmacists in addition to well-defined, evidence-based protocols.[22]

Our study was not designed to determine whether or not antibiotic prescribing behavior discordant to the PCT value was clinically appropriate in each individual case, however it is clear that if the results of the

PCT assay are disregarded almost half the time, opportunities to apply the assay to a more targeted patient population exist. Conservative estimates of potential waste in laboratory costs alone were greater than $200,000 over the 2-year study. Additional drug costs incurred by any excess antibiotic use, and associated antibiotic adverse effects were not assessed, implying that the potential cost implications are much greater.

LIMITATIONS

Our study had several limitations. The single-center design impacts the generalizability of our results to other settings, though similarly low adherence to PCT-guided antibiotic prescribing protocols has been demonstrated elsewhere.[8,20,21] As a large retrospective database review, we were unable to assess whether or not individual antibiotic decisions were clinically appropriate; thus, we opted to characterize prescribing behavior as concordant or discordant with the PCT value, rather than as appropriate or inappropriate. Our findings speak more to overuse of the laboratory than to antibiotic misuse.

Furthermore, our definitions of concordance did not distinguish between evidence-based use of PCT (i.e. for sepsis and lower respiratory tract infections) and PCT ordered for conditions with weaker clinical indications (e.g., urinary tract infections, cellulitis). Hence, the prevelance of discordant use is likely an underestimate.

Finally, our design does not offer insight into the reasons for such widespread discordance between testing and clinical prescribing behavior. Some speculative reasons include differences between the ordering provider and the provider empowered to act on the test, as in when the emergency department obtains a PCT assay which the admitting team may not find clinically useful. Lack of comfort with shorter course antibiotic therapy, clinical inertia around antibiotic de-escalation, confusion about appropriate PCT cutoff levels, and conflicting opinions about the utility of PCT in the current literature may all be contributors. Further investigation of the root causes is warranted.

The conservative cutoffs for antibiotic prescribing we used in this study likely led us to underestimate the true prevalence of low-value PCT use at our institution. For many patients, a PCT threshold of 0.25 ng/mL would be a clinically appropriate cutpoint.

CONCLUSIONS

Effective use of the laboratory in clinical practice involves an empiric assessment of the probability of a given condition. When clinical uncertainty exists, additional information from a test may influence the decision by increasing or decreasing the likelihood of the condition in question. If the results of the test are not likely to alter the probability sufficiently to change the clinical decision, then testing is felt to be superfluous.[23] Creating a culture change that includes PCT guided antibiotic stewardship will be challenging if clinician experience with the assay is predominantly driven by inappropriate use.

Nonetheless, efforts to improve antibiotic stewardship remain pressing. It may be difficult to truly grasp the potential impact of PCT-guided therapy as a tool until its use is more consistently applied. We view the findings of this and other studies as an opportunity to shift the research agenda toward improving test utilization, rather than a call to abandon the assay altogether.

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Table 1

	Antibiotic Decision				
	Start	Hold	SUM**	% discordant	p value*
High (>0.5 ng/mL)	668[C]	844[D]	1,512	55.8	<0.0001
Indeterminate	477	859	1,336	N/A	N/A
Low (< 0.1 ng/mL)	430[D]	1,232[C]	1,662	25.9	<0.0001
Total	1,575	2,935	4,510	N/A	N/A

Table 1. Rate of antibiotic decisions concordant with initial PCT value for hospitalized patients not on antibiotics prior to PCT assay.
[C]Concordant: PCT elevated and antibiotic started OR PCT low and antibiotic withheld
[D]Discordant: PCT low and antibiotic started OR PCT elevated and antibiotic withheld
*Chi-square test with antibiotic decision for all PCT results (ie row labeled 'Total')

