ORIGINAL ARTICLE

# Development and Validation of a Simple and Easy-to-Employ Electronic Algorithm for Identifying Clinical Methicillin-Resistant *Staphylococcus aureus* Infection

**Westyn Branch-Elliman, MD, MMSc;[1,2,3] Judith Strymish, MD;[1,3,5] Kalpana Gupta, MD, MPH[1,4,5]**

BACKGROUND. With growing demands to track and publicly report and compare infection rates, efforts to utilize automated surveillance systems are increasing. We developed and validated a simple algorithm for identifying patients with clinical methicillin-resistant *Staphylococcus aureus* (MRSA) infection using microbiologic and antimicrobial variables. We also estimated resource savings.

METHODS. Patients who had a culture positive for MRSA at any of 5 acute care Veterans Affairs hospitals were eligible. Clinical infection was defined on the basis of manual chart review. The electronic algorithm defined clinical MRSA infection as a positive non-sterile-site culture with receipt of MRSA-active antibiotics during the 5 days prior to or after the culture.

RESULTS. In total, 246 unique non-sterile-site cultures were included, of which 168 represented infection. The sensitivity (43.4%–95.8%) and specificity (34.6%–84.6%) of the electronic algorithm varied depending on the combination of antimicrobials included. On multivariable analysis, predictors of algorithm failure were outpatient status (odds ratio, 0.23 [95% confidence interval, 0.10–0.56]) and respiratory culture (odds ratio, 0.29 [95% confidence interval, 0.13–0.65]). The median cost was $2.43 per chart given 4.6 minutes of review time per chart.

CONCLUSIONS. Our simple electronic algorithm for detecting clinical MRSA infections has excellent sensitivity and good specificity. Implementation of this electronic system may streamline and standardize surveillance and reporting efforts.

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As electronic medical records become standard,[1] utilization of automated surveillance systems is increasing.[1,2] Much prior work focused on *International Classification of Diseases, Ninth Revision* (ICD-9) codes to identify patients with various conditions,[3] including methicillin-resistant *Staphylococcus aureus* (MRSA). However, several studies have demonstrated that ICD-9-based searching for MRSA infection has low sensitivity and specificity.[4,5] Natural language processing of Veterans Affairs (VA) data has also been used to identify MRSA-positive cultures, but it has not been employed to designate infection status and is not available at most facilities.[6]

Previous studies of electronic definitions have demonstrated that automated systems save time;[7,8] however, they have lower sensitivity and specificity than manual review. Thus, the overall cost-effectiveness of using electronic systems remains in question.[9]

Alternative options for identifying MRSA infections include microbiologic data and hospital discharge data.[10,11] Microbiologic data alone is insufficient to classify infected versus noninfected patients. Until recently, definitions based on antimicrobial usage have been impractical because of difficulties in obtaining prescribing information.[11] Studies evaluating surgical site infection (SSI) detection have found that combinations of pharmacy and administrative data improve standard manual chart review surveillance methods.[12,13]

Although ICD-9-based definitions are clearly deficient, alternative strategies are lacking. To this end, we sought to develop and validate a simple and easy-to-employ electronic definition of clinical MRSA infection using microbiologic and prescription data within the VA Healthcare System (HCS). Our goal was to maximize sensitivity, as manual review may be used as an ancillary process to adjudicate electronically identified infections and optimize specificity. Secondary aims were (1) to determine predictors of algorithm failure and identify areas where electronic algorithms do not function well to inform future electronic surveillance systems and (2) to estimate the cost savings generated from the reduced person-time required for manual chart review.

Affiliations: 1. Boston Veterans Affairs Healthcare System, Boston, Massachusetts; 2. Divisions of Infectious Diseases and Infection Control, Beth Israel Deaconess Medical Center, Boston, Massachusetts; 3. Harvard University Medical School, Boston, Massachusetts; 4. Boston University School of Medicine, Boston, Massachusetts; 5. Patient Safety Center of Inquiry on Measurement to Advance Patient Safety, Veterans Affairs National Healthcare System, Boston, Massachusetts.

