Title

A Randomized Clinical Trial Comparing Use of Rapid Molecular Testing for Staphylococcus aureus for Patients With Cutaneous Abscesses in the Emergency Department With Standard of Care

Journal

Infection Control and Hospital Epidemiology, 36(12)

ISSN

0899-823X

Authors

May, Larissa S
Rothman, Richard E
Miller, Loren G
et al.

Publication Date

2015-12-01

DOI

10.1017/ice.2015.202

Peer reviewed

HHS Public Access

Author manuscript

Infect Control Hosp Epidemiol. Author manuscript; available in PMC 2017 March 03.

Published in final edited form as:

Infect Control Hosp Epidemiol. 2015 December ; 36(12): 1423–1430. doi:10.1017/ice.2015.202.

A Randomized Clinical Trial Comparing Use of Rapid Molecular Testing for *Staphylococcus aureus* for Patients With Cutaneous Abscesses in the Emergency Department With Standard of Care

Larissa S. May, MD[1], **Richard E. Rothman, MD**[2], **Loren G. Miller, MD**[3], **Gillian Brooks, MS**[4], **Mark Zocchi, MPH**[5], **Catherine Zatorski, BA**[4], **Andrea F. Dugas, MD**[3], **Chelsea E. Ware, MS**[4], and **Jeanne A. Jordan, PhD**[6]

[1]Emergency Department Antibiotic Stewardship, Department of Emergency Medicine, University of California–Davis, Sacramento, California [2]Department of Emergency Medicine, Johns Hopkins University, Baltimore, Maryland [3]Los Angeles BioMedical Research Center at Harbor-UCLA Medical Center, Torrance, California [4]Department of Emergency Medicine, George Washington University, Washington, DC [5]Office for Clinical Practice Innovation, George Washington University, Washington, DC [6]Department of Epidemiology and Biostatistics, School of Public Health, George Washington University, Washington, DC

Abstract

OBJECTIVE—To determine whether real-time availability of rapid molecular results of *Staphylococcus aureus* would impact emergency department clinician antimicrobial selection for adults with cutaneous abscesses.

DESIGN—We performed a prospective, randomized controlled trial comparing a rapid molecular test with standard of care culture-based testing. Follow-up telephone calls were made at between 2 and 7 days, 1 month, and 3 months after discharge.

SETTING—Two urban, academic emergency departments.

PATIENTS—Patients at least 18 years old presenting with a chief complaint of abscess, cellulitis, or insect bite and receiving incision and drainage were eligible. Seven hundred seventy-eight people were assessed for eligibility and 252 met eligibility criteria.

METHODS—Clinician antibiotic selection and clinical outcomes were evaluated. An ad hoc outcome of test performance was performed.

Address correspondence to Larissa S. May, MD, University of California–Davis, Department of Emergency Medicine, 4150 V St, Ste 2100, Sacramento, CA 95817 (larissa.may@gmail.com).

Disclaimer. The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of the National Center for Advancing Translational Sciences or the National Institutes of Health.

Potential conflicts of interest. L.S.M. reports that she has received honoraria for consulting and educational presentation for Cepheid; travel and meeting expenses for Cepheid; and advisory board honorarium and travel expenses from Durata. L.G.M. reports that he has received consulting fees from Cubist, Durata, and Pfizer. R.E.R. reports that he has a Cooperative Agreement with BARDA, HHS (Influenza Diagnostic Study); a grant with Cepheid (sexually transmitted disease diagnosis); and meeting expenses for unpaid consultation by Cepheid. J.A.J. reports that she has received clinical trial funding for HIV qualitative, HIV quantitative, Trichomonas vaginalis (TV), all on GeneXpert by Cepheid. All other authors report no conflicts of interest relevant to this article.

RESULTS—We enrolled 252 patients and 126 were randomized to receive the rapid test. Methicillin-susceptible *S. aureus*–positive patients receiving rapid test results were prescribed beta-lactams more often than controls (absolute difference, 14.5% [95% CI, 1.1%–30.1%]) whereas methicillin-resistant *S. aureus*–positive patients receiving rapid test results were more often prescribed anti–methicillin-resistant *S. aureus* antibiotics (absolute difference, 21.5% [95% CI, 10.1%–33.0%]). There were no significant differences between the 2 groups in 1-week or 3-month clinical outcomes.

CONCLUSION—Availability of rapid molecular test results after incision and drainage was associated with more-targeted antibiotic selection.