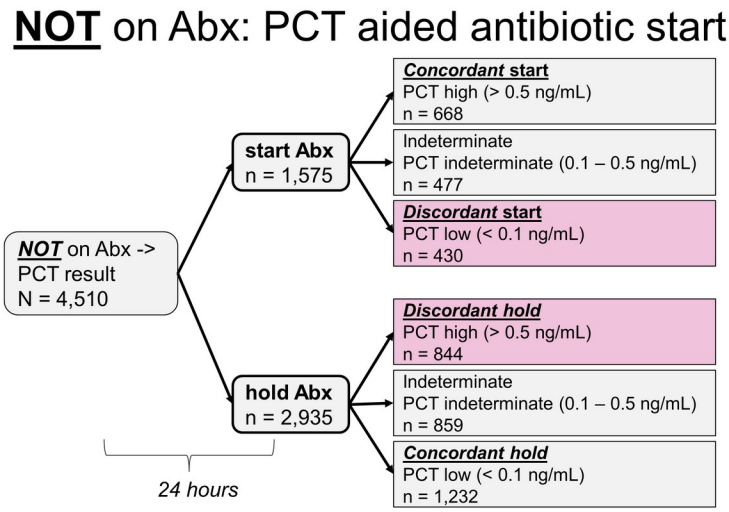
Table 2

Single PCT result during encounter					
	Antibiotic Decision				
	Continue	Stop	SUM**	% discordant	p value*
High (>0.5 ng/mL)	1,503[C]	188[D]	1,691	11.1	<0.0001
Indeterminate	815	146	961	N/A	N/A
Low (< 0.1 ng/mL)	728[D]	178[C]	906	80.4	<0.0001
Subtotal	3,046	512	3,559	N/A	N/A
Multiple PCT results during encounter	Antibiotic Decision				
	Continue	Stop	SUM	% discordant	p value*
High (> 0.5 ng/mL) AND stable (> 20 % of peak)	4,986[C]	500[D]	5,486	9.9	0.67
Low (<0.1 ng/mL) OR downtrending (< 20% of peak)	1,516[D]	159[C]	1,675	90.5	0.67
Subtotal	6,502	659	7,161	52.0	N/A
Total	9,548	1,171	10,720	N/A	N/A

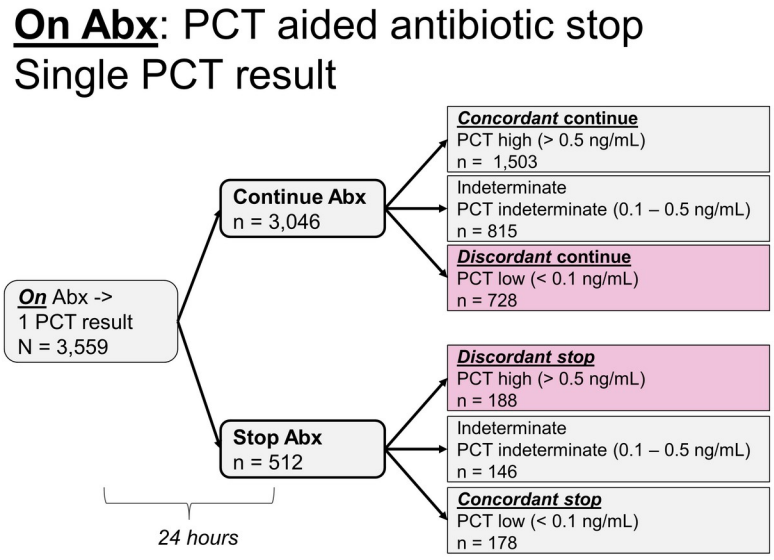
Table 2. Rate of antibiotic decision making concordant with initial PCT value for hospitalized patients on antibiotics prior to PCT assay.
Top: sample limited to patients with only a single PCT value.
[C]Concordant: PCT elevated AND stable and antibiotic continued or PCT low OR downtrending and antibiotic stopped
[D]Discordant: PCT low OR downtrending antibiotic continued or PCT elevated AND stable and antibiotic stopped
Bottom: Sample limited to patients with multiple PCT values.
*Chi-square test with antibiotic decision for all PCT results (ie row labeled ‘subtotal’)

