Article title: Comments on “Impact of Antibiotic Stewardship Rounds in the Intensive Care Setting: A Prospective Cluster-Randomized Crossover Study”

Authors: Hideharu Hagiya[1]

Affiliations: Department of General Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan[1]

Orcid ids: 0000-0002-5086-1891[1]

Contact e-mail: hagiya@okayama-u.ac.jp

License information: This work has been published open access under Creative Commons Attribution License http://creativecommons.org/licenses/by/4.0/, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Conditions, terms of use and publishing policy can be found at https://www.scienceopen.com/.

Preprint statement: This article is a preprint and has not been peer-reviewed, under consideration and submitted to ScienceOpen Preprints for open peer review.

Funder: None

DOI: 10.14293/S2199-1006.1.SOR-.PPLMVBN.v1

Preprint first posted online: 07 August 2022

Keywords: antimicrobial resistance, antimicrobial stewardship, intensive care unit, risk of bias
Comments on “Impact of Antibiotic Stewardship Rounds in the Intensive Care Setting: A Prospective Cluster-Randomized Crossover Study”

Hideharu Hagiya¹

¹Department of General Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Keywords: antimicrobial resistance; antimicrobial stewardship; intensive care unit; risk of bias

Running title: Comments on article by Seidelman et al.

Corresponding author:
Hideharu Hagiya, MD, PhD
Department of General Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
E-mail: hagiya@okayama-u.ac.jp
As an infectious disease specialist struggling to propel the proper use of antibiotics, I have gone through the most recent article in your esteemed journal written by Seidelman et al. [1]. In this age of antimicrobial resistance [2], promoting antimicrobial stewardship is increasingly highlighted worldwide [3]. Therefore, evaluating the clinical impacts of antibiotic stewardship rounds in intensive care units (ICU) where broad-spectrum antibiotics are prescribed is vital. As described in the literature, a cluster-randomized crossover design has probably never been applied to assess antimicrobial stewardship in ICU settings full of clinical and multidisciplinary complexities. Although their intervention was offered once a week, it must have been laborious and tough, considering their efforts in collecting prerequisite information for discussion and maintaining continuous communication with intensivists. Thus, I praise their hard work in unveiling unsolved matters. However, I would like to make several suggestions to avoid possible bias and provide positive feedback to accurately evaluate the clinical impact of antibiotic stewardship rounds.

Based on the Risk of Bias 2 tool [4], I noticed several points to be addressed. First, a selection bias at the time of ICU admission may have influenced the results. As mentioned, the intervention’s allocation (low or high side) could not be blinded to frontline practitioners. Thus, patients requiring intensive antimicrobial treatment might have been favorably allotted to intervention beds. Second, the outcome data had a high risk of bias. The unblinded study design allowed clinical data such as days of therapy (DOT) as the primary outcome and ICU length of stay to be arbitrarily adjusted. Third, a reporting bias should also be mentioned. The authors reported that the rate ratio of antibiotic DOT per 1,000 patient-days was significant (0.93 [95% confidential interval, 0.89–0.98]) when excluding the data from the cardiothoracic ICU. Due to the unavailability of a pre-submitted research protocol, I could not confirm this. However, a post hoc analysis was not described in the article’s Methods section and thus should not be highlighted in the Abstract. This could be a kind of “spin,” possibly misleading readers in evaluating study results [5]. Finally, the authors concluded that the decline in post-intervention antibiotic use was derived from the indirect effects of antimicrobial stewardship rounds. I agree with their remarks; however, to negate the direct effect, quasi-experimental time-series analysis could be of choice, as has been done in a previous study [6].

I would also like to deliver positive comments. I believe that acceptance rates of
recommendations by the antibiotic stewardship round teams could be far better than those reported when clinical and microbiological diagnoses were confirmed. During the intervention, 26.7% and 44.2% of the cases were classified into “clinical diagnosis without microbiological data” and “clinical diagnosis workup pending,” respectively. This suggests that 70.9% of the intervened cases lacked sufficient data to propose appropriate antimicrobial therapy, leading to an underestimation of the impact of antibiotic stewardship rounds. Hopefully, the authors share the results of stratified analysis limited to cases with “diagnosis confirmed with microbiological data.”

**Funding:** None to report.

**Conflict of interests:** None to declare.

**References**


