

2017

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Maria M. Reyes
Washington University School of Medicine

Satish Munigala
Washington University School of Medicine

Emily L. Church
Barnes Jewish Hospital

Tobias B. Kulik
Washington University School of Medicine in St. Louis

Salah G. Keyrouz
Washington University School of Medicine in St. Louis

See next page for additional authors

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Recommended Citation

Reyes, Maria M.; Munigala, Satish; Church, Emily L.; Kulik, Tobias B.; Keyrouz, Salah G.; Zipfel, Gregory J.; and Warren, David K., "Comparing external ventricular drains-related ventriculitis surveillance definitions." *Infection Control and Hospital Epidemiology*. 38, 5. 574-579. (2017).
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Authors

Maria M. Reyes, Satish Munigala, Emily L. Church, Tobias B. Kulik, Salah G. Keyrouz, Gregory J. Zipfel, and David K. Warren

Comparing External Ventricular Drains-Related Ventriculitis Surveillance Definitions

Maria M. Reyes, MD;¹ Satish Munigala, MBBS, MPH;¹ Emily L. Church, MPH;⁴ Tobias B. Kulik, MD, PhD;² Salah G. Keyrouz, MD, FAHA;² Gregory J. Zipfel, MD;³ David K. Warren, MD, MPH¹

OBJECTIVE. To evaluate the agreement between the current National Healthcare Safety Network (NHSN) definition for ventriculitis and others found in the literature among patients with an external ventricular drain (EVD)

DESIGN. Retrospective cohort study from January 2009 to December 2014

SETTING. Neurology and neurosurgery intensive care unit of a large tertiary-care center

PATIENTS. Patients with an EVD were included. Patients with an infection prior to EVD placement or a permanent ventricular shunt were excluded.

METHODS. We reviewed the charts of patients with positive cerebrospinal fluid (CSF) cultures and/or abnormal CSF results while they had an EVD in place and applied various ventriculitis definitions.

RESULTS. We identified 48 patients with a total of 52 cases of ventriculitis (41 CSF culture-positive cases and 11 cases based on abnormal CSF test results) using the NHSN definition. The most common organisms causing ventriculitis were gram-positive commensals (79.2%); however, 45% showed growth of only 1 colony on 1 piece of media. Approximately 60% of the ventriculitis cases by the NHSN definition met the Honda criteria, approximately 56% met the Gozal criteria, and 23% met Citerio's definition. Cases defined using Honda versus Gozal definitions had a moderate agreement ($\kappa = 0.528$; $P < .05$) whereas comparisons of Honda versus Citerio definitions ($\kappa = 0.338$; $P < .05$) and Citerio versus Gozal definitions ($\kappa = 0.384$; $P < .05$) had only fair agreements.

CONCLUSIONS. The agreement between published ventriculostomy-associated infection (VAI) definitions in this cohort was moderate to fair. A VAI surveillance definition that better defines contaminants is needed for more homogenous application of surveillance definitions between institutions and better comparison of rates.

Infect Control Hosp Epidemiol 2017;38:574–579

Ventriculostomy-associated infection (VAI) is one of the most serious complications of external ventricular drain (EVD) use. These infections can result in increased morbidity, mortality, prolonged hospital stay, and higher healthcare costs.^{1,2} The reported incidence of VAI varies from <1% to 45%.^{1,3} This wide variability in VAI incidence may be due in part to the challenge of diagnosing VAI in the presence of an abnormal cerebrospinal fluid (CSF) profile from underlying central nervous system (CNS) disease, recent surgery,^{1,4} and differences among VAI definitions.^{1,5}

The Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) has defined ventriculitis.⁶ A single positive CSF culture or non-culture-based microbiological test meets the NHSN ventriculitis definition. Because CSF samples for culture are generally

drawn through the EVD in the course of routine care, intraluminal colonization of the device may result in a positive culture,¹ thereby meeting the NHSN definition.

A recent study by Lewis et al³ compared the performances of multiple VAI definitions. The NHSN definition was not included in the comparison, and the antibiotic length of therapy was used as the gold standard for ventriculitis, which may have introduced bias due to variations in antibiotic prescribing practices.⁷

NHSN surveillance data are increasingly being linked to hospital reimbursement by regulatory agencies and payers (eg, the Centers for Medicare and Medicaid Services). Therefore, understanding the performance characteristics of NHSN definitions is important. In this study, we compared VAI rates using the NHSN definition versus other published definitions.

