sities for colonization or infection with either MRSA or VRE, and for colonization or infection with MRSA, and for colonization or infection with VRE. The study is powered to detect a moderate (40%) decrease in the composite outcome (MRSA or VRE colonization or infection) associated with the intensive control strategy. A smaller decrease could yield a *P* value greater than .05, a negative study result, as noted by Dr. Farr.[1] However, given that the strategy of using active surveillance and contact precautions strategy involves additional workload and cost, we believed that decision-makers would require at least a moderate reduction to justify wider use of this strategy, especially since many acute care facilities are already committing substantial resources to the prevention of infections in general, not just those caused by MRSA or VRE.

It is premature to judge the contribution of the STAR-ICU trial to the base of evidence regarding the effectiveness of using active surveillance and contact precautions in controlling the spread of MRSA and VRE in healthcare facilities. We encourage readers to evaluate the study critically after its design, methods, results and conclusions have been reported fully.

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Reply to Huskins et al.

TO THE EDITORS—Huskins et al.[1] say they addressed the "principal criticisms" I made in my article,[2] but they only discussed inadequate sample size and statistical power and intervention in a single ICU of a large hospital with a high prevalence (ie, among about a dozen reasons I gave that favor false-negative results).

Regarding the former concern, they say increasing the sample size wouldn't effectively increase power, but readers of this journal probably know better. Rosner's *Fundamentals of Biostatistics*, 3rd edition, states that power increases "as sample size increases."[3(p209)] Huskins et al.[1] then defend the trial's intentionally marginal power (ie, power to detect only a 40% reduction), saying active detection and isolation cost more and thus should be required to show a bigger bang for the extra bucks, but some say the most expensive measure really is one that doesn't work, and 14 studies have reported cost savings using active detection and isolation of methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant *Enterococcus* (VRE).[4]

Regarding the latter concern, Huskins et al.[1] say cluster randomization was necessary because spread occurs throughout an ICU and could confound a trial randomizing individual patients; this observation is correct, but fails to address spread throughout the hospital and entire healthcare system that could confound the single-ICU intervention. A study by da Silva et al. showed that spread extends far beyond a single unit; 80% of cases of MRSA bacteremia in 12 hospitals across 7 states from New York to Georgia were due to just 2 clones.[5] For example, an unisolated, uncolonized patient in an ICU randomized to use isolation may be visited by a consultant or technician carrying equipment contaminated elsewhere in a hospital that is generally not controlling MRSA and VRE, or this patient may be transported outside the ICU for a diagnostic or therapeutic procedure and acquire MRSA or VRE as a result. The trial likely will count these as failures of ICU isolation, but it would represent confounding. Huskins et al.[1] say intervening more broadly would have been

"unfeasible" and would have prevented "insur[ing] reliable implementation"; however, broad, reliable implementation has been achieved in entire hospitals[2,4,6,7] and even entire healthcare systems,[2,8-10] yielding tight control.

Huskins et al.[1] say the trial's multicenter approach helps ensure generalizability, but the findings of a multicenter study with inadequate power and false-negative results wouldn't be generalizable. And even if spread halts with use of standard precautions, it won't be clear that this finding would be generalizable to real-world settings outside the limelight (and transient Hawthorne effect) of the world's first randomized trial of this question. Active detection and isolation have worked in real-world settings for decades across entire nations in Northern Europe and in Western Australia.[10,11] But after a decade of federal regulations requiring hand hygiene before and after every patient contact in thousands of US healthcare facilities and after more than 4 years of alcohol hand rubs being recommended for most hand hygiene, we still have scant credible evidence this will work to control MRSA and VRE in a real-world (non-study) setting.[2,4] Huang et al.[12] reported 80% hand hygiene compliance during the first year of a campaign (with no effect on the rate of MRSA bacteremia), but also reported that this high level of compliance proved to be unsustainable, raising questions about generalizability of that measure to real-world situations over the long term.

Huskins et al.[1] say certain statistical tests shouldn't have been used, because "nonindependence of colonization events" due to spread could have favored false-positive results in the many studies showing control of MRSA or VRE with active detection and isolation. However, if so, the same should have occurred with other approaches studied using the same tests, and positive results usually weren't seen with use of standard precautions,[13-15] antibiotic control,[16] or isolation only of patients detected by clinical culture.[6] Consistently positive results were seen only with active detection and isolation, suggesting that the result was validly associated with the control measure used, not an artifact of the statistical test. Moreover, active detection and isolation worked similarly well with smallpox, tuberculosis, and severe acute respiratory syndrome (as evaluated with the same type of statistical tests and assumptions), and it would be difficult to say that their control was a false-positive result because for 2 of those infections human transmission was eradicated worldwide.[2,4]

In addition to multiple factors previously enumerated that favor a false-negative trial result,[2] here are a couple more to consider. First, the protocol says the trial will include ICUs that "collect data for at least 3 months." If 6 months was marginal, having only 3 would be bleak. Second, one of the trial's coinvestigators told me that nurses at that particular hospital "opposed" active detection and isolation. If so, this may have boded ill for conduct of dispassionate science in that study unit, especially if those nurses believed differential performance of study control measures could "prove" their point of view in a study that multiple opponents of isolation precautions kept lauding in advance as more definitive science. It seems likely that exuberant use of one approach would work better than poor implementation of the other approach, regardless of which approach works better if both are perfectly implemented. Because the trial is unblinded, concern exists that uneven performance could occur and go undetected by the planned 5 hours of monitoring per week in each study ICU (ie, less than 0.3% of all patient-hours in fully occupied ICUs of 10 beds or larger), and bias results. Data from the tiny fraction of patient-hours monitored couldn't exclude differential performance during the 99.7% of unobserved patient-hours in such units.

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