TRIAL REGISTRATION—clinicaltrials.gov Identifier: NCT01523899

Increasingly resistant pathogens stem from inappropriate antibiotic use or overuse. One important strategy for combating this growing public health threat is rapid molecular-based diagnostic testing to guide therapy. Rapid molecular tests can provide real-time information on pathogen identification and genotypic resistance profile, which may decrease inappropriate or unnecessary and overly broad-spectrum antibiotic use.[1]

Cutaneous abscesses are common in the emergency department (ED) but little effort has been invested to date in evaluating newer rapid molecular-based technologies to improve ED antimicrobial stewardship by allowing earlier detection and identification of methicillin-resistant *Staphylococcus aureus* (MRSA). Several molecular assays recently approved by the US Food and Drug Administration can detect MRSA in less than 90 minutes, directly from clinical specimens, with high sensitivity and specificity.[2–5] Although some early implementation studies conducted in inpatient settings found integrating these tests in practice decreases broad-spectrum antibiotic use, other studies report mixed results, perhaps attributable to the assay used, clinical setting, or target population studied.[6,7]

To date, few studies have evaluated incorporating rapid molecular-based testing in evaluating and treating patients with abscesses in the ED, where empirical antibiotic use is common.[8] One recent ED investigation sought to assess the impact of using rapid testing with physician education alone or with pharmacist-guided antibiotic selection for admitted patients with abscesses.[9] Despite this test's potential impact on antibiotic selection, no reduction in empirical prescription of anti-MRSA antibiotics was observed in either intervention arm.[9]

Given that more than 90% of ED patients with abscesses are discharged home, the potential impact of real-time results on clinician prescribing behavior in the broader ED population has not been studied. Therefore, we conducted a randomized controlled trial to determine whether providing real-time results using the US Food and Drug Administration–approved Xpert MRSA/methicillin-susceptible *S. aureus* (MSSA) skin and soft-tissue infection (SSTI) assay (Cepheid) would impact antibiotic selection for patients with abscesses.

METHODS

Study Setting

The study was conducted in 2 urban academic EDs: the George Washington (GW) and Johns Hopkins (JH) EDs from April 1, 2011, through April 30, 2014. Before initiation, the study was approved by both institutional review boards and registered on clinicaltrials.gov (NCT01523899).

Eligibility and Recruitment

Trained research staff in each ED screened participants for eligibility from approximately 9 AM to approximately 8 PM, and ED providers also identified potential participants. Eligibility criteria included age at least 18 years, chief complaint consistent with a possible cutaneous abscess (eg, abscess, skin infection, wound, insect bite), and an incision and drainage (I&D) procedure. Patients were excluded if they had had previous treatment, medically or surgically, for the same abscess, had taken oral or parenteral antibiotic therapy in the previous 14 days, or had a surgical site or postprocedure infection. Patients who met enrollment criteria were approached for written informed consent.

Randomization

A random-number generator was used to assign patients to either the test or the control group. A 1:1 simple randomization was used and generated before study initiation. Study arm randomization was given in sequentially numbered, sealed, and opaque envelopes containing the randomized testing allocation and was prepared by the study coordinator. Study staff enrolling participants and treating physicians were masked to randomization until after enrollment.

Patients randomly assigned to the test group had wound specimens collected and analyzed by both molecular and culture methods, whereas control patients' specimens were cultured only.

Data Collection

After consenting, patients provided demographic information (age, sex, race, comorbidities, insurance type), epidemiologic factors (antibiotic use within 6 months, hospitalization in previous year, number of household contacts, including children younger than 18), and abscess characterization (size, location, presence of fever). For reporting purposes, clinical data were collected for the largest abscess (eg, size, extent of erythema) when patients presented with multiple abscesses. Providers documented choice and duration of antimicrobial therapy. Wound culture and susceptibility results, where applicable, were obtained electronically from the clinical microbiology laboratory report. All data were entered into a password-protected database accessible only to the researchers.

Laboratory Testing

Wound cultures—Specimens obtained during I&D were collected with a Copan transport swab. At GW, wound swabs were cultured in the hospital's Clinical Laboratory Improvement Amendments–approved clinical microbiology laboratory by direct plating onto

5% sheep blood agar, MacConkey agar, colistin nalidixic acid agar, and MRSA-Select CHROMagar (Bio-Rad) and incubated at 37°C for 20 to 24 hours. Specimens were plated within 2 hours of receipt unless received between midnight and 8 AM, when swabs were held at 2°C to 8°C and then processed. Coagulase production was tested on mauve-colored colonies from the MRSA-Select CHROMagar.

