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CME Information: Troponin Testing and Coronary Syndrome in Geriatric Patients With Nonspecific Complaints: Are We Overtesting?

CME Editor: Corey Heitz, MD

Authors: Alfred Z. Wang, MD, Jason T. Schaffer, MD, Daniel B. Holt, MD, Keaton L. Morgan, MD, and Benton R. Hunter, MD

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Educational Objectives
After reading the article, participants should be able to discuss the utility of routine troponin testing in geriatric patients with nonspecific complaints.

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Troponin Testing and Coronary Syndrome in Geriatric Patients With Nonspecific Complaints: Are We Overtesting?

Alfred Z. Wang, MD, Jason T. Schaffer, MD, Daniel B. Holt, MD, Keaton L. Morgan, MD, and Benton R. Hunter, MD

ABSTRACT

Background: Elderly patients presenting to the emergency department (ED) with nonspecific complaints (NSCs) often undergo troponin testing to assess for atypical acute coronary syndrome (ACS). However, the rate of ACS and utility of troponin testing in this population is unknown. We sought to determine the rate of ACS and diagnostic yield of troponin testing in elderly patients with NSCs.

Methods: We retrospectively identified all patients aged ≥65 years triaged in the ED with NSCs from January 1, 2017, to June 30, 2017. NSCs were defined a priori and included complaints such as weakness, dizziness, or fatigue. NSCs were verified in ED provider notes by trained abstractors blind to testing results. Exclusions were focal chief complaint in provider notes, fever, and no troponin ordered. ACS was strictly defined and independently adjudicated by two trained physician researchers blind to the study hypothesis. We calculated the proportion of patients with ACS within 30 days and the test characteristics of troponin to diagnose ACS.

Results: Screening identified 1,146 encounters, and 552 were excluded for fever or focal chief complaints in the provider notes. Of the remaining 594 patients, troponin was ordered in 412 (69%), comprising the study cohort. The mean (±SD) age was 78.7 (±8.3) years, with 58% female and 75% admitted. Troponin elevation occurred in 81 patients (20%). ACS occurred in 5 of 412 (1.2%). Troponin was 100% sensitive (95% confidence interval [CI] = 48% to 100%) and 81% specific (95% CI = 77% to 85%) for ACS. Of patients with elevated troponin, 93.8% were false positives (no ACS). All patients with troponin elevation were admitted, but only one underwent angiography and no patients received reperfusion therapy.

Conclusions: While consideration for ACS is prudent in selected elderly patients with NSCs, ACS was rare and no patients received reperfusion therapy. Given the false-positive rate in our study, our results may not support routine troponin testing for ACS in this population.

Patients aged 65 years or older account for approximately 15% of all emergency department (ED) visits in the United States.1 These elderly patients often require significant resource utilization and are at increased risk of adverse outcomes such as functional decline, prolonged hospitalization, and death.1−5 The assessment of this high-risk population can be complicated by the fact that elderly patients frequently...
present with nonspecific complaints, such as “weakness,” “dizziness,” or “not feeling well.”\textsuperscript{6,7} Furthermore, the medical history can be obscured by comorbidities, polypharmacy, and cognitive or functional impairment.\textsuperscript{6,8} Elderly patients in the ED are often diagnosed with serious or life-threatening acute medical problems, including those who present with vague or nonspecific complaints.\textsuperscript{9}

Since nonspecific complaints often have a broad differential diagnosis and there are no recommended diagnostic algorithms for patients with nonspecific presentations, practitioners often embark upon extensive testing to assess for a wide array of serious conditions.\textsuperscript{10} Acute coronary syndrome (ACS) is among the life-threatening conditions in the differential diagnosis of elderly patients with nonspecific complaints. Compared to younger populations, the elderly with ACS more frequently present without chest pain\textsuperscript{11} and up to 20\% of elderly patients with myocardial infarction may present with weakness as part of the chief complaint.\textsuperscript{12,13} Further, cardiovascular disease is the leading cause of mortality and morbidity in the elderly.\textsuperscript{14,15} Despite this, the frequency of ACS among elderly ED patients with nonspecific complaints has not been previously defined. Assessment for the presence of ACS typically includes troponin testing, but the utility of routine troponin testing in elderly patients with nonspecific symptoms is also unknown. The primary objectives of this study were to determine the frequency of ACS in elderly patients presenting to the ED with nonspecific complaints and to define the frequency and utility of troponin testing in this population.

**METHODS**

**Study Design and Setting**

This is a retrospective study of patients seen at an academic Level I trauma and tertiary referral center in the United States. The hospital is located near the center of a major metropolitan area and the ED sees approximately 100,000 patients per year. This study was approved by the local institutional review board.

**Patient Identification and Data Abstraction**

The target population was patients aged ≥ 65 years presenting to the ED with nonspecific complaints who underwent troponin testing. The cutoff of 65 years is consistent with previous studies and definitions\textsuperscript{16} and based on evidence that patients older than 65 have an increased mortality and higher rate of hospitalization due to cardiac vascular disease.\textsuperscript{17,18} The electronic medical record (EMR) was searched for patients registered in the ED aged 65 or older with triage chief complaints representing vague or nonspecific presentations. Potential triage complaints were defined a priori, including weak or weakness, dizzy or dizziness, fatigue, lethargy, altered mental status, light-headed, medical problem, examination requested, failure to thrive, or “multiple complaints.” These complaints were based on a combination of previous definitions of nonspecific presentations and institutional EMR codified complaints suggesting patient inability to articulate the specific reason for visit in triage.\textsuperscript{8,19} The EMR search included the 6-month period from January 1, 2017, through June 30, 2017.

Since some patients receive a triage complaint different than the chief complaint documented by the provider, we then performed a review of the provider note for each encounter with a nonspecific triage complaint. If the provider documented a focal chief complaint (e.g., any focal pain or injury complaint, shortness of breath, vomiting, diaphoresis, syncope, fever, cough, focal neurologic deficit), then the patient was excluded. In cases of multiple complaints, unless otherwise specified, the first symptom mentioned in the provider’s note was counted as the chief complaint. Secondary focal complaints were allowed if a nonspecific complaint was documented first or as primary.

Determination of a “nonspecific complaint” was made by two trained physician researchers who were blind to test results, including troponin. The ED physician note was opened in the EMR and a determination was made about whether the patient had presented with a nonspecific chief complaint. This determination was documented on a standardized data collection sheet. After a nonspecific chief complaint had been verified, the abstractor determined whether a troponin was ordered by viewing diagnostic test results in the EMR. Since a primary objective of the study was to assess the utility of troponin testing, patients in whom no troponin was ordered in the ED were excluded. The only other exclusion criteria applied was fever ≥ 38.0°C at triage. Patients were not excluded for reporting fevers prior to ED arrival, as long as fever was not the chief complaint (considered a focal complaint) and they were not documented to be febrile upon arrival. We chose to exclude febrile patients because fever strongly suggests infection and much less likely ACS. Other vital sign abnormalities were permitted.
Since the determination of “nonspecific” is not entirely objective, the first month of patient charts were reviewed by two researchers independently. Agreement about inclusion and exclusion criteria was measured and reported as a kappa value. Discrepancies were resolved through discussion. If agreement was sufficiently high, the remaining charts were to be divided between the two researchers for assessment of inclusion and exclusion criteria.

Once inclusion criteria were verified, additional objective data were abstracted from the EMR using a standardized data collection form, including age, sex, triage chief complaint, admission status, initial troponin positive or negative, results of any subsequent troponin testing during the index visit, and whether or not the patient was documented to have chest pain or shortness of breath on review of systems. Troponin positive was strictly defined according to the institutional cutoffs. The index visit included the ED visit and hospital stay if the patient was admitted. Only the ED visit was counted as index if the patient was discharged from the ED. Abstraction of outcome data and ACS determination were performed by two different physician researchers, as described below.

Outcomes
The outcomes of interest were: 1) the proportion of patients with verified nonspecific complaints who underwent troponin testing; 2) the proportion of such patients who had elevated troponin; 3) the proportion of patients with ACS at the index visit or within 30 days; 4) the utility of troponin testing to diagnose or exclude ACS; and 5) the frequency of other causes of troponin elevation in this population.

During the time period studied, two different troponin assays were utilized. A troponin I point of care whole blood assay (istat, Abbott) with cutoff of 0.08, based on 99th percentile, was primarily used in the ED. Inpatient troponin testing was performed with a troponin I fourth generation (Access, Beckman Coulter). The cutoff is 0.04, also based on 99th percentile. To avoid any subjectivity, we strictly applied the institutional cutoffs in all patients.

Adjudication of ACS
Using the 2014 American Heart Association (AHA) definition for ACS as the standard, we defined ACS as acute myocardial ischemia caused by a partial or complete occlusion of a coronary artery. We further specified ACS as not secondary to noncoronary factors such as demand ischemia or hypoperfusion from sepsis or anemia. To assess for the presence of ACS, each chart was reviewed independently by two trained physician researchers who were blind to the hypothesis and all other aspects of the study. Criteria for the diagnosis of ACS were predefined: 1) any documented ST-elevation myocardial infarction; 2) any coronary revascularization procedure or anatomic test showing acute occlusion or stenosis ≥ 70%; 3) stress test or echocardiogram (ECHO) read as consistent with inducible ischemia unless troponins negative and anatomic testing showed no flow restricting lesion; 4) troponin rise and fall in a pattern typical of ACS without an obvious alternative cause (e.g., sepsis, pulmonary embolism). This definition generally conforms to the AHA definition of ACS. Of note, unstable angina (cardiac chest pain without elevation in biomarkers) is considered ACS by the AHA. Our population, by definition, did not have cardiac chest pain, so we limited the diagnosis of ACS to objective findings consistent with cardiac ischemia. Non-ACS causes of troponin elevation were assigned based off the primary team or cardiology team’s explanation of troponin elevation.

Agreement was measured and reported. Disagreements were adjudicated through discussion. For any deaths within 30 days, the cause was determined through chart review performed independently by two physicians blinded to the hypothesis of the study. Cause of death, as defined by the clinical team in the discharge or death note, was generally assumed to be accurate. Disagreements were resolved by discussion.

Thirty-day follow-up included a search of the institutional EMR as well as a regional database of medical records compiled from all of the major regional hospital systems (Indiana Healthcare Information Exchange, Careweb). This database includes laboratory results, physicians’ notes, discharge summaries, and operative reports from each of the primary hospital systems in the area.

Data Analysis
We assessed the diagnostic utility of troponin as a test for ACS by calculating sensitivity, specificity, negative and positive predictive values (NPV, PPV), and likelihood ratios. We explored how troponin testing performed based on a single blood draw using the first troponin drawn in the ED, as well as the performance accounting for all troponin draws during the index visit, counting any elevated troponin above the institutional cutoff as a “positive” test.
The main objectives were to calculate a rate of ACS in the population, which was assumed to be low, and a false-positive rate (specificity) of troponin testing. As there is no prior literature from which to define the rate of ACS in the population being studied, an assumption based on clinical experience was made that the ACS rate was unlikely to be greater than 2%. To target a 95% confidence interval (CI) with a width of ≤3%, assuming an ACS rate of 2%, approximately 375 patients would be required to provide a 95% CI between 1 and 4%. Assuming a specificity of 90% for troponin, 375 patients would allow for a CI of 86% to 93% for specificity, which was felt unlikely to be viewed as clinically important (i.e., providers would not change their use of the test based on the difference between 86 and 93%).

RESULTS

Patient Identification and Characteristics

The EMR search identified 1,146 unique encounters of ED patients aged 65 and older with nonspecific triage chief complaints between January 1, 2017, and June 30, 2017. After the first 195 encounters (all of January) had been assessed for inclusion by two authors, agreement was 90% (κ = 0.79, 95% CI = 0.74–0.90). To improve agreement going forward, two additional clarifications were made; dizziness was counted as a nonspecific complaint, regardless of how it was described in the chart (vertiginous versus other) and “troponin ordered in the ED” was defined as drawn within 1 hour of the first blood draw done in the ED. After these clarifications, 100 additional charts were assessed, with 100% agreement. The remaining charts were divided between the two authors for eligibility screening.

Figure 1 outlines the flow of patient identification and exclusions. Of 1,146 encounters, 515 were excluded for having a focal chief complaint upon review of the ED physician note. Thirty-seven patients were then excluded for triage temperature ≥ 38.0°C. Of the remaining 594 patients, 412 (69%) had a troponin drawn in the ED and were included in the study population.

Baseline characteristics for the study cohort are shown in Table 1. The mean (±SD) age was 78.7 (±8.3), and 75% of patients were admitted. Eighty-two patients (20%) had at least one elevated troponin at some point during the index hospitalization. Of these, 52 (63%) had troponin elevation on the first draw in the ED and 30 (37%) had an initially negative troponin. Patients with elevated troponin were more likely to be admitted; more likely to present with a chief complaint of altered mental status; and less likely to present with dizziness, weakness, or fatigue (Table 1).

Main Results

Five patients (1.2%) were determined to have had ACS within 30 days. Details of these patients’ courses are provided in Table 2. All cases were identified during the index hospitalization, and no patient developed ACS after being discharged. Agreement for adjudication of ACS was 99.5%. Only one patient was taken for cardiac catheterization and was found to have diffuse coronary disease that was not amenable to intervention. This patient subsequently had a
cardiac arrest likely secondary to an acute myocardial infarction and was the only patient who died of ACS. No other patients underwent any attempt at reperfusion or had ACS therapy beyond aspirin. The other four ACS diagnoses were all based on troponin elevations without any further formal ACS workup besides nonstress echocardiography.

Counting any elevation as a positive, troponin was 100% sensitive (95% CI = 48%–100%) and 81% specific (95% CI = 77%–85%). The NPV was 100%, and PPV was 6.1%. The positive likelihood ratio (LR+) was 5.26, and the negative likelihood ratio (LR−) was 0. The first troponin drawn in the ED in isolation was 80% sensitive and 88% specific.

Table 1
Cohort Demographics

<table>
<thead>
<tr>
<th>All Patients</th>
<th>Positive Troponin</th>
<th>Negative Troponin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>412</td>
<td>82</td>
</tr>
<tr>
<td>Age (years), mean (±SD)</td>
<td>78.7 (±8.3)</td>
<td>78.8 (±9.4)</td>
</tr>
<tr>
<td>Admitted, n (%)</td>
<td>311 (75)</td>
<td>82 (100)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>239 (58)</td>
<td>36 (46)</td>
</tr>
</tbody>
</table>

Table 2
Details of Five Patients With ACS

<table>
<thead>
<tr>
<th>Patient</th>
<th>Chief Complaint</th>
<th>Peak Troponin (ng/mL)</th>
<th>Imaging for ACS</th>
<th>Discharge Diagnoses</th>
<th>ACS Diagnosis by Clinical Team?</th>
<th>Narrative</th>
</tr>
</thead>
<tbody>
<tr>
<td>82 y/o F</td>
<td>Weakness</td>
<td>&gt;73.0</td>
<td>Angiography showing severe coronary disease and acute thrombus in obtuse marginal vessel</td>
<td>NSTEMI, acute kidney injury, septic shock, pneumonia, hyperkalemia, respiratory failure, ventricular tachycardia</td>
<td>Yes</td>
<td>In ED seen for weakness, diagnosed with hyperkalemia, pneumonia, elevated trop. Inpatient had sepsis requiring vasopressors, troponin peaked at 9, angiography with small acute thrombus. Recovered, off vasopressors, then suddenly developed recurrent arrest and trop &gt; 73, care withdrawn.</td>
</tr>
<tr>
<td>92 y/o F</td>
<td>AMS</td>
<td>6.90</td>
<td>ECHO with no WMA, EF 56%</td>
<td>NSTEMI, cerebral contusion, delirium, dementia</td>
<td>Yes</td>
<td>Found confused with evidence of fall, small parietal contusion. No further ACS assessment due to goals of care.</td>
</tr>
<tr>
<td>82 y/o F</td>
<td>Dizziness</td>
<td>1.42</td>
<td>ECHO with no WMA</td>
<td>Dizziness, chest pain, troponin elevation medication reaction</td>
<td>No</td>
<td>Seen for dizziness, with subacute CP and SOB on ROS. Troponin 0 in ED. Got fentanyl and desaturated to 45%, recovered with naloxone and sternal rub. Troponin then rose up to 1.4, then down. Treating team felt troponin elevation was due to sternal rub. No cardiology consult.</td>
</tr>
<tr>
<td>96 y/o M</td>
<td>Examination requested</td>
<td>3.24</td>
<td>ECHO with no WMA</td>
<td>NSTEMI, unresponsive episode, paroxysmal atrial fibrillation</td>
<td>Yes</td>
<td>Unresponsive episode resolved by ED arrival. Systolic blood pressure 70s in the field. Diagnosed with NSTEMI and transient AMS, no further workup due to goals of care.</td>
</tr>
<tr>
<td>78 y/o M</td>
<td>AMS</td>
<td>0.10</td>
<td>ECHO with possible RCA distribution WMA</td>
<td>Unresponsive episode, “CAD with slight trop elevation,” multiple myeloma</td>
<td>No</td>
<td>Brought to ED with brief unresponsive episode. Resolved and workup negative. After ECHO, patient deemed poor candidate for angiography due to multiple myeloma, no further workup pursued.</td>
</tr>
</tbody>
</table>

ACS = acute coronary syndrome; AMS = altered mental status; CAD = coronary artery disease; ECHO = echocardiogram; EF = ejection fraction; NSTEMI = non-ST-elevation myocardial infarction; RCA = right coronary artery; WMA = wall motion abnormalities.
(NPV = 99.7%, PPV = 7.7%). The LR+ was 6.67, and LR− was 0.23.

