Reply to Parra-Ruiz

We thank Dr Parra-Ruiz for his interest in our article [1]. He disagrees with our conclusion [2] and suggests that vancomycin should no longer be regarded as first line therapy except for non-critically ill patients, infected with a susceptible (minimum inhibitory concentration $\leq 1$ mg/mL) methicillin resistant S. aureus (MRSA) isolate and in whom vancomycin and renal function can be closely monitored. Dr Parra-Ruiz provides several arguments to substantiate his point of view.

First, he argues that infection related and not overall mortality is augmented by antimicrobial therapy, and therefore in critically ill patients other measures of success should be evaluated. In other words, clinical or microbiological success (determined by pathogen clearance) should be seen as measures of success in the Zephyr trial [3]. This is highly controversial as persistent pathogen isolation in nonsterile site infections (such as pneumonia) does not necessarily represent failure or ongoing infection but rather colonization. Similarly, the relevance of clinical success is this study is unclear, as it did not result in either reduced ventilator days or lengths of stay.
Second, Dr Parra-Ruiz points to a mortality benefit observed with 2 recently published studies [4, 5]. We agree that these data are intriguing, but due to multiple limitations [6, 7] they are suggestive at best and require confirmation.

Third, the increased acute renal injury (AKI) was seen with the vancomycin treatment arms in the 2 recent randomized controlled studies for MRSA pneumonia [3] and bacteremia [8]. These adverse events are associated with increased morbidity, mortality, and costs. Surely, given the size of the effect described, one would expect a reduction in overall mortality in both these studies with nonvancomycin based therapy? This was not the case and reflects the multifactorial nature of AKI and the complexities of differentiating causation from association especially with renal excreted antibiotics such as vancomycin [9].

Fourth, antimicrobial resistance to alternative antibiotics remains uncommon and ensuring these agents longevity is the role of antimicrobial stewardship (AMS) programs. Although resistance is rare based on large surveillance studies, these are unlikely to detect slow changes in resistance secondary to sampling bias and susceptibility methodology employed. Irrespective, there is a clear link between usage and resistance that persists despite reduced consumption [10]. Furthermore, the role of any AMS program in controlling usage is not feasible if vancomycin is deemed inferior, as optimal prescribing remains an important tenant of such a program.

Finally, drug-acquisition cost is only one component of the overall cost, which is reduced with alternative therapy based on several recent publications [11, 12]. We agree that drug acquisition costs, although more expensive, may be offset by other savings. This argument is only effective, however, in healthcare systems that do not approach expenditure through compartmentalized departmental budgets. Furthermore, it is empirical antimicrobial prescribing that drives cost, which to our knowledge, has yet to be included in any economic analysis.

In conclusion, unlike Dr Parra-Ruiz who wishes to relegate vancomycin to second-line therapy, our review of the data confirms that the optimal antibiotic option for MRSA therapy remains unknown. Consequently, vancomycin remains an important therapeutic option in patients with MRSA infections.

Note
Potential conflicts of interest. Both authors: No reported conflicts. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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