Affiliations: 1. Department of Medicine Washington University School of Medicine, St. Louis, Missouri; 2. Department of Neurology, Washington University School of Medicine, St. Louis, Missouri; 3. Department of Surgery, Washington University School of Medicine, St. Louis, Missouri; 4. Department of Hospital Epidemiology and Infection Prevention, Barnes Jewish Hospital, St. Louis, Missouri.

Received August 14, 2016; accepted January 17, 2017; electronically published February 21, 2017

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METHODS

Study Cohort

We conducted a retrospective study of patients who underwent placement of an EVD between January 2009 and December 2014 and were cared for in the Barnes-Jewish Hospital neurological and neurosurgical intensive care unit.

Inclusion and Exclusion Criteria

A total of 965 EVDs were identified during the study period. We excluded EVDs placed in patients <18 years old and those who had a permanent shunt, a cerebral abscess, and/or a positive CSF culture at the time of EVD insertion. From the remaining patients with EVDs, we included only those whose EVD and culture status satisfied the NHSN definition for ventriculitis.⁶ These included patients having a positive CSF culture while the EVD was in place or an abnormal CSF analysis result or positive blood cultures in the presence of neurological symptoms. We considered only tests that were performed while an EVD was in place and up to 2 days after removal.

NHSN CSF Culture-Positive Episodes

We included all patients with a positive CSF culture during the study period. If multiple organisms grew from a single CSF culture, we considered it a polymicrobial case. If a patient had multiple CSF cultures that grew the same organism, we considered it a single case with the date of initial positive culture as the case date. If a patient had multiple CSF cultures performed and different organisms grew from >1 culture, we considered each culture as a different case. Cultures drawn on the same day or within 1 calendar day were part of the inclusion criteria unless the patient had a pre-existing infection.

NHSN CSF Culture-Negative Cases

Patients with at least 1 CSF glucose measurement <50 mg/dL were included. Patients with all 3 additional criteria were included for further review: CSF protein >50 mg/dL, CSF nucleated cells >5 cells/mm³, and fever >38°C.

Cerebrospinal fluid analysis data (ie, protein level, density of nucleated cells, glucose level) obtained contemporaneously with CSF culture were considered. If no CSF analysis was obtained when the culture specimen was obtained, we considered the CSF analysis temporally closest to the CSF culture performed while the EVD was in place.

To assess the cases of patients who did not meet either the positive CSF culture or the abnormal CSF criteria, we conducted a chart review of all patients with a positive blood culture(s) while the EVD was in place. If there was suspicion of a CNS infectious source, the patient was included for further evaluation.

Other Definitions

We applied 3 other published VAI definitions (ie, those of Honda et al,⁸ Gozal et al,⁹ and Citerio et al¹⁰) to our cohort (Table 1).⁶ All of these definitions required the growth of an organism from a CSF culture; therefore, the patients who met these definitions comprised a subset of the patients who met the NHSN VAI definition by virtue of a positive CSF culture.

Data Collection

Patient demographics, CSF testing, culture results, and blood culture data were abstracted from the hospital medical informatics database. We collected the following data from the charts: date of EVD insertion and removal (ie, extracted from the per shift nursing assessment), EVD indication for placement, clinical information (ie, maximal temperature, new meningeal or cranial nerve signs within 72 hours of CSF testing), and systemic antibiotic therapy while the EVD was in place.

We defined treatment as receiving an antibiotic with activity against the organism(s) detected in CSF cultures, based upon susceptibilities. In the case of common commensals with no susceptibilities reported, agents with activity against methicillin-resistant bacteria were considered active. We defined ≥14 days as an appropriate length of antibiotic therapy for ventriculitis. Notably, prior to May 2012, all EVD patients in our study received either cefazolin or vancomycin prior to EVD placement and then as long as the catheter remained in place. After May 2012, patients received only periprocedural antibiotics.

Statistical Analyses

SPSS version 22 software (IBM; Armonk, NY) was used for statistical analyses. Percentage agreements of the Honda, Gozal, and Citerio definitions with NHSN definition were calculated. The unweighted κ statistic was used to assess the agreement between Honda, Gozal, and Citerio definitions.