Neither chest pain nor shortness of breath on review of systems was associated with either troponin elevation or ACS. Thirteen patients were positive for chest pain on review of systems; two had troponin elevation at index and none had ACS. Thirty patients were positive for shortness of breath on review of systems; nine had troponin elevation and none had ACS.

Sepsis was the most common cause of troponin elevation. Table 3 lists all the causes of non-ACS troponin elevation during index visit. Thirty-two patients (7.8%) died within the 30-day follow-up, mostly from sepsis. One patient died of ACS. Table 4 lists all causes of death. Mortality was 19.5% (16/82) in patients with troponin elevation and 4.8% (16/330) in patients with normal troponin. The relative risk for death with elevated troponin was 4.0 (95% CI = 2.0–8.1).

DISCUSSION

In this series of elderly patients presenting to the ED with nonspecific complaints, most patients underwent troponin testing, and although 20% of those tested had an elevated troponin, the diagnostic yield for ACS was low. Only 1.2% of patients (6.0% of those with elevated troponin) were determined to have ACS. Further, only one patient underwent angiography, and no patients received reperfusion therapy.

To our knowledge this is the first study to define the rate of ACS and evaluate the utility of troponin testing in elderly patients with nonspecific complaints. Previous work has found that elderly patients, especially those patients older than 75, with ACS can present with nonspecific complaints.17,21–23 No previous studies, however, have described the percentage of elderly patients with nonspecific complaints who are diagnosed with ACS. Instead, previous studies, such as the GRACE registry, have examined the percentage of elderly patients with specific complaints, such as vomiting, shortness breath, syncope, and diaphoresis, who had ACS.23 On the other hand, studies that have examined nonspecific complaints such as weakness have started with a cohort of patients diagnosed with ACS and reported how many ACS patients presented with nonspecific complaints.23–25 Small series of patients with nonspecific complaints have not reported ACS as an individual diagnosis, instead bundling “circulatory system” problems together.6,8 This makes comparisons of the rate of ACS with the current study impossible. Our study provides an estimate of the rate of ACS given nonspecific complaints, providing a previously unknown baseline risk estimate or pretest probability in this population. We would note that, for several reasons outlined in the limitations section, the 1.2% risk of ACS in this population may be a conservatively high estimate.

Table 3
Non-ACS Reasons for Troponin Elevation During Initial Visit

<table>
<thead>
<tr>
<th>Reason</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>22</td>
</tr>
<tr>
<td>Dehydration</td>
<td>7</td>
</tr>
<tr>
<td>Heart failure</td>
<td>6</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>5</td>
</tr>
<tr>
<td>Hypertensive emergency</td>
<td>5</td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td>4</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>4</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>3</td>
</tr>
<tr>
<td>Hypotension</td>
<td>3</td>
</tr>
<tr>
<td>Anemia</td>
<td>2</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>2</td>
</tr>
<tr>
<td>Hyperosmolar hyperglycemic state</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>2</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>2</td>
</tr>
<tr>
<td>Adrenal crisis</td>
<td>1</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>1</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>1</td>
</tr>
<tr>
<td>Alcohol withdrawal</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>1</td>
</tr>
<tr>
<td>Influenza</td>
<td>1</td>
</tr>
<tr>
<td>Seizure</td>
<td>1</td>
</tr>
<tr>
<td>Supraventricular tachycardia</td>
<td>1</td>
</tr>
<tr>
<td><strong>Sum</strong></td>
<td>77</td>
</tr>
</tbody>
</table>

ACS = acute coronary syndrome.

Table 4
Causes of Death Within 30 Days

<table>
<thead>
<tr>
<th>Cause</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>11</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>5</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
</tr>
<tr>
<td>Cancer</td>
<td>2</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>2</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>2</td>
</tr>
<tr>
<td>Heart failure</td>
<td>2</td>
</tr>
<tr>
<td>Colchicine toxicity</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal bleed</td>
<td>1</td>
</tr>
<tr>
<td>Liver failure</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
</tr>
<tr>
<td><strong>Sum</strong></td>
<td>32</td>
</tr>
</tbody>
</table>
There is a wide body of literature demonstrating that troponin elevation predicts worse outcomes in a variety of noncardiac conditions. We found a raw association between troponin elevation and mortality that was very similar to previous works. Since our intention was not to explore troponin as a prognostic marker, we did not collect other prognostic information necessary to perform analyses to calculate whether troponin was an independent predictor of death. We are thus unable to comment on whether troponin added valuable prognostic information on top of clinical judgment and other markers of poor prognosis.

Since there are elderly patients with nonspecific complaints who ultimately have ACS, routine troponin testing might seem like the safest option to avoid missing this important diagnosis. However, in terms of attempting to diagnose ACS, our study did not suggest any patient benefit with this strategy, and there are likely risks that are difficult to quantify. Of the five patients determined to have ACS, four did not undergo any formal testing beyond troponins and nonstress echocardiography, generally due to limited goals of care. The only patient to undergo angiography did not receive reperfusion therapy and ultimately died in the hospital. Although in our study, it seems unlikely that any patient actually benefitted from ACS testing, the elderly population is a very heterogenous one. Our study’s patients may have different goals of care than other populations, and it is possible that other elderly patients may request and benefit from more aggressive treatment.

Given the unclear benefit, the potential harm of routine troponin testing in this population should be considered. All 82 patients who had troponin elevation during their index visit were admitted, and almost all received cardiology consultations. Multiple studies have demonstrated a high rate of adverse events in elderly patients who are hospitalized, including delirium and somnolence or nosocomial infections such as pneumonias and urinary tract infections. While coronary angiography can benefit elderly patients with diagnosed ACS, and should probably be pursued in certain cases, it is a higher risk procedure in this age group. Some elderly patients with nonspecific complaints would no doubt benefit from the identification and treatment of ACS, but our findings suggest that such cases are rare. Rather than routine troponin testing, we suggest that the risks, costs, and consequences of downstream testing should be weighed against the potential for benefit and the likelihood of ACS prior to initiating troponin testing in these patients, especially given a false-positive rate of almost 20%.

**Limitations**

There are several important limitations to our study. This was a descriptive study with no comparison group, so our findings cannot clearly determine whether liberal troponin testing is associated with any change in admissions, downstream testing, or patient outcomes. Although all patients with troponin elevation were admitted, this should not be interpreted as a causal relationship. The admission rate was high even in patients without troponin elevation, and it is possible that all patients admitted with troponin elevation had other markers.

The determination of what constitutes a “nonspecific” complaint is not entirely objective, and we may have included patients who actually had focal complaints. We attempted to minimize this risk by using triage complaint as a screening tool only and confirming a nonspecific presentation in the providers’ notes. Chart reviewers were blinded to whether a troponin had been drawn to limit inclusion bias, and we used two independent reviewers to try to ensure that the determination of a “nonspecific complaint” was reproducible.

Alternatively, our screening criteria could have missed patients with nonspecific complaints who did not present with a triage complaint identified by our EMR search. We consulted with a systemwide IT expert with emergency medicine expertise to ensure that our screening included all triage complaints that would meet the spirit of the study, and we believe that any such misses were rare.

As this was a retrospective chart review, troponin was drawn entirely at the providers’ discretion. Since a primary goal of the study was to determine the utility of troponin testing, only patients who underwent troponin testing were included. There were 182 patients with nonspecific complaints excluded for not having a troponin drawn in the ED. Since patients who underwent troponin testing were likely deemed higher risk for ACS by the treating clinician than those who did not, inclusion of these additional patients may have diluted the overall prevalence of ACS, which was only 1.2% among those with troponin testing.
Another limitation of the retrospective nature of the study is that it is impossible to determine why troponin testing was ordered. We have generally assumed that troponin testing is undertaken to assess for ACS, but in some cases, it may have been drawn for prognostic purposes rather than significant concern for ACS.

There are no clear diagnostic criteria for ACS in this population. The diagnostic criteria we set forth included troponin elevation as one method to define ACS, even in the absence of other confirmatory testing, as long as no other clear cause for troponin elevation was identified. We tried to minimize the impact of this limitation by blinding the adjudicators of ACS to the hypothesis of the study and defining what constitutes ACS objectively. Nonetheless, the incorporation of the test we were evaluating (troponin) into the criteria for diagnosing ACS may have artificially increased the apparent diagnostic accuracy of the test. This may have played into our results substantially, as four of the five patients diagnosed with ACS had no confirmatory testing beyond abnormal troponins and nonstress echocardiography. Further, two of the five were not felt by their treating clinicians to have ACS. The end result of this limitation is that our finding of a 1.2% ACS rate in this population may have been an overestimation.

Cases of ACS occurring within 30 days but after the initial hospitalization could have been missed. In addition to our institutional EMR, we searched the regional combined EMR database (IHIE Careweb) for cardiology reports and discharge summaries to ensure catchment of any patients diagnosed with ACS at any of the major hospitals within the city and surrounding areas, but diagnoses occurring outside of the regional centers could have been missed.

Finally, this was a single-center study. There could be patient differences in other settings and the threshold for troponin testing could differ in other practice environments.

CONCLUSIONS

Elderly patients with nonspecific complaints in the ED underwent frequent troponin testing, and 20% of those tested had elevated troponin. However, our findings suggest that acute coronary syndrome is rare in this population and the vast majority of patients with elevated troponin do not have acute coronary syndrome. No patients in this study underwent reperfusion therapy. Given the false-positive rate in our study, our results may not support routine troponin testing for acute coronary syndrome in this population.

References

13. Wroblewski M, Mikulowski P, Steen B. Symptoms of myocardial infarction in old age: clinical case,


Predictive Accuracy of Electrocardiographic Monitoring of Patients With Syncope in the Emergency Department: The SyMoNE Multicenter Study

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ABSTRACT

Background: Arrhythmia is one of the most worrisome causes of syncope. Electrocardiographic (ECG) monitoring is crucial for the management of non–low-risk patients in the emergency department (ED). However, its diagnostic accuracy and optimal duration are unknown. We aimed to assess the diagnostic accuracy of ECG monitoring in non–low-risk patients with syncope in the ED.

Methods: This prospective multicenter observational study included adult patients presenting to the ED after syncope. Patients without an obvious etiology after ED evaluation who were classified by ED physicians as being at non–low risk of adverse events underwent ECG monitoring. We assessed sensitivity, specificity, and diagnostic yield (defined as the proportion of patients with true-positive ECG monitoring findings) of ECG monitoring in the identification of 7- and 30-day adverse and arrhythmic events according to monitoring duration.

Results: Of 242 patients included in the study, 29 patients had 7-day serious outcomes. Ten additional patients had serious outcomes at 30 days. The overall sensitivity, specificity, and diagnostic yield of ECG monitoring in the identification of 7-day adverse events were 0.55 (95% confidence interval [CI] = 0.36 to 0.74), 0.93 (95% CI = 0.89 to 0.96), and 0.07 (95% CI = 0.04 to 0.10), respectively. The sensitivity, specificity, and diagnostic yield of >12-hour ECG monitoring in the identification of 7-day adverse events were 0.89 (95% CI = 0.65 to 0.99), 0.78 (95% CI = 0.67 to 0.87), and 0.18 (95% CI = 0.12 to 0.28), respectively. Similar results were observed for 30-day adverse events. The median (interquartile range) ECG monitoring time was 6.5 (6 to 15) hours. ECG monitoring findings were positive in 31 patients.
Conclusions: Although the overall diagnostic accuracy of ECG monitoring is fair, its sensitivity at >12 hours’ duration is substantially higher. These results suggest that prolonged (>12 hours) monitoring is a safe alternative to hospital admission in the management of non–low-risk patients with syncope in the ED.

Despite international efforts to improve the emergency department (ED) management of patients with syncope through the development of consensus papers, risk prediction tools, and clinical guidelines, many issues remain unresolved. Physicians often find it difficult to distinguish among the many potential causes of syncope, which include benign and life-threatening conditions. As a result, a considerable proportion of patients is hospitalized for diagnostic evaluation to exclude a cardiac cause. However, hospital admission has a low diagnostic yield and high cost. Moreover, it does not appear to positively affect outcomes and might even be harmful to patients.

Arrhythmia is one of the most worrisome causes of syncope. As arrhythmia tends to occur in clusters, with a higher recurrence rate early after an event, the early use of electrocardiographic (ECG) monitoring may increase the likelihood of detecting significant arrhythmia related to a syncopal episode.

Two randomized clinical trials have assessed the roles of a structured ED observation protocol and syncope evaluation unit, respectively, in the management of patients with syncope in the ED. The study protocols involved ECG monitoring for 6 and 12 hours, respectively. The researchers reported a higher diagnostic yield and decreased hospital admission rate in the observation protocol/syncope unit group compared with the standard care group, but they did not report on the diagnostic accuracy of ECG monitoring. A study involving 4 weeks of external ECG monitoring for patients discharged from the ED after unexplained syncope showed an actuarial diagnostic yield of 29.4%, suggesting that early monitoring after syncope is more likely to detect significant arrhythmia.

Although ECG monitoring is considered to be the cornerstone of the ED management of patients with syncope, its diagnostic accuracy and optimal duration remain undefined. The aim of the current study was to assess the diagnostic accuracy of ECG monitoring in the ED according to its duration in non–low-risk patients with syncope.

METHODS

Population

The Syncope Monitoring and Natriuretic peptides in the Emergency department (SyMoNE) study was a prospective multicenter investigation conducted in six hospitals in northern Italy to assess the roles of brain natriuretic peptides and ECG monitoring in the ED management of patients with syncope. The Niguarda, Policlinico, and Sacco hospitals in Milan; the Humanitas Research Hospital in Rozzano (Milan); and the Alessandria and Santa Croce hospitals in Moncalieri (Torino) participated in the SyMoNE study. The enrollment of adult (age ≥ 18 years) patients who presented with syncope to the EDs of the participating centers extended from September 1, 2015, to February 28, 2017. Exclusion criteria were: 1) loss of consciousness (LOC) following head trauma; 2) nonspontaneous recovery of consciousness; 3) episodes of falling, dizziness, or lightheadedness without LOC; 4) LOC associated with alcohol or drug abuse; 5) pregnancy or breastfeeding status; 6) inability to provide informed consent to study participation or to complete follow-up; 7) syncope as an underlying symptom of an acute condition diagnosed in the ED or requiring therapeutic intervention irrespective of syncope (acute myocardial infarction, pulmonary embolism, aortic dissection, cerebral hemorrhage, carotid sinus syndrome, or arrhythmia diagnosed before ECG monitoring in the ED); 8) nonsyncopal LOC (i.e., history of epilepsy); and 9) poor prognosis in the next 30 days. Collected data included participants’ personal data and past medical histories as well as data on the features of the syncopal episodes, according to previous consensus.

Based on their clinical judgment, we asked the ED physicians to assess the patients’ risk of adverse events, classified as low, intermediate, and high. ED physicians managed patients regardless of patients’ participation in the study. For the purpose of the current investigation, we considered patients deemed to be at low risk by the ED physicians and those discharged without ECG monitoring (e.g., those with clear vasovagal histories or other benign explanations) to be at low risk. All remaining patients underwent ECG
monitoring and were enrolled in the study. We imposed no constraint on the duration of monitoring, but recommended a minimum duration of 6 hours. In cases of hospital admission, we retrieved copies of discharge letters. We followed patients by telephone at 7 and 30 days to assess the occurrence of any adverse events.

This study complied with the Declaration of Helsinki and received approval from the institutional review board of the coordinating center (L. Sacco Hospital, approval number 608/2015). All participants provided written consent and oral consent to telephone interviews as applicable.

Definitions

For this study, we defined syncope as transient LOC likely due to transient global cerebral hypoperfusion and characterized by rapid onset, short duration, and spontaneous complete recovery.\(^2,4\) We took the presence of any of the following abnormalities at ED presentation to constitute abnormal ECG status:\(^3,15\) nonsinus rhythm (including paced rhythm), 2) sinus bradycardia ≤ 50 beats/min, 3) left bundle branch block, 4) delta waves, 5) prolonged QRS (>120 msec), 6) prolonged QTc (>450 msec), 7) Brugada pattern, and 8) Q/ST/T changes consistent with acute or chronic ischemia. According to a previous consensus, we considered the presence of any of the following conditions to indicate ECG monitoring positivity:\(^3\) sinus arrest with cardiac pause > 3 seconds; 2) sustained or nonsustained, symptomatic or asymptomatic, ventricular tachycardia; 3) high-grade (second-degree type 2 or third-degree) atrioventricular (AV) block; 4) symptomatic or asymptomatic bradycardia < 30 beats/min; 5) symptomatic bradycardia < 50 beats/min; 6) tachycardia > 120 beats/min in a symptomatic patient; and 7) sick sinus syndrome with alternating bradycardia and tachycardia. We also recorded other conditions, such as new-onset atrial fibrillation, asymptomatic bradycardia < 50 beats/min, and tachycardia < 120 beats/min, although we did not consider them to contribute directly to definitive diagnoses. According to the “Standardized reporting guidelines for emergency department syncope risk-stratification research,”\(^15\) adverse events included any of the following: 1) all-cause and syncope-related death, 2) ventricular fibrillation, 3) sustained and symptomatic nonsustained ventricular tachycardia, 4) sinus arrest with cardiac pause > 3 seconds, 5) sick sinus syndrome with alternating bradycardia and tachycardia, 6) second-degree type 2 or third-degree AV block, 7) permanent pacemaker (PM) or implantable cardioverter defibrillator (ICD) malfunction with cardiac pauses, 8) aortic stenosis with valve area ≤ 1 cm\(^2\), 9) hypertrophic cardiomyopathy with outflow tract obstruction, 10) left atrial myxoma or thrombus with outflow tract obstruction, 11) myocardial infarction, 12) pulmonary embolism, 13) aortic dissection, 14) occult hemorrhage or anemia requiring transfusion, 15) syncope or fall resulting in major traumatic injury (requiring admission or procedural/surgical intervention), 16) PM or ICD implantation, 17) cardiopulmonary resuscitation, 18) syncope recurrence with hospital admission, and 19) cerebrovascular events.

