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Reply: From the "Door-to-Antibiotic" to the "Antibiotic-at-Door" Concept?

From the Authors:

We appreciate the thoughtful comments from Jouffroy and Vivien regarding our study. We agree completely regarding the need for validated methods to risk stratify likely patients with sepsis well before the Sequential Organ Failure Assessment score becomes available. We are also eager for results from SAMU Save Sepsis and other innovative trials in early sepsis care that will help guide quality improvement efforts and also address persistent concerns that early antibiotic initiation is a marker of overall better sepsis care, rather than a direct driver of improved sepsis mortality (1). Data from these studies should also inform the debate currently raging on the potential adverse effects of accelerated antibiotic initiation (2–4) by quantifying any adverse effects and distinguishing between the process outcome of antibiotic overtreatment and actual patient harms (e.g., anaphylaxis, antibiotic-associated infections).

On a side note, similar to other recent authors (4, 5), Jouffroy and Vivien describe as "negative" Alam and colleagues' pioneering randomized trial of prehospital ceftriaxone for patients with infection plus the systemic inflammatory response syndrome (6). Setting aside the fact that 20% of patients were already receiving antibiotics and the unfortunate and extensive failures of randomization, this trial was powered for control group mortality fivefold higher than observed and an effect size 20–100% too large, given the achieved difference in antibiotic timing and the effect predicted from observational data. We would advise sepsis clinicians and researchers that referring to this randomized trial as "negative" without also noting that it was severely underpowered implies the trial provides considerably stronger evidence against early or prehospital antibiotics than it does in reality, particularly when the goal is to argue for more cautious efforts to accelerate antibiotics (4, 5).

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