This study was approved by the Washington University Human Research Protection Office.

RESULTS

After exclusions, our study cohort included 48 patients with 49 EVDs and 52 cases of ventriculitis, which included 41 culture-positive and 11 culture-negative cases (Figure 1). The median age of the patients was 54 years (interquartile range [IQR], 47–64 years) and 58.3% were female (n = 28). Several EVD characteristics are listed in Table 2.

CSF Culture-Positive Cases

Overall, 37 patients with 38 EVDs contributed to 41 CSF culture-positive cases of ventriculitis. The median time from EVD insertion to first positive culture was 8 days (IQR, 4–12 days). Of the 41 CSF culture-positive samples, 2 were not

TABLE 1. Ventriculitis Definitions Used in the Study

Name	Definition Criteria	Culture Criteria	Gram Stain	Clinical Criteria	CSF Analysis Criteria	Other Criteria
CDC/ NHSN ⁶	Culture criteria alone OR 2 of 3 clinical criteria and <ul style="list-style-type: none"> All CSF analysis criteria OR Abnormal gram stain OR Positive blood culture 	Any growth	Organism present	<ul style="list-style-type: none"> Fever >38°C Meningeal Cranial nerve signs 	↑ CSF nucleated cells AND ↓ CSF glucose AND ↑ CSF protein	...
Honda et al ⁸	Culture alone OR if skin flora, ^a then at least one of CSF analysis criteria must be met.	Any growth	Should match culture growth		<ul style="list-style-type: none"> CSF WBC ≥10 cells/mm³ OR CSF glucose <25 mg/dL OR CSF protein >50 mg/dL 	Consider only if at least 48 h after EVD inserted
Gozal et al ⁹	Culture AND clinical criteria AND CSF analysis criteria	Any growth		Fever >38.6°C	<ul style="list-style-type: none"> CSF glucose < 50 mg/dL OR CSF glucose/serum glucose ratio ≤ 50% 	Includes even those in whom criteria were met within 72 h of EVD removal
Citerio et al ¹⁰	Culture criteria AND clinical criteria AND CSF analysis criteria	Any growth		Fever > 38°C	CSF WBC >5 cells/μL AND CSF glucose/ serum glucose ratio ≤50%	...

NOTE. CDC/NHSN, Centers for Disease Control and Prevention/National Healthcare Safety Network; CSF, cerebrospinal fluid; WBC, white blood cell count; EVD, external ventricular drain.

^aCommon skin flora: coagulase-negative staphylococci, *Corynebacterium*, *Bacillus*, *Micrococcus*, or *Propionibacterium* spp.

