After controlling for the percentage of physicians with waivers using multivariate regression, the adjusted percentage of NPs with waivers was 4.73% in less restrictive states and 2.70% in more restrictive states, with a mean difference of 2.03 percentage points (95% CI, 2.02-2.04 percentage points) (Table). There remained no significant association between less restrictive PA scope of practice and the percentage of PAs with waivers.

Discussion | Greater practice restrictions were associated with a lower percentage of NPs, but not PAs, with waivers. The difference in NPs with waivers was modest in terms of percentage points, but was more than 75% larger in less restrictive states compared with more restrictive states. Differences in characteristics between NP and PA scope of practice restrictions, such as PA regulations in all states requiring collaboration with a physician, unlike NPs, may explain the result.

Limitations of this study include that the denominators may include nonpracticing clinicians, leading to underestimation of clinicians with waivers, and that NPs and PAs have been able to obtain waivers for only 2 years.

The results of this study suggest that states in which NP practice is restricted may be less able to expand the opioid treatment workforce.

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Accepted for Publication: January 25, 2019.

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Conflict of Interest Disclosures: Dr Spetz reported receiving grants from the National Council of State Boards of Nursing during the conduct of the study and personal fees from the Center to Champion Nursing in America (American Association of Retired Persons) and grants from the Robert Wood Johnson Foundation, National Council of State Boards of Nursing, and California Health Care Foundation outside the submitted work. Dr Tierney reported receiving grants from the National Council of State Boards of Nursing's Center for Regulatory Excellence during the conduct of the study and honoraria from Contemporary Forums, the American Society of Addiction Medicine, Cabezon Group, and the American Psychiatric Nurses Association; grants from the Substance Abuse and Mental Health Services Administration; and honorarium from Johnson & Johnson outside the submitted work. No other disclosures were reported.

Funding/Support: This research was supported by the National Council of State Boards of Nursing's Center for Regulatory Excellence (grant R101026).

Role of the Funder/Sponsor: The funder was not involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript. They approved of the decision to submit the manuscript for publication to *JAMA*, without review of the manuscript, per the terms of the grant.

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COMMENT & RESPONSE

Decontamination Strategies for Critically Ill Patients

To the Editor Dr Wittekamp and colleagues concluded that the use of selective digestive tract decontamination (SDD), compared with standard care, did not lead to a reduction in bloodstream infections acquired in the intensive care unit (ICU) caused by multidrug-resistant gram-negative bacteria.[1] Their conclusion is misleading because they studied only the effect of topically administered antimicrobials and not the effect of the full SDD strategy, which is based on 4 components.[2]

The authors omitted an important component of SDD; ie, the administration of parenteral antibiotics. A 3- to 4-day course of parenteral antibiotics is required to prevent or control primary endogenous infections.[3] Approximately 55% of all infections in critically ill patients are of primary endogenous pathogenesis.

Another potential explanation for the negative results of the study is that patients who were carriers of antibiotic-resistant gram-negative bacteria in the SDD group were not decontaminated (eFigure in Supplement 2 of the article[1]). The authors did not adjust the SDD medication based on the results of the susceptibility tests of the isolated microorganisms. Depending on the antimicrobial susceptibility of the isolated microorganisms, the enteral antimicrobials should be adjusted.[4,5] Part of the SDD strategy is not the administration of topical antimicrobials but the administration of appropriate antimicrobials resulting in successful decontamination. Successful decontamination reduces bloodstream infections and mortality in critically ill patients.[2]

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Conflict of Interest Disclosures: None reported.

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To the Editor A randomized clinical trial investigated the incidence of bloodstream infections with antibiotic-resistant microorganisms in ventilated patients with sequential phases of chlorhexidine 2% mouthwash, selective oral decontamination, and SDD.[1] The SDD strategy is aimed at the detection and elimination of the patient's enteral carrier state of aerobic gram-negative bacteria.[2] The authors concluded that the SDD strategy did not prevent bloodstream infections in ICUs with a high prevalence of β-lactamase–resistant Enterobacteriaceae. We would like to raise several questions.

First, the high prevalence (14.8%) of rectal cultures still growing gram-negative bacteria on day 14 of SDD application is surprising if SDD paste and suspension with colistin sulfate, tobramycin, and nystatin was applied according to protocol, especially because the authors reported a low prevalence of colistin resistance (1.3%) among the participants. The latter prevalence may be due to the intrinsic colistin resistance that occurs with *Morganella* and *Serratia* species. Also, the authors did not report any data about defecation. Can decontamination be successful if the SDD products do not reach the rectum?

Second, the authors did not report on the day that bloodstream infections occurred after the interventions were commenced, nor did they report whether an association could be demonstrated in patients who were enteral carriers of gram-negative bacteria. This is important because an initial bloodstream infection, especially if the wrong systemic antibiotics are selected, cannot be prevented by applying the SDD strategy because it is aimed at the prevention of secondary infections. Can the authors provide data on the patients for whom decontamination was actually successful, ie, rectal cultures became negative for gram-negative bacteria?

Third, the power calculation may be invalid, there was no a priori presentation of an intracluster coefficient or calculation of required cluster number, there was an unclear error statement about "calculation of variance between study groups," there was an unjustified inflation of the sample size, and there was presentation of an invalid post hoc power calculation.[3] The power of the study for the presented outcomes is unclear and may be limited.