FIGURES

1A



1B



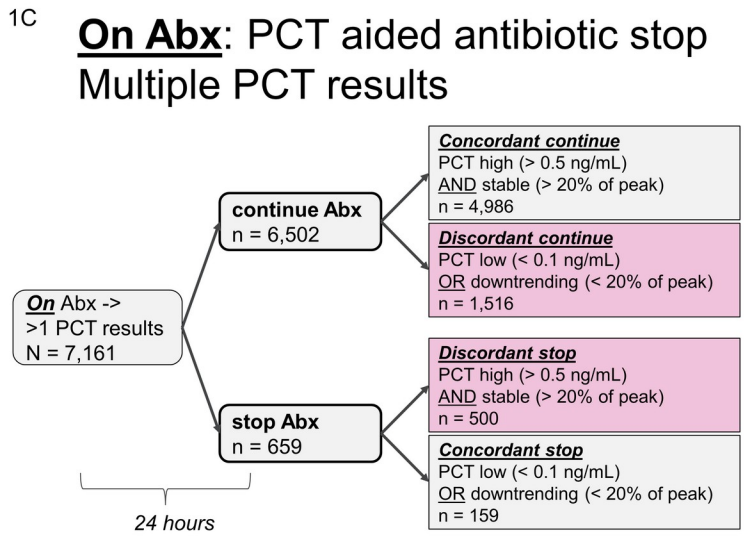
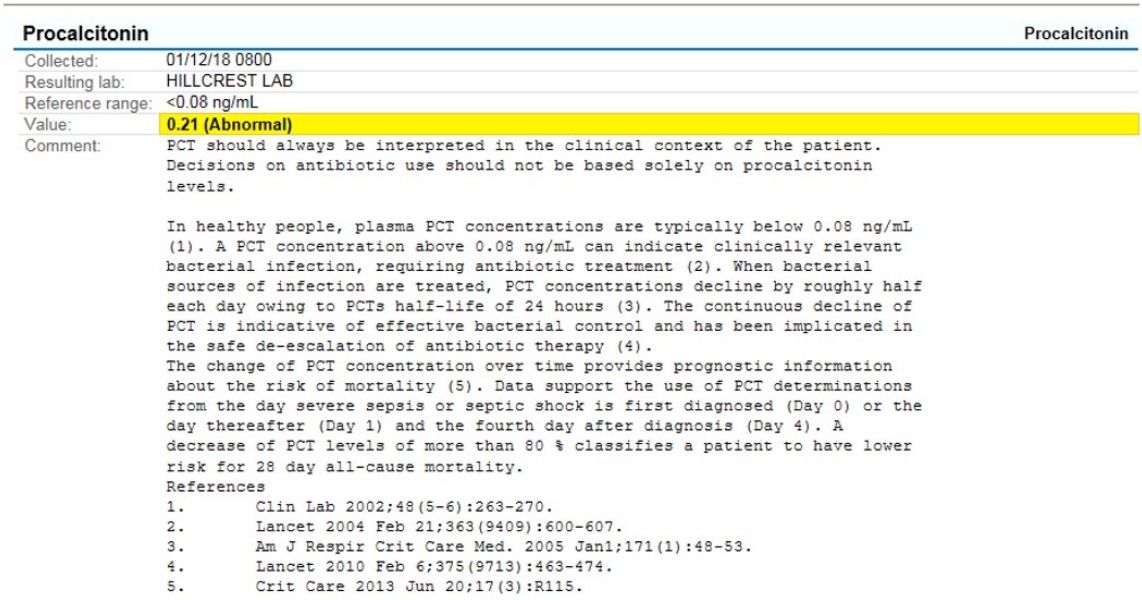


Figure 1: Algorithms for categorizing discordant and concordant antibiotic prescribing following PCT results. Figure 1A demonstrates the algorithm for patients not on antibiotics prior to PCT testing. Figure 1B demonstrates the algorithm for patients on antibiotics prior to PCT testing who had a single PCT result during their encounter. Figure 1C demonstrates the algorithm for patients on antibiotics prior to PCT testing who had multiple PCT results during their encounter.

