Is a Single Initial Procalcitonin Test Sufficient in Septic, Critically Ill Patients to Minimize Antibiotic Use?

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of the financial outcomes of our report[1] are helpful for properly designing high-quality studies that can support causal inference.

We also agree with Dr Taylor et al that cost-effectiveness studies, like those reported to date,[3] are important and standard state of the art methods for judging whether the costs of an intervention are justifiable based on their health benefits. The ICU Telemedicine Financial Outcomes study[1] and an externally conducted, reported, and audited study of an ICU telemedicine Centers for Medicare and Medicaid Services demonstration project[5] conducted at Emory, have indicated that comprehensive ICU telemedicine programs can have financially significant favorable effects on case volume and on the costs of posthospital care that may not be visible using conventional cost-effectiveness methods. In addition to effects on the cost-quality axis, ICU telemedicine programs can affect the costs of providing access to high-quality critical care depicted on the quality-access and cost-access axes of Figure 1.

We appreciate the opportunity to explain that our study was intended to share useful sustainability and financial metric variation information, ICU telemedicine associations with case volume, and associations with access to care with the critical care community, and to provide a financial argument for performing more definitive trials. We believe that granular financial data that are linked to process and outcomes and measurement of effects along the cost-access, quality-access, and cost-quality axes of ICU finance depicted in Figure 1 are useful considerations for properly designing, budgeting, financing, and performing comparative interventional trials of this multifaceted technological intervention.

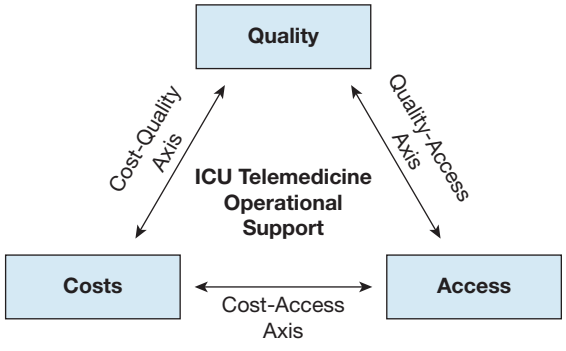

Figure 1 – *ICU financial analyses of cost-quality, quality-access, and cost-access.*

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References

1. Lilly CM, Motzkus C, Rincon T, et al. ICU telemedicine program financial outcomes. *Chest*. 2017;151(2):286-297.
2. Lilly CM, Cody S, Zhao H, et al. Hospital mortality, length of stay, and preventable complications among critically ill patients before and after tele-ICU reengineering of critical care processes. *JAMA*. 2011;305(21):2175-2183.
3. Yoo BK, Kim M, Sasaki T, Melnikow J, Marcin JP. Economic evaluation of telemedicine for patients in ICUs. *Crit Care Med*. 2016;44(2):265-274.
4. Kahn JM, Hill NS, Lilly CM, et al. The research agenda in ICU telemedicine: a statement from the Critical Care Societies Collaborative. *Chest*. 2011;140(1):230-238.
5. ABT Associates. Evaluation of hospital-setting HCIA awards, third annual report. 2017:34-46. https://downloads.cms.gov/files/cmmi/hcia-hospitalsetting-thirdannualrpt.pdf. Accessed March 14, 2017.

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To the Editor:

We read with great interest the article by Balk and colleagues in *CHEST* (January 2017),[1] in which the authors retrospectively evaluated critically ill patients with suspected sepsis, systemic inflammatory response syndrome, or shock. From the U.S. Premier Healthcare Database, 33,569 patients with procalcitonin (PCT) testing on day 1 of ICU admission and 98,543 propensity score-matched patients without PCT testing were compared. PCT utilization was associated with significant reductions in total antibiotic exposure (16.2 vs 16.9 days), total hospital and ICU length of stay (11.6 vs 12.7 and 5.1 vs 5.3 days, respectively), and total hospital costs ($30,454 vs $33,213). They conclude that PCT testing on day 1 could rule in or rule out sepsis

and thus may explain their results. However, despite the use of a propensity score this study has the potential for significant bias; especially considering the fact that various previous studies have advocated against the use of a single PCT measurement to "prove" bacterial infection.[2] The test characteristics of PCT (ie, specificity and negative predictive value) are not high enough to rule out bacterial infection in a mixed ICU population.[2] In addition, most physicians want to start antimicrobial therapy immediately after they've made the presumptive diagnosis of sepsis.[3] Research on PCT has shifted toward serial PCT measurements for the discontinuation of antimicrobial therapy. In the Stop Antibiotics on Procalcitonin Guidance Study (SAPS)[4] we performed a randomized controlled trial with daily PCT vs no PCT in 1,546 ICU patients in whom antibiotic treatment was started. We demonstrated a significant reduction in initial antibiotic duration (5.0 vs 7.0 days). This result was driven by earlier discontinuation of antibiotic treatment on the basis of an absolutely (≤ 0.5 μg/L) or relatively (≤ 20% peak value) low PCT. We believe an initial PCT measurement followed by daily measurements will allow earlier and safe discontinuation of antibiotics in septic ICU patients. The utility of PCT as a marker largely arises from its unique kinetics: a rapid rise within hours after bacterial infection and an approximate half-life of 24 h once the infection abates.[5] We agree with Balk and colleagues[1] that PCT helps guide antimicrobial therapy, but in our opinion a single measurement will not suffice to withhold such therapy in patients suspected of having (severe) sepsis or septic shock. We are aware that serial measurements will inevitably be more costly, which may undercut the cost-effectiveness of this strategy.

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References

1. Balk RA, Kadri SS, Cao Z, Robinson SB, Lipkin C, Bozzette SA. Effect of procalcitonin testing on health-care utilization and costs in critically ill patients in the United States. *Chest*. 2017;151(1):23-33.
2. Wacker C, Prkno A, Brunkhorst FM, Schlattmann P. Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis. *Lancet Infect Dis*. 2013;13(5):426-435.
3. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock: 2016. *Intensive Care Med*. 2017;43(3):304-377.
4. de Jong E, van Oers JA, Beishuizen A, et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. *Lancet Infect Dis*. 2016;16(7):819-827.
5. Nijsten MW, Olinga P, The TH, et al. Procalcitonin behaves as a fast responding acute phase protein in vivo and in vitro. *Crit Care Med*. 2000;28(2):458-461.

Response

To the Editor:

We appreciate the comments of Dr van Oers and colleagues concerning the limitations of a single or even two procalcitonin (PCT) determinations on the initial day of ICU care. The use of a large hospital administrative database does not afford the ability to answer specific important questions related to the ability of PCT to diagnose septic patients, to identify bacterial infection, or to identify the need for antibiotic therapy. While there is certainly the potential for bias in how centers applied the use of PCT testing, we used propensity score matching to help mitigate the potential for confounding by indication.[1]

Certainly, a single PCT level does not provide the ability to look for change over time, which may aid in prognosis or the duration of antibiotic therapy. However, our study was designed to evaluate the health care utilization and economic impact of using PCT as a potential tool to assist with the identification of sepsis in a manner that was approved for use by the U.S. Food and Drug Administration at that point in time.[1] For this purpose, we restricted our analysis to patients who had one or two PCT evaluations at the