Study Endpoints

The primary endpoint was the accuracy of ECG monitoring for the identification of 7- and 30-day adverse events in non–low-risk patients with syncope in the ED according to the duration of monitoring. Specifically, we assessed the following monitoring lengths: 1) < 6 hours (including data on monitoring lasting < 6 hours and data from the first 6 hours in patients monitored longer); 2) 6 to 12 hours (including data on monitoring lasting ≥6 hours but < 12 hours, data from the first 12 hours in patients monitored longer, and data from patients with positive monitoring findings within the first 6 hours [with positivity considered to be present even if monitoring had lasted longer]); and 3) >12 hours (including data on monitoring lasting >12 hours and data from patients with positive monitoring findings within the first 12 hours). Major secondary endpoints were: 1) the accuracy of ECG monitoring in the identification of arrhythmic events at 7 and 30 days according to the duration of monitoring and 2) the prevalence of all adverse events and arrhythmic adverse events at 7 and 30 days in patients who did not undergo ECG monitoring. We examined the latter endpoint to test the safety of ECG monitoring only in non–low-risk patients. According to the aim of the study, we did not consider adverse events occurring during ECG monitoring to be acute conditions diagnosed in the ED and thus included these events in the analyses. Two independent researchers blinded to the monitoring results subsequently revised all the patients’ charts to confirm, and possibly to readjudicate, the presence and nature of the adverse events observed during follow-up.
Data Analysis
A researcher at the coordinating center collected all data and stored them in a prospectively designed database. Descriptive statistics were calculated for continuous and categorical variables to summarize the baseline characteristics of patients enrolled, ECG monitoring results, and adverse events. We created 2 × 2 contingency tables for all endpoints. We assessed sensitivity, specificity, diagnostic yield (defined as the proportion of patients with true-positive ECG monitoring findings), and the number needed to diagnose (NND; the number of patients requiring ECG telemetry for the correct identification of one adverse event, computed as the inverse of the prevalence of true-positive ECG monitoring findings), and the calculation of 95% confidence intervals (CIs). We used the Kaplan–Meier method to estimate the probability of ECG monitoring positivity. As this report is part of a larger study of the roles of brain natriuretic peptides and ECG monitoring in the ED management of patients with syncope, the sample size was calculated to test the specificity of relative N-terminal pro–B-type natriuretic peptide variation in the prediction of adverse events. We performed the analyses using SAS statistical software (release 9.4, SAS Institute Inc.).

RESULTS
During the enrollment period, the researchers screened 414 patients who presented to the participating hospitals’ EDs for syncope for potential study participation. A total of 284 patients underwent ECG monitoring, and we included 242 of them in the study (Figure 1). Table 1 shows the demographic and clinical characteristics of the study population.

After 7 days of follow-up, 29 (12%) patients had serious outcomes and one of these patients died. At the 30-day follow-up, 10 additional patients had serious adverse events. Table 2 summarizes the incidence of 7- and 30-day adverse events in patients with and without arrhythmia during ECG monitoring.

The median (interquartile range) ECG monitoring duration was 6.5 (6–15) hours. Monitoring durations were >12 hours in 71 (29%) patients, 6 to 12 hours in 121 (50%) patients, and <6 hours in 50 (21%) patients. ECG monitoring findings were positive in 31 (13%) patients. The recorded arrhythmias were: 1) bradycardia in 18 patients (sinus arrest with cardiac pause > 3 seconds in five patients, high-grade AV block in two patients, bradycardia < 30 beats/min in one patient, symptomatic bradycardia < 50 beats/min in three patients, asymptomatic bradycardia < 50 beats/min in seven patients), 2) tachyarrhythmia in 12 patients (ventricular tachycardia in one patient, asymptomatic tachycardia > 120 beats/min in three patients, supraventricular tachycardia in eight patients), and 3) sick sinus syndrome with alternating atrial fibrillation and severe bradycardia in one patient.

The sensitivity, specificity, and diagnostic yield of ECG monitoring in the identification of 7-day adverse events were 0.55 (95% CI = 0.36–0.74), 0.93 (95% CI = 0.89–0.96), and 0.07 (95% CI = 0.04–0.10), respectively. The analysis of patients monitored for <6 hours showed poor diagnostic accuracy; the sensitivity, specificity, and diagnostic yield were 0.07 (95% CI = 0.01–0.23), 0.98 (95% CI = 0.95–0.99), and 0.01 (95% CI = 0.002–0.03), respectively. ECG monitoring for 6 to 12 hours performed slightly better, the sensitivity, specificity, and diagnostic yield were 0.29 (95% CI = 0.13–0.51), 0.95 (95% CI = 0.90–0.98), and 0.04 (95% CI = 0.02–0.07), respectively. Finally, the sensitivity, specificity, and diagnostic yield of ECG monitoring for >12 hours in the identification of 7-day adverse events were 0.89 (95% CI = 0.65–0.99), 0.78 (95% CI = 0.67–0.87), and 0.18 (95% CI = 0.12–0.28), respectively. The NNDs to identify 7- and 30-day adverse events were 16 (95% CI = 10–25) and 13 (95% CI = 9–20), respectively. In the subgroup of patients with >12 hours monitoring, the NNDs for 7- and 30-day adverse events were 6 (95% CI = 4–9) and 5 (95% CI = 4–8), respectively. Table 3 shows the accuracy of ECG monitoring in the identification...
of all adverse events and arrhythmic adverse events at 7 and 30 days according to the duration of monitoring. Figure 2 depicts the Kaplan–Meier curve for the probability of ECG monitoring positivity over time.

Follow-up data were available for 103 of the 130 patients who did not undergo ECG monitoring because of low estimated risks of adverse events (Data Supplement S1, available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13842/full). Three patients had 7-day adverse events. Hospital staff discharged one patient with ischemic cardiomyopathy after excluding arrhythmia by ICD testing, but the patient returned to the ED on the next day with dyspnea and hypotension and died of electromechanical dissociation, likely due to myocardial infarction. One patient had sick sinus syndrome and one had traumatic syncope recurrence. At the 30-day follow-up, one additional patient exhibited PM malfunction with cardiac pauses.

Table 1. Characteristics of Enrolled Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (% or median [IQR])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients enrolled</td>
<td>242</td>
</tr>
<tr>
<td>Patient characteristics</td>
<td></td>
</tr>
<tr>
<td>Sex (male)</td>
<td>129 (53.3)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>76 (62–83)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>130 (115–150)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>75 (64–85)</td>
</tr>
<tr>
<td>Admitted to hospital</td>
<td>95 (39.3)</td>
</tr>
<tr>
<td>Syncopal episode characteristics</td>
<td></td>
</tr>
<tr>
<td>During working activity</td>
<td>13/239 (5.4)</td>
</tr>
<tr>
<td>During exertion</td>
<td>4 (1.6)</td>
</tr>
<tr>
<td>While driving</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>In supine position</td>
<td>6 (2.5)</td>
</tr>
<tr>
<td>In seated position</td>
<td>79 (32.6)</td>
</tr>
<tr>
<td>In orthostatic position</td>
<td>135 (55.8)</td>
</tr>
<tr>
<td>While standing from a seated position</td>
<td>20 (8.3)</td>
</tr>
<tr>
<td>Postprandial</td>
<td>25 (10.3)</td>
</tr>
<tr>
<td>With postsyncope trauma</td>
<td>92 (38.0)</td>
</tr>
<tr>
<td>Without prodrome</td>
<td>132 (54.6)</td>
</tr>
<tr>
<td>Without vagal prodrome</td>
<td>121 (50.0)</td>
</tr>
<tr>
<td>Associated with</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>19 (7.8)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>15 (6.2)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>11 (4.5)</td>
</tr>
<tr>
<td>Lightheadedness</td>
<td>60 (24.8)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>47 (19.4)</td>
</tr>
<tr>
<td>Sensation of warmth</td>
<td>23 (9.5)</td>
</tr>
<tr>
<td>Sweating</td>
<td>50 (20.7)</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>38 (15.7)</td>
</tr>
<tr>
<td>Triggered by pain/stressors</td>
<td>13 (5.3)</td>
</tr>
<tr>
<td>Triggered by cough/micturition/defecation</td>
<td>18 (7.4)</td>
</tr>
<tr>
<td>Hematocrit &lt; 30%</td>
<td>8/241 (3.3)</td>
</tr>
<tr>
<td>Hemoglobin &lt; 9 g/dL</td>
<td>7/241 (2.9)</td>
</tr>
<tr>
<td>Systolic arterial blood pressure &lt; 90 mm Hg</td>
<td>7 (2.9)</td>
</tr>
<tr>
<td>Past medical history</td>
<td></td>
</tr>
<tr>
<td>Syncope in the previous year</td>
<td>70 (28.9)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>7 (2.9)</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>45 (18.6)</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>20 (8.3)</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>7 (2.9)</td>
</tr>
<tr>
<td>Left ventricular outflow obstruction</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>7 (2.9)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction &lt; 40%</td>
<td>9 (3.7)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>9 (3.7)</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>8 (3.3)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>29 (12.0)</td>
</tr>
<tr>
<td>Previous PM implantation</td>
<td>8 (3.3)</td>
</tr>
</tbody>
</table>

Table 1. (continued)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (% or median [IQR])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous ICD implantation</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Mobitz 2 second- or third-degree AV block</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>153 (63.2)</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>25 (10.3)</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>34 (14.0)</td>
</tr>
<tr>
<td>Chronic kidney disease (serum creatinine ≥ 2 mg/dL)</td>
<td>9 (3.7)</td>
</tr>
<tr>
<td>COPD</td>
<td>18 (7.4)</td>
</tr>
</tbody>
</table>

Abnormal ECG findings (ECG results available for 239 patients)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (% or median [IQR])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardia &lt; 50 beats/min</td>
<td>8 (3.3)</td>
</tr>
<tr>
<td>First-degree AV block</td>
<td>31 (13.0)</td>
</tr>
<tr>
<td>Right bundle branch block</td>
<td>31 (13.0)</td>
</tr>
<tr>
<td>Left bundle branch block</td>
<td>8 (3.3)</td>
</tr>
<tr>
<td>Left anterior fascicular block</td>
<td>25 (10.5)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>21 (8.8)</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Ventricular ectopic beats</td>
<td>10 (4.2)</td>
</tr>
<tr>
<td>Supraventricular ectopic beats</td>
<td>11 (4.7)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>18 (7.5)</td>
</tr>
<tr>
<td>Sinus bradycardia &lt; 60 beats/min</td>
<td>27 (11.3)</td>
</tr>
<tr>
<td>Sinus tachycardia &gt; 100 beats/min</td>
<td>18 (7.5)</td>
</tr>
<tr>
<td>Prolonged QT interval</td>
<td>5 (2.1)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (1.7)</td>
</tr>
</tbody>
</table>

AV = atrioventricular; COPD = chronic obstructive pulmonary disease; ECG = electrocardiography; ICD = implantable cardioverter defibrillator; IQR = interquartile range; PM = pacemaker; TIA = transient ischemic attack.
DISCUSSION

The results of this study suggest that the overall diagnostic accuracy of ECG monitoring in ED patients with syncope is imperfect. However, monitoring for >12 hours showed increased sensitivity (89%) and diagnostic yield (18%), with a low NND to correctly identify patients with adverse events. Notably, such sensitivity and diagnostic yield are higher than those of the diagnostic tests and clinical prediction tools commonly used in the management of patients with syncope. Moreover, the Kaplan–Meier curve shows that, although the probability of ECG monitoring positivity is low with <6 hours’ duration, this probability increases constantly between 6 and 24 hours. As few patients underwent ECG monitoring for >24 hours, we cannot draw a robust conclusion for such a monitoring length.

Two randomized clinical studies have assessed the potential role of ECG monitoring as part of syncope observation protocols in the ED. The prospective, randomized, single-center Syncope Evaluation in the Emergency Department study involved the random allocation of intermediate-risk patients to syncope unit evaluation or standard care. Patients in the syncope unit arm received continuous cardiac monitoring for ≤6 hours, as well as orthostatic blood pressure, ECG, tilt-table testing, carotid sinus massage, and electrophysiologic consultation when clinically indicated. The diagnostic yield was significantly higher and the hospital admission rate was lower for these patients than for those in the standard care group. The second multicenter study compared an ED observation syncope protocol with routine inpatient admission for intermediate-risk patients after unrevealing ED evaluation for syncope. All observation protocol patients received continuous cardiac monitoring for ≥12 hours, and the ED treatment teams could perform two serial cardiac troponin tests, ECG, and additional testing at their discretion. The ED observation protocol substantially reduced hospital inpatient admissions, lengths of stay, and index hospital costs, with no difference in safety events. Both of these studies enrolled intermediate-risk patients, as low-risk patients are generally discharged without further investigation, and high-risk patients are usually admitted to hospital. Locati et al. performed a prospective multicenter observational study in which patients discharged from the hospital or ED after unexplained syncope underwent 4-week external ECG monitoring. The actuarial diagnostic yields were 13.2% at 1 week, 19.1% at 2 weeks, and 29.4% at 4 weeks. Multivariate logistic regression analysis revealed that the early initiation of monitoring after the index syncopal event independently predicted diagnosis. This finding is consistent with some preliminary observations suggesting that syncopal events occur in clusters early after the index event, which makes the prompt initiation of ECG monitoring crucial.

<p>| Table 2 | Incidence of 7- and 30-Day Adverse Events in Patients With and Without Arrhythmia During ECG Monitoring of Any Duration |</p>
<table>
<thead>
<tr>
<th>Adverse event</th>
<th>7 Days</th>
<th>30 Days</th>
<th>7 Days</th>
<th>30 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse event</td>
<td>16 (6.6)</td>
<td>13 (5.4)</td>
<td>19 (7.9)</td>
<td>20 (8.3)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>1 (0.4)</td>
<td>0</td>
<td>1 (0.4)</td>
<td>0</td>
</tr>
<tr>
<td>Sustained/symptomatic nonsustained VT</td>
<td>1 (0.4)</td>
<td>0</td>
<td>1 (0.4)</td>
<td>0</td>
</tr>
<tr>
<td>Paroxysmal or new-onset AF</td>
<td>1 (1.2)</td>
<td>1 (0.4)</td>
<td>2 (0.8)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Sinus arrest with cardiac pause &gt; 3 seconds</td>
<td>2 (0.8)</td>
<td>0</td>
<td>2 (0.8)</td>
<td>0</td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>4 (1.7)</td>
<td>1 (0.4)</td>
<td>5 (2.1)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Second-degree type 2 or third-degree AV block</td>
<td>2 (0.8)</td>
<td>1 (0.4)</td>
<td>2 (0.8)</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>1 (0.4)</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Occult hemorrhage or anemia requiring transfusion</td>
<td>1 (0.4)</td>
<td>0</td>
<td>2 (0.8)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>PM or ICD implantation</td>
<td>10 (4.1)</td>
<td>10 (4.1)</td>
<td>11 (4.5)</td>
<td>13 (5.4)</td>
</tr>
<tr>
<td>Syncope recurrence with hospital admission</td>
<td>1 (0.4)</td>
<td>0</td>
<td>3 (1.2)</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Cerebrovascular events</td>
<td>1 (0.4)</td>
<td>0</td>
<td>2 (0.8)</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are presented as n (%). Data for 30-day events include those for 7-day events. AF = atrial fibrillation; AV = atrioventricular; ECG = electrocardiography; ICD = implantable cardioverter defibrillator; PM = pacemaker; VT = ventricular tachycardia.
Table 3
Diagnostic Accuracy of ECG Monitoring for 7- and 30-Day Adverse Events and Arrhythmic Events According to Monitoring Duration