At JH, wound culturing was not always performed as standard of care, so specimens were stored at 2°C to 8°C and shipped weekly to Cepheid where swabs were inoculated directly onto sheep blood agar (Remel), HardyCHROM MRSA agar (Hardy Diagnostics), and HardyCHROM *S. aureus* agar (Hardy Diagnostics) and incubated at 35°C for 20 to 24 hours. The wound swabs themselves were then incubated overnight in 2.2 mL tryptic soy broth with 6.5% NaCl (Remel). The enrichment broths from specimens with negative or ambiguous results after direct culturing were plated onto HardyCHROM *S. aureus* and HardyCHROM MRSA agar and incubated at 35°C for 20 to 24 hours before colonies were tested for catalase and coagulase production.

Xpert MRSA/S. aureus SSTI assay—Wound swabs were tested directly for *S. aureus* using the Xpert MRSA/MSSA SSTI assay according to the manufacturer's recommendation at both study sites. Testing was performed immediately following specimen collection by nonlaboratory personnel trained by Cepheid representatives.

Data Analysis

Patients were included in the analysis if their abscess(es) yielded purulent material that could be sent for diagnostic testing.

Outcomes

Our primary objective was to assess clinician antibiotic selection (anti-MRSA, beta-lactam, or no antibiotic therapy), stratified by whether MRSA or MSSA was detected by the rapid test. Our secondary objectives were to assess clinical outcomes of the 2 groups at 1 week, 1 month, and 3 months and to compare performance characteristics of the rapid test to direct culture.

Antibiotic selection (anti-MRSA, beta-lactam, or none) in test vs control groups—We hypothesized that providing real-time results to ED clinicians would (1) decrease overall antibiotic use in the test compared with control groups and (2) increase appropriate antibiotic selection, including anti-MRSA antibiotic use (eg, clindamycin or trimethoprim/sulfamethoxazole [TMP-SMX]) in patients whose real-time result was MRSA-positive, while reducing anti-MRSA antibiotic use in patients with MSSA-positive results. Antibiotic categories prescribed included beta-lactams (cephalexin or dicloxacillin) and non–beta-lactams (TMP-SMX; TMP-SMX plus another antibiotic; clindamycin). We defined *unnecessary combination therapy* as using at least 2 antibiotics, such as cephalexin plus TMP-SMX. The study was powered at 80% to detect an expected reduction in anti-MRSA antibiotic use (TMP-SMX, clindamycin) from 80% to 64% (n=125 per group) on the basis of prior institutional data.[10,11]

Clinical outcomes after discharge—Patient-reported symptom improvement (decreasing erythema, pain, swelling, drainage, and presence/absence of fever) was determined during the 2- to 7-day follow-up telephone call. Abscess recurrence was determined during the patient follow-up telephone interviews at months 1 and 3. All patients reached at either the 1- or 3-month follow-up call were included in the analysis. Baseline patient characteristics were compared between those who were reached for follow-up (n = 193) and those who were not (n =59).

For those not responding to their 1-week follow-up phone call, a medical chart review was performed and patients returning to the ED for their 2-day wound check visit (standard of care visit for SSTIs) or for subsequent ED visits for abscesses were evaluated for the same criteria, if documented in the patient's EMR. Trained abstractors used explicit protocols, precisely defined variables, and standardized abstraction instruments to document variables. Missing variables were recorded as missing or unknown. Ambiguous chart elements occurred in fewer than 5 cases and were resolved by the principal investigator.

Performance characteristics of Xpert MRSA/S. aureus SSTI assay compared with direct culture—Measures of diagnostic accuracy of the molecular-based test were estimated with 95% confidence intervals and included sensitivity, specificity, positive predictive value, and negative predictive value.

Pearson χ^2, Fisher exact, and 2-sample *t* tests were used to compare baseline participant characteristics. Two-sample tests of proportions were used to estimate absolute differences and 95% CI in prescribing patterns and sensitivities and specificities of the molecular test. All analyses were conducted with Stata, version 13.1 (StataCorp).

RESULTS

Study Population

Over the study period, 252 patients were recruited (215 at GW, 37 at JH); 126 each were randomly assigned to the test or control group (Figure 1). Mean age of the study population was 36.2 years (95% CI, 34.5–37.9); there were more women (54.0%). No baseline differences existed in demographic or clinical characteristics between test and control groups (Table 1), whereas differences between sites were found and included disposition (no JH patients required admission, whereas 7 GW patients [3.3%] were admitted despite plans for outpatient treatment) and prescriber type (131 GW patients [61%] were treated by a physician assistant compared with 7 JH patients [18.9%]).

