Hospital-wide Rollout of Antimicrobial Stewardship: A Stepped-Wedge Randomized Trial

To the Editor—We commend Palmay et al on their large study of an antimicrobial stewardship program across 6 hospital departments, following its success in the intensive care unit (ICU) [1, 2]. Prospective audit and feedback is a well-validated stewardship intervention [3], and they measured a wide range of outcomes. While they showed reduced antimicrobial use in their target group, the authors highlight that there was no significant reduction in any key outcome measures when applied to all patients. We are concerned that the negative outcomes from this impressively resourced study could discourage efforts to institute stewardship programs in similar settings.

The authors chose a stepped-wedge randomized design in response to a 2013 Cochrane review, which highlighted the lack of methodologically robust evidence in stewardship [4, 5]. Stepped-wedge trials are a form of crossover cluster randomized trial, a design identified as particularly susceptible to bias by the same review [4, 5]. Although randomization does control for allocation bias, the potential for bias at outcome assessment remains high; this is in contrast to the low risk of bias in, for example, interrupted time-series trials.

The other methodological issue is the intervention itself. Patients receiving targeted antimicrobials on day 3 and day 10 of admission were selected for the intervention. These criteria would exclude many general medical and surgical patients who are likely to receive different antibiotics and be rapidly discharged. An intervention that targets all antibiotic usage on day 2 of admission would be more appropriate. Additionally, it is not clear whether the assessment of appropriateness of antibiotic therapy had the same criteria as in the ICU study and therefore whether this influenced the number of eligible patients.

There are also issues with the choice of microbiological outcome measures. Clostridium difficile and resistant gram-negative pathogens are less clinically relevant outside the ICU, and, as acknowledged by the authors, the follow-up period was insufficient to detect changes. Potential short-term benefits including drug toxicity and catheter-related bloodstream infections were not measured.

The acceptability of the intervention and reduction in days of therapy of targeted antimicrobials in eligible patients shows its efficacy in selected patient groups. However, it is not surprising that this benefit was not significant when applied to the whole study population. The stewardship team reviewed only 20% of all admitted patients; 47% of these had recommendations, of which 80% were accepted. Therefore, only 7.5% of admitted patients had a change in therapy resulting from the intervention. We appreciate that the extent of the intervention may have been limited by resource constraints.

While reporting of negative results is important, we believe that the authors have potentially done their antimicrobial stewardship program a disservice through the inappropriate application of an ICU strategy to general wards. This study highlights the importance of tailoring antimicrobial stewardship interventions and outcomes to individual departments.

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.

Bridget Freyne,1,2,3 Jeremy Carr,1 Joshua Osowicki,1,2 Andrew Steer,1,2,3 Nigel Curtis,1,2,3 and Penelope A. Bryant1,2
1Infectious Diseases Unit, Department of General Medicine, The Royal Children’s Hospital Melbourne, 2The Murdoch Children’s Research Institute, and 3Department of Paediatrics, University of Melbourne, Australia

References

Correspondence: Bridget Freyne, MBChBBA, MRCPI, MIH, Infectious Diseases Unit, Department of General Medicine, The Royal Children’s Hospital, 50 Flemington Rd, Parkville, Vic 3052 (bridget.freyne@rch.org.au).

Clinical Infectious Diseases 2015;60(4):666 © The Author 2014. Published by Oxford University Press on behalf of the Infectious Diseases Society of America. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com. DOI: 10.1093/cid/ciu899