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## METHODS

### Case Selection

VISN-1 is comprised of 5 acute care hospitals, 3 long-term care facilities, and several outpatient clinics. In total, there are 1,084 inpatient beds, and approximately 240,000 unique patients are cared for on an annual basis. Data from all facilities within VISN-1, including outpatient clinics, were included in the study.

Details on cohort inclusion criteria have been published elsewhere.[14] Briefly, patients who were admitted to an acute care hospital in VISN-1 and underwent active surveillance screening for MRSA colonization during the period from January 1, 2008, through December 31, 2010, were eligible for inclusion. From this larger cohort, patients with non-sterile-site cultures positive for MRSA were identified, and a random sample was chosen for manual chart review. Patients with multiple positive cultures were potentially included more than once; however, if 2 non-sterile-site cultures were positive within a 2-week window, only 1 was eligible for inclusion.

### Data Extraction

Baseline demographic data (age, sex, race), clinical data (diabetes, renal disease, human immunodeficiency virus infection, smoking status), microbiologic data (culture result and date), and data on antimicrobial prescriptions within 5 days of a positive culture were extracted electronically using FileMan routines as well as Structured Query Language. Oral and intravenous as well as inpatient and outpatient antimicrobial prescription data were evaluated.

Manual chart review was conducted to confirm culture results and date as well as prescription data. Charts were also reviewed for inpatient versus outpatient status of patient at the time of clinical culture, clinical characteristics suggestive of underlying infection, and provider diagnosis.

### Electronic Definition

MRSA infections were defined electronically as any positive culture from a sterile site (blood, bone, device) or a positive culture from a nonsterile site (fluid, respiratory, skin, swab, tissue, urine) in association with 1 or more MRSA-active antimicrobials within 5 days prior to or after a positive culture (Figure 1). To maintain simplicity of the algorithm, any dose of a MRSA antibiotic within the window was considered positive. Sterile-site cultures and cultures sent for surveillance purposes only were excluded from the analysis of the operating characteristics of the electronic algorithm. Antimicrobials extracted electronically and potentially included in the definition were clindamycin, daptomycin, doxycycline, linezolid, trimethoprim-sulfamethoxazole, and vancomycin. Additional antimicrobials that were evaluated included $\beta$-lactam antibiotics (amoxicillin, ampicillin, cefazolin, cefepime, cefpodoxime, ceftriaxone, cephalexin, dicloxacillin, nafcillin, oxacillin, piperacillin) and fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin).

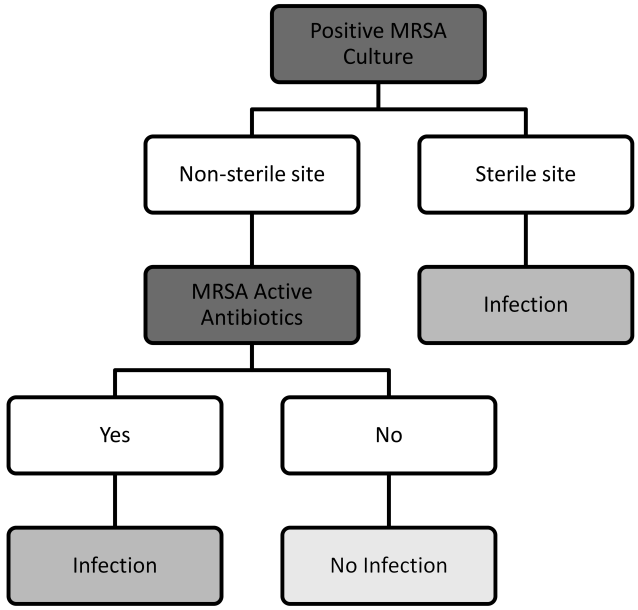


FIGURE 1. Proposed electronic algorithm for identifying clinical methicillin-resistant *Staphylococcus aureus* (MRSA) infection.

