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initially omitted due to limited space. To elaborate, during his therapy, our patient was diligently monitored weekly and C-reactive protein was used as a surrogate marker of response, which decreased from an initial measure of 30.1 mg/L to 6.2 mg/L by week 9, a point at which we could not justify prolonging the treatment further. We emphasize that our patient’s treatment comprised doses of daptomycin (8 mg/kg daily) and ceftriaxone (2 g twice daily) higher than those shown to be sufficient for synergy. Although we cannot directly specify the cause of death, this regimen was clearly insufficient to attain microbiological cure, evidenced by relapse occurring almost immediately after stopping treatment and the isolation of bacteria from blood cultures and from the patient’s valve tissue days later. We were surprised to find that the organism’s MIC of daptomycin increased 4-fold while on treatment, which strongly suggests that the development of resistance probably contributed to treatment failure despite the high doses of both daptomycin and ceftriaxone.

Although this case resulted in our patient expiring, we stand beside our clinical decisions, as well as those leading us to submit our case for publication. The work by Hall Snyder et al. describing synergy between daptomycin and ceftriaxone is of high quality and offers a microbiologically sound therapeutic option where first-line therapies are not feasible. Publishing our case marked the transition from the laboratory to clinical practice, and despite possessing biases intrinsic to case reports, it stands as a valid addition to the medical literature and not as a platform to criticize desperately needed research for novel therapies. In fact, we had made an a priori decision to submit this case for publication, and having obtained signed patient consent at the beginning of treatment, we would have objectively reported any outcome observed, positive or negative. While we agree with Hall Snyder et al. that our experience with this regimen, along with any other non-randomized research on daptomycin against Enterococcus, should be interpreted with caution when making therapeutic decisions, we also respectfully underscore the bias inherent to research from laboratories funded by the pharmaceutical industry. Nevertheless, we feel that we speak for many clinicians who manage challenging infections such as enterococcal IE, look forward to the results of future evidence, be it laboratory or clinical, regarding novel therapies, and encourage those with unreported clinical experience to submit their data for publication.

Transparency declarations
None to declare.

References
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Efficacy and safety of daptomycin for the treatment of infectious disease: a meta-analysis based on randomized controlled trials—authors’ response

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Sir,

We appreciate the comment on our published meta-analysis1 by Potashman et al.2 They made the criticism that a trial3 about daptomycin for the treatment of community-acquired pneumonia (CAP) was included in our study, as it showed that daptomycin was not as effective as its comparator. We would like to remind readers that daptomycin was not advised for the treatment of pneumonia, which was clearly acknowledged in our paper.

In fact, our study indicated that daptomycin showed a similar efficacy among the ITT population and was less efficacious among the clinically evaluable (CE) population than its comparators. These results were further explored by subgroup and sensitivity analysis regarding the controversy between CAP and other kinds of infectious diseases. The samples from the trial3 indeed constituted >25% of our ITT population, but when we appraised the efficacy of daptomycin according to type of infection, no different conclusion was drawn, as illustrated in Figure 2.1 Furthermore, daptomycin showed lower efficacy compared with other treatments with regard to clinical success among the CE population. Our study also emphasized that the removal of the trial from the analysis led to a result with no difference in clinical success between daptomycin and comparators.

Randomized controlled trials are a critical source for the practice of meta-analysis, which should collect samples as much as possible according to the QUOROM statement.4 This is really of importance to circumvent bias rather than to decrease the quality of meta-analysis.5 Our study focused on both the efficacy of daptomycin and its safety; data from the trial were significant for the evaluation of daptomycin safety. If the samples from that trial were not included just because of their lower clinical success for CAP, we would be less convinced that daptomycin resulted in more creatine phosphokinase elevation effects and fewer adverse events in total.

As we mentioned in our article, one of the limitations of our study was that various kinds of infectious diseases were included. However, subgroup and sensitivity analysis can minimize and compensate for this. In conclusion, daptomycin may be a promising alternative antimicrobial agent for serious infectious diseases, but not for CAP.

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Transparency declarations

M. H. P. and J. F. M. are employees of Cubist Pharmaceuticals and own stock. D. N. F. is an employee of Northeastern University and Cubist Pharmaceuticals. K. H. is an employee of Novartis Pharmaceuticals Corporation and owns stock.

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