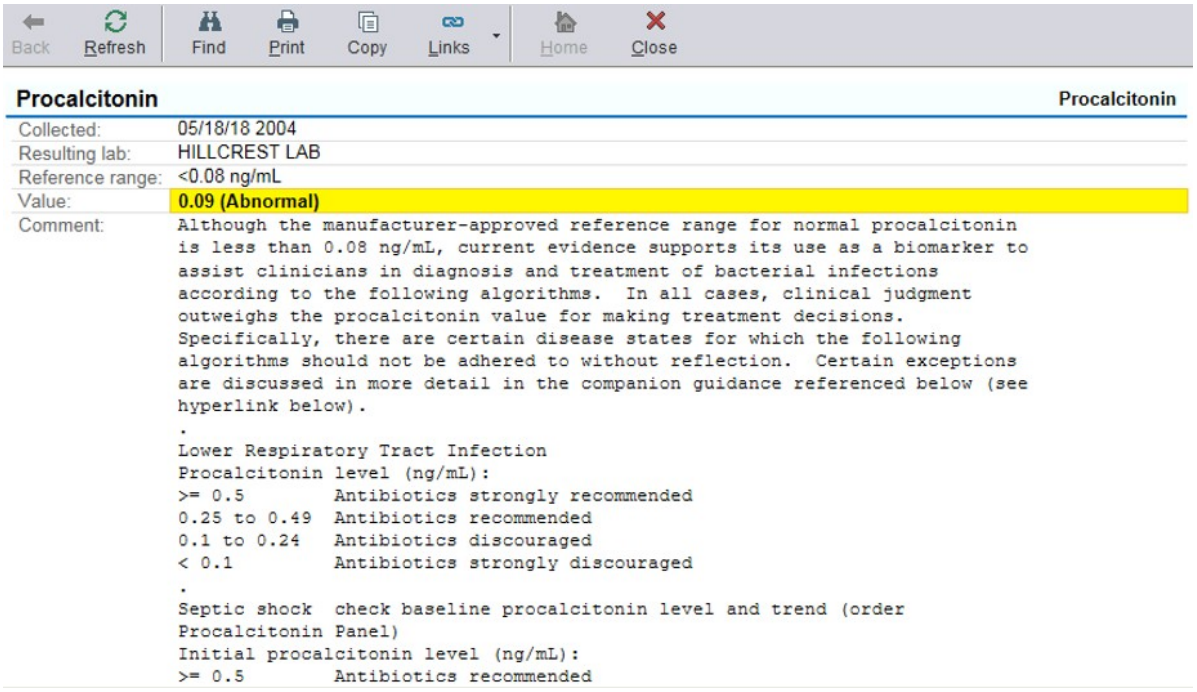
Figure 2A



Procalcitonin — **Procalcitonin**

Collected:	01/12/18 0800
Resulting lab:	HILLCREST LAB
Reference range:	<0.08 ng/mL
Value:	**0.21 (Abnormal)**
Comment:	PCT should always be interpreted in the clinical context of the patient. Decisions on antibiotic use should not be based solely on procalcitonin levels. In healthy people, plasma PCT concentrations are typically below 0.08 ng/mL (1). A PCT concentration above 0.08 ng/mL can indicate clinically relevant bacterial infection, requiring antibiotic treatment (2). When bacterial sources of infection are treated, PCT concentrations decline by roughly half each day owing to PCTs half-life of 24 hours (3). The continuous decline of PCT is indicative of effective bacterial control and has been implicated in the safe de-escalation of antibiotic therapy (4). The change of PCT concentration over time provides prognostic information about the risk of mortality (5). Data support the use of PCT determinations from the day severe sepsis or septic shock is first diagnosed (Day 0) or the day thereafter (Day 1) and the fourth day after diagnosis (Day 4). A decrease of PCT levels of more than 80 % classifies a patient to have lower risk for 28 day all-cause mortality. References 1. Clin Lab 2002;48(5-6):263-270. 2. Lancet 2004 Feb 21;363(9409):600-607. 3. Am J Respir Crit Care Med. 2005 Jan1;171(1):48-53. 4. Lancet 2010 Feb 6;375(9713):463-474. 5. Crit Care 2013 Jun 20;17(3):R115.