### Clinical Definition and Review

A random selection of patients with non-sterile-site cultures positive for MRSA were reviewed for clinical diagnosis of infection. Clinical determination of infection was based on published definitions of skin and soft-tissue infections,[15] bronchitis/pneumonia,[16] and urinary tract infection.[17,18] National Healthcare Safety Network (NHSN) definitions were used to define SSIs. Cultures labeled as swabs or fluid were evaluated for the source and then designated as infection on the basis of published infection definitions, as above.[3,18]

Charts received an initial clinical review by one of the authors (W.B.-E.), who was blinded to the electronic determination of infected versus noninfected. If the initial clinical and electronic evaluations of infection agreed, no further clinical review was undertaken. If the clinical and the electronic definitions disagreed, then a second clinician (J.S.) reviewed the chart and determined infection status. The second reviewer was blinded to both the first clinical evaluation and the electronic determination. If the 2 clinical reviews agreed, then the case was classified accordingly. If the first and second clinical reviewers disagreed, then a third clinician (K.G.) reviewed the chart, and the case was classified according to the 2 agreeing clinical reviews, regardless of the results of the electronic algorithm.

### Person-Time Requirements

To determine the amount of time required to classify a positive culture as representing an infection, the length of time

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TABLE 1. Baseline Characteristics of the Cohort Used to Derive Electronic Definition of Clinical Methicillin-Resistant *Staphylococcus aureus* Infection

| | Infected ($n$ = 168) | Noninfected ($n$ = 78) |
|---|---|---|
| Clinical characteristics | | |
| Provider diagnosis of infection | 92.9 (156/168) | 91.0 (71/78) |
| Drug use | 8.9 (15/168) | 3.8 (3/78) |
| HIV positive | 0.6 (1/168) | 1.3 (1/78) |
| Renal disease | 14.3 (24/168) | 11.5 (7/78) |
| Culture characteristics | | |
| Inpatient status when culture taken | 81.5 (137/168) | 81.1 (60/74) |
| Mixed culture | 29.2 (49/168) | 39.2 (29/74) |
| Receipt of any antimicrobial | 95.8 (161/168) | 65.4 (51/78) |
| Respiratory culture | 22.0 (37/168) | 30.8 (24/78) |
| Urine culture | 1.2 (2/168) | 2.6 (2/78) |
| Abscess, drainage, fluid culture | 26.8 (45/168) | 20.5 (16/78) |
| Swab | 26.8 (45/168) | 30.8 (24/78) |
| Other | 23.2 (39/168) | 15.4 (12/78) |

NOTE. Data are % (proportion). HIV, human immunodeficiency virus.

required for data abstraction was collected. The time required for chart abstraction was recorded only after the first 100 charts were reviewed, to avoid bias. Only cases that received evaluation and treatment at the VA Boston HCS were included in the person-time analysis.

### Statistical Analysis

*Accuracy of electronic algorithm.* To determine the optimal electronic algorithm, the clinical review of infection versus no infection was compared with the electronic algorithm designation. Different combinations of antimicrobials were included in the electronic definition, with clinical review used as the gold standard for infection diagnosis. We also compared the clinical gold standard diagnosis to the provider diagnosis. The sensitivity and specificity of the algorithm were calculated. $\kappa$ agreement statistics and receiver operating curves were generated and used to determine the optimal electronic MRSA infection definition. A subanalysis was completed on cases meeting NHSN criteria for SSI to determine algorithm success.

*Predictors of agreement and discordance.* After the optimal electronic definition was determined, potential predictors of algorithm success and failure were evaluated using $t$ tests, Fisher exact tests, and $\chi^2$ tests, as appropriate. Variables significant to a $P < .2$ level were then entered into a multivariable stepwise logistic regression model, and variables significant to $P < .05$ were included in the final model. Odds ratios (ORs) and $P$ values are reported. Finally, the Hosmer-Lemeshow test was calculated to determine model goodness of fit.

*Cost calculation and presentation.* The cost of manual surveillance was calculated by determining the mean length of time required by chart review and multiplying the time by the median hourly wage for a registered nurse, as determined by the US Department of Labor Statistics (median wage of infection control practitioner not available).[19] We assumed that clinical chart review was part of the usual workflow of infection control practitioners and that resources would not be diverted from other activities for this purpose.

The incremental cost of clinical review was calculated as the cost of using the electronic algorithm subtracted from the cost of manual chart review by an experienced practitioner. Costs are presented in 2012 US dollars, and descriptive statistics are presented.

## RESULTS

In total, 1,139 cultures were identified. Of these, 201 were clearly marked from sterile sites, and no further evaluation was undertaken (157 blood, 41 bone, 3 device). Five swabs were performed for surveillance purposes only; these were also excluded.