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Conflict of Interest Disclosures: None reported.

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To the Editor In 13 ICUs in 6 European countries, Dr Wittekamp and colleagues[1] found that use of chlorhexidine mouthwash, selective oropharyngeal decontamination, and SDD, compared with standard care, were not associated with reductions in ICU-acquired bloodstream infections caused by multidrug-resistant gram-negative bacteria among patients receiving mechanical ventilation. We have several concerns.

First, the authors did not show the sources of bloodstream infections. In a recent meta-analysis,[2] oral hygiene care, including chlorhexidine mouthwash or gel, reduced the risk of developing ventilator-associated pneumonia in critically ill patients from 25% to about 19%. Therefore, the incidence of bloodstream infection secondary to ventilator-associated pneumonia may be reduced by chlorhexidine mouthwash. In contrast, the effect of chlorhexidine mouthwash on the incidence of bloodstream infections secondary to sources other than the respiratory tract may not be affected. Further analysis is needed to clarify the issue.

Second, the type of chlorhexidine used was changed from 2% mouthwash to 1% gel during the study period. However, the effects of the mouthwash and gel may be different. In a previous study, Tang et al[3] showed that chlorhexidine gel may be more effective than chlorhexidine mouthwash for preventing ventilator-associated pneumonia. Thus, the different effects between chlorhexidine mouthwash and gel should be taken into account in the analysis.

Third, the authors did not evaluate the possibility of clonal spread of antibiotic-resistant bacteria during the study period. Because this study was conducted in ICUs with

moderate to high prevalence of antibiotic resistance, it is possible that the development of bloodstream infections could be due to the clonal spread of antibiotic-resistant bacteria.

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Conflict of Interest Disclosures: None reported.

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In Reply As mentioned by Ms Taylor and colleagues, the SDD strategy did not include systemic cephalosporins, as this was considered inappropriate in settings that were selected for having a high prevalence of multidrug-resistant gram-negative bacteria.[1] We acknowledge that this may have reduced prevention of episodes of bloodstream infection during the first days in the ICU. Therefore, we provided a post hoc sensitivity analysis that failed to support this hypothesis; the number of ICU-acquired bloodstream infections that could have been prevented by cephalosporin prophylaxis was low (17 in 16 patients) during days 0 to 4 of SDD. The median time to onset of ICU-acquired bloodstream infection was 7 days (interquartile range, 4-14 days).

We concur with Taylor and colleagues and with Drs Spronk and Cuthbertson that suboptimal decontamination of the gut might have reduced the effectiveness of SDD to prevent ICU-acquired bloodstream infections. Whether a more reactive approach in adapting the decontamination regimen on receiving culture results of individual patients or pursuing more rapid defecation would have resulted in lower carriage rates and incidences of ICU-acquired bloodstream infections caused by multidrug-resistant gram-negative bacteria and better patient outcomes is unknown. Persistent rectal colonization in some SDD patients was not primarily caused by intrinsic colistin-resistant gram-negative bacteria because the average proportion of rectal cultures (ESBL ChromID) with such bacteria was 0.8% vs 0.7% during days 0 to 14 of the baseline and SDD periods, respectively (and 2.6% vs 2.7% in the respiratory samples). Evaluation of associations between carriage state with gram-negative bacteria and the occurrence of ICU-acquired bloodstream infection, as recently studied in the Dutch setting,[2] is planned.

Spronk and Cuthbertson question the sample size calculation of our study. Yet, regardless of how a certain sample size is derived, the actual power of a study is reflected by the confidence intervals around the effect estimates. For clarity we mentioned the actual power, which might be considered unusual but is not invalid. The correct interpretation of the primary end point is that the study had 78.7% power to demonstrate that SDD was associated with a 50% reduction in ICU-acquired bloodstream infections, which does not exclude the possibility of a benefit of lower magnitude.

In response to the comments by Drs Chao and Lai, we can say that, as in previous studies,[3,4] the occurrence of ventilator-associated pneumonia was not measured because of the inherent problems in establishing this diagnosis. Chlorhexidine had no effect on the occurrence of ICU-acquired bloodstream infections compared with baseline. The change from 2% chlorhexidine mouthwash to 1% chlorhexidine oral gel occurred early in the study, precluding a sensible comparison of effectiveness for any of the end points. The occurrence of clonal spread is a subject of ongoing research. Yet, as we investigated unit-wide interventions without changing other infection control measures, any difference in clonal spread between study periods may well reflect consequences of the interventions studied rather than a factor disturbing a sound comparison of the interventions.

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Conflict of Interest Disclosures: All authors reported receiving grants from the European Commission.

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Multifaceted Program to Reduce Job Strain in ICU Nurses

To the Editor Ms El Khamali and colleagues[1] found that, among nurses working in an intensive care unit (ICU), those who participated in a multifaceted skills enhancement program had a lower prevalence of job strain after 6 months compared with those who did not participate in the program. However, as mentioned in the Editorial by Seaman et al,[2] "there is a lack of clarity about the theorized and actual mechanism by which the intervention exerted its effect." Accordingly, some aspects need clarification.