Primary Outcomes

Antibiotic selection (anti-MRSA, beta-lactam, or none) in test vs control groups—Clinicians prescribed antibiotics to 193 (77%) of 252 study participants. The most frequently prescribed antibiotics were clindamycin (58%) and TMP-SMX plus beta-lactams (19%), with unnecessary combination therapy given in 16% of participants, most commonly TMP-SMX plus cephalexin (Table 2). Among 32 test patients diagnosed with MRSA, none received a beta-lactam and 30 (94%) received anti-MRSA antibiotics. Among 126 controls, 6 (5%) received a beta-lactam and 91 (72%) received anti-MRSA antibiotics (Table 3).

Among 26 test patients diagnosed with a MSSA, 5 (19%) received a beta-lactam compared with 6 (5%) of 126 controls (absolute difference, 14.5% [95% CI, 1.1%–30.1%]).

Twenty-five control patients and 26 test patients were given a diagnosis of MSSA. MSSA-positive controls were less likely than test patients to be prescribed any antibiotic and less likely to be prescribed an anti-MSSA antibiotic. This finding was also true among test and control patients given a diagnosis of MRSA, although the difference was not statistically significant (Table 4). Forty-nine (39%) of 126 test patients waited for the molecular result, with missing data for 22 patients (data not shown).

We did not find a decrease in overall antibiotic use. More than 75% of patients with a real-time MRSA result still received MRSA-active antibiotic, with nearly a quarter of all patients receiving no antibiotic at discharge.

Clinical outcomes—No significant differences were found in 1-week or 3-month outcomes between test patients and controls (data not shown). Negative 1-week outcomes were found in 12 (11.7%) of 103 controls and 9 (8.7%) of 103 test patients. Abscess recurrence at either 1 or 3 months after discharge occurred in 24 (27.3%) of 88 controls and 26 (28.6%) of 91 test patients. Seventy-nine patients could not be reached for follow-up at 1 or 3 months and were more likely to be homeless (7.7% vs 0.5%, $P = .02$) and treated by less experienced providers (20.3% vs 11.6%, $P = .047$).

Analytic performance characteristics of Xpert MRSA/MSSA SSTI assay compared with direct culture—Mean turnaround time for the molecular test was 82 minutes. Test performance in MRSA or MSSA detection was compared between direct culture and test patients. Sensitivities of the molecular tests for MRSA and MSSA detection were 87.9% and 95.7%, respectively (absolute difference, 7.8% [95% CI, −6.1% to 21.7%]), whereas specificities for MRSA and MSSA detection were 98.8% and 95.7%, respectively (absolute difference, 3.1% [95% CI, −1.8% to 8.0%]) (Table 5).

DISCUSSION

In this trial we found real-time reporting of molecular test results during an ED visit for SSTIs resulted in significant prescribing behavior changes with no impact on clinical outcomes. Specifically, access to real-time results reduced use of anti-MRSA agents for patients with a diagnosis of MSSA and increased use of anti-MRSA therapy for MRSA-infected patients. Our findings suggest incorporation of real-time reporting in the ED could lead to improved antibiotic selection, compared with the traditional paradigm of empirical therapy. Interestingly, real-time result availability did not change overall antibiotic use. However, this may be attributed to provider selection of empirical antibiotics where the provider or patient chose not to wait for results. Despite this, real-time testing could help target therapy in cases where clinicians decide to prescribe antibiotics.

Broad-spectrum antibiotic overuse is one of the most important drivers in MRSA emergence and is associated with an additional $22 billion per year in healthcare costs for hospitalized patients.[12] Antibiotic overuse not only leads to increased antimicrobial resistance rates but

also exposes patients unnecessarily to potential adverse events. For example, *Clostridium difficile* infection, which accounts for up to 20% of antibiotic-associated diarrhea, is associated with clindamycin use.[13] In addition, approximately 3% of patients have adverse reactions to sulfa drugs and the incidence of severe adverse effects increases to 60% for those infected with human immunodeficiency virus.[14]

Emergence of community-acquired MRSA represents a major clinical and public health challenge. Empirical treatment of abscesses with a beta-lactam, the standard of care for decades, is no longer recommended given many US communities have greater than 50% prevalence of MRSA among *S. aureus*.[5] Although differentiating MRSA from non-MRSA causes of abscesses has important patient care implications, this is not possible by clinical characteristics alone.[15] The Infectious Diseases Society of America guidelines recommend empirical treatment of MRSA-infected abscesses in patients at risk for complications.[10] However, clinician concern regarding the possible presence of MRSA has prompted increasing rates of broad-spectrum antibiotics,[16,17] despite data suggesting antibiotics may not be needed for relatively healthy patients receiving I&D for uncomplicated abscesses.[18–20] The Infectious Diseases Society of America guidelines for SSTI treatment, published after completion of our study, include several important changes[21]: routine antibiotic therapy is not recommended for mildly severe SSTIs undergoing I&D, with first-line targeted treatment for moderate MRSA infection using TMP-SMX. For MSSA infection, beta-lactams are first-line agents for both moderate and severe infections. Our results suggest real-time molecular testing could improve targeted treatment for these infections, especially given guidelines recommending antibiotics for moderate to severe suppurative SSTIs.