Two hundred fifty clinical charts were randomly selected for clinical review. Four charts were excluded because of inability to access the patient's electronic medical record, which left 246 charts included in the analysis.

Of the 246 cultures, 68.3% (168/246) were classified as MRSA infection and 31.7% (78/246) were classified as no infection, according to the clinical definitions used for the study (Table 1). Of these, 31.7% (78/246) were mixed cultures and 80.1% (197/246) were performed on an inpatient basis. The clinical chart review and the provider diagnosis agreed in 92.3% of cases (227/246). The $\kappa$ agreement statistic between the gold standard infection diagnosis and the provider diagnosis was 0.825 (95% confidence interval [CI], 0.749–0.900), in the excellent range.

The sensitivity and specificity of the electronic algorithm varied from 43.4% to 95.8% (sensitivity) and from 34.6% to 84.6% (specificity), depending on the combination of antimicrobials included in the definition (Table 2). The combi-

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TABLE 2. Test Characteristics Varied by Number and Type of Antibiotic Included for the Electronic Algorithm for Identifying Clinical Methicillin-Resistant *Staphylococcus aureus* Infection

| Antibiotics included in electronic definition | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| V[a] | D[b] | L[c] | C[d] | D[e] | T[f] | FQ[g] | BL[h] | Sensitivity, % | Specificity, % | $\kappa$ (95% CI) |
| • | | | | | | | | 68.5 | 80.8 | 0.44 (0.33–0.54) |
| | | • | • | • | • | | | 43.5 | 84.6 | 0.22 (0.13–0.31) |
| • | • | • | • | | • | | | 86.9 | 73.1 | 0.60 (0.49–0.71) |
| • | • | • | • | • | • | | | 91.1 | 68.0 | 0.61 (0.50–0.72) |
| • | • | • | • | • | • | • | • | 95.8 | 34.6 | 0.36 (0.24–0.48) |

NOTE. CI, confidence interval.
[a] Vancomycin.
[b] Daptomycin.
[c] Linezolid.
[d] Clindamycin.
[e] Doxycycline.
[f] Trimethoprim-sulfamethoxazole.
[g] Fluoroquinolones evaluated included ciprofloxacin, levofloxacin, and moxifloxacin.
[h] $\beta$-Lactams evaluated included amoxicillin, ampicillin, cefazolin, cefepime, cefpodoxime, ceftriaxone, cephalexin, dicloxacillin, nafcillin, oxacillin, and piperacillin.

nation of antibiotics that maximized sensitivity while maintaining specificity included clindamycin, daptomycin, doxycycline, linezolid, trimethoprim-sulfamethoxazole, and vancomycin (Figure 2). The $\kappa$ agreement statistic between the clinical review call and the electronic algorithm call was 0.61 (95% CI, 0.50–0.72). Including fewer antimicrobials in the electronic definition improved specificity but reduced sensitivity. Similarly, including additional antimicrobials improved sensitivity but markedly reduced specificity.

No demographic variables were found to be significantly associated with algorithm failure on univariate analysis. Clinical and microbiologic variables that were predictive of electronic algorithm success included inpatient status at the time of culture collection and culture classified as coming from an abscess, drainage, or fluid. Cultures identified as coming from a respiratory source (bronchoalveolar lavage or sputum) were predictive of electronic algorithm failure. On multivariable analysis, we found that having a positive non-sterile-site culture collected on an inpatient basis (compared with outpatient) was significantly associated with algorithm success (OR, 4.3 [95% CI, 1.8–10.3]), and a positive culture from a respiratory source was significantly associated with algorithm failure (OR, 0.29 [95% CI, 0.13–0.65]; Table 3). Although having a positive non-sterile-site culture from an abscess, drainage, or fluid was significantly associated with predicting algorithm success (OR, 4.8; $P = .0046$), it did not meet criteria to stay in the final adjusted model ($P = .053$). The Hosmer-Lemeshow statistic for goodness of fit of the model was 0.62.

Among the positive clinical culture isolates, 33 cases of SSI were identified. The electronic algorithm correctly identified these cases as infections in 87.9% (29/33).

