CRITICAL CARE

LETTER

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Importance of a registered and structured protocol when conducting systematic reviews: comments about nebulized antibiotics for ventilator-associated pneumonia

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See related Letter by Gu, http://www.ccforum.com/content/19/1/236, and related research by Zampieri et al., http://ccforum.com/content/19/1/150

We appreciate Gu's [1] interest in our study. We apologize and agree with his comment about attributing units to standardized mean difference (SMD). Nevertheless, similar to the SMD, results in mean difference (control – nebulized) were unaffected by nebulized antibiotics (2.67 days, 95 % confidence interval (CI) −2.89, 8.23 for ICU length of stay (LOS); and 0.70 days, 95 % CI −3.40, 4.80 for mechanical ventilation). However, we strongly disagree with other points raised by the letter.

First, the study protocol was defined a priori [2]. We disagree that combining observational studies with intervention studies is reserved only for safety evaluation. This topic has been discussed in the literature and combining both types of studies was adequate for our aim [3]. Furthermore, we presented the main results separating interventional studies from observational studies, thereby allowing the reader to interpret both analyses independently.

Second, both of the studies cited as "case–control studies" [1] received this denomination in their title and abstract. However, by reading their methods it becomes clear that they are actually matched cohort studies [4, 5]. Indeed, they matched exposed patients ("nebulized group") to unexposed patients ("no-nebulized group"). A case–control design starts with the outcome (case = "clinical success") and matches them with controls ("clinical failures"). Therefore, our measure of effect was correct [5]. For exploration, we report the analysis for clinical cure using the odds ratio (OR) (Fig. 1). The results are unchanged.

Third, Kalin's study was included because it fulfilled our inclusion/exclusion criteria [2]. Gu's suggestion to exclude this study based solely on its effects in heterogeneity could be considered selective reporting [1].
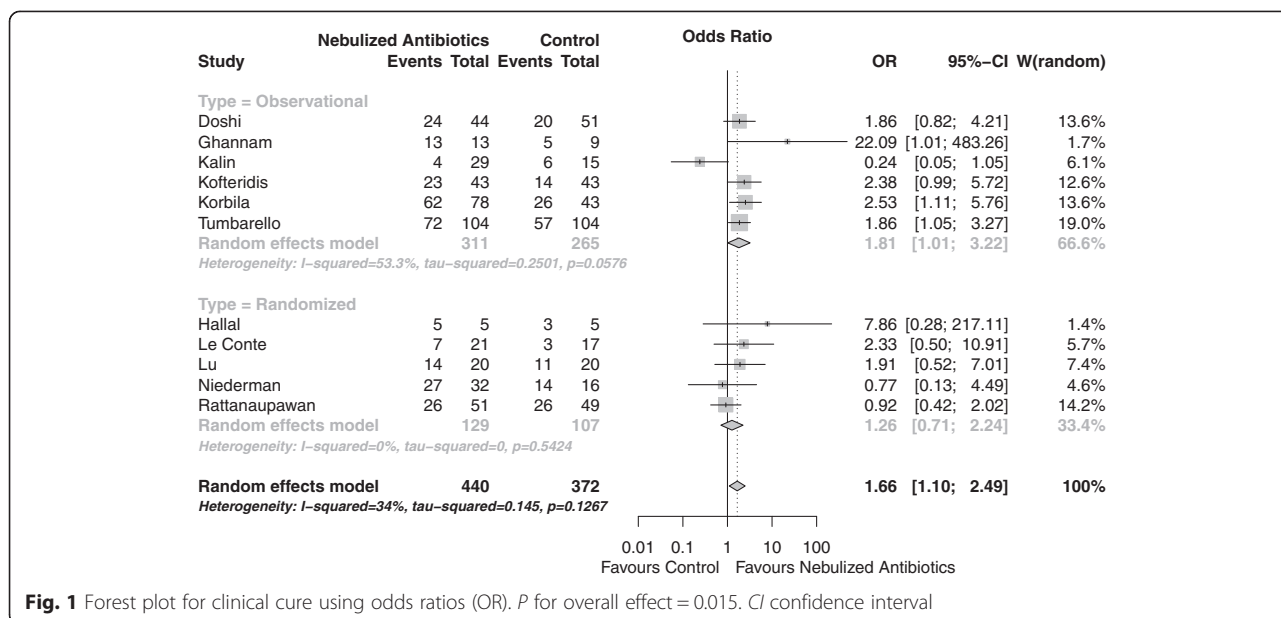
Our study provided data for further trials aiming to evaluate the effect of nebulized antibiotics in ventilator-associated pneumonia (VAP) [2].

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Fig. 1 Forest plot for clinical cure using odds ratios (OR). *P* for overall effect = 0.015. *CI* confidence interval

Abbreviations
CI: Confidence interval; LOS: Length of stay; OR: Odds ratio; SMD: Standardized mean difference; VAP: Ventilator-associated pneumonia.

Competing interests
The authors declare that they have no competing interests.

Author contributions
FGZ conceived the study, participated in data acquisition, data analysis, and interpretation, and helped to revise the manuscript for important intellectual content. APN participated in conception of the study, data acquisition, data analysis, and interpretation, and helped to revise the manuscript for important intellectual content. DG-F participated in conception of the study and interpretation, and helped to revise the manuscript for important intellectual content. LUT participated in conception and design of the study and interpretation, and helped to revise the manuscript for important intellectual content. AT participated in conception and design of the study and interpretation, and helped to revise the manuscript for important intellectual content. OTR conceived the design of the study, participated in data acquisition and interpretation, and wrote the draft of the manuscript. All authors read and approved the final manuscript.

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