

LETTERS TO THE EDITOR

Effectiveness of Alcohol-Based Hand Hygiene Gels in Reducing Nosocomial Infection Rates

To the Editor—We have read with great interest the article by Rupp et al.¹ The results challenge current infection control policies.² The study has been carefully conducted and the results appear to be valid. Surprisingly, the improved compliance with hand hygiene recommendations associated with the use of alcohol-based hand hygiene products did not result in lower nosocomial infection rates. As the authors pointed out, the results may be interpreted in several ways. We want to add points to be discussed that may be associated with or even responsible for these negative results.

First, the level of antimicrobial efficacy of 62% ethanol may not suffice to interrupt transmission of nosocomial pathogens. In fact, the product does not meet the requirement of European standard EN 1500,³ which is needed to clear the product for the European market.⁴ Incidentally, the exact concentration of the ethanol is not described by Rupp et al¹: it may be 62% by volume (equivalent to 49 g/dL) or 62% by weight. Second, we have shown that training in the application of alcohol-based hand hygiene products is crucial to optimize antimicrobial killing.^{5,6} No formal training is described by Rupp et al¹; an absence of training may have reduced the effect of the gel. Third, coagulase-negative staphylococci were cultured mainly from the hands of healthcare workers. However, data regarding detection of clinically important pathogens such as methicillin-resistant *Staphylococcus aureus* are not given. Finally, a formal sample size calculation was not mentioned, and lack of this calculation potentially limits the impact of the negative results of the trial. The low baseline rate of nosocomial infection may have jeopardized the possibility of detecting the clinical effect of the introduction of the gel. In addition, under conditions of high patient occupancy or understaffing, hand hygiene alone is unlikely to prevent nosocomial infection.⁷

We congratulate the authors for conducting this important trial. It may be the first hint that the antimicrobial activity of such gels is not sufficient to reduce the incidence of nosocomial infections.

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“Cannot Detect a Change” Is Not the Same as “There Is Not a Change”

To the Editor—The recent article by Rupp et al.¹ has generated a great deal of media attention. Unfortunately, the value of the article in terms of increasing hand hygiene compliance, use of alcohol-based hand gel, and useful adherence data from observations was lost. However, we believe the following remarks provide evidence that the conclusion of “no detectable change” in nosocomial infection rates may not be supported by their analysis.

The authors had a null hypothesis of “no change” and an alternative of “change.” They have concluded that their findings support the null hypothesis. What this means is that there is not enough evidence to overturn the null hypothesis—but that is not the same as saying that the null hypothesis is true. If you collect very few data or assemble a very uninformative data set, then it is unlikely that you will have enough evidence to overturn the null hypothesis—even if it should be overturned.

There are so few infections over the time period in the study¹ that the data sets are likely to be uninformative with respect to the question of infection rates. These units had 12 beds, and the

patients in each unit were observed for 1 year in each branch of the crossover study. Twelve beds multiplied by 365 days is 4,380 bed-days; so they had 4,380 bed-days as a maximum (we do not know if the units were consistently fully occupied). Their reported infection rates are approximately 1 to 4 infections per 1,000 bed-days. This means that they observed approximately 4 to 16 infections over the entire year of the intervention for each arm of the study. This range represents a very small number of infections, and without getting into the details of the underlying Poisson regression model, the inherent variability on these numbers will be relatively high.

So, what does this mean? It means that the data are very noisy, and the study is unlikely to be able to demonstrate an effect even if it is there. Rough calculations suggest that even if improvements in hand hygiene adherence were able to decrease infection rates by 50%, then this study would have only roughly a 20% chance of demonstrating the effect.

Another issue important to this data set is whether the infections themselves are independent or whether they occurred in clusters (clumped in time). If they were clustered (which would mean that they were not statistically independent), then this analysis would be weakened even more, because ignoring the clustering would give a false sense of the amount of information contained in the data. If the infections are clustered in time, then the analysis is inappropriate.

To the authors' credit, they do acknowledge that the study is "underpowered to detect small differences in rates of infection,"¹ but it may be underpowered to demonstrate larger differences, too. The reviewers of this article should have noted to the authors that this is a good article but requested that they leave out the comments on "detectable changes in the incidence of healthcare-associated infection," because there does not appear to be enough information to generate a reliable conclusion.

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Trial of Alcohol-Based Hand Gel in Critical Care Units

To the Editor—We congratulate Rupp et al.¹ for their well-designed and well-performed study. However, we have some concerns. In contrast to the findings of several studies,^{2–7} this study did not find an association between increased hand hygiene adherence and a reduction in nosocomial infections in intensive care units. The authors reported the incidence of 3 types of medical device-related infections (central venous catheter-related bacteremia, urinary catheter-associated urinary tract infection, and ventilator-associated pneumonia) and 3 types of infections associated with multidrug-resistant pathogens (methicillin-resistant *Staphylococcus aureus* [MRSA], vancomycin-resistant enterococci [VRE], and *Clostridium difficile*). Our major concern is that active surveillance cultures were not performed to identify patients colonized with MRSA or VRE. This is an important shortcoming, because the rate of importation of MRSA or VRE into intensive care units and the proportion of ICU patients colonized with such organisms ("colonization pressure") are factors shown to affect the rate of transmission and, most likely, the incidence of infection.⁸ Because no surveillance cultures were performed, the present study was not able to assess the impact of hand hygiene on nosocomial transmission of these organisms.

The study was statistically underpowered to show a difference in the measured outcomes, and in fact no formal power analysis was conducted. With detection of such low rates of nosocomial infections, the findings can be explained by chance variability, regression to the mean, and, because nosocomial infections tend to cluster, overdispersion of infection rates relative to chance variation. The authors might consider pooling the data on the incidence of infections due to MRSA, VRE, *C. difficile*, and *Pseudomonas aeruginosa* to ascertain if there was a difference in the total number of infections caused by these pathogens during the periods under study, but it is unclear if this would overcome the above-mentioned problems. In addition, the study compares infection rates aggregated by time period. As stated in gold standard guidelines for the reporting of intervention studies of nosocomial infections,⁹ measurement at regular intervals (weekly or monthly) would have better demonstrated trends.

Two of the device-related infections selected as outcomes—namely, catheter-related bloodstream infections and ventilator-associated pneumonia—often necessitate a combination ("bundle") of preventive measures, not just hand hygiene alone, to achieve substantial reductions in incidence. However, the authors did not mention if bundles were used during any of the study periods and, if they were, the degree of compliance with the bundles or other interventions that may have confounded the results.

The authors noted that their inability to demonstrate an association between hand hygiene adherence levels and rates of nosocomial infections may have been due to a failure to