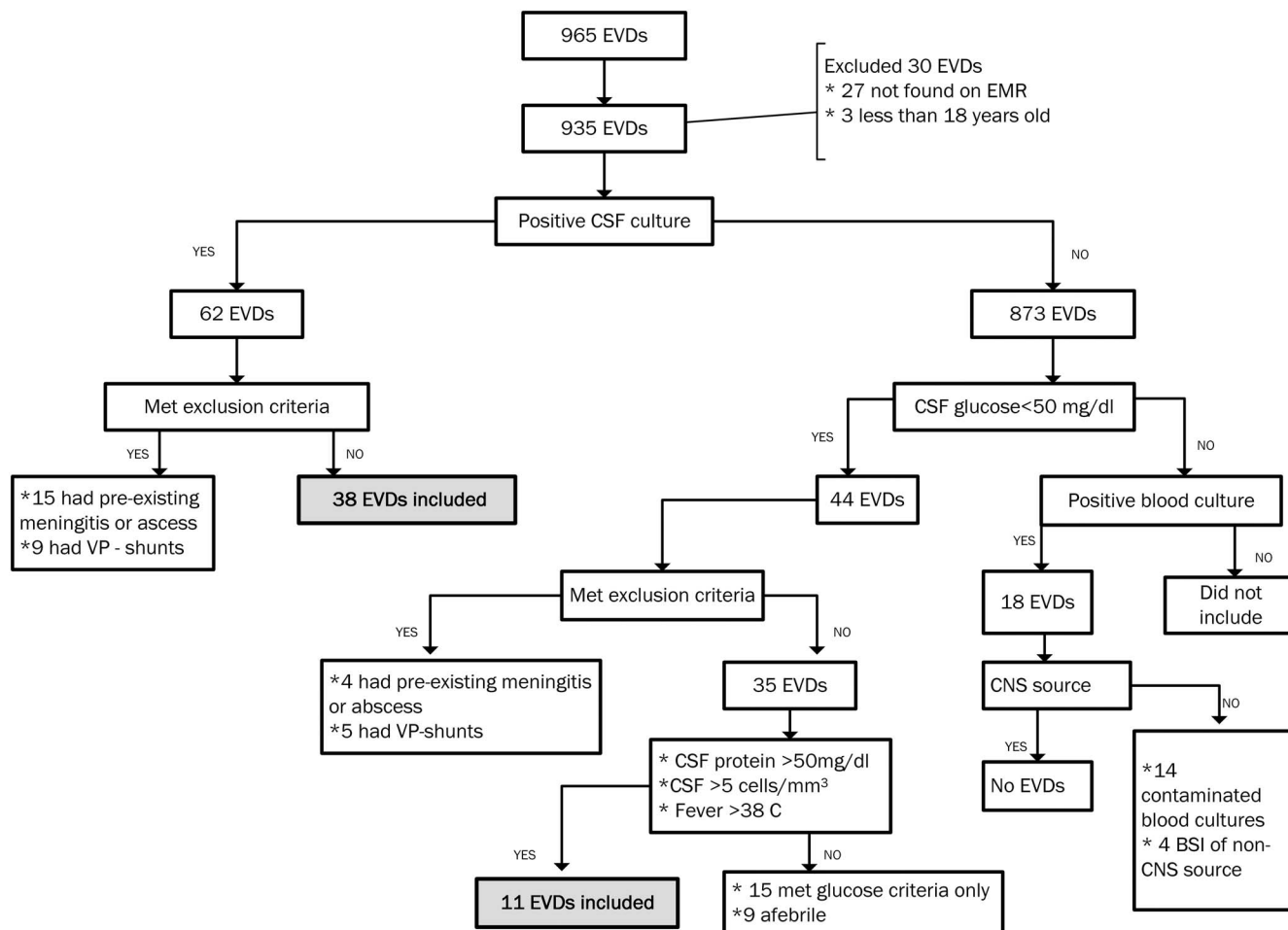


FIGURE 1. Inclusion of patients in the study. Abbreviations: EVDs, external ventricular drains; EMR, electronic medical record; CSF, cerebrospinal fluid; CNS, central nervous system, BSI, bloodstream infections; VP, ventriculoperitoneal.

sent for CSF analysis. The median number of nucleated cells in the remaining 39 CSF samples was 60 cells/mm³ (range, 0–8,440). In total, 30 samples (76.9%) had ≥ 5 nucleated cells/mm³. The median concentration of protein was 48 mg/dL (IQR, 27–87), and 19 samples (48.7%) had a protein level > 50 mg/dL. The median glucose level was 74 mg/dL (IQR, 66–90); only 3 samples (7.6%) had a glucose level < 50 mg/dL.

The microbiology of CSF cultures is shown in Table 3. Notably, 20 of 41 culture-positive cases (49%) had an annotation of “1 colony on 1 piece of media” for an organism. The organisms growing only a single colony in culture were coagulase-negative *Staphylococcus* spp (n = 11 cultures), *Micrococcus* spp (n = 4), *Corynebacterium* spp (n = 2), *Bacillus* spp, *Propionibacterium* spp, and unidentified yeast.

Overall, 40 positive-culture CSF (97.6%) case patients received some antibiotic therapy, and 22 patients (53.6%) received appropriate antibiotic for the organisms cultured. The median length of antibiotic use was 5 days (IQR, 3–11 days). In addition, 5 patients received treatment for ≥ 14 days; 4 of these patients had gram-negative bacteria and 1 had *Candida*

parapsilosis. From the 20 cultures that had the annotation “1 colony on 1 piece of media,” 7 corresponding patients (35%) received an antibiotic with activity against the isolated organism; none received antibiotics for > 14 days.

Among the 38 EVDs in patients with ≥ 1 positive CSF culture, 9 (23.6%) were removed and 3 (7.9%) were exchanged within 48 hours of the positive culture.