To combat rising antibiotic-resistant rates, federal agencies recently released a strategy implementing antimicrobial stewardship interventions in key healthcare settings, including the ED, emphasizing rapid point-of-care testing for resistant pathogens.[22] The ED should implement antimicrobial stewardship programs given its high rates of overall antibiotic use[8] and the extremely high variability with regard to clinician decision-making.[23] Current practice in most adult and pediatric EDs for patients with abscesses consists of I&D and empirical treatment with MRSA-active antibiotics, regardless of whether culture was performed or patients are at low risk for complications.[1,6]

Increasing ED patients' access to point-of-care testing is a cornerstone of the Infectious Diseases Society of America strategy to curb antimicrobial resistance.[4] However, US EDs do not currently incorporate these assays in practice, even though they represent an important venue for antimicrobial stewardship improvement. Lack of ED access to these highly accurate tests leads to frequent unnecessary broad-spectrum antibiotic use. Molecular-based testing has already improved antimicrobial stewardship in inpatient settings.[3,4] To our knowledge, ours is the first trial to show a clinical impact when providing real-time results during an ED visit. Although rapid tests significantly decrease unnecessary antibiotic use in streptococcal pharyngitis,[5] Terp et al[9] found that using rapid MRSA tests for hospitalized patients with complicated SSTI, along with physician education and pharmacist guidance, did not reduce excessive empirical treatment with anti-MRSA antibiotics. Although we employed a minimal educational strategy in comparison with that

study, we believe the reason clinical practice changed in our trial was because the test targeted an outpatient population, where clinicians were less concerned about morbidity. On the basis of results from our largely outpatient ED population (97% of subjects were discharged home), using real-time testing could improve antibiotic stewardship for those diagnosed with either MRSA or MSSA.

Finally, the Xpert MRSA/MSSA SSTI assay accurately detected both MRSA and MSSA from abscesses, with a negative predictive value of 95.3% for MRSA and an 82-minute turnaround time. Importantly, these results were consistent with the greater than 95% negative predictive value we observed when trained nonlaboratory operators performed the Xpert *S. aureus* Nasal Complete assay, suggesting molecular-based testing has the potential to be a point-of-care test in the ED, under Clinical Laboratory Improvement Amendments waiver.[24]

Our investigation had limitations. First, although we attempted to enroll patients consecutively, study staff were not available 24 hours a day. Thus the number of patients missed is unknown. Second, although trained nonlaboratory research personnel performed the testing at GW, at JH laboratory technicians performed the testing. Third, not all patients or providers waited for test results. This likely contributed to a reduction in the observed impact of having real-time data on clinician decision-making. Further analysis was not possible because it was unknown whether decisions were based on test results or on follow-up calls by the physician instructing them to take or not take an antibiotic. Relevant to this issue, prior research demonstrates the ideal turnaround time for a rapid diagnostic test in the ED is less than 45 minutes.[25] Fourth, cost per test and possible capital investment for the instrument could be a potential limitation with regard to generalizability. Our study was not designed to evaluate cost-effectiveness and focused investigations in this area are warranted. Fifth, although a substantial proportion of our population had comorbidities, most infections were mild (lack of fever; patient not admitted) and thus arguably would not have required antibiotics or culturing. Finally, it was impossible to mask the abstractor (research coordinator) to the study hypothesis or group assignment, although medical chart elements were objective on the basis of a structured abstraction instrument.

In summary, our investigation found that rapid diagnostic testing for *S. aureus*, including detection of methicillin resistance, in ED patients with cutaneous abscesses improved antibiotic stewardship. Consideration should be made to developing protocols that incorporate this type of real-time testing to facilitate patient evaluation and management of ED patients with cutaneous abscesses.

Acknowledgments

We thank Isabella Tickler, for her time and effort in performing the masked culture-based procedures used for wound specimens; and Fred Tenover, for his critical feedback.

Financial support. National Institutes of Health National Center for Advancing Translational Sciences (UL1RR031988/UL1TR000075 and KL2RR031987/KL2TR000076); and Cepheid (test materials and support for laboratory testing).

