Reply to Hurley

To the Editor—We gratefully acknowledge Dr Hurley for his very useful commentary. First, Dr Hurley questioned
the inclusion of randomized studies with various designs in our metaanalysis (randomization clinical trial [RCT] or cluster-randomized studies). To the best of our knowledge, the hierarchy of research design is still a matter of debate [1], and the clinical studies that provide the best evidence are not necessarily the ones that use a randomization of patients per patient [2]. The exclusion of the cluster-randomized studies would have exposed our results to a significant bias, and we thus decided to include these studies in our metaanalysis.

Second, Dr Hurley proposed an attractive hypothesis, that is, the apparent reduction regarding the risk of death attributed to selective digestive decontamination (SDD) may be explained by an increased risk of death in the placebo group rather than a protective effect of SDD. To support his hypothesis, Dr Hurley showed that the rate of death was higher in the placebo group of double-blind randomized studies that mixed SDD and placebo patients in the same intensive care units (ICUs), and he proposed that a contextual hazard of SDD (ie, a side effect in controlled patients) could explain this surprising result [3]. Of note, a contextual hazard of the topical antibiotic component of SDD has already been proposed to be responsible for an increased rate of bacteremia in the placebo groups of RCTs evaluating SDD [4]. However, we doubt that the reduction of the death rate observed with SDD could be entirely explained by an increased risk of mortality for control patients concurrently located in the ICU. First, this hypothesis would imply an effect of SDD only in RCTs subjected to a contextual hazard toward bacteremia within the literature did not detect any relation between the use of SDD and the development of resistance in the ICU [6]. Finally, the higher mortality rates in the controlled groups of RCTs compared with those from studies with another design could be explained by the use of more severe inclusion criteria in the RCT than in cluster-randomized or observational studies.

Interestingly, Dr Hurley found that the systemic antibiotic component of SDD mitigates the contextual hazard of the topical antibiotic component on the risk of bacteremia [4]; we found that when SDD is used, systemic antibiotic administration is required in order to decrease the risk of mortality of ICU patients [5]. We concluded that SDD with systemic antimicrobial therapy should be administered in ICU patients at high risk of death. However, we recommend that future research include before and after studies to assess the balance of benefit to risk of SDD in “real life” and to evaluate any side effects, even in untreated patients.

Finally, we agree with Dr Hurley that there is a typographical error in Figure 3 (a study with a relative risk >2 is missing from Figure 3A). We have reevaluated this exploratory analysis. The trends remain similar. An erratum has been issued to correct this in *Clinical Infectious Diseases*.

### Note

**Potential conflicts of interest.** All authors: No reported conflicts.

All 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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**References**


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