Review of 102 charts were timed to determine the person-time required to classify a positive non-sterile-site culture for MRSA as an infection versus colonization. The mean length of time required for clinical review was 4.6 minutes per chart, with a range of 2–12 minutes depending on degree of clinical complexity. According to the US Department of Labor Statistics, the median hourly wage for registered nurses is $31.71 (interquartile range, $25.85–$46.46). Thus, the median cost of reviewing a single chart is $2.43, with the median cost varying depending on the wage of infection control practitioners at a given institution. If the time required for clinical review is on the higher end (12 minutes), then the median cost is $6.34; if the time required is less (2 minutes), then the median cost is $1.06. In our institution, an electronic medical record and programming for an electronic MRSA infection definition were already in place. Thus, the cost of using the electronic definition was negligible.

## DISCUSSION

Identification of patients with clinical and healthcare-associated MRSA infections is increasingly being required as part of infection prevention, quality, and public health programs.[20] Manual review of all patients with potential MRSA is an onerous task that may defer resources away from other prevention activities. Thus, there is a need for strategies that facilitate classification of MRSA infection using easily obtainable criteria.

Our simple electronic definition of MRSA infection had high sensitivity and specificity; the definition performed as well or better than older algorithms being used in other medical centers and systems.[10] By providing a structured, systematic process for MRSA infection designation, efficiency and objectivity and validity of comparing rates within or across hospitals improves.[10] In addition, this algorithm can be applied to large databases for research or quality improvement

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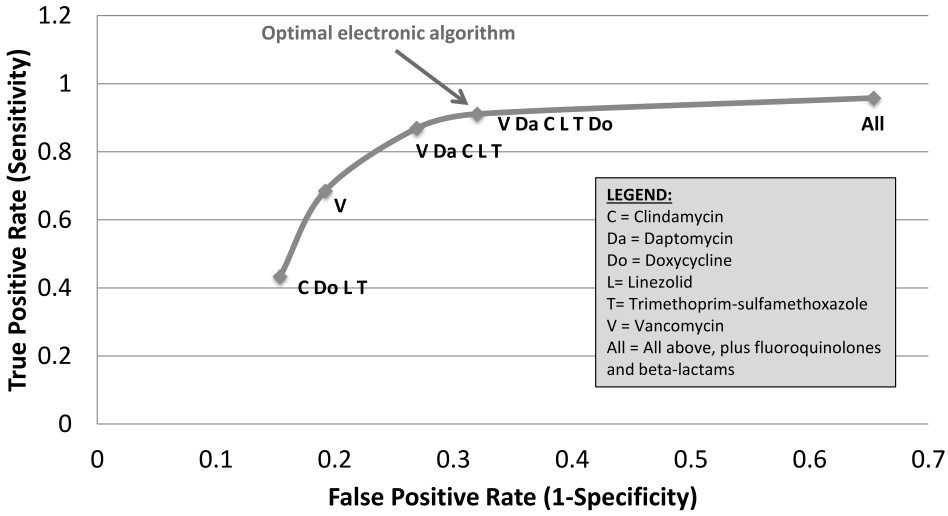


FIGURE 2. Receiver operating characteristics of different combinations of antimicrobials for identifying clinical methicillin-resistant *Staphylococcus aureus* (MRSA) infection. As more antimicrobials are added to the electronic algorithm, the sensitivity improves but the specificity suffers.

activities that might otherwise be precluded if manual review were required to identify each infection.

In comparison to methicillin-susceptible *S. aureus*, there is a small and well-characterized collection of antimicrobials that are used to treat MRSA infections. Both the strength and the weakness of our electronic definition was its reliance on antimicrobial usage and clinical prescribing practice. The primary reason for loss of sensitivity was clinical MRSA infections being treated with antimicrobials not active against MRSA, most commonly $\beta$-lactams.[21] Because some of the variability in algorithm performance was the result of differences in local prescribing practices, we also considered using a wider range of antibiotics in our electronic definition, including some not active against MRSA. When we included additional antimicrobials, we were able to achieve high algorithm sensitivity (95.8%); however, the specificity suffered considerably (34.6%). Future algorithms could potentially include additional clinical variables and administrative data, such as procedure codes or ICD-9 codes, to improve the overall operating characteristics of the algorithm.

