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The authors reply

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We thank Ishii et al (1) for their comments on our recently published study (2) in *Critical Care Medicine*, examining a sepsis quality improvement program. We have summarized the authors' concerns as the following: 1) a broad case definition of suspected infection that may bias the cost-savings by including more patients with milder disease; 2) paucity of evidence to provide sepsis care to patients with suspected infection but without meeting sepsis criteria; 3) lack of information detailing the pathogens and antibiotic stewardship.

The lack of diagnostic tools and the heterogeneous presentation of sepsis continues to impede providers' ability to differentiate cases from noncases, so what is pragmatic for prompt investigation and management of patients at-risk for sepsis? Hospitals have built customized protocols to guide adherence to the 3- and 6-hour sepsis bundle and they report their compliance rate for patients coded as septic, severely septic, or septic shock (3). Our study (2) was not based on administrative data and case definition was inclusive of providers suspecting infection as determined through the electronic health record orders. The focus of our intervention was to improve provider knowledge and awareness through education and system alerts so no qualifying patients were missed for the Severe Sepsis/Septic Shock bundle. The program augmented decision-making but it was ultimately at the discretion of the provider to administer treatment. We did not measure if treatments were appropriate or not.

Our health system's approach to initiate early treatment was with an early warning score (EWS), but we recognize this also brings false-positives with it and lower specificity (4). In our analysis, we examined the cohort of suspected infections that may have been prompted by our EWS, and we also examined the cohort with explicit sepsis *International Classification of Diseases* codes, which trades a higher specificity for a lower sensitivity. Although there is promise in EWS for detecting cases at-risk for sepsis, it was not designed for this intention and there remains limited evidence that they improve outcomes (5). We focused our primary analysis in patients with suspected infection as the more pragmatic population, but we did not collect data to examine which part of the intervention was the most beneficial.

Prospective studies are needed to examine the unintended consequences of protocols targeting patients at-risk for sepsis, including over-treating patients without sepsis. In sensitivity analyses, the subgroup admitted with less severe organ dysfunction (Sequential Organ Failure Assessment score ≤ 5) demonstrated the most benefit from our implementation bundle and had the greatest cost-effectiveness. We agree with the authors that the benefit in our results was driven by milder cases, but we postulate that early identification and treatment would be most beneficial in preventing development or advancement of sepsis. Hospital charges serve as one surrogate measure for over-treatment, and we found no substantial changes in the median hospitalization cost between periods when adjusted for confounders in our cost-effectiveness analysis.

We believe our findings support quality improvement programs to implement sepsis bundles with an early detection protocol, but disentangling the pieces of the protocol including sites of infection, antibiotic stewardship, and predominant pathogens were outside the scope of our current study by Afshar et al (2). Our findings are hypothesis-generating for future clinical trials to examine treatment protocols in patients at-risk for sepsis.

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REFERENCES

1. Ishii J, Ohshimo S, Shime N: Potential Confounders for Applying a Novel Sepsis Care Quality Improvement Program. *Crit Care Med* 2020; 48:e161–e162 [PubMed: 31939826]
2. Afshar M, Arain E, Ye C, et al.: Patient outcomes and cost-effectiveness of a sepsis care quality improvement program in a health system. *Crit Care Med* 2019; 47:1371–1379 [PubMed: 31306176]
3. Levy MM, Gesten FC, Phillips GS, et al.: Mortality changes associated with mandated public reporting for sepsis. The results of the New York state initiative. *Am J Respir Crit Care Med* 2018; 198:1406–1412 [PubMed: 30189749]
4. Churpek MM, Snyder A, Han X, et al.: Quick sepsis-related organ failure assessment, systemic inflammatory response syndrome, and early warning scores for detecting clinical deterioration in infected patients outside the intensive care unit. *Am J Respir Crit Care Med* 2017; 195:906–911 [PubMed: 27649072]
5. McLymont N, Glover GW: Scoring systems for the characterization of sepsis and associated outcomes. *Ann Transl Med* 2016; 4:527 [PubMed: 28149888]