Figure 2B



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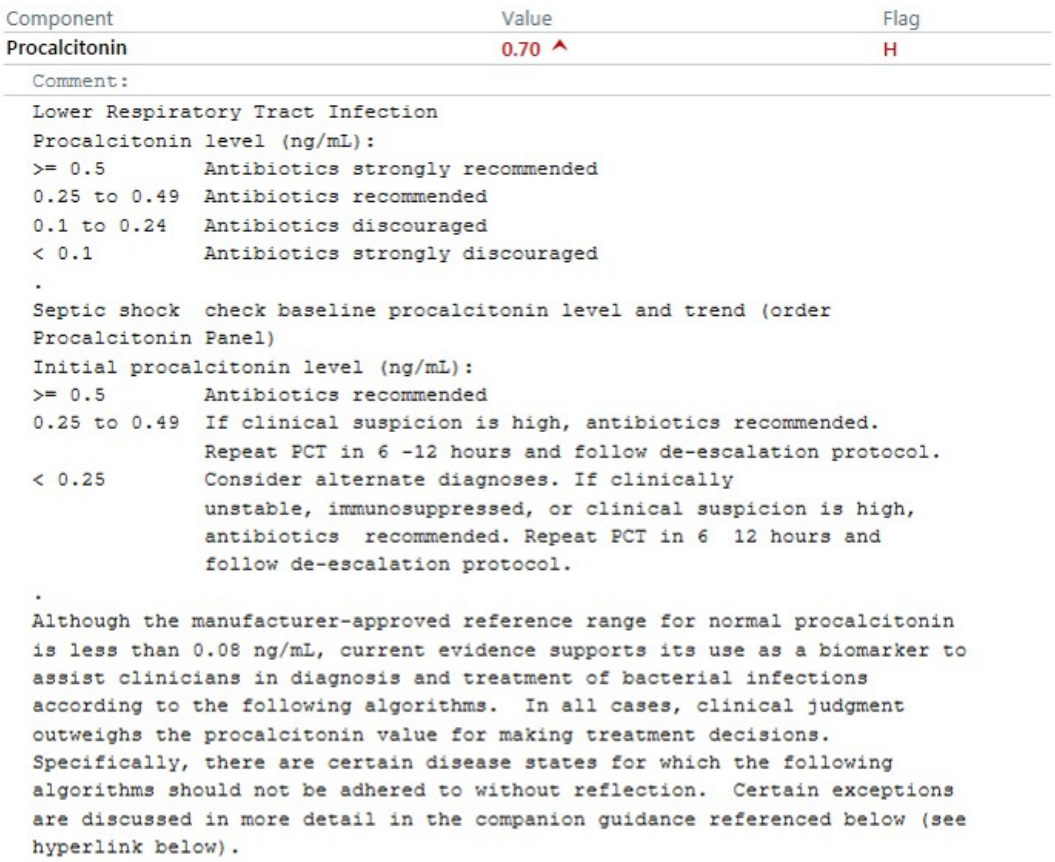
Procalcitonin — **Procalcitonin**

Collected:	05/18/18 2004
Resulting lab:	HILLCREST LAB
Reference range:	<0.08 ng/mL
Value:	**0.09 (Abnormal)**
Comment:	Although the manufacturer-approved reference range for normal procalcitonin is less than 0.08 ng/mL, current evidence supports its use as a biomarker to assist clinicians in diagnosis and treatment of bacterial infections according to the following algorithms. In all cases, clinical judgment outweighs the procalcitonin value for making treatment decisions. Specifically, there are certain disease states for which the following algorithms should not be adhered to without reflection. Certain exceptions are discussed in more detail in the companion guidance referenced below (see hyperlink below). . Lower Respiratory Tract Infection Procalcitonin level (ng/mL): >= 0.5 Antibiotics strongly recommended 0.25 to 0.49 Antibiotics recommended 0.1 to 0.24 Antibiotics discouraged < 0.1 Antibiotics strongly discouraged . Septic shock check baseline procalcitonin level and trend (order Procalcitonin Panel) Initial procalcitonin level (ng/mL): >= 0.5 Antibiotics recommended

Figure 2C



Component	Value	Flag
Procalcitonin	0.70 ^	H

Comment:

Lower Respiratory Tract Infection
Procalcitonin level (ng/mL):
>= 0.5 Antibiotics strongly recommended
0.25 to 0.49 Antibiotics recommended
0.1 to 0.24 Antibiotics discouraged
< 0.1 Antibiotics strongly discouraged
.
Septic shock check baseline procalcitonin level and trend (order Procalcitonin Panel)
Initial procalcitonin level (ng/mL):
>= 0.5 Antibiotics recommended
0.25 to 0.49 If clinical suspicion is high, antibiotics recommended. Repeat PCT in 6 -12 hours and follow de-escalation protocol.
< 0.25 Consider alternate diagnoses. If clinically unstable, immunosuppressed, or clinical suspicion is high, antibiotics recommended. Repeat PCT in 6 12 hours and follow de-escalation protocol.
.
Although the manufacturer-approved reference range for normal procalcitonin is less than 0.08 ng/mL, current evidence supports its use as a biomarker to assist clinicians in diagnosis and treatment of bacterial infections according to the following algorithms. In all cases, clinical judgment outweighs the procalcitonin value for making treatment decisions. Specifically, there are certain disease states for which the following algorithms should not be adhered to without reflection. Certain exceptions are discussed in more detail in the companion guidance referenced below (see hyperlink below).

Figure 2 Legend:

Evolution of results display and decision support for PCT results. Figure 2A is a screenshot of the original support language. Figure 2B is a screenshot of revised results display which added evidence-based guidance for antibiotic decisionmaking. The implementation of the decision support in in Figure 2B corresponds to event 1 in the control charts. Figure 2C is a screenshot of a further revised results discplay which moved prescribing guidance text to the top of the screen. The implementation of the decision support in in Figure 2C corresponds to event 4 in the control charts.

Figure 3

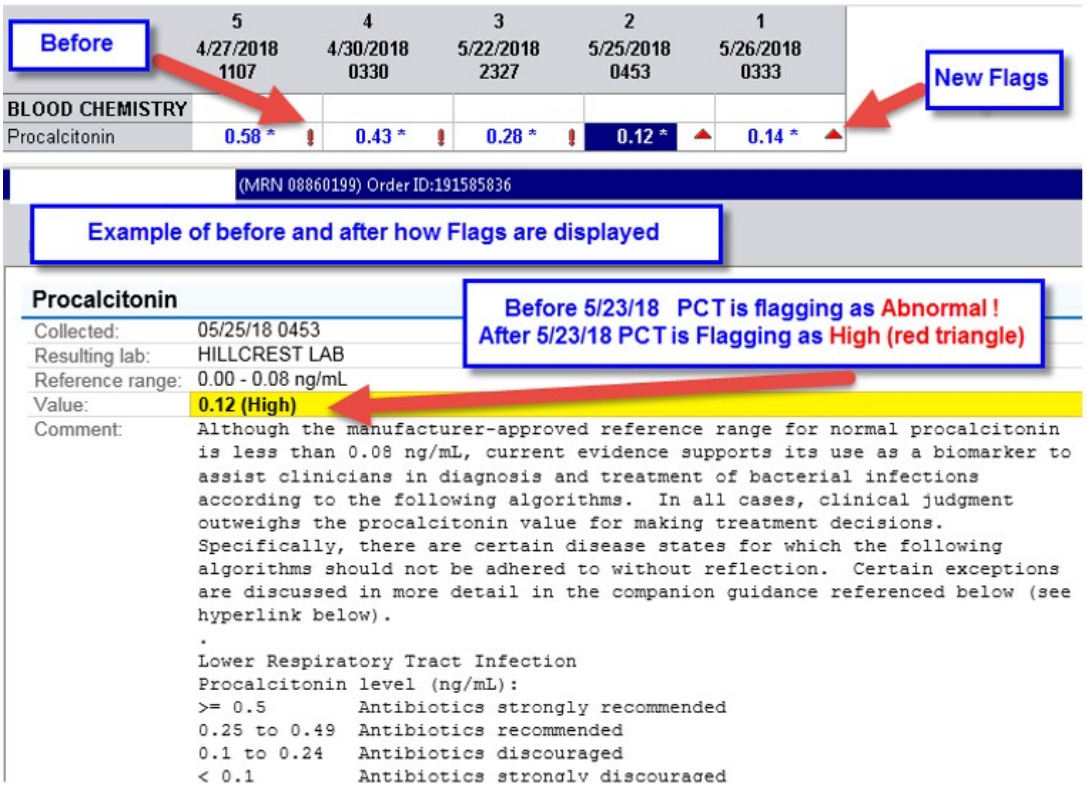


Figure 3 Legend

Evolution of results display for PCT results. Screenshot showing a change in flagging elevated PCT values with an “abnormal!” symbol to a “high” symbol. The implementation of the decision support showin in Figure 3 corresponds to event 2 in the control charts.

