conditions for nutrient-rich conditions and replacing the validated recommended test organism (biofilm forming strain of *Pseudomonas aeruginosa*) for *E coli*. Both deviations appear rather unwarranted: it is widely accepted that the biofilm in endoscope lumens is most likely to occur during storage when airborne *P aeruginosa* is contaminating washed and disinfected (ie, nutrient poor) lumen. The scenario envisaged by the authors—biofilm resulting from *E coli* from patient feces—is extremely unlikely.

The biofilm removal and accessibility of bacteria to disinfectant action should be regarded as a major risk when assessing the feasibility of replacing manual brushing with automated reprocessing in automatic endoscope reprocessors. The research on removal of biofilms is expensive, time consuming, and limited to specialized laboratories only. This is why the wider infection control community heavily relies on the published results—the conclusions of the articles similar to Ren et al[1] and Vickery et al[3] are copied-and-pasted into process risk assessment reports and product marketing sheets. The erroneous test methodologies result in erroneous conclusions that in turn lead to underestimating the risks and might cause major outbreaks, similar to the recent incident at University of California, Los Angeles.[9]

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Effect of geographic region and seasonality on *Clostridium difficile* incidence and hospital mortality

To the Editor:

The recent study by Argamany et al[1] concluded that the incidence and hospital mortality for *Clostridium difficile* infection (CDI) differed between major regions of the United States and across different seasonal times of the year. However, these conclusions were not supported by the data in their study because the authors based them exclusively on statistical significance without considering the effect size of their findings. The effect sizes of region and season on CDI were very low or near zero, contradicting their conclusion, as subsequently explained.

The effect sizes for U.S. region (Northeast, Midwest, South, and West) and seasonality (winter, spring, summer, and fall) were estimated using the data for patients overall and presented in their Figures 1-5.[1] The population rates provided were first converted into a contingency table with population counts from which Pearson χ^2 was calculated. The χ^2 was converted to a Pearson correlation coefficient, which is a standard estimator of effect size[2] using the conversion formula of $r = \chi^2 / (\chi^2 + N)$, for when the degrees of freedom are >1. The effect sizes were interpreted using Cohen's recommended criteria.[3]

The reanalysis of data showed that effect sizes (r) for the effect of U.S. region on CDI incidence was $r = 0.016$, and the effect of season was $r = 0.003$. The effect of region on CDI hospital mortality was $r = 0.014$, and the effect of season was $r = 0.023$. By Cohen's criteria,[3] an effect size of $r = 0.10$ is considered a small effect size, but these effect sizes average less than a tenth of that value, approaching zero. Although statistically significant because of the enormous sample size in the study ($N = 2{,}279{,}004$), the differences of the CDI incidence and patient mortality, as the effect sizes estimates indicated, are so trivial that the regional and seasonal differences can be safely ignored. This is consistent with the small percentage differences reported in the study: the CDI mortality for all patients differed only by approximately 1% between regions or seasons, and incidence differed across seasons by a fraction of a percent.

An additional complication is that there was little agreement on the riskiest region and season. For overall CDI mortality, the highest risk seasons were fall for adults and winter for older adults. On the other hand, for CDI incidence, the riskiest seasons were spring for both adults and older adults. Therefore, there was no agreement between incidence and mortality measures for CDI, which leaves open the question of whether any single season can be identified as the highest risk season. The same is true regarding regional differences, with the Northeast having the highest risk for CDI incidence, but the Midwest region having the worst for hospital mortality. The lowest risk was the Northeast for mortality and West for incidence. Therefore, similar to seasonality, no single region can really be identified as the high-risk region overall.

To sum up, the conclusion that the CDI incidence and hospital mortality of patients significantly differed among regions and seasons is contradicted by the calculated effect sizes and other inconsistencies in the findings. Our additional analysis does not support the authors' suggestion that "These results underscore the need for improved infection control and antimicrobial stewardship measures to prevent CDI and its transmission, particularly in high-risk regions and seasons." Instead, our estimates that the effect size

was near zero appear to support the conclusion that CDI incidence and hospital mortality of patients is nearly the same across all 4 regions and seasons. We would suggest a replacement conclusion that there is a very similar CDI risk across regions and seasons, with possible exception of particular subsets (eg, older adults).

The study by Argamany et al[1] has many of strengths, including large sample size, clear study design, excellent writing, an excellent discussion section that includes a thorough examination on the limitations of the data set, and finally, a focus on an important problem in infection control. Despite these strengths, because of the near-zero effect sizes of the findings, the conclusion of the study that the CDI incidence and patient mortality differed significantly across regions and seasons is not sufficiently supported. We suggest that there is no need at this time to redirect resources or implement targeted control measures according to region and seasons.

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Response to "Effect of geographic region and seasonality on *Clostridium difficile* incidence and hospital mortality"

To the Editor:

We appreciate the comments regarding our recently published article on the regional and seasonal variation in *Clostridium difficile* infection (CDI) among hospitalized patients in the United States.[1] We agree that measuring effect size is important in any study, particularly with a large sample size where small variations between groups could result in a statistically significant difference. However, effect size is calculated without accounting for the meaning of the measures used. We believe that the use of Cohen's criteria[2] without regard to clinical significance results in underestimation of the importance of our study findings.

From a public health perspective, the regional and seasonal variations in CDI incidence and mortality identified in our study are meaningful. Based on the actual percentage difference between the regions with the lowest (West, 6.2%) and highest (Midwest, 7.3%) mortality observed in our study, patients hospitalized with CDI in the Midwest have a 17.7% higher rate of death than hospitalized patients in the West. Similarly, a patient in the Northeast (8.0 CDIs/1,000 discharges) is 63% more likely to be hospitalized with CDI than a patient in the West (4.9 CDIs/1,000 discharges). If the observed regional and seasonal rates were reduced across the United States to the lowest rates observed in our study, a total of 42,532 cases of CDI and 1,595 deaths could be avoided each year. Using conservative estimates, each case of CDI results in an additional $2,871 in costs, potentially leading to an additional economic burden of approximately $122 million annually in our study.[3] We do not believe that these numbers can be safely ignored.

Finally, we agree that the regional and seasonal effects differed based on the measure of interest (ie, mortality vs incidence); however, this is not an inconsistency in our findings. It is quite plausible that one region might have higher mortality among patients with CDI, whereas another might have higher CDI incidence caused by differences in population characteristics and patient care. This calls for differential application of interventions to reduce the burden of CDI (eg, enhanced recognition and treatment to prevent mortality, improved antibiotic stewardship and infection control measures to reduce incidence), but does not invalidate the results.

In summary, we believe that focusing on statistical measurements alone risks leaving the human and economic consequences of CDI to be forgotten. The regional and seasonal variations identified in our study are not of minimal consequence. We affirm our original conclusion that the results of this study may be used to direct preventative and therapeutic resources where and when they are needed most.

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