<table>
<thead>
<tr>
<th>Monitoring Duration</th>
<th>No. of Patients</th>
<th>SE</th>
<th>SP</th>
<th>DY</th>
<th>NND</th>
<th>SE</th>
<th>SP</th>
<th>DY</th>
<th>NND</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adverse events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>242</td>
<td>0.55 (0.36–0.74)</td>
<td>0.93 (0.89–0.96)</td>
<td>0.07 (0.04–0.10)</td>
<td>16 (10–25)</td>
<td>0.49 (0.32–0.66)</td>
<td>0.94 (0.90–0.97)</td>
<td>0.08 (0.05–0.12)</td>
<td>13 (9–20)</td>
</tr>
<tr>
<td>&lt;6 hours</td>
<td>242</td>
<td>0.07 (0.01–0.23)</td>
<td>0.98 (0.95–0.99)</td>
<td>0.01 (0.00–0.03)</td>
<td>121 (4–435)</td>
<td>0.08 (0.02–0.21)</td>
<td>0.98 (0.96–1.00)</td>
<td>0.01 (0.00–0.04)</td>
<td>81 (28–239)</td>
</tr>
<tr>
<td>6-12 hours</td>
<td>198</td>
<td>0.29 (0.13–0.51)</td>
<td>0.95 (0.90–0.98)</td>
<td>0.04 (0.02–0.07)</td>
<td>29 (15–58)</td>
<td>0.24 (0.11–0.42)</td>
<td>0.95 (0.91–0.98)</td>
<td>0.04 (0.02–0.08)</td>
<td>25 (19–49)</td>
</tr>
<tr>
<td>&gt;12 hours</td>
<td>88</td>
<td>0.89 (0.65–0.99)</td>
<td>0.78 (0.67–0.87)</td>
<td>0.18 (0.12–0.28)</td>
<td>6 (4–9)</td>
<td>0.86 (0.65–0.97)</td>
<td>0.82 (0.70–0.90)</td>
<td>0.22 (0.14–0.31)</td>
<td>5 (4–8)</td>
</tr>
<tr>
<td><strong>Arrhythmic events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>242</td>
<td>0.58 (0.37–0.77)</td>
<td>0.93 (0.88–0.96)</td>
<td>0.06 (0.04–0.10)</td>
<td>17 (2–27)</td>
<td>0.53 (0.34–0.72)</td>
<td>0.93 (0.89–0.96)</td>
<td>0.07 (0.04–0.10)</td>
<td>16 (10–25)</td>
</tr>
<tr>
<td>&lt;6 hours</td>
<td>242</td>
<td>0.08 (0.01–0.25)</td>
<td>0.98 (0.95–0.99)</td>
<td>0.01 (0.00–0.03)</td>
<td>121 (4–435)</td>
<td>0.07 (0.01–0.22)</td>
<td>0.98 (0.95–0.99)</td>
<td>0.01 (0.00–0.03)</td>
<td>81 (28–239)</td>
</tr>
<tr>
<td>6-12 hours</td>
<td>198</td>
<td>0.27 (0.11–0.50)</td>
<td>0.94 (0.90–0.97)</td>
<td>0.03 (0.01–0.06)</td>
<td>33 (16–72)</td>
<td>0.23 (0.09–0.44)</td>
<td>0.94 (0.90–0.97)</td>
<td>0.03 (0.01–0.06)</td>
<td>33 (16–72)</td>
</tr>
<tr>
<td>&gt;12 hours</td>
<td>88</td>
<td>0.88 (0.64–0.99)</td>
<td>0.77 (0.66–0.86)</td>
<td>0.17 (0.11–0.26)</td>
<td>6 (4–10)</td>
<td>0.84 (0.60–0.97)</td>
<td>0.78 (0.66–0.87)</td>
<td>0.18 (0.12–0.28)</td>
<td>5 (4–8)</td>
</tr>
</tbody>
</table>

Numbers in parentheses are 95% CI.

- DY = diagnostic yield; ECG = electrocardiography; NND = number needed to diagnose; SE = sensitivity; SP = specificity.
- Patients monitored for <6 hours and the first 6 hours in patients monitored longer.
- Patients monitored >6 hours but <12 hours, the first 12 hours in patients monitored longer, and patients with positive monitoring findings within the first 6 hours.
- Patients monitored ≥12 hours and those with positive monitoring findings within the first 6 hours.

In a recently published large prospective multicenter study of patients presenting to the ER with syncope, researchers tried to identify the optimal duration of cardiac rhythm monitoring based on the timing of arrhythmia identification and costs. The authors reported relatively prompt ED identification of the location of serious arrhythmia identification. The diagnostic accuracy of ECG monitoring in non-low-risk patients with no obvious serious condition on arrival (within the first 2 hours in low-risk patients and 6 hours in medium- or high-risk patients) is suggested to be the diagnostic accuracy of ECG monitoring in non-low-risk patients with no obvious serious condition on arrival (within the first 2 hours in low-risk patients and 6 hours in medium- or high-risk patients). 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LIMITATIONS

This study has some limitations. Adverse events in patients with syncope are relatively uncommon, usually not serious, and very heterogeneous, as they can be related to different underlying conditions. Therefore, the choice to assess the accuracy of ECG monitoring in the identification of arrhythmic and nonarrhythmic adverse events might be questioned. However, we decided to include all outcomes to assess the feasibility of ECG monitoring as part of a management strategy, rather than as a single diagnostic tool for the identification of arrhythmia. Moreover, as most of the adverse events were arrhythmic, the diagnostic accuracy for the identification of arrhythmic events and all events was similar.

The diagnostic yield of ECG monitoring might seem to be poor, and some might argue that the routine use of prolonged telemetry in non–low-risk patients with syncope might lead to unnecessary testing and ED stays. However, the NND, which takes into account the prevalence of adverse events, was low in this study. Indeed, the need to monitor six patients for >12 hours to correctly identify one patient who will experience a 7-day serious adverse event is a feasible requirement.

The specificity of ECG monitoring declined in patients with longer monitoring durations. However, the false-positive results reflect the use of ECG monitoring as a prognostic, rather than diagnostic, tool. Indeed, the criteria adopted to define ECG monitoring positivity included not only diagnoses (i.e., ventricular tachycardia or high-grade AV block), but also worrisome findings (i.e., severe sinus bradycardia or unexplained tachycardia) that warranted hospital admission for further evaluation and adequate therapy. For example, according to the study protocol, unexplained symptomatic sinus tachycardia is a positive monitoring finding likely resulting in hospital admission. Careful evaluation might reveal that this finding is the manifestation of another condition, such as sepsis or a respiratory problem, which would constitute a false-positive monitoring result. However, the identification of patients with potentially serious conditions beyond arrhythmia is crucial, and telemetry might become a comprehensive tool for the assessment of patients with syncope. From this perspective, we argue that the reduction of specificity is not a true limitation.

On the other side, some authors have questioned the inclusion of PM and ICD implantation among study outcomes. Indeed, as device implantation is a treatment and not a diagnosis, a clinician’s decision to perform it might be the consequence of a more comprehensive subjective evaluation beyond simple testing. For example, an elderly patient with traumatic syncope without prodrome and a bifascicular block might undergo PM implantation even after negative ECG monitoring. In this case, some might question the consideration of the monitoring result as a false negative. However, we decided to include these procedures as outcomes to ensure consistency with previous consensus documents.

We did not use a standardized protocol to guide ECG monitoring duration and patient management, which some might consider a limitation of the current study, as monitoring durations were likely longer for patients considered to be at higher risk. However, as no evidence for the optimal duration of monitoring existed up to now, we decided not to set an a priori monitoring length, although we recommended a minimum of 6 hours.

CONCLUSIONS

Our study shows that, whereas the overall diagnostic accuracy of ED electrocardiographic monitoring of non–low-risk patients syncope is imperfect, the sensitivity of prolonged telemetry is high. These results suggest that the use of prolonged (>12 hours) monitoring is a safe alternative to hospitalization for the management of non–low-risk patients with syncope.

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References


Supporting Information

The following supporting information is available in the online version of this paper available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13842/full

Data Supplement S1. Characteristics of the non-monitored patients.
Can Emergency Physician Gestalt “Rule In” or “Rule Out” Acute Coronary Syndrome: Validation in a Multicenter Prospective Diagnostic Cohort Study

Govind Oliver\textsuperscript{1,2}\textsuperscript{a}, Charlie Reynard, MBChB\textsuperscript{1,2}\textsuperscript{a}, Niall Morris, MBChB, PhD\textsuperscript{1,2}\textsuperscript{a}, and Richard Body, MBChB, PhD\textsuperscript{1,2}\textsuperscript{a}

A related article appears on page 80.

ABSTRACT

\textbf{Background:} Chest pain is a common problem presenting to the emergency department (ED). Many decision aids and accelerated diagnostic protocols have been developed to help clinicians differentiate those needing admission from those who can be safely discharged. Some early evidence has suggested that clinician judgment or gestalt alone could be sufficient.

\textbf{Objectives:} Our aim was to externally validate whether emergency physician’s gestalt could “rule in” or “rule out” acute coronary syndromes (ACS).

\textbf{Methods:} We performed a multicenter prospective diagnostic accuracy study including consenting patients presenting to the ED in whom the physician suspected ACS. At the time of arrival, clinicians recorded their perceived probability of ACS using a 5-point Likert scale. The primary outcome was a diagnosis of ACS, defined as acute myocardial infarction or major adverse cardiac events within 30 days.

\textbf{Results:} A total of 1,391 patients were included; 240 (17.3\%) had ACS. Overall, gestalt had fair diagnostic accuracy with a C-statistic of 0.75 (95\% confidence interval = 0.72 to 0.79). If ACS was “ruled out” in the 60 (4.3\%) patients where clinicians perceived that the diagnosis was “definitely not” ACS, a sensitivity of 98.0\% and negative predictive value of 95.0\% could have been achieved. If ACS was only ruled out in patients who also had no electrocardiographic (ECG) ischemia and a normal initial cardiac troponin (cTn) concentration, 100.0\% sensitivity and NPV could be achieved. However, this strategy only applied to 4.1\% of patients. If patients with “probably not” ACS who had normal ECG and cTn were also ruled out (n = 418, 30.8\%), sensitivity fell to 86.2\% with 99.2\% NPV. Using gestalt “definitely” ACS to rule in ACS gave a specificity of 98.5\% and positive predictive value of 71.2\%.

\textbf{Conclusion:} Clinician gestalt is not sufficiently accurate or safe to either rule in or rule out ACS as a decision-making strategy. This study will enable emergency physicians to understand the limitations of our clinical judgment.

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The authors have no relevant financial information or potential conflicts to disclose.

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Chest pain is a common problem in the emergency department (ED) representing over 5% to 6% of all attendances and over 25% of all acute medical admissions. Most of these patients do not have an acute coronary syndrome (ACS) with prevalence at 8% to 10%.

Prompt identification of patients presenting with chest pain who have ACS (“rule in”), and exclusion of ACS in those who do not (“rule out”), is a priority. Multiple accelerated diagnostic protocols have been developed to assist and guide clinicians’ decision-making. Many are now available including the HEART score, the Global Registry of Acute Coronary Events (GRACE) score, the Thrombolysis and Myocardial Infarction (TIMI) score, the Troponin only Manchester Acute Coronary Syndrome decision aid (TMACS), and the Emergency Department Assessment of Chest Pain Score (EDACS). Recent work has focused on the use of highly sensitive cardiac troponin (hs-cTn) assays to rule out acute myocardial infarction (AMI) early in the patient journey; these have been incorporated into 1- and 3-hour AMI rule-out strategies recommended by the European Society of Cardiology. However, while the “typicality of chest pain” has been shown to be of limited discriminatory value in the assessment of suspected ACS, early evidence suggests that clinician’s global diagnostic assessment or gestalt may be sufficient in “ruling in” or “ruling out” the diagnosis.

One prospective study found no statistical difference between gestalt and the HEART score in identifying “low-risk” patients for ACS rule out. Another found that clinician gestalt of “probably not” or “definitely not” ACS combined with a normal electrocardiogram (ECG) and arrival troponin could effectively rule out 23.1% of patients presenting with suspected cardiac chest pain. The sensitivity of this strategy was 99.0% (95% confidence interval [CI] = 94.6% to 100.0%) and negative predictive value (NPV) 99.1% (95% CI = 93.7% to 99.9%). Incorporation of a normal hs-cTnT concentration on arrival increased the number of patients identified as low risk to 41.7% with no missed AMIs and a 1.6% incidence of major adverse cardiac events (MACE) at 30 days. The sensitivity of this strategy for MACE was 97.0% (95% CI = 91.5% to 99.4%), and NPV was 98.4% (95% CI = 95.3% to 99.5%). The primary aim of our study was to externally validate the diagnostic accuracy of clinician gestalt for ruling in or ruling out ACS in adults presenting to the ED with suspected cardiac chest pain.

METHODS

Study Design
The Bedside Evaluation of Sensitive Troponin (BEST) study was a prospective multicenter diagnostic accuracy study at 18 hospitals, including adults presenting to the ED with suspected ACS (Data Supplement S1, available as supporting information in the online version of this paper, which is available at http://online library.wiley.com/doi/10.1111/acem.13836/full). This is a preplanned secondary analysis of the BEST study. Ethical approval was obtained from the National Research Ethics Service (reference 14/NW/1344). Patients were recruited over a 2.5-year period from February 2015 to July 2017.

Study Setting and Population
We included adult patients (>18 years) presenting to the ED with suspected cardiac chest pain peaking within the past 12 hours (symptoms compatible with the American Heart Association case definition for ACS) that the treating physician identified as requiring investigation for ACS. Exclusion criteria were patients with unmistakable ST-elevation myocardial infarction, those whose symptoms peaked over 12 hours ago, those presenting with other non-ACS medical complaints necessitating hospital admission, and patients unable to provide written informed consent.

Study Protocol
Potential participants meeting the study inclusion criteria were given verbal and written information about the study by an investigator. Written consent was obtained from all participants. Each patient had an ECG performed. Blood was drawn for cTn testing on arrival. The treating physician and study nurse, on a standardized study case report form at the time of inclusion in accordance with international standards, captured study-specific key clinical data. Data were collected on multiple variables including patient demographics, past medical history including risk factors for cardiovascular disease, 12-lead ECG findings, and the clinician’s assessment or unstructured gestalt about the probability of ACS. The latter had to be stated by the clinician responsible for providing clinical care to the patient and was recorded on a 5-point Likert scale as follows: “definitely not” ACS, “probably not” ACS, “could be” ACS, “probably” ACS, and “definitely” ACS. These data were recorded at the time of initial review following assessment; clinicians were unblinded.

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to both the ECG and the initial cTn results but were blinded to serial cTn results and the final outcome. The ECG was available to clinicians at the time of their review; the availability of the initial cTn was dependent on local factors influencing the time of the clinicians assessment and the return of the laboratory result. All patients underwent reference standard serial troponin testing over at least 3 hours (when hs-cTn assays were in use) or at least 6 hours (for contemporary assays).

Follow-up was conducted for 30 days. Patients were followed by the research team throughout their admission and were contacted by telephone, e-mail, or letter or in person after 30 days. If the patient could not be reached, follow-up information was collected from their general practitioner.

Outcome Measures
The primary outcome was a diagnosis of ACS, defined as prevalent AMI or incident MACE at 30 days. MACE included all cause death, coronary revascularization, and incident AMI. All outcomes were adjudicated by two investigators blinded to each other’s adjudication and to clinician gestalt. AMI was diagnosed in accordance with the Third Universal Definition of Myocardial Infarction. This required a rise and/or fall of cTn with at least one level above the 99th percentile for a healthy reference population.16

Data Analysis
As the sample size for this study was driven by the primary analysis, no formal a priori sample size calculation was performed for this secondary analysis. However, the primary analyses were powered such that a diagnostic test with 100% sensitivity and NPV would achieve 95% CIs with lower bounds that did not fall below 95% for sensitivity and 99% for NPV. Estimating prevalence 10 and 5% losses to follow-up, this would be achieved with a total sample of 1,575 patients. Descriptive statistics and receiver operator characteristic (ROC) curve analysis were performed using IBM SPSS (version 23.0, IBM Corp.). Sensitivity, specificity, positive predictive value (PPV), and NPV were calculated using MedCalc (version 18.11.3).

RESULTS
In total, 1,613 cases were screened from the BEST study for inclusion in this secondary analysis. The flow of participants and reasons for exclusion are shown in Figure 1. Of these patients, 207 (14.9%) were given an adjudicated diagnosis of AMI and additional 33 developed MACE within 30 days (including five cardiac deaths and 28 coronary revascularizations), giving a total of 240 (17.3%) patients meeting criteria for the target condition of ACS. The population was predominantly male (n = 893, 64.2%) with and mean age of 58.7 years (range = 19–93 years, SD ± 15.4 years). The population cardiovascular risk factors are shown in Table 1. The clinician recorded the presence of acute ischemic features on the ECG in 99 (7.1%) patients, and the initial troponin was greater than the 99th percentile in 344 (24.7%) cases.

Clinician gestalt had an area under the ROC curve of 0.75 (95% CI = 0.72–0.79) for ACS. The proportion of patients with ACS stratified by clinician’s gestalt is shown in Table 2. Despite being investigated for ACS, in 60 (4.3%) of cases, the clinician felt that ACS was actually “definitely not” the diagnosis. Interestingly three (5.0%) of these patients did in fact have AMI. Allowing for a degree of uncertainty, gestalt was recorded as “probably not” ACS in 493 (35.4%) of cases with 24 (4.9%) having AMI and 27 (5.5%) ACS. At the other end, clinicians perceived that the diagnosis was “definitely” ACS in a similarly small
Diagnostic Accuracy of Clinician Gestalt for ACS Rule Out, Both Alone and in Combination With the ECG and Initial cTn Concentration

The diagnostic accuracy of gestalt alone and also combined with ECG and initial troponin, for ruling out ACS is shown in Table 3. In the cases where the clinician felt the diagnosis was “definitely not” ACS, the diagnostic accuracy was high with a sensitivity of 98.8% and NPV of 95.0%. If ACS had been “ruled out” in all cases where the clinician felt the diagnosis was either “definitely not” or “probably not” ACS, then sensitivity would have dropped to 87.8% and NPV to 94.8%. Interestingly, the diagnostic accuracy of gestalt as a rule-out strategy was not substantially changed much by combining it with an ECG without ischemic features and an initial cTn concentration below the 99th percentile upper reference limit. The high accuracy of gestalt in the “definitely not” ACS group was improved to a sensitivity of 100.0% and an NPV of 100.0% when combined with ECG and troponin, but this rule-out strategy would only have ruled out ACS in 55 (4.1%) patients.

