Reply to Mills and Linkin

To the Editor—In their letter [1], Mills and Linkin question the conclusion of our recent study that patient-to-patient transmission of Staphylococcus aureus rarely occurs on an intensive care unit [2]. Over 14 months, we detected only 7 patient-to-patient transmissions using whole-genome sequencing, a finding that strongly supports our conclusions. Furthermore, patient-to-patient transmission accounted for only a minority of the observed acquisitions. It is important to emphasize that we conducted our study in the context of enhanced infection prevention measures including scrupulous hand hygiene, environmental decontamination, and washing of patients with chlorhexidine. Our results suggest that these measures are highly effective in preventing transmission.

Mills and Linkin base their criticism on calculation of confidence intervals (CIs) around proportions; in fact our observed 18.9% (7/37) of S. aureus acquisitions that could plausibly represent patient-to-patient transmissions, based on whole-genome sequencing, has an exact binomial 95% CI [3] of 8.0%–35.1% (this method better allows for the small number of acquisitions than the Wald/normal approximation used in [1]).

Mills and Linkin pay particular attention to methicillin-resistant S. aureus (MRSA) acquisitions (actually 5/15 [33%; 95% CI, 11.8%–61.6%] patient-to-patient transmissions from Figure 2 in our article; patient 35 acquired 2 MRSA strains of differing spa types). Approaches that focus on effects within small subgroups that have not been predefined are widely recognized as flawed [4,5]. We did not predefine subgroups as we knew the number of S. aureus acquisitions to be limited before we performed sequencing to identify transmissions. The 95% CI within any subgroup will widen substantially because of the even smaller size, making inference on the basis of 95% CI alone problematic. If, as recommended [4,5], we consider heterogeneity across subgroups (albeit in exploratory/post-hoc analyses), comparing the 33% of MRSA acquisitions that are plausible transmissions with the corresponding 9% (2/22; 95% CI, 1.1%–29.2%) of methicillin-sensitive S. aureus (MSSA) acquisitions, we find weak evidence for such an effect (two-sided P = .10 by Fisher’s exact test). In our study context of enhanced infection prevention practice, larger numbers would be needed to confirm whether or not MRSA could be responsible for greater patient-to-patient transmission than MSSA, and to estimate the proportion of acquisitions that could be due to patient-to-patient transmission more precisely.
Notes

Financial support. This work was supported by the Wellcome Trust; the Medical Research Council; the Biotechnology and Biological Sciences Research Council; and the National Institute for Health Research on behalf of the Department of Health.

Potential conflicts of interest. All authors: No potential 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.

James R. Price,1 Tanya Golubchik,2 Daniel J. Wilson,3,4 Derrick W. Crook,3,5 A. Sarah Walker,2,5 Timothy E. A. Peto,3,5 John Paul,1,6 and Martin J. Llewelyn1,7

1Department of Microbiology and Infection, Royal Sussex County Hospital, Brighton; 2Department of Statistics, University of Oxford; 3Nuffield Department of Clinical Medicine, Experimental Medicine Division, John Radcliffe Hospital, 4Wellcome Trust Centre for Human Genetics, 5NIHR Oxford Biomedical Research Centre, John Radcliffe Hospital, Oxford; 6Public Health England, Royal Sussex County Hospital, Brighton; and 7Division of Medicine, Brighton and Sussex Medical School, Falmer, United Kingdom

References


Correspondence: Martin Llewelyn, MBBS, PhD, Division of Medicine, Brighton and Sussex Medical School, University of Sussex, Falmer, East Sussex, BN1 9PS, UK (m.j.llewelyn@bsms.ac.uk).

Clinical Infectious Diseases 2014;59(5):752–3

© 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/ciu370