On the flip side, one of the major contributors to a lack of specificity was patients receiving MRSA-active antimicrobials for non-MRSA infections, which resulted in patients being incorrectly classified as having a MRSA infection when they did not. Examples of this included the following: treatment for other types of gram-positive organisms with vancomycin in the setting of a $\beta$-lactam allergy, use of vancomycin for perioperative surgical prophylaxis, broad-spectrum treatment for sepsis of an unidentified source, use of trimethoprim-sulfamethoxazole for non-MRSA urinary tract infections, and use of doxycycline for acne or MRSA decolonization. Adjustment for lack of specificity could be obtained by changing the window for antimicrobial usage; our definition included any active antimicrobial during the 5 days prior to or after a positive clinical MRSA culture. Shortening the window or requiring multiple doses of antimicrobials may improve the specificity of the algorithm by excluding some of the patients who briefly received antimicrobials for other purposes. Changing the time frame could also be used to designate an infection as community or healthcare associated.

Because of our reliance on a positive clinical culture, the electronic definition failed to identify patients with suspected MRSA infection who did not have a culture sent. Previous studies suggest that relying on microbiologic data may miss up to 6% of cases of nosocomial infection in medical units and greater than 10% of cases in surgical units.[22] While this

TABLE 3. Predictors of Success and Failure for the Electronic Algorithm for Identifying Clinical Methicillin-Resistant *Staphylococcus aureus* Infection

| Variable | Univariate OR (95% CI) | Univariate *P* | Multivariable OR (95% CI) | Adjusted *P* |
|---|---|---|---|---|
| Inpatient status at time of culture | 2.8 (1.3–6.0) | .012 | 4.3 (1.8–10.3) | <.001 |
| Respiratory culture | 0.48 (0.23–0.98) | .048 | 0.29 (0.13–0.65) | .003 |
| Culture labeled as abscess, drainage, or fluid | 4.8 (1.4–16.3) | .0046 | ... | ... |

NOTE. CI, confidence interval; OR, odds ratio.

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is clearly a downside of our algorithm, nearly all existing electronic algorithms use a positive microbiologic result to identify cases.[7,8,11,13] Definitions that do not depend on a positive culture, such as ICD-9-based algorithms, are known to have suboptimal operating characteristics for identifying MRSA-infected patients.[4] Development of a fully automated system will likely require integrating simple clinical data with administrative data for optimal results.

Because our study included patients from all of VISN-1, practice related to a single center was unlikely to affect our results; however, regional trends may have impacted results, particularly if providers at our facilities were more likely to prescribe certain types of antimicrobials or were more or less likely to order bacterial cultures than clinicians in other settings. The closed nature of the VA HCS combined with our robust electronic medical record almost certainly improved our capture of infections; however, it may limit the generalizability of our results to open healthcare systems and to centers lacking an electronic prescription program.

Our cost estimate was based on the person-time required for clinical chart review in a system with a robust and long-standing electronic medical record. The time required for manual chart review may vary depending on type of medical record (paper vs electronic) and experience of the clinical reviewer. Unfortunately, we were not able to address these issues in our cost analysis. Furthermore, at our institution the necessary tools for implementing the electronic definition were already in place, and thus the electronic algorithm was cost-free. If the required infrastructure is not in place, then developing and maintaining an electronic system for identifying infections could be very expensive.

Strengths of our study included that both inpatient and outpatient results were included. Although the algorithm was found to have better operating characteristics for inpatients (Table 2), overall it performed well and could be used on a broader scale than many previously published systems.

In conclusion, our simple electronic definition of MRSA infection, including a positive MRSA culture with MRSA-active antimicrobials within a 10-day window surrounding the culture date, had excellent sensitivity and good specificity. This easy-to-use algorithm works well in both inpatient and outpatient settings and could be utilized to identify patients with MRSA infection for surveillance reporting purposes. In addition, our study highlights areas where improvement is needed before a fully automated system can be adopted.

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*Potential conflicts of interest.* All authors report no conflicts of interest relevant to this article. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

Address correspondence to Westyn Branch-Elliman, MD, MMSc, 330 Brookline Avenue, Boston, MA 02215 (wb-e@fsm.northwestern.edu).

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