Figure 4A

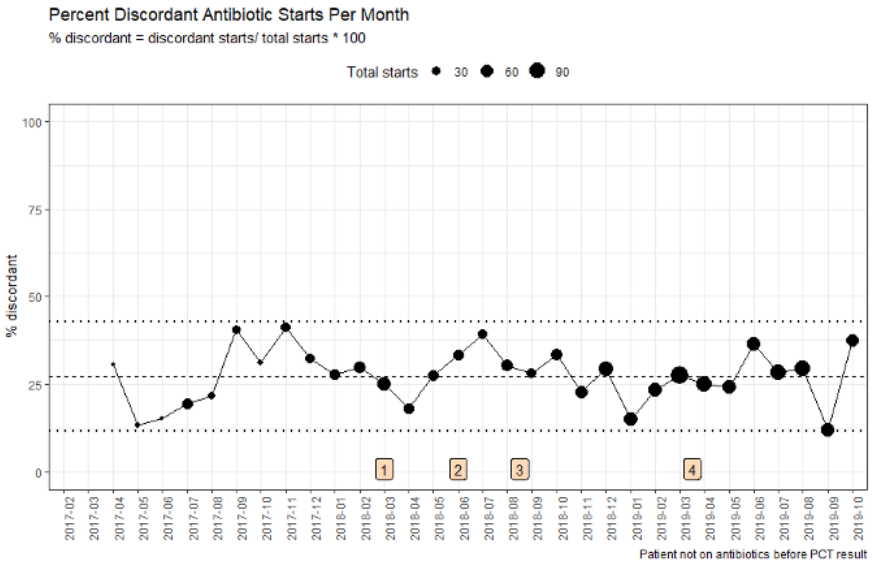


Figure 4B

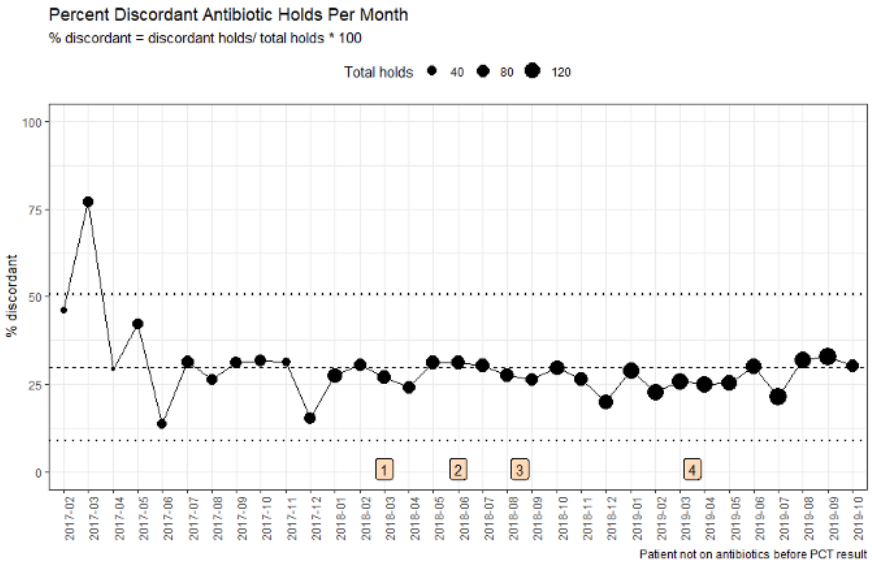


Figure 4: Discordance of procalcitonin result and antibiotic decision for patients not receiving antibiotics prior to the PCT result. Y-axis is discordance rate as described in the text and figure 1A. X-axis is the month and year. Size of the dot at each month is proportional to the total number of PCT results and antibiotic starts for patients not receiving antibiotics. Figure 4A demonstrates discordant antibiotic starts, and Figure 4B demonstrates discordant antibiotic holds. Timeline annotations 1-4 correlate to the interventions described in the text.