References

1. Spellberg B, Blaser M, Guidos RJ, et al. Infectious Diseases Society of America (IDSA). Combating antimicrobial resistance: policy recommendations to save lives. Clin Infect Dis. 2011; 52:S397–S428. [PubMed: 21474585]
2. Huletsky A, Giroux R, Rossbach V, et al. New real-time PCR assay for rapid detection of methicillin-resistant *Staphylococcus aureus* directly from specimens containing a mixture of staphylococci. J Clin Microbiol. 2004; 42:1875–1884. [PubMed: 15131143]
3. Renwick L, Hardie A, Girvan EK, et al. Detection of methicillin-resistant *Staphylococcus aureus* and Panton-Valentine leukocidin directly from clinical samples and the development of a multiplex assay using real-time polymerase chain reaction. Eur J Clin Microbiol Infect Dis. 2008; 27:791–796. [PubMed: 18357477]
4. Wassenberg MW, Kluytmans JA, Box AT, et al. Rapid screening of methicillin-resistant *Staphylococcus aureus* using PCR and chromogenic agar: a prospective study to evaluate costs and effects. Clin Microbiol Infect. 2010; 16:1754–1761. [PubMed: 20219077]
5. Wolk DM, Struelens MJ, Pancholi P, et al. Rapid detection of *Staphylococcus aureus* and methicillin-resistant *S aureus* (MRSA) in wound specimens and blood cultures: multicenter preclinical evaluation of the Cepheid Xpert MRSA/SA skin and soft tissue and blood culture assays. J Clin Microbiol. 2009; 47:823–826. [PubMed: 19144803]
6. Yang S, Rothman RE. PCR-based diagnostics for infectious diseases: uses, limitations, and future applications in acute-care settings. Lancet Infect Dis. 2004; 4:337–348. [PubMed: 15172342]
7. Polisena J, Chen S, Cimon K, McGill S, Forward K, Gardam M. Clinical effectiveness of rapid tests for methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitalized patients: a systematic review. BMC Infect Dis. 2011; 11:336. [PubMed: 22151575]
8. May L, Cosgrove S, L'Archeveque M, et al. A call to action for antimicrobial stewardship in the emergency department: approaches and strategies. Ann Emerg Med. 2013; 62:69–77. e2. [PubMed: 23122955]
9. Terp S, Krishnadasan A, Bowen W, et al. Introduction of rapid methicillin-resistant *Staphylococcus aureus* polymerase chain reaction testing and antibiotic selection among hospitalized patients with purulent skin infections. Clin Infect Dis. 2014; 58:e129–e132. [PubMed: 24457337]
10. Elashoff, JD. nQuery Advisor Version 3.0 User's Guide. Los Angeles, CA: Statistical Solutions; 1999.
11. May L, Harter K, Yadav K, et al. Practice patterns and management strategies for purulent skin and soft-tissue infections in an urban academic ED. Am J Emerg Med. 2012; 30:302–310. [PubMed: 21277138]
12. Cassell GH, Mekalanos J. Development of antimicrobial agents in the era of new and reemerging infectious diseases and increasing antibiotic resistance. JAMA. 2001; 285:601–605. [PubMed: 11176866]
13. Schroeder MS. *Clostridium difficile*–associated diarrhea. Am Fam Physician. 2005; 71:921–928. [PubMed: 15768622]
14. Tilles SA. Practical issues in the management of hypersensitivity reactions: sulfonamides. South Med J. 2001; 94:817–824. [PubMed: 11549195]
15. Moran GJ, Krishnadasan A, Gorwitz RJ, et al. Methicillin-resistant *S aureus* infections among patients in the emergency department. N Engl J Med. 2006; 355:666–674. [PubMed: 16914702]
16. Hammond SP, Baden LR. Clinical decisions: management of skin and soft-tissue infection—polling results. N Engl J Med. 2008; 359:e20. [PubMed: 18843122]
17. Talan DA, Krishnadasan A, Gorwitz RJ, et al. Comparison of *Staphylococcus aureus* from skin and soft-tissue infections in US emergency department patients, 2004 and 2008. Clin Infect Dis. 2011; 53:144–149. [PubMed: 21690621]
18. Schmitz GR. How do you treat an abscess in the era of increased community-associated methicillin-resistant *Staphylococcus aureus* (MRSA)? J Emerg Med. 2011; 41:276–281. [PubMed: 21658881]

19. Duong M, Markwell S, Peter J, Barenkamp S. Randomized, controlled trial of antibiotics in the management of community-acquired skin abscesses in the pediatric patient. Ann Emerg Med. 2010; 55:401–407. [PubMed: 19409657]

20. Rajendran PM, Young D, Maurer T, et al. Randomized, double-blind, placebo-controlled trial of cephalexin for treatment of uncomplicated skin abscesses in a population at risk for community-acquired methicillin-resistant *Staphylococcus aureus* infection. Antimicrob Agents Chemother. 2007; 51:4044–4048. [PubMed: 17846141]

21. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections: 2014 update by the Infectious Diseases Society of America [published correction appears in *Clin Infect Dis* 2015;60:1448]. Clin Infect Dis. 2014; 59:e10–e52. [PubMed: 24973422]

22. Executive order—combating antibiotic-resistant bacteria. White House website. http://www.whitehouse.gov/the-press-office/2014/09/18/executive-order-combating-antibiotic-resistant-bacteria. Published September 14, 2014

23. Tamma P, Cosgrove SE. Antimicrobial stewardship. Infect Dis Clin North Am. 2011; 25:245–260. [PubMed: 21316003]

24. May L, McCann C, Brooks G, Rothman R, Miller L, Jordan J. Dual-site sampling improved detection rates for MRSA colonization in patients with cutaneous abscesses. Diagn Microbiol Infect Dis. 2014; 80:79–82. [PubMed: 24958641]

25. May L, Gudger G, Armstrong P, et al. Multisite exploration of clinical decision making for antibiotic use by emergency medicine providers using quantitative and qualitative methods. Infect Control Hosp Epidemiol. 2014; 35:1114–1125. [PubMed: 25111919]

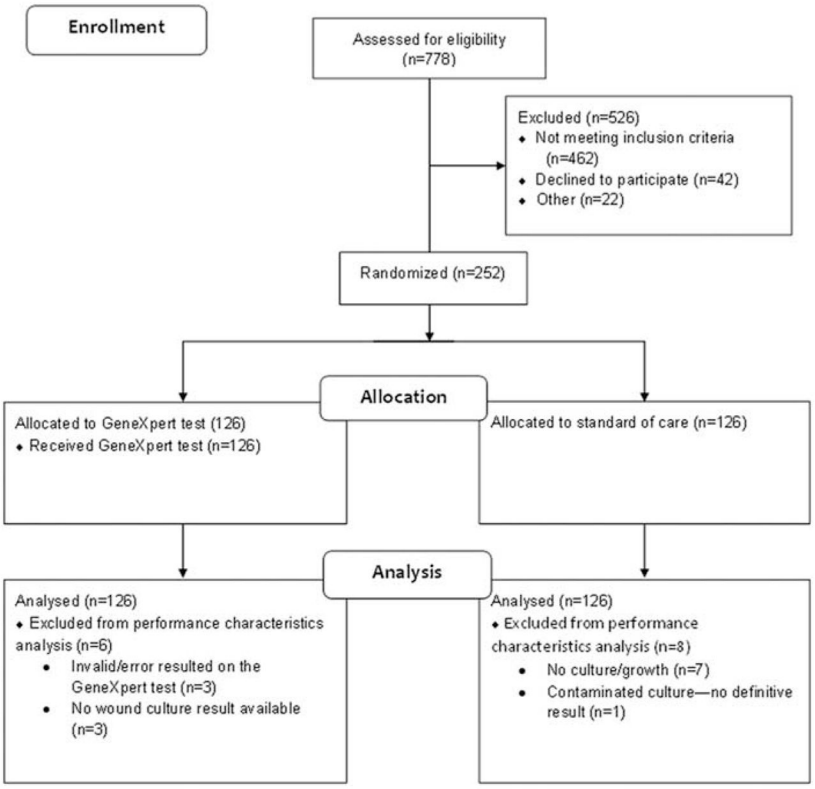

FIGURE 1.
Study Flow Diagram

TABLE 1

Baseline Participant Characteristics

	Control *(n = 126)*	Test *(n = 126)*
Age, mean ± SD, y	36.5 ± 13.8	36.0 ± 13.4
Female sex	73 (57.9)	63 (50.0)
Race (available for GW only)		
Black	90 (71.4)	83 (65.9)
White	4 (3.2)	4 (3.2)
Other	12 (9.5)	21 (16.7)
Missing or NA	20 (15.9)	18 (14.3)
Insurance status		
Private	53 (42.1)	48 (38.1)
Medicaid	49 (38.9)	58 (46.0)
Medicare	9 (7.1)	10 (7.9)
Self-pay	15 (11.9)	10 (7.9)
Comorbid condition		
Diabetes mellitus	17 (13.5)	16 (12.7)
HIV/immunocompromised	6 (4.8)	9 (7.1)
Multiple	5 (4.0)	11 (8.7)
Other	14 (11.1)	8 (6.3)
None	84 (66.7)	82 (65.1)
Prior hospitalization	25 (19.8)	25 (19.8)
Prior abscess	74 (58.7)	81 (64.3)
Adherence	73 (57.9)	72 (57.1)
Wound culture		
MRSA	36 (28.6)	33 (26.2)
MSSA	25 (19.8)	23 (18.3)
Other	57 (45.2)	62 (49.2)
Missing or NA	8 (6.3)	8 (6.3)
Disposition		
Routine discharge	122 (96.8)	122 (96.8)
Admission	4 (3.2)	3 (2.4)
Left without being evaluated	0 (0)	1 (0.8)
Prescribed antibiotics	97 (77.0)	96 (76.2)
Prescriber		
Attending	40 (31.7)	29/124 (23.4)
Physician assistant	65 (51.6)	72/124 (58.1)
Resident	21 (16.7)	23/124 (18.5)