The diagnostic accuracy of gestalt alone, and also combined with ECG and troponin, for ruling in ACS is shown in Table 4. Where the gestalt was “definitely” ACS, the diagnostic accuracy was high with a specificity of 98.5% and PPV of 71.2%. Interestingly,

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**Table 1**

Baseline Characteristics and Cardiovascular Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Present</th>
<th>MACE</th>
<th>Not Present</th>
<th>MACE</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>893 (64.2)</td>
<td>173 (19.4)</td>
<td>488 (35.8)</td>
<td>67 (13.5)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>688 (49.5)</td>
<td>147 (21.4)</td>
<td>702 (50.5)</td>
<td>67 (13.5)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>523 (37.6)</td>
<td>114 (21.8)</td>
<td>855 (61.5)</td>
<td>93 (13.3)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>387 (27.8)</td>
<td>91 (23.5)</td>
<td>1001 (72.0)</td>
<td>123 (14.4)</td>
</tr>
<tr>
<td>Previous angina</td>
<td>389 (28.0)</td>
<td>96 (24.7)</td>
<td>979 (70.5)</td>
<td>149 (14.9)</td>
</tr>
<tr>
<td>Diabetes Type 1</td>
<td>24 (1.7)</td>
<td>9 (37.5)</td>
<td>1359 (97.7)</td>
<td>142 (14.5)</td>
</tr>
<tr>
<td>Diabetes Type 2</td>
<td>267 (19.2)</td>
<td>68 (25.5)</td>
<td>1119 (80.5)</td>
<td>229 (16.9)</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>273 (20.0)</td>
<td>55 (20.2)</td>
<td>1085 (79.7)</td>
<td>172 (15.4)</td>
</tr>
</tbody>
</table>

Data are reported as n (%).

MACE = major adverse cardiac events; MI = myocardial infarction.

---

**Table 2**

Proportion of Patients With AMI and ACS Stratified by Clinician Gestalt

<table>
<thead>
<tr>
<th>Gestalt Likert Scale</th>
<th>“Definitely Not” ACS</th>
<th>“Probably Not” ACS</th>
<th>“Could Be” ACS</th>
<th>“Probably” ACS</th>
<th>“Definitely” ACS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number (%)</td>
<td>60 (4.3)</td>
<td>493 (35.4)</td>
<td>466 (33.5)</td>
<td>313 (22.5)</td>
<td>59 (4.3)</td>
</tr>
<tr>
<td>Number with AMI (%)</td>
<td>3 (5.0)</td>
<td>24 (4.9)</td>
<td>59 (12.7)</td>
<td>84 (26.8)</td>
<td>37 (62.7)</td>
</tr>
<tr>
<td>Number with ACS (%)</td>
<td>3 (5.0)</td>
<td>27 (5.5)</td>
<td>67 (14.4)</td>
<td>100 (32.0)</td>
<td>42 (71.2)</td>
</tr>
</tbody>
</table>

Data are reported as n (%).

ACS = acute coronary syndrome; AMI = acute myocardial infarction.

---

**Table 3**

Diagnostic Accuracy of Clinician Gestalt for ACS Rule Out, Both Alone and in Combination With the ECG and Initial cTn Concentration

<table>
<thead>
<tr>
<th>Rule-out Strategy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinician believes the diagnosis is “definitely not” ACS</td>
<td>98.8 (96.4–99.7)</td>
<td>5.1 (3.9–6.5)</td>
<td>95.0 (85.7–98.4)</td>
<td>18.2 (17.9–18.4)</td>
<td>60 (4.4)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “definitely not” or “probably not” ACS</td>
<td>87.8 (82.9–91.8)</td>
<td>45.5 (42.5–48.4)</td>
<td>94.8 (92.8–96.3)</td>
<td>24.8 (23.4–26.1)</td>
<td>480 (35.4)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “definitely not” ACS + ECGa</td>
<td>98.3 (95.2–99.7)</td>
<td>5.2 (3.9–6.7)</td>
<td>94.9 (85.5–98.3)</td>
<td>14.8 (14.5–15.1)</td>
<td>59 (4.4)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “definitely not” or “probably not” ACS + ECGa</td>
<td>86.1 (80.2–90.8)</td>
<td>46.3 (43.3–49.4)</td>
<td>95.2 (93.3–96.7)</td>
<td>21.1 (19.8–22.5)</td>
<td>466 (34.4)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “definitely not” ACS + ECG + troponinb</td>
<td>100.0 (88.1–100.0)</td>
<td>5.9 (4.4–7.6)</td>
<td>100.0</td>
<td>3.2 (3.1–3.2)</td>
<td>55 (4.1)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “definitely not” or “probably not” ACS + ECG + troponinb</td>
<td>86.2 (68.4–96.1)</td>
<td>50.0 (46.7–53.2)</td>
<td>99.2 (97.9–99.7)</td>
<td>5.1 (4.3–5.9)</td>
<td>418 (30.8)</td>
</tr>
</tbody>
</table>

Data are reported as % (95% CI) or n (%).

ACS = acute coronary syndrome; cTn = cardiac troponin; ECG = electrocardiogram; NPV = negative predictive value; PPV = positive predictive value.
aGestalt combined with an ECG with no ischemic features to rule out ACS.
bGestalt combined with an ECG with no ischemic features and an initial troponin < 99th percentile (normal) to rule out ACS.
while the PPV increased to 95.0 and 94.1% when gestalt was combined with an ECG with ischemic features and both an ECG with ischemic features and an initially elevated troponin as a diagnostic strategy, the specificity decreased to 97.9 and 90.0%, respectively. With lower levels of clinical certainty, the accuracy of rule in strategies dropped (Table 4).

**DISCUSSION**

In this multicenter study we have robustly demonstrated that clinician gestalt alone is not sufficiently accurate or safe to either rule in or rule out ACS as a clinical decision-making and management strategy in patients who the physician decided to proceed with an ACS evaluation. We prospectively evaluated clinicians’ global diagnostic assessment or gestalt in a large cohort of undifferentiated patients with suspected cardiac chest pain. Gestalt has not been extensively studied but the limited evidence has suggested potential diagnostic value. In a single-center prospective cohort study, the diagnostic accuracy of gestalt (low risk, intermediate risk, or high risk) performed similarly to the HEART score.14

A previous single-center prospective cohort study performed by our group found that gestalt, assessed in the same way, performed well. When combined with cTn, that study found that gestalt could be used to rule out ACS and discharge up to one-quarter of patients who presented with suspected ACS with no missed AMI and a low incidence of 30-day MACE (0.9%).13 In that study of 458 patients with suspected cardiac chest pain, 17.7% of whom had AMI, the area under the ROC curve for gestalt in diagnosing AMI was 0.76 (95% CI = 0.70 to 0.82).13 In our study of 1,391 patients with suspected cardiac chest pain, 14.9% of whom had AMI and 17.3% ACS, the area under the ROC curve for gestalt in diagnosing ACS is very similar at 0.75 (95% CI = 0.72 to 0.79). The consistency suggests that the true diagnostic value lies around this mark.

The first key role that gestalt could play in decision making and management is in ruling out ACS to discharge and avoid unnecessary admissions. Using gestalt alone, as a strategy to discharge patients, was less accurate than previously noted in the literature. In the earlier single-center study, discharging patients whom the clinician believed the diagnosis was “definitely not” or “probably not” ACS had a sensitivity of 95.1% (95% CI = 87.8 to 98.6) and NPV of 96.8% (95% CI = 92.0% to 99.1%).13 Our data showed that in the notably small number (4.4%) of patients whom the clinician felt the diagnosis was “definitely not” ACS, the sensitivity was high at 98.8% (95% CI = 96.4%–99.7%) and NPV was 95.0% (95% CI = 85.7% to 98.4%). Although these figures show that we are accurate, even at this highest rule out threshold, the posttest probability of missing ACS at 5% is too high risk for use in clinical practice. A survey of acceptable risk of MACE following discharge from the ED among emergency physicians showed that almost half of clinicians accepted a miss rate of 1% or less with a majority accepting a miss rate of 0.5% or less.17

In this study gestalt alone, even at this highest

<table>
<thead>
<tr>
<th>Rule in strategy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinician believes the diagnosis is “definitely” ACS</td>
<td>18.3 (13.5–23.9)</td>
<td>98.5 (97.6–99.1)</td>
<td>85.5 (84.7–86.3)</td>
<td>71.2 (58.9–81.0)</td>
<td>59 (4.4)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “probably” or “definitely” ACS</td>
<td>60.0 (53.4–66.4)</td>
<td>79.8 (77.3–82.1)</td>
<td>90.7 (89.3–91.9)</td>
<td>37.7 (34.1–41.5)</td>
<td>307 (22.6)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “definitely” ACS + ECGa</td>
<td>38.0 (24.7–52.8)</td>
<td>97.9 (88.7–100.0)</td>
<td>59.7 (54.3–64.9)</td>
<td>95.0 (72.6–99.3)</td>
<td>20 (1.5)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “probably” or “definitely” ACS + ECGa</td>
<td>86.0 (73.3–94.2)</td>
<td>44.7 (30.2–59.9)</td>
<td>75.0 (58.5–86.5)</td>
<td>62.3 (55.6–68.7)</td>
<td>49 (3.6)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “definitely” ACS + ECG + troponinb</td>
<td>39.0 (24.2–55.5)</td>
<td>90.0 (55.5–99.8)</td>
<td>26.5 (20.7–33.2)</td>
<td>94.1 (70.6–99.1)</td>
<td>17 (1.3)</td>
</tr>
<tr>
<td>Clinician believes the diagnosis is “probably” or “definitely” ACS + ECG + troponinb</td>
<td>87.8 (73.8–95.9)</td>
<td>50.0 (18.7–81.3)</td>
<td>50.0 (26.3–73.7)</td>
<td>87.8 (79.3–93.1)</td>
<td>24 (1.8)</td>
</tr>
</tbody>
</table>

Data are reported as % (95% CI) or n (%).

ACS = acute coronary syndrome; cTn = cardiac troponin; ECG = electrocardiogram; NPV = negative predictive value; PPV = positive predictive value.

aGestalt combined with an ECG with ischemic features to rule in ACS.
bGestalt combined with an ECG with ischemic features and an initial troponin > 99th percentile (elevated) to rule in ACS.

Table 4
Diagnostic Accuracy of Clinician Gestalt for ACS Rule In, Both Alone and in Combination With the ECG and Initial cTn Concentration
threshold, did not achieve this. Discharging patients whom the clinician believed the diagnosis was “definitely not” or “probably not” ACS as per the earlier study had a comparatively lower sensitivity at 87.8% (95% CI = 82.9% to 91.8%) and NPV was 94.8% (95% CI = 92.8% to 96.3%). Adding an ECG without ischemic features for a rule-out strategy of gestalt and ECG performs similarly to gestalt alone and adding an initial troponin below the 99th percentile is also insufficient. Adding criteria of a normal ECG and normal first troponin to gestalt “definitely not” made a very accurate diagnostic rule out strategy achieving a sensitively and NPV of 100%. However, this would only rule out ACS in 4.1% of patients and would thus have a minimal impact in clinical practice.

Prior to this study, the field was faced with the vital unanswered question about whether cTn testing is undertaken too often in the context of patients with possible ACS. Our multicenter study has clearly shown that gestalt cannot be reliably be used as a rule-out strategy. When clinicians deemed that the diagnosis was “definitely not” ACS, they were incorrect on 5% of occasions. This suggests that it would be unsafe to reduce cTn testing in this patient group. It is, however, crucial to emphasize that we only included patients with chest pain or discomfort where ACS was suspected (even if the treating clinician felt that the diagnosis was highly unlikely) with no other apparent cause. Our findings do not apply to patients who did not pass the clinicians pretest probability threshold for warranting investigation for ACS. Our findings cannot be extrapolated to patients with other symptoms.

The second key role that gestalt could play in decision making and management is in ruling in those with ACS to promptly treat and manage the condition. How should our clinical judgment impact our management strategy? Should we start treatment based on clinical suspicion while awaiting the serial troponin result? There is very little previous evidence on the accuracy of gestalt as a diagnostic rule in strategy. In the small number of patients (4.4%) where the treating clinician believed the patient “definitely” had ACS, there was a high level of accuracy with specificity of 98.5% (95% CI = 97.6% to 99.1%) and PPV of 71.2% (95% CI = 58.9% to 81.0%) with a positive likelihood ratio of 12.1 (95% CI = 7.01 to 20.87). When those who the clinician felt “probably” had ACS are considered, which is 22.6% of patients, gestalt accuracy drops to having a specificity of 79.8% (95% CI = 77.3% to 82.1%), PPV of 37.7% (95% CI = 34.1%–41.5%), and positive likelihood ratio of 3.0 (95% CI = 2.53 to 3.47). This clearly is not accurate enough to rule in ACS or consider treatments or interventions with considerable risk. It could, however, help shape our communication with the patient, relatives, and onward medical team and inform our decision making around administering antiplatelet therapy. Having an ECG with ischemic features and an initial troponin above the 99th percentile increase the PPV and positive likelihood ratio of a combined gestalt, ECG, and troponin rule in strategy but only applied to <2% of patients and saw a drop in specificity.

LIMITATIONS

In this study, clinicians were not blinded to the ECG or initial cTn results. It was considered to be unethical to blind the clinician to these results given the potential for this to delay the identification and treatment of ACS. Our results cannot, therefore, truly assess the diagnostic accuracy of “gestalt” in isolation. However, our method represents an entirely pragmatic evaluation of gestalt in practice, where practicing clinicians also have access to this information. The accuracy of the clinician recording the presence of acute ischemic ECG features was not validated for this analysis; however, this pragmatic approach also replicates a real-world practice setting.

CONCLUSIONS

Our study confirms that, once a clinician has decided that a patient warrants investigation for a possible diagnosis of acute coronary syndromes, the gestalt of the clinician is insufficiently accurate to either rule in or rule out that diagnosis, even when they perceive that the diagnosis is present or absent with certainty. The findings give statistical evidence to what emergency physician clinical judgment represents from a probabilistic decision-making perspective and can be used to advise patients, family, and the medical professionals involved in ongoing care.

References

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Supporting Information

The following supporting information is available in the online version of this paper available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13836/full

Data Supplement S1. List of study sites and troponin assays.
An Implementation Science Approach to Antibiotic Stewardship in Emergency Departments and Urgent Care Centers

Kabir Yadav, MDCM, MS, MSHS1,2, Aubyn Stahmer, PhD3, Rakesh D. Mistry, MD, MS4, and Larissa May, MD, MSPH, MSHS5

ABSTRACT

Background: Antibiotic stewardship efforts have expanded focus from inpatient to include outpatient settings. However, stewardship is urgently needed in acute care ambulatory settings: emergency departments (EDs) and urgent care centers (UCCs). Implementation of antibiotic stewardship in acute ambulatory care settings has been limited. Two major barriers to effective implementation exist: 1) lack of adaptation of successful outpatient stewardship interventions to the acute care ambulatory setting and 2) absence of rigorous measurement of implementation processes in EDs and UCCs in a manner that informs future scale and spread.

Objectives: Our objective was to apply an implementation science approach to address antibiotic overuse and inappropriate use in EDs and UCCs.

Methods: This study was a redesign of an evidence-based outpatient antibiotic stewardship intervention at participating EDs and UCCs using an innovative implementation science framework (dynamic adaptation process), adaptable for local clinical workflow and local champion provision. We evaluated multiple implementation outcome metrics throughout a cluster-randomized comparative effectiveness clinical trial of two approaches to the adapted antibiotic stewardship interventions.

Results: Our preimplementation phase included 21 in-depth interviews and online provider surveys (52% response rate). For the postimplementation survey, we had a 39% response rate. We identified common themes including patient expectations, lack of knowledge of existing guidelines, and maintenance of education over time. Additional themes indicated differences in modifications needed by type of clinical setting. Adoption of public commitment was high, with 79% of providers signing a commitment log, and 84% received public commitment flair. Signing of public commitment posters rate was 62%, as several sites chose not to use this component. Acceptability, fidelity, and appropriateness were also measured.

Conclusions: We demonstrate that implementation science approaches can help address the problem of unnecessary antibiotic use in EDs and UCCs with high acceptability and adoption. Similar approaches could be used to tailor quality improvement interventions in these settings.

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This work was supported by CDC’s investments to combat antibiotic resistance under award number 200-2016-91939.

The authors have no potential conflicts to disclose.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Author contributions: LM, KY, RDM, and AS conceived the study, designed the trial, and obtained research funding; LM, KY, and RDM supervised the conduct of the trial and data collection; LM, KY, and RDM undertook recruitment of participating sites and providers and managed the data, including quality control; KY and AS provided methodologic advice on study design and analyzed the data; KY, AS, and LM drafted the manuscript; and all authors contributed substantially to its revision. KY takes responsibility for the paper as a whole.