CSF Culture-Negative Cases

Overall, 11 patients with 11 EVDs contributed to 11 CSF culture-negative cases (Figure 1). The median number of nucleated cells in these cultures was 375 cells/mm³ (IQR, 100–2,067). The median concentration of protein in patients in this cohort was 113 mg/dL (IQR, 71–332). The median glucose level of this cohort was 45 mg/dL (IQR, 27–48). All 11 case patients received intravenous antibiotics, but none completed 14 days of therapy. Moreover, 2 EVDs (18%) were removed within 48 hours of the abnormal CSF test results. The remaining 9 EVDs (81.8%) were neither removed nor exchanged.

TABLE 2. Characteristics of External Ventricular Drains in the Study Population

Variable	EVDs, No. (%) (n = 49) ^a
Indication for EVD placement ^b	
Hydrocephalus	43 (87.8)
Intracranial bleeding	42 (85.7)
Intracranial tumor	9 (18.4)
Trauma	3 (6.1)
Where was the EVD placed?	
Neuro intensive care unit	28 (57.1)
Operating room	13 (26.5)
Outside hospital	5 (10.2)
Emergency department	3 (6.1)
Neurosurgical history?	
≤30 d before EVD placement	8 (16.3)
Surgery while EVD was in place	22 (44.9)

NOTE. EVD, external ventricular drain.

^aIncludes 48 patients. One patient had 2 EVDs during study period.

^bEVDs may have been placed for ≥1 indication.

Comparison of Ventriculitis Rates

We identified 52 cases of ventriculitis using the NHSN definition: 41 cases were based on a positive CSF culture, and 11 cases were based on abnormal CSF test results. Of these cases, 31 (59.6%) met the ventriculitis criteria using the Honda definition; 29 cases (55.8%) met the ventriculitis criteria using the Gozal definition; and 12 cases (23.1%) met the ventriculitis criteria using the Citerio definition. The ventriculitis rate varied widely by definition: 6.7 cases per 1,000 EVD days using the NHSN definition; 4.0 using the Honda criteria, 3.7 using the Gozal criteria, and 1.5 using the Citerio criteria. No cases were identified using the other 3 definitions but not the NHSN definition.

Comparing the agreement among the definitions, we found that the Honda and Gozal definitions had moderate agreement ($\kappa = 0.528$; $P < .05$). The other comparisons had only fair agreements: Honda versus Citerio ($\kappa = 0.338$; $P < .05$) and Citerio versus Gozal ($\kappa = 0.384$; $P < .05$).

DISCUSSION

Ventriculitis rates in our study varied widely according to the definition applied. Compared to 3 culture-based definitions in the literature, the NHSN definition resulted in substantially more cases of VAI being identified. This finding is most likely due to the NHSN definition defining any growth on CSF culture, no matter the organism, the number of abnormal CSF cultures or the degree of growth on media as infection. This definition also classified cases as VAI based upon CSF abnormalities plus neurological symptoms, irrespective of culture findings.

In our study, gram-positive commensals were the predominant organisms recovered from CSF cultures (79.3%).

TABLE 3. Characteristics of Cerebrospinal Fluid (CSF)-Positive Cultures

Organisms	CSF-Positive Cultures, No. (%) (n = 54) ^a
Gram-positive bacteria	
Coagulase-negative <i>Staphylococcus</i> spp	24 (44.4)
<i>Micrococcus</i> spp	6 (11.1)
<i>Corynebacterium</i> spp	4 (7.4)
<i>Propionibacterium</i> spp	3 (5.6)
<i>Streptococcus</i> spp	3 (5.6)
<i>Bacillus</i> spp	2 (3.7)
<i>Arthrobacter</i> spp	1 (1.9)
Gram-negative bacteria	
<i>Enterobacter</i> spp	3 (5.6)
<i>Neisseria</i> spp	2 (3.7)
<i>Moraxella</i> spp	1 (1.9)
<i>Klebsiella</i> spp	1 (1.9)
<i>Serratia</i> spp	1 (1.9)
<i>Brevudimonas</i> spp	1 (1.9)
Fungal	
<i>Candida parapsilosis</i>	1 (1.9)
Unidentified yeast	1 (1.9)

^aOf 41 cases, 4 cultures were polymicrobial: 2 cultures had 2 organisms, 1 culture had 4 organisms, and 1 culture had 9 organisms.

These organisms are the most commonly implicated as a cause of VAI,^{5,1} but they also frequently cause culture contamination or catheter colonization. We found that 45% of the common commensals had an annotation by the laboratory of "1 colony on 1 piece of media," which calls into question their significance as a pathogen. Of the other VAI definitions available in the literature,^{1,3,9} only 1 used quantification of colony forming units, and none required >1 positive culture.³ Therefore, most definitions may identify either catheter colonization or contamination during collection as a VAI.

The NHSN definition also includes the presence of new cranial nerve signs, meningeal signs, or headache. Given their underlying pathology, neurosurgical patients may have these signs and symptoms, regardless of infection. Other infection surveillance definitions relying on clinical signs and symptoms have been reported to miss cases. A study examining chart-documented signs and symptoms of catheter-associated urinary tract infections found that only 9.5% case patients had documented dysuria, frequency or urgency, and only 4.1% had suprapubic tenderness or costovertebral angle pain.¹¹ In our cohort, only 9 patients (17.3%) had new or worsening cranial nerve signs, and none had new or worsening meningeal signs.

A surveillance definition that cannot adequately discern VAIs from culture contamination may lead to a misinterpretation of clinical practice patterns. In our cohort, only 53.6% of NHSN-defined VAI cases received organism-specific antibiotic therapy, and only 5 patients received treatment for ≥14 days. Among "1 colony on 1 piece of media" cases, we

found a significantly lower proportion of associated CSF protein >50 mg/dL and CSF glucose <50 mg/dL versus other cases (data not shown). Among the NSHN-defined VAI cases that grew 1 colony on 1 piece of culture media, only 35% received organism-specific antibiotic therapy, and in all these cases, treatment duration was <9 days. Analogous to central-line-associated bloodstream infections, EVD removal is recommended in VAI cases.¹² However, among the EVDs in our cohort with a positive CSF culture, 9 (23.6%) were removed, and 3 (7.8%) were exchanged. Among VAI cases with negative CSF cultures, only 2 EVDs (18%) were removed, and none were exchanged.

Our VAI rate varied considerably, depending on the definition applied. For instance, using the Citerio definition,¹⁰ there were no cases of VAI in 2012; however, using the NSHN definition, there were 12 VAI cases, a rate of 10.7 infections per 1,000 EVD days. When comparing rates among hospitals, this variability becomes problematic.⁵ Currently, US hospitals are mandated to report certain hospital-acquired infections for quality of care metrics, which are linked to reimbursement.¹³ Therefore, it is increasingly important that surveillance definitions are reproducible and align well with clinical definitions. We call for refining the NSHN VAI definition and adopting a definition similar to the current NSHN central-line-associated bloodstream infection definition.⁹ This measure would increase definition specificity, and by removing subjective clinical criteria, would allow for automated surveillance.¹⁴

Our study has several limitations. It was conducted in a single care center. Also, it was retrospective and relied on pre-existing documentation. We calculated the Cohen's κ coefficient for the 3 published definitions, but we could not directly compare them to the NSHN definition because the ventriculitis cases in all 3 definitions were a subset of NSHN-defined VAI cases. The strengths of our study include the placement of a large number of EVDs in our institution and a high number of CSF cultures, which allowed the comparison of various ventriculitis definitions.

The current NSHN ventriculitis definition has limitations that make it difficult to use to compare VAI rates among institutions and for surveillance. Our data suggest that a modification to the current NSHN definition is needed to improve such comparisons in the future.

ACKNOWLEDGMENTS

We thank the Barnes-Jewish Hospital Neurology and Neurosurgical Intensive Care Unit and Infection Prevention staff for providing data for this study. The findings and conclusions in this document are those of the authors who are responsible for its content and do not necessarily represent the official view of the Centers for Disease Control and Prevention.

Financial support: Funding for this project was provided in part by the Centers for Disease Control and Prevention Epicenters Program (grant no. U54CK000162).

Potential Conflicts of Interest. All authors report no conflicts of interest relevant to this article.

Address correspondence to Maria Reyes, MD, 7777 Hennessy Blvd, Ste 7000, Baton Rouge, LA 70808 (Mariareyesa@gmail.com).

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