NOTE. Data are no. (%) unless otherwise specified. No characteristics were found to be statistically different at $P < .05$. GW, George Washington University emergency department; HIV, human immunodeficiency virus; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*; NA, not applicable.

TABLE 2

Antibiotic Selection

Prescriptions	No.	%
Clindamycin	111	57.5
Trimethoprim/sulfamethoxazole	37	19.2
Overprescribing combinations/prescriptions	30	15.5
Beta-lactams	15	7.8
Total	193	100.0

TABLE 3

Clinical Actions Based on Rapid Test Results: Comparing Controls With Entire Test Group or MRSA-Positive or MSSA-Positive Test Subjects

Prescriptions	**Controls[a] (n = 126)**	**All tests (n = 126)**	**Difference (95% CI)**
Beta-lactams	6 (4.8)	9 (7.1)	−2.4 (−8.2 to 3.5)
MRSA active	91 (72.2)	87 (69.0)	3.2 (−8.1 to 14.4)
None prescribed	29 (23.0)	30 (23.8)	−0.8 (−11.2 to 9.7)
Prescriptions	Controls[a] (n = 126)	Tests MRSA+ (n =32)	Difference (95% CI)
Beta-lactams	6 (4.8)	0 (0.0)	4.8 (1.0 to 8.5)
MRSA active	91 (72.2)	30 (93.8)	−21.5 (−33.0 to −10.1)
None prescribed	29 (23.0)	2 (6.3)	16.7 (5.6 to 27.9)
Prescriptions	Controls[a] (n = 126)	Tests MSSA+ (n = 26)	Difference (95% CI)
Beta-lactams	6 (4.8)	5 (19.2)	−14.5 (−30.1 to 1.1)
MRSA active	91 (72.2)	20 (76.9)	−4.7 (−22.7 to 13.3)
None prescribed	29 (23.0)	1 (3.8)	19.2 (8.7 to 29.6)

NOTE. MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus.*

[a]Comparisons are against all control patients, regardless of test results.

TABLE 4

Antibiotics Prescribed to Test Group and Controls MRSA-Positive or MSSA-Positive

	Controls	Tests	Difference (95% CI)
MRSA+	(n = 36)	(n = 32)	
Prescribed a MRSA-active antibiotic[a]	30 (83.3)	30 (93.8)	− 10.4 (−25.2 to 4.4)
No antibiotic prescribed	6 (16.7)	2 (6.2)	
MSSA+	(n = 25)	(n = 26)	
Prescribed a MSSA-active antibiotic[a]	16 (64.0)	23 (88.5)	− 24.5 (−46.9 to −2.0)
No antibiotic prescribed[b]	9 (36.0)	3 (11.5)	

NOTE. Data are no. (%) unless otherwise specified. MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus.*

[a]MSSA-active antibiotics = trimethoprim/sulfamethoxazole, clindamycin, cephalexin; MRSA-active antibiotics =clindamycin, trimethoprim/sulfamethoxazole, doxycycline, vancomycin.

[b]Includes cases where non MSSA-active antibiotics were prescribed.

TABLE 5

Performance Analyses: Xpert vs Culture-Based Testing

Performance Analysis: Xpert vs Standard of Care					**95% CI**
MRSA	Xpert (+)	Xpert (−)	**Sensitivity**	87.9	71.8–96.6
Culture (+)	29	4	**Specificity**	98.8	93.4–100.0
Culture (−)	1	81	**Positive predictive value**	96.7	82.8–99.9
			Negative predictive value	95.3	88.4–98.7
MSSA	Xpert (+)	Xpert (−)	**Sensitivity**	95.7	78.1–99.9
Culture (+)	22	1	**Specificity**	95.7	89.2–98.8
Culture (−)	4	88	**Positive predictive value**	84.6	65.1–95.6
			Negative predictive value	98.9	93.9–100.0

NOTE. MRSA, methicillin-resistant *Staphylococcus aureus;* MSSA, methicillin-susceptible *S. aureus.*