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Our objective was to apply an implementation science approach to address the problem of antibiotic overuse and inappropriate use, which jeopardizes patient safety, increases health care costs, and is accelerating the epidemic of drug-resistant bacteria—a true patient care and public health crisis. To date, antibiotic stewardship efforts have almost exclusively focused on inpatient settings, with a recent emphasis on office-based ambulatory care settings. Stewardship is now urgently needed in acute care ambulatory settings, which include emergency departments (EDs) and urgent care centers (UCCs). These settings share similar time-pressured, episodic care challenges that represent an overlooked but growing setting for antibiotic overprescribing. Each year 10 million antibiotic prescriptions are written from EDs, and many for children and the elderly with acute viral respiratory tract infections, for which treatment with antibiotics does not improve outcomes. Approximately 85% to 95% of antibiotic use by volume occurs in outpatient settings, and 39% of urgent care and 14% of ED visits lead to an antibiotic prescription. Given the rising number of ED and UCC visits in the United States, effective strategies are desperately needed to adapt evidence-based antibiotic stewardship interventions for these settings. Strong antibiotic stewardship in ED and UCC is necessary to reduce inappropriate antibiotic prescribing for antibiotic nonresponsive conditions such as acute bronchitis and nonspecific upper respiratory infection in these acute episodic care ambulatory settings to prevent associated adverse events and future development of resistance.

The Centers for Disease Control and Prevention (CDC) has suggested a framework for effective antibiotic stewardship activities for outpatient clinic settings. The CDC Core Elements of Outpatient Antibiotic Stewardship uses a variety of stewardship interventions broadly classified under four core elements: commitment, action for policy and practice, tracking and reporting, and education and expertise. There is a moderate evidence base for outpatient antibiotic stewardship interventions in office-based ambulatory care settings. There has been limited success implementing antibiotic stewardship interventions in EDs and UCCs, in part a result of barriers unique to these acute ambulatory care settings. Two identified barriers to effective implementation are 1) need to adapt effective outpatient stewardship interventions to the acute care ambulatory setting and 2) inability to rigorously measure the impact of implementation processes in EDs and UCCs in a manner that confirms fidelity, informs sustainability, and identifies best practices for scale and spread.

Systematic, flexible implementation models are needed to adapt evidence-based interventions and rigorously deploy them in heterogeneous acute care ambulatory settings. Implementation science calls for the adaptation process to be tailored to the organizational context to integrate the intervention with the features of local settings to ensure effective implementation. Fitting the intervention to the context increases the likelihood of successful outcomes. One model, the dynamic adaptation process (DAP; Figure 1), was developed to guide, monitor, and evaluate adaptation of empirically validated practices into new settings while maintaining fidelity to the core intervention functions. DAP takes into account the multilevel context to develop robust implementation strategies to facilitate service delivery (system, resources, provider, patient, workflow) and engages stakeholders from all levels throughout the process of adaptation and implementation (i.e., preimplementation, adaptation, implementation, and effectiveness), using data, technical assistance, and feedback between the practitioners and administrators using the intervention and the research team to iteratively adapt the intervention throughout all phases. Our objective is to apply this theory-driven approach to guide locally driven adaptation of evidence-based interventions within a generalizable framework to balance fidelity and adaptation.

The aims of this paper are to report on the adaptation process and detail the implementation outcomes for the recently published “Multifaceted Intervention Improves Prescribing for Acute Respiratory Infection for Adults and Children in Emergency Department and Urgent Care Settings,” or MITIGATE, trial. The MITIGATE trial was a cluster-randomized multicenter comparative effectiveness study of two adapted antimicrobial stewardship interventions incorporating behavioral science techniques. The results of the clinical effectiveness of these adapted antimicrobial stewardship interventions have been previously reported.

**METHODS**

**Study Design**

The implementation project was divided into two phases: 1) redesign of an outpatient antibiotic
stewardship intervention at participating EDs and UCCs using an innovative implementation science framework (DAP), adaptable for local clinical workflow and local champion provision; and 2) evaluation of multiple implementation outcome metrics throughout a cluster-randomized comparative effectiveness clinical trial of antibiotic stewardship interventions to reduce inappropriate prescribing rates for acute respiratory infections. The conceptual model of the project was adapted from the DAP framework (Figure 1).

Institutional review boards (IRBs) at all participating sites approved the study protocol. Written consent was obtained from all clinician participants at all sites, and a waiver from consent was granted for all secondary patient participants. The clinical trial was registered on ClinicalTrials.gov (Identifier: NCT03022929).

**Study Setting and Population**

Emergency physicians, advanced care practitioners, internists, and pediatricians treating a diverse and underserved patient population from three academic health systems across two states were approached for consent to participate in stewardship toolkit components. Regardless of refusal to consent for identifiable research activities, anonymous data from all providers were included in the outcome measurement using an intention-to-treat analysis. Due to determinations by the IRB, we were not able to collect demographic data on the providers enrolled in the study.

The institutional and contextual features of the participating sites were as follows:

- **University of California–Davis (contributing one ED site):** This site is a quaternary care center Level I trauma center with approximately 65,000 adult and 20,000 pediatric visits per year caring for a mix of urban and rural populations. The providers were familiar with antibiotic stewardship insofar as they had recently been a part of a skin and soft tissue infection stewardship project and had a faculty member with a designated role of director of emergency department antibiotic stewardship.

- **Harbor–UCLA Medical Center (one ED site, one urgent care site):** This site was a Level I trauma center and pediatric critical care center with 65,000 adult ED visits, 24,000 pediatric ED visits, and 11,000 adult UCC visits. No formal acute ambulatory care antibiotic stewardship activities had previously taken place at this site.

- **Children’s Hospital Colorado (CHCO; three EDs and three urgent care sites):** CHCO is composed of an urban, pediatric tertiary care ED that is the region’s only pediatric trauma center and receives 73,000 pediatrics visits annually. The tertiary care ED has two associated satellite EDs and three satellite UCCs that operate using linked health records. Across all ED and UCC sites, CHCO receives 170,000 pediatric visits each year. The lead investigator at CHCO is a member of the hospital-wide antimicrobial stewardship committee and was conducting preliminary efforts to develop sustainable methods of ED and UCC antimicrobial stewardship for common pediatric bacterial infections prior to the initiation of this study.
In terms of broad environmental features of the study setting, it is important to note that California sites were operating under the Public Hospital Redesign and Incentives in Medi-Cal (PRIME) program, which incentivizes value-based care with performance benchmarks that included an optional one for reduction in unnecessary antibiotic prescribing for acute bronchitis (Harbor–UCLA Medical Center was using that performance benchmark, University of California–Davis was not).

**Study Protocol**

**Phase 1: Adaptation of Outpatient Stewardship.** The evidence-based outpatient stewardship framework we sought to adapt was the CDC Core Elements for Outpatient Antimicrobial Stewardship (commitment, action for policy and practice, tracking and reporting, and education and expertise). Commitment refers to a demonstrable willingness of health care providers and the health system to support and adhere to antibiotic stewardship principles in practice. Action represents undertaking key evidence-based activities to promote stewardship, including communication skills training and clinical decision support. Tracking and reporting include quality improvement activities like audit and feedback. Education and expertise include academic detailing, continuing education activities, timely access to experts, and provision of patient education materials.

Our approach to adapting the CDC core elements was a series of preimplementation processes that included stakeholder interviews, validated provider surveys, workflow analyses, and engagement with key personnel. The implementation team consisted of leadership from each participating site to provide operational insight and administrative support, clinical experts, implementation scientists, behavioral scientists, frontline providers, and informatics specialists. At study initiation all eligible providers were invited via e-mail to participate in an anonymous survey. We sought to enroll a representative sample of providers, staff, and administration from each site for interviews using purposeful sampling via e-mails from local champions, with a minimum of one of each type of stakeholder from each participating site. No participation incentives were offered. We performed grounded theory analysis of semistructured stakeholder interview transcripts, double-coded independently with consensus on disagreements, and triangulated the data with electronic survey data of providers and clinical workflow analyses to identify barriers, facilitators, and novel intervention approaches. The electronic surveys also explored acceptability and adaptation of each stewardship component to inform implementation outcomes analysis in Phase 2.

**Phase 2: Implementation Analysis.** The impact of the acute care ambulatory stewardship interventions was evaluated using a cluster-randomized study design in which all sites receive one of two versions of the intervention, allowing us to both collect useful effectiveness data while still offering benefit from the intervention to all participating sites. Beyond impact, to test the implementation of this approach, data were collected on implementation process outcomes such as adoption and adaptation, and members of the research team performed site visits to evaluate fidelity and feasibility (interviews/surveys completed, workflow assessment, components selected).

**Measurements or Key Outcome Measures**

The reporting of our study conforms to the Standards for Reporting Implementation Studies (StaRI) standard for implementation science.

**Phase 1**

Qualitative data collection was conducted by trained research assistants under the supervision of the two study implementation scientists through a process of triangulation.

**Provider Survey.** Providers from each study site were invited to complete the anonymous survey prior to site-specific implementation of the assigned intervention and again after the intervention period. Due to staff turnover and the anonymity of the survey, individual follow-up surveys were not able to be linked to the preintervention surveys.

**Provider and Stakeholder Interviews.** Individual providers, nurses, and administrators from each site were invited to participate in in-depth one-on-one semistructured interviews prior to implementation at their site. Interviews were conducted by trained research assistants or implementation scientists in a private setting. Interviewers were often not known to the interviewees or, if known, did not have any supervisory authority over the interviewees. Survey materials and interview guides were created based on prior survey work in this area.
Phase 2
In line with the StaRI framework and where feasible, we measured several implementation processes and outcome measures for the MITIGATE trial, described in detail below.

Acceptability. We measured the perception of feasibility of an antibiotic stewardship intervention in general among implementation stakeholders by assessing knowledge, attitudes, and beliefs about antimicrobial stewardship in ED and UCCs during the preimplementation phase of the trial.

Fidelity. Balanced against the need for adaptation, we assessed how true to intended mode, or adherence to the original operative model, the components of the intervention were when deployed at each site. Our effectiveness was partially limited by the constraints of a research study. For example, delays at one of our institutions due to IRB staffing issues delayed deployment of critical components of the intervention by several months for over half of our sites.

Adoption. We measured adoption of individual components of the stewardship intervention. For instance, we measured public commitment adoption by reporting percentage of eligible clinicians who signed a public commitment log. We also measured public commitment by willingness to wear CDC stewardship campaign-branded "flair" (badge reels, pins) to demonstrate public commitment. Finally, providers were asked to sign publicly displayed commitment posters signaling their intention to avoid prescribing antibiotics unnecessarily.

Appropriateness. We evaluated the perceived relevance of the antimicrobial stewardship intervention at each site by soliciting feedback during the implementation process. We also surveyed clinicians on their postimplementation knowledge, attitudes, and beliefs about antimicrobial use and stewardship.

Data Analysis
For Phase 1, empirical material contained in the interviews were extracted via professional transcription from audio recordings and personal identifiers were removed. Electronic survey data were downloaded and independently coded by the project investigators. Data were analyzed using NVivo 11 (QSR International) using an iterative coding and review process informed by grounded theory. Robust understanding of the issues was obtained through a process of triangulation in which accounts of specific events and behaviors obtained from interviews, and surveys were compared with one another to determine if they converge in providing the similar answers to questions. Key results for Phase 1 included identification of adaptations necessary to implement an outpatient stewardship intervention in acute care ambulatory settings and development of a toolkit describing that process for future scale and spread.

For Phase 2, survey data and implementation process data were summarized and presented as counts and frequencies and graphically to gauge the success of the implementation. Sample size determinations were driven by the comparative effectiveness cluster-randomized clinical trial, whose design and results are described in a separate article. The funding organization for the study, the CDC, approved the clinical trial study proposal and reporting of the clinical trial, but did not influence the conduct or data analysis of the trial. As such, the conclusions, findings, and opinions expressed by the study authors do not necessarily reflect the official position of the U.S. Department of Health and Human Services, the Public Health Service, or the CDC.

RESULTS
Phase 1: Stewardship Intervention Adaptation
Our preimplementation work including surveys of clinicians and our site stakeholder interviews with physicians, advanced care practitioners, nurses, and administrators were used to inform the adaptation of the evidence-based antimicrobial stewardship intervention components. For the preimplementation survey, 159 of 303 (52.4%) eligible providers across all sites completed the survey. For the postimplementation survey, 120 of 312 (38.5%) of eligible providers completed the survey. For the in-depth interviews, 21 interviews were completed, with at least one stakeholder of each category (provider, staff, administrator) from each site. Eight interviews were conducted at UC Davis, three interviews at Harbor–UCLA UCC, and five interviews at Harbor–UCLA ED. Because of the considerable overlap in staffing and administration at the six CHCO sites, five instead of 18 interviews were conducted there. Common themes that were elucidated were consistent with previously identified
barriers and facilitators for clinical decision making around antibiotic use in the ED (Tables 1 and 2).\textsuperscript{10} Saturation, or the mention of similar concepts across participating sites, was noted in these common themes.

Additional themes indicated differences in modifications needed for pediatric ED patients, adult ED patients, and patients seen in UCCs, including tailoring materials to patients versus parents and the location of specific educational materials due to clinical workflow differences (Table 3).

**Contextual Changes.** At one of the study sites, the Harbor–UCLA ED, a pediatric ED antibiotic stewardship consultation service was initiated during the study period and lasted about 6 months. The stewardship team visited the pediatric ED three times during the day on weekdays at noon to performed case-based teaching cases about antibiotic appropriateness.

A potential unintended effect of our stewardship intervention was concern for diagnostic code shifting, measurable as an increase in percentage of antibiotic-eligible respiratory infections to circumvent stewardship efforts. These data were not readily available across all the participating sites, but a subgroup analysis of the Harbor–UCLA ED and UCC (6,475 visits) found no evidence of diagnostic drift, with percentage of antibiotic-eligible diagnoses going from 26.2\% to 27.4\% (p = 0.27).

**Implementation Outcomes**

**Acceptability.** Key survey questions informed determination of feasibility of the proposed antibiotic stewardship interventions. This was administered to providers at all sites during both the preimplementation phase and the postimplementation phase of the trial (Figure 2). Responding providers overwhelmingly felt that antibiotic stewardship was important in the ED and UCC settings, and similarly reported low rates of perception that such stewardship interventions would interfere with their usual clinical approach. Unexpectedly, however, providers provided conflicting postimplementation attitude changes around acceptability insofar as more providers felt that stewardship was important in ED and UCC settings and that more patients got educated about antibiotics, but more also felt that such efforts interfered with their usual clinical approach.

**Fidelity.** Based on preimplementation surveys, interviews, and workflow analysis adaptations, DAP teams adapted the outpatient antibiotic stewardship program to increase feasibility for different acute ambulatory care settings (Table 3). To ensure that adaptations remained effective, assessing fidelity to the original interventions was an important implementation outcome. Using the lens of the CDC Core Elements for Antimicrobial Stewardship (commitment, action for policy and practice, tracking and reporting, and education and expertise),\textsuperscript{9} we paid close attention to how true to intended mode the components of the intervention were deployed at each site. Commitment, referring to a demonstrable willingness of health care providers and the health system to support and adhere to antibiotic stewardship principles in practice, was met through seeking support by each health system for the project, identifying a local champion, and seeking public forms of commitment from individual providers. Each site supported the project at the hospital and departmental leadership levels, each site had a committed local champion, and public forms of commitment were successfully sought from providers (detailed under “Adoption” outcome below). Action for policy and practice, referring to adoption of key evidence-based activities to promote stewardship, was met

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Barriers and Facilitators From Interviews</th>
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<tbody>
<tr>
<td><strong>Barriers</strong></td>
<td><strong>Facilitators</strong></td>
</tr>
<tr>
<td>Patient expectations for antibiotics</td>
<td>Incorporation of patient education materials into the triage and discharge processes</td>
</tr>
<tr>
<td>Providers lack of knowledge of current guidelines</td>
<td>Provider education during resident didactics, nursing briefings, and department meetings</td>
</tr>
<tr>
<td>Underutilization of existing patient education materials</td>
<td>Routine display of bilingual patient education materials in triage areas and patient examination rooms</td>
</tr>
<tr>
<td>Maintaining awareness of the stewardship program over time</td>
<td>Systematic placement of stewardship material among provider spaces</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Barriers to stewardship (choose all that apply), n (% of respondents)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient expectations</strong>, 131 (82%)</td>
<td><strong>Psychosocial barriers</strong>, 38 (24%)</td>
</tr>
<tr>
<td><strong>Lack of clear guidelines</strong>, 37 (23%)</td>
<td><strong>Lack of access to guidelines</strong>, 35 (22%)</td>
</tr>
<tr>
<td><strong>Electronic health record</strong>, 4 (3%)</td>
<td><strong>Provider education</strong>, 27 (17%)</td>
</tr>
<tr>
<td><strong>Individual feedback</strong>, 19 (12%)</td>
<td><strong>Patient education</strong>, 1 (1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preferred method of stewardship, rank order, ordered from most to least preferred (% first choice)</th>
<th>Provision of guidelines, 52 (33%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electronic decision support, 43 (27%)</td>
<td>Provider education, 27 (17%)</td>
</tr>
<tr>
<td>Individual feedback, 19 (12%)</td>
<td>Patient education, 1 (1%)</td>
</tr>
</tbody>
</table>
through communication skills training at staff meetings and resident didactic conferences. While electronic clinical decision support was considered, it was simply not feasible in the project timeline given the differing electronic health records (EHRs) being used at different sites and the deliberate pace of EHR change cycles. Tracking and reporting, referring to quality improvement activities to measure change, was

Table 3
Adaptations Proposed Based on Site Type

<table>
<thead>
<tr>
<th>All-setting Acute Care Modifications</th>
<th>Adult ED Modifications</th>
<th>UCC Modifications</th>
<th>Pediatric ED Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilingual patient education posters, brochures, and handouts from CDC Get Smart campaign materials</td>
<td>Display in waiting rooms and triage areas (long wait)</td>
<td>Display in waiting room, triage areas, and patient examination rooms</td>
<td>Poster display in individual patient rooms (Harbor) and waiting rooms (UC Davis)</td>
</tr>
<tr>
<td>Provider public commitment flair (badges; pins) and signing of commitment logs</td>
<td>Bilingual handouts provided to patients after triage process to review while they are waiting for provider</td>
<td>Bilingual handouts provided to patients after intake process to review while they are waiting for provider</td>
<td>Include handouts for families</td>
</tr>
<tr>
<td>Monthly individualized provider feedback and peer comparison of antibiotic prescribing practices</td>
<td>Resident didactic sessions</td>
<td>Presentation at monthly UCC provider meetings</td>
<td>Resident didactic sessions</td>
</tr>
<tr>
<td>Stewardship program education in monthly department meetings and daily nurse briefings</td>
<td>Included in departmental newsletter to all nurses and technicians</td>
<td>Initiatives discussed at UCC nursing briefings</td>
<td>Departmental quarterly provider meetings</td>
</tr>
<tr>
<td>Viral prescription pads and discharge workstations supplied with educational handouts for patients to fit clinical workflow</td>
<td>Viral prescription pads and handouts available in provider workrooms</td>
<td>Viral prescription pads on each mobile provider workstation</td>
<td>Viral prescription pads and school notes in provider workroom</td>
</tr>
</tbody>
</table>

UCC = urgent care center.

Figure 2 Attitudes toward antibiotic stewardship, pre- and postimplementation.
met through selection of audit and feedback as an intervention component, which we enhanced with behavioral science nudging to be personalized peer comparison using positive reinforcement. Education and expertise, referring to educational activities and availability of experts, was met with academic detailing using locally sourced guidelines at staff meetings, continuing education activities at resident didactic conferences and other venues (see supplementary material in MITIGATE trial publication, Yadav et al.).

Adoption. We measured adoption of individual components of the stewardship intervention. In particular, public commitment adoption measured by 242 of 317 (79%) of eligible clinicians signing a public commitment log, 266 of 317 (84%) receiving flair to be worn as a personal display of public commitment, and 195 of 317 (62%) signing publicly displayed commitment posters signaling their intention to avoid prescribing antibiotics unnecessarily (Table 4). Of note, the low rate of public commitment posters was largely due to several sites being unwilling to display public commitment posters with signatures and headshots of providers due to concerns over drug diversion and staff privacy. Only one provider out of 317 declined to receive the personalized peer comparison feedback. All planned patient handout stations were deployed and informational posters in waiting areas and treatment rooms were mounted after appropriate approvals. Our adoption was potentially limited by the constraints of a research study. For example, delays due to IRB staffing issues delayed deployment of critical components of the intervention at over half of our sites by several months, although every planned component was rolled out eventually.

Appropriateness. We evaluated the relevance of the antimicrobial stewardship intervention in each site by soliciting feedback prior to the implementation process and surveying clinicians on their postimplementation knowledge, attitudes, and beliefs about antibiotic stewardship (Figure 2). Responding providers understood the nature of both the public health crisis and the contribution of inappropriate prescribing to bacterial resistance. More directly speaking to appropriateness, providers reported that antibiotic stewardship was important in the ED and UCC settings.

**Toolkit Development**

To both inform sustainability at participating sites and meet our longterm goal of scale and spread of successful interventions, we recorded and organized our implementation processes into a stewardship toolkit to inform assessment of local settings and use the results to adapt available components of an acute care stewardship program. The toolkit provides user-friendly instructions for assessing client-emergent issues, available resources to use (posters, handouts, public commitment flair), workflow considerations to guide initial implementation, and surveys and interview guides to gauge provider knowledge, skills, and abilities. DAP procedures informed how the toolkit could guide local ED and UCC teams in how to make adaptations specific to their own context and then test the effectiveness of adaptations to ensure ongoing impact. Following the DAP model, the toolkit outlines core components (“functions”) of the intervention and adaptable characteristics (“forms”) chosen based on the assessment input. The DAP enabled a phased implementation process that takes into account the multilevel context of health care delivery, engages stakeholders, and leverages appropriate expertise and feedback during implementation to monitor and address adaptations while maintaining fidelity to the toolkit’s core elements.

The toolkit is available online at the Society for Academic Emergency Medicine and the Society for Healthcare Epidemiology of America, and it is linked from the CDC.

<table>
<thead>
<tr>
<th>Site</th>
<th>Commitment Log</th>
<th>Poster Signatures</th>
<th>Badge Reels</th>
<th>Pins</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC Davis (one site), n = 54</td>
<td>22 (40.7%)</td>
<td>33 (61.1%)</td>
<td>13 (24.1%)</td>
<td>53 (98.1%)</td>
</tr>
<tr>
<td>Harbor-UCLA (two sites), n = 108</td>
<td>107 (99.1%)</td>
<td>49 (45.4%)</td>
<td>61 (56.5%)</td>
<td>39 (36.1%)</td>
</tr>
<tr>
<td>CHCO (six sites), n = 145</td>
<td>113 (77.9%)</td>
<td>113 (77.9%)</td>
<td>–70 (–48%)</td>
<td>–30 (–21%)</td>
</tr>
</tbody>
</table>

*Distribution wasn’t tallied, based on number supplied to site.
CHCO = Children’s Hospital Colorado.
Table 5 lists the intervention components that were included in the toolkit.

In the course of our study, we encountered several unexpected barriers, including challenges in operationalizing data extraction methods, buy-in from peers regarding feedback data, and the need to include a large number of stakeholders. We successfully overcame these barriers using strategies of engagement with stakeholders and education of participating providers. Anticipating these challenges and proposed solutions were incorporated into the toolkit.

**DISCUSSION**

Prior literature on the barriers and facilitators to antibiotic stewardship have identified that unique factors exist in the acute care ambulatory care setting. This is reinforced by our results during the preimplementation mixed-methods preparatory work. Additional insight gained from our study is that local context of EDs and UCCs inform the specific tools to be implemented to match clinical workflow and provider-perceived needs. While we cannot state that locally driven implementation led to more effective reductions in inappropriate antibiotic prescribing because both arms of our comparative effectiveness study used implementation adaptation, which led to significant decreases in inappropriate prescribing. Failure to perform adaptation may partially explain why prior successful outpatient stewardship interventions have not been easily translated to EDs or UCCs. However, implementation challenges still remain in that providers likely understood the importance of stewardship more after the intervention, but more also felt that it interfered with their usual clinical practice.

We did not find prior literature on the use of implementation science for improving antibiotic stewardship in EDs or UCCs, but there is an emerging literature for the use of implementation science for antibiotic stewardship in other settings. As such, our study lends further support to the promising application of implementation science to antibiotic stewardship efforts, by demonstrating the utility of implementation science in the ED and UCC settings. Similarly, the human factors approach to antibiotic stewardship also recommends addressing system change at multiple levels of engagement, from the individual to the health systems. It should come as no surprise that there are parallels to an implementation science approach when both of these fields are applied rigorously with a firm theoretical foundation.

An urgent challenge to healthcare improvement is how to balance competing interests in acute ambulatory care settings, such as antibiotic stewardship quality metrics “pitted against” sepsis guidelines that expect early administration of broad-spectrum antibiotics.
within an hour of suspected sepsis. In keeping with a body of literature on quality improvement, engagement of stakeholders in the process of intervention implementation may identify competing interests that would lead to more successful compromise outcomes. Rather than expect elimination of use of antibiotics in cases where a severe viral infection mimics sepsis (and unintentionally delay sepsis patients from receiving needed antibiotics), rapid deescalation of intravenous antibiotics once viral infection is identified (and no prescription for antibiotics) would be more clinically appropriate.

Examining the broader issue to adapting evidence-based practices to the ED and UCC settings, our study’s findings support the value of a implementation science approach to developing a tailored adaptation strategy. This is supported by stakeholders identifying multiple site-specific and acute ambulatory care adaptations during our study and participating providers in survey responses prioritizing the need for local guidelines, such as those utilizing the model of an expected practice. ED stewardship needs assessments in the past similarly noted that providers cite need for local guidelines as important, in that it takes the best evidence and contextualizes it to the local practice environment and the local patient population served. We believe that key to the utility of an implementation science approach is provision of a process or framework to be followed by other settings in replicating the work. As such, we highlight the potential value of an implementation toolkit that can be used to address local adaptation and implementation.

LIMITATIONS

One perceived limitation of this study was the use of an existing framework (CDC Core Elements) as the foundational basis for the interventions. While we recognize that this framework was developed for the outpatient setting incorporating limited evidence from ED and UCC settings, the CDC and The Joint Commission consider the ED and UCC to be outpatient health care settings. The targeted patient visits included patients with presumed viral respiratory infections based on ICD-10 without comorbidity or exclusionary diagnoses and represents a similar population to other outpatient settings. While survey respondents indicated that the EHR would be a preferred method of stewardship delivery, due to logistic and time constraints, we did not incorporate clinical decision support into our intervention, although this is a subject of ongoing research and implementation. The use of the DAP and multiple preimplementation readiness methods provided information regarding adaptation. For example, although only 1% of survey respondents indicated that patient education was the preferred method of stewardship, 82% of respondents felt that patient expectations were a barrier to stewardship and in-depth stakeholder interviews revealed that the need for patient education appeared as a consistently strong theme. Therefore, the teams chose to remain consistent to the use of the CDC Core Educational Element using patient-facing materials (commitment posters, brochures, flair, handouts, viral pads, etc.). During postimplementation surveys, providers reported greater patient education around antibiotic stewardship. In the end, Core Elements did not need extensive adaptation; however, having a clear method for choosing specific elements and how to implement them (e.g., where to fit education into the workflow) likely led to increased feasibility, acceptability, and adoption of the stewardship intervention.

Although we sought to measure multiple implementation outcome components of the StaRI framework, we did not assess the cost of the antimicrobial stewardship interventions, their penetration, or the sustainability of the interventions. Due to our inability to solicit information directly from identifiable individual providers due to IRB restrictions, neither were we able to characterize survey responders versus nonresponders nor were we able to evaluate the integration of the antimicrobial stewardship interventions at the provider level throughout the project period (penetration). However, we did track delivery of different intervention components across all nine sites included in the MITIGATE trial (such as the provision of monthly audit and feedback). Our adoption measure was somewhat constrained by the fact that we did not perform spot checks in the clinical areas to confirm that those who received flair actually displayed them as a form of public commitment. While we did not have an effective method to measure use of patient education materials, patient handouts and viral prescription pads were restocked at each site.

While ideally this study would have had a postintervention period to evaluate sustainability, we were not able to evaluate the extent to which the antimicrobial stewardship implemented interventions were maintained within our study sites due to funding period constraints. However, ongoing and planned projects to
scale and spread the MITIGATE toolkit should provide future data on sustainability of the MITIGATE interventions.

Future work should evaluate whether an implementation science approach that is more impactful in community settings, the challenge being the need for implementation science experts and use of a mixed methods framework. An opportunity therefore exists for developing “train the trainer” partnerships with academic centers, explore use of simplified analytic approaches, and reliance on user-friendly implementation toolkits to facilitate scale and spread to community settings. We acknowledge that development and uptake of a user-friendly toolkit will depend upon operational buy-in and integration of toolkit processes within the clinical workflow; however, this approach is one in which implementation science excels.

CONCLUSIONS

We found that an implementation science approach including a preimplementation phase to assess barriers and facilitators to implementing antibiotic stewardship interventions by key stakeholders, with adaptation of the intervention components to the local site and setting followed by an implementation phase led to successful uptake of the intervention. We demonstrate that an implementation science approach can be used to address the problem of unnecessary antibiotic use in ED and urgent care settings with high acceptability and adoption. Similar approaches could be used to tailor quality improvement interventions in these settings.

The authors acknowledge the contributions of Samuel Gaona, Reagan Miller, and Dr. Kristi Shigyo, who all assisted with subject recruitment and assisted with data analysis.

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Geriatric Emergency Department Innovations: The Impact of Transitional Care Nurses on 30-day Readmissions for Older Adults

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ABSTRACT

Objectives: Transitional care nurse (TCN) care has been associated with decreased hospitalizations for older adults in the emergency department (ED). The objective of this study was to evaluate the association between TCN care and readmission for geriatric patients who visit the ED within 30 days of a prior hospital discharge.

Methods: We studied a prospective cohort of ED patients aged 65 and older with an ED visit within 30 days of inpatient discharge. Patients with an Emergency Severity Index of 1 or prior TCN contact were excluded. Entropy balancing and logistic regression were used to estimate the average incremental effect of the TCN intervention on risk of admission during the index ED visit and within 30 days of prior discharge.

Results: Of 6,838 visits, 608 included TCN care. TCN patients had lower risk of readmission during the index ED visit at Mount Sinai Medical Center (MSMC), −10.1 percentage points (95% confidence interval [CI] = −18.5 to −2.7), and Northwestern Memorial Hospital (NMH), −17.3 percentage points (95% CI = −23.1 to −11.5), but not St. Joseph’s Regional Medical Center (SJWMC), −2.5 percentage points (95% CI = −10.5 to 5.5). TCN patients had fewer readmissions within 30 days of prior hospital discharge at NMH, −16.2 percentage points (95% CI = −22.0 to −10.3), but not at MSMC, −5.6 percentage points (95% CI = −13.1 to 1.8), or at SJWMC, 0.5 percentage points (95% CI = −7.2 to 8.2).

Conclusions: Transitional care nurse care in the ED after a prior hospitalization was associated with decreased readmission of older adults during the index ED visit at two of three hospitals, with sustained reduction for the entire 30-day readmission window at one hospital. TCN interventions in the ED may decrease readmissions for geriatric patients in the ED; however, these results may be dependent on implementation of the program and availability of ED, hospital, and local resources for older adults.

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Hospital readmissions within 30 days of discharge (30-day readmissions) are associated with increased mortality and health care costs. In 2011, they accounted for $24 billion in Medicare costs. Rate of 30-day readmission has become an increasingly important metric for hospitals since the implementation of the Centers for Medicare & Medicaid Services’ Hospital Readmissions Reduction Program (HRRP), which reduces payments to hospitals with excess readmissions. Readmissions for older adults are particularly important because patients age 65 and older represent 85% of all Medicare beneficiaries and older patients are more likely to be readmitted than patients under age 65.

As many as 25% of patients of all ages who are discharged from the hospital return to the emergency department (ED) within 30 days. Of these patients who visit the ED within 30 days of hospital discharge, 36% to 56% are readmitted. Given the high rate of patients returning to the ED after hospitalization and the high risk of readmission when they arrive, the ED is a logical location for targeted programs to safely discharge patients at high risk for readmission.

One such program, Geriatric Emergency Department Innovations in Workforce, Informatics, and Structural Enhancements (GEDI WISE), is a model of geriatric emergency care that operationalizes the structural and process interventions of the geriatric ED guidelines that national geriatric and emergency medicine organizations have endorsed. GEDI WISE improves care for older adults in the ED using geriatric clinical protocols; informatics for monitoring and clinical decision making; and structural enhancements to meet the triple aim of better geriatric emergency care, better older adult health, and lower health care costs. GEDI WISE includes an ED-based transitional care nurse (TCN) program to identify individuals with geriatric-specific health-related needs and coordinate their transition from ED to home with the goal of avoiding inpatient admissions when feasible and safe.

We have previously demonstrated that older adults who received a TCN intervention in the ED had a reduction in risk of hospital admission by 10 to 17 percentage points. However, it is yet unknown if the TCN program has similar effects on readmissions for older adults who return to the ED within 30 days of hospital discharge, as this represents a population at high risk of readmission. The objective of this study was to evaluate the association between receipt of a TCN intervention during an ED visit and risk of inpatient readmission for patients with recent inpatient discharges. The primary outcome was readmission during the index ED visit. Secondary outcome was any readmission within 30 days of the prior inpatient discharge.

**METHODS**

**Study Design**

This was a multicentered prospective cohort study of unique patients 65 years and older who were discharged from inpatient status (henceforth called the prior admission) and had a subsequent ED visit within 30 days after hospital discharge (henceforth called the index ED visit). This study was approved by institutional review boards at all three sites.

**Study Setting and Population**

Eligible patients age 65 and older had an index ED visit during the study period (January 1, 2013, to July 30, 2015, for Mount Sinai Medical Center [MSMC] and St. Joseph’s Regional Medical Center [SRMC]; April 1, 2013, to July 30, 2015, for Northwestern Memorial Hospital [NMH]). Patients were excluded if they had prior contact with a TCN within the 30 days prior to their index ED visit (e.g., during a prior ED visit). Patients with an Emergency Severity Index (ESI) of 1 were also dropped, because patients with high acuity were not targeted by the TCN.

**Study Protocol**

Details of the TCN protocol and hospital characteristics were described in previous publications. In brief, GEDI WISE TCNs assessed patients for geriatric syndromes that would be responsive to an ED-based transitional care program. Likelihood of discharge was not explicitly considered when determining eligibility for TCN evaluation. The TCN evaluation included assessment of functional and cognitive impairment, physical frailty, and medical complexities common in older adults. Patients targeted by the TCN were assessed for cognitive function (Short Portable Mental Status Questionnaire or Mini-Cog), delirium (Confusion Assessment Method, Richmond Agitation Sedation Scale, CAM-ICU, or brief Confusion Assessment Method), functional status (Katz Activities of Daily Living), falls risk (Timed Up and Go Test), care transitions (Care Transitions Measure-3), and caregiver strain (Modified Caregiver Strain Index).
Based on needs revealed during the GEDI WISE patient assessment, the TCN initiated an interdisciplinary ED geriatric care plan using resources available to the ED. Sites customized the TCN intervention to address patient needs using site-specific resources available, for example, MSMC and SJMC used nurse practitioners as TCNs while NMH used registered nurses. The interdisciplinary care plan could involve pharmacy, physical therapy, social work, or palliative care consultation and interventions in the ED as available. The interdisciplinary care plan was communicated with the ED team and with the patient's primary care clinician when possible. Admission decisions were ultimately determined by the ED attending physician. Up to four phone calls from 1 to 28 days post-ED visit were made depending on the site-specific protocol for TCN patients. ED spaces with dedicated structural enhancements such as diurnal lighting; glass doors; and nonslip, nonglare floors were available to older adults at all three sites. However, not all older adults were seen in spaces with structural enhancements. Additionally, nursing case managers were available at all sites; however, they did not perform any of the TCN roles. Rather, they reviewed whether or not admitted patients met inpatient or observation criteria. All TCN interactions were recorded in the medical record or in logs kept by the TCN staff and imported to a secure database from the institutions' data warehouses.

The TCN intervention targeted patients based on Identification of Seniors at Risk (ISAR) score and ESI per site-specific protocol. For all sites, there were hours during the nights and weekends when a TCN was not available. Even when a TCN was available, they often were unable to see all patients meeting eligibility criteria because of staffing constraints. Thus, there were many patients who did not receive the intervention for reasons unrelated to patient risk factors who were similar to those who did receive the intervention. We sought to identify comparison patients who were eligible for the TCN intervention with similar acuity, complexity, and similar likelihood of discharge as the treatment group patients but who were not see by the TCN.

Measures

Transitional care nurse interventions were recorded in the medical record through medical record notes and consult requests. Patients were assigned to the treatment group if there was TCN contact on the index ED visit regardless of duration or extent of associated ED geriatric care provided. Patients who had no contact with a TCN during the index visit were included in the comparison group. For individual patients with multiple ED visits within 30 days of a hospital discharge, only the first visit was included in this analysis. Analyses were stratified by site using standardized data for all three sites.

Data for patient demographics and outcomes were collected from institutional electronic health records, data warehouses, and TCN logs. Through a data use agreement, NMH and SJRMC transmitted files securely to MSMC so that a standardized three-site database could be created.

The primary multinomial outcome of interest was inpatient disposition (discharge with no subsequent readmission within 30 days of prior admission [the ideal outcome], discharge on index ED visit but a subsequent inpatient admission within 30 days of the prior admission, or inpatient readmission during the index ED visit). The secondary outcome was any subsequent inpatient readmission within 30 days of the prior admission (both admission from the ED and direct inpatient admissions; Figure 1). Patients who were not admitted to inpatient care at the time of the index ED visit but subsequently returned again to the health care system and were admitted as an inpatient within the 30-day window from prior hospitalization would be included in this secondary outcome along with any admissions to inpatient care during the index ED visit.

Data Analysis

Analyses were conducted and reported by site; data were not pooled because hospitals varied in implementation of clinical programs and TCN workflow as well as in duration of geriatric ED (GED) programs (e.g., SJRMC had a GED program since 2009 prior to CMMI funding, while NMH began a GED program in 2013).

To account for possible selection bias and to ensure that patients in our intervention and comparison groups were as similar as possible except for TCN contact, we used entropy balancing to obtain a weighted comparison group with similar covariate means and distributions as the TCN (intervention) group for each site. Entropy balancing drops observation without complete data. We treated “missing” as informative for variables that had high rates of missing data so that observations with missing data were
appropriately balanced in the comparison group. Data were cleaned and examined prior to model building. Bivariate analyses were performed on balanced data using weighted univariate logistic regression. Multivariable regression models were run on the balanced data sets. Details of these methods were previously described. We chose entropy balancing over other methods as it best accounted for the number of confounders of interest (traditional matching is only practicable with a small number of confounders) and was not limited by its ability to specify a propensity score, a limitation of propensity score models previously described in the literature. We also tested coarsened exact matching, but entropy balance achieved better covariate balance in our sample, and it allowed us to retain a greater number of observations in our data set, thus improving the efficiency of our estimates. All analyses were conducted with Stata 15.

Our treatment and comparison groups were balanced on the following variables, all measured during the index ED visit: sociodemographic characteristics (age, sex), likelihood of not encountering TCN interventions (index ED visit occurred during evening hours [9 PM–9 AM] or the weekend [yes/no], if the patient was placed in a geriatric ED structural environment [yes/no]), risk of adverse outcome (ESI = 2 [more urgent], 3, 4-5 [less urgent], ISAR = 0–1 vs. ISAR ≥ 2), overall clinical status (Charlson comorbidity scores [0, 1, 2, 3, ≥4]), the six most common chief complaints at all sites for patients 65+ in age (pain, falls, difficulty breathing, weakness, altered mental status, or psychiatric). Balance in covariates across treatment groups was assessed by standardized differences, with differences of less than 10% considered ideal.

Regression Models
Adjusted regression models on balanced samples allowed us to account for potential covariate imbalance that could remain after entropy balancing. Models also included all covariates used to create entropy balance weights, allowing for doubly robust estimations. Within each site, we used a multinomial logistic regression to examine the relationship between TCN intervention and three outcomes: discharge with no subsequent readmission within 30 days of prior admission (the ideal outcome), discharge on index ED visit but a subsequent inpatient admission within 30 days of the prior admission, and inpatient readmission during the index ED visit. Results are presented as average incremental effects (AIE) by percentage points (i.e., the mean change in likelihood of hospital admission that occurs when a patient is moved from the comparison group to the TCN group, holding all other covariates at their weighted values). We also used logistic regression to examine the relationship between TCN intervention and any readmission within 30 days of the prior admission. Logistic regression models include all variables hypothesized to be associated with likelihood of receiving a TCN intervention and with readmission, in line with a direct modeling approach.

RESULTS
Characteristics of Study Participants
During the study period, there were 57,287 ED visits by patients age 65 and older at the three participating hospitals. Of these ED visits, 6,838 (11.9%) occurred within 30 days of a prior hospital discharge. These
index ED visits occurred a median of 11 days (interquartile range [IQR] = 4–19) after inpatient discharge at MSMC, 10 days (IQR = 4–18) at NMH, and 10 days (IQR = 4–19) at SJRMC. Forty-eight visits (14 at MSMC, 22 at NMH, and 12 at SJRMC) were by patients who had prior contact with the TCN during the 30 days prior to the index ED visit, these visits were not included in the analysis. Patients received a TCN intervention during 608 (8.9%) of index ED visits. At MSMC, 6.8% (160 of 2,340 visits) of patients were exposed to a TCN, 13.0% (304 of 2,333 visits) at NMH, and 6.7% (144 of 2,165 visits) at SJRMC. Of the ED visits which occurred within 30 days of a prior hospital discharge, 4,210 (61.6%) visits resulted in readmission during the index ED visit: 1,469 (62.8%) at MSMC, 1,375 (58.9%) at NMH, and 1,366 (63.1%) and SJRMC. After discharge from the ED on the index visit, 404 patients (5.9%) were subsequently readmitted within 30 days of the prior hospitalization: 159 visits (6.8%) at MSMC, 117 patients (5.0%) at NMH, and 128 patients (5.9%) at SJRMC. Overall, 4,614 (67.4%) visits resulted in any readmission within 30 days of the prior hospitalization at all sites, 1,628 (69.6%) at MSMC, 1,492 (64.0%) at NMH, and 1,494 (69.0%) at SJRMC.

**Entropy Balancing**

We used entropy balancing to create weighted comparison groups for each site that were similar to the TCN group, except for receipt of the TCN intervention. At SJRMC, 83% of records were missing ISAR scores. Therefore, we treated “missing” as informative. That is, scores were grouped into three categories (1 = missing, 2 = 0 or 1, or 3 = 2 or higher). Therefore, the weighted comparison group and TCN intervention group had similar rates of missing ISAR data at SJRMC (Table 1). Standardized differences approached 0% across treatment and comparison groups after matching patients in risk for adverse outcomes, clinical characteristics, and sociodemographics (Figure 2). As a sensitivity analysis, we included days from prior hospitalization to index ED visit in the entropy balancing model. The sensitivity analysis yielded no significant changes in the results.

**Weighted Bivariate Analysis**

In weighted univariate logistic regression analyses of balanced samples for the primary outcome, patients cared for by the TCN in the ED had a significantly lower rate of readmission than comparison patients on their index visit at NMH (AIE = −17.4 percentage points, 95% confidence interval [CI] = −25.2 to −9.6), but not at MSMC (AIE = −10.1 percentage points, 95% CI = −20.9 to 0.8) nor SJRMC (AIE = −2.45 percentage points, 95% CI = −13.7 to 8.8). For patients who were discharged during their index ED visit, there were no statistically significant differences in subsequent inpatient hospitalization within the 30-day readmission window for TCN patients versus comparison patients (MSMC—10.0% TCN vs. 5.6% comparison, p = 0.10; NMH—5.6% TCN vs. 4.4% comparison, p = 0.62; SJRMC—9.0% TCN vs. 6.0% comparison, p = 0.10). For the secondary outcome, TCN patients were less likely than comparison patients to have any readmission within the 30-day readmission window at MSMC (57.5% TCN vs. 63.1% comparison, p < 0.001) and NMH (51.0% TCN vs. 67.2% comparison, p < 0.01), but not at SJRMC (69.4% TCN vs. 68.8% comparison, p = 0.91; Table 2). There was no significant difference in returns to the ED within 72 hours at any hospital: MSMC AIE, 2.19 (95% CI = −1.1 to 7.49); NMH AIE, 0.12 (95% CI = −3.19 to 3.43); and SJRMC AIE, 0.84 (95% CI = −3.14 to 4.81).

**Multivariable Regression Models**

In our multivariable multinomial logistic regression model, we examined associations between TCN intervention and three outcomes: inpatient admission during the ED visit, ED discharge but subsequent 30-day readmission, and ED discharge with no readmission (reference category). We continued to observe a significant relationship between TCN intervention and reduced risk of admission during the ED visit among patients at MSMC and NMH: MSMC AIE, −11.0 percentage points (95% CI = −18.5 to −2.7), and NMH AIE, −17.3 percentage points (95% CI = −23.1 to −11.5). As in our bivariate analyses, this relationship was not observed at SJRMC: AIE, −2.5 percentage points (95% CI, −10.5 to 5.5; Table 3). However, at MSMC, TCN intervention was associated with an increased risk of subsequent readmission after ED discharge: AIE, 4.8 percentage points (95% CI = 0.4 to 9.2). There was no evidence of this relationship at NMH, AIE 1.1 percentage points (95% CI −1.8 to 4.0); or SJRMC, AIE 3.0 percentage points (95% CI = −1.6 to 7.5).

We then examined the secondary outcome: likelihood of any 30-day readmission (on the index visit or any time within the 30 days). In multivariable logistic.
Table 1
Baseline Demographic and Clinical Factors by Site

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mount Sinai Medical Center</th>
<th>Northwestern Memorial Hospital</th>
<th>St. Joseph’s Regional Medical Center</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years, mean ± SD)</strong></td>
<td>77.1 ± 8.7</td>
<td>79.0 ± 9.1</td>
<td>79.0 ± 8.5</td>
</tr>
<tr>
<td><strong>Charlson Comorbidity Score (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>13.9</td>
<td>17.5</td>
<td>17.5</td>
</tr>
<tr>
<td>2</td>
<td>15.7</td>
<td>12.5</td>
<td>12.5</td>
</tr>
<tr>
<td>3</td>
<td>15.1</td>
<td>8.8</td>
<td>8.7</td>
</tr>
<tr>
<td>≥4</td>
<td>43.0</td>
<td>41.9</td>
<td>41.9</td>
</tr>
<tr>
<td><strong>Chief complaint (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altered mental status</td>
<td>4.4</td>
<td>3.7</td>
<td>3.8</td>
</tr>
<tr>
<td>Difficulty breathing</td>
<td>13.9</td>
<td>13.7</td>
<td>13.8</td>
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<tr>
<td>Falls</td>
<td>2.6</td>
<td>6.9</td>
<td>6.9</td>
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<tr>
<td>Pain</td>
<td>6.7</td>
<td>15.6</td>
<td>15.6</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>2.7</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Weakness</td>
<td>5.7</td>
<td>7.5</td>
<td>7.5</td>
</tr>
<tr>
<td><strong>ESI (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>42.2</td>
<td>27.5</td>
<td>27.5</td>
</tr>
<tr>
<td>3</td>
<td>55.1</td>
<td>69.4</td>
<td>69.4</td>
</tr>
<tr>
<td>4 or 5</td>
<td>2.3</td>
<td>2.9</td>
<td>3.13</td>
</tr>
<tr>
<td>Missing ESI (%)</td>
<td>0.3</td>
<td>0.2</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Geriatric ED space (%)</strong></td>
<td>28.7</td>
<td>66.9</td>
<td>66.9</td>
</tr>
<tr>
<td><strong>ISAR score (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 or 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 or more</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing ISAR</td>
<td>17.8</td>
<td>0.0</td>
<td>14.4</td>
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<tr>
<td>0</td>
<td>1.19</td>
<td>0.81</td>
<td>0.6</td>
</tr>
<tr>
<td>1</td>
<td>7.7</td>
<td>11.9</td>
<td>11.9</td>
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<tr>
<td>2</td>
<td>24.0</td>
<td>27.5</td>
<td>27.5</td>
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<tr>
<td>3</td>
<td>13.8</td>
<td>17.5</td>
<td>17.5</td>
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<tr>
<td>4</td>
<td>21.1</td>
<td>16.3</td>
<td>16.2</td>
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<tr>
<td>5 or 6</td>
<td>14.4</td>
<td>11.9</td>
<td>11.9</td>
</tr>
<tr>
<td>Male (%)</td>
<td>46.6</td>
<td>38.8</td>
<td>38.7</td>
</tr>
<tr>
<td>Night or weekend (%)</td>
<td>41.7</td>
<td>30.6</td>
<td>30.6</td>
</tr>
</tbody>
</table>

ESI = Emergency Severity Index; ISAR = Identification of Senior at Risk; Std.Diff. = standardized difference; TCN = transitional care nurse.
*ISAR data at St. Joseph’s Regional Medical Center recorded as dichotomous (0–1 or 2+).
Figure 2. Standardized differences by site entropy balancing resulted in better covariate balance (smaller absolute value of standardized difference across treatment and comparison groups for each site. Closed circles are weighted and open circles are unweighted. ESI = Emergency Severity Index; ISAR = Identification of Seniors at Risk.
regression models, TCN patients were less likely to have any 30-day readmissions than comparison patients at NMH: AIE $-16.2$ percentage points (95% CI $=-22.0$ to $-10.3$). At MSMC and SJRMC, there was no significant difference in likelihood of readmission: MSMC AIE, $-5.6$ percentage points (95% CI $=-13.1$ to $1.8$); and SJRMC AIE, $0.5$ percentage points (95% CI $=-7.2$ to $8.2$; Table 3).

**DISCUSSION**

This study demonstrates that older adults with an ED visit within 30 days of a prior admission may be less likely to be readmitted if they receive a TCN intervention. However, the impact of the TCN intervention varied by site. At NMH the TCN intervention was associated with a significant decrease in admissions during the index visit and the entire 30-day readmission window. At MSMC, TCN intervention was associated with a significant decrease in admissions only during the index visit, not the entire 30-day readmission window. At SJRMC, TCN intervention was not associated with any change in readmission rate on the index visit or the 30-day readmission window.

Like our previous study demonstrating decreased admissions for all older adults seen by the TCN

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**Table 2**

Weighted Comparison Group Rates and Univariate Logistic Regressions of TCN Intervention and Readmission Outcomes by Site

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mount Sinai Medical Center (n = 2,340)</th>
<th>Northwestern Memorial Hospital (n = 2,333)</th>
<th>St. Joseph’s Regional Medical Center (n = 2,165)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Readmission during ED visit</td>
<td>57.6%</td>
<td>$-10.1$ ($-20.9$ to $0.8$)</td>
<td>62.8%</td>
</tr>
<tr>
<td>Discharge during ED visit, but subsequent readmission within 30 days of previous hospitalization</td>
<td>5.6%</td>
<td>$4.4$ ($-1.4$ to $10.3$