Figure 5A

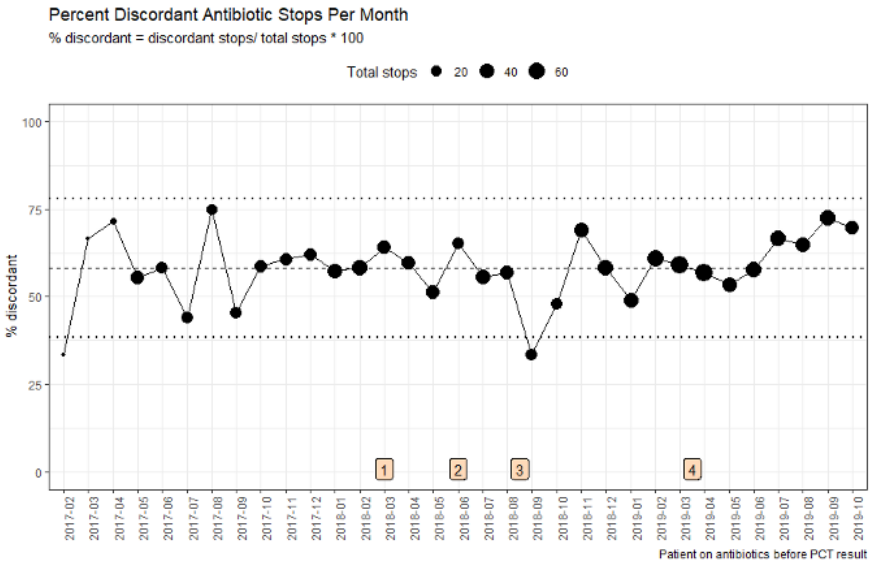


Figure 5B

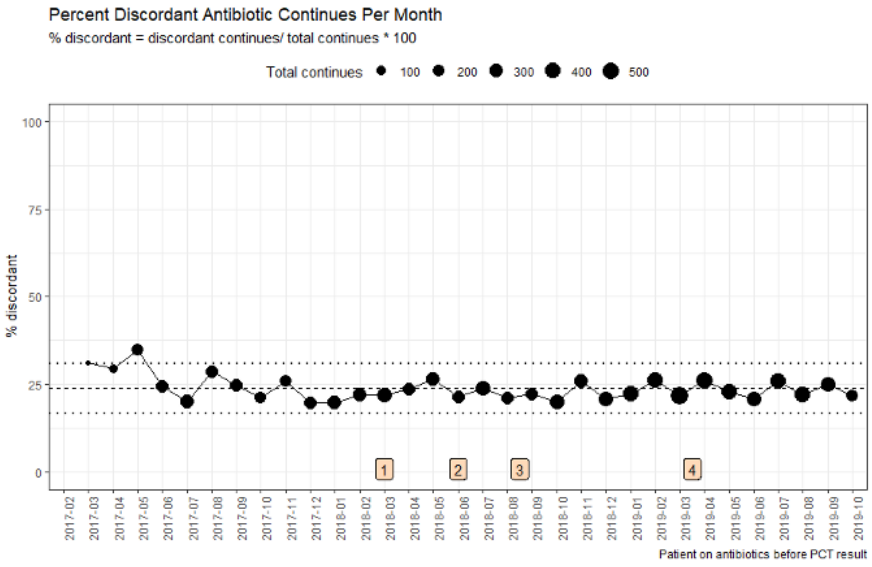


Figure 5: Discordance of procalcitonin result and antibiotic decision for patients already receiving antibiotics prior to the PCT result. Y-axis is discordance rate as described in the text and figures 1B and 1C. X-axis is the month and year. Size of the dot at each month is proportional to the total number of PCT results and antibiotic starts for patients not receiving antibiotics. Figure 5A demonstrates discordant antibiotic stops, and Figure 5B demonstrates discordant antibiotic continuations. Timeline annotations 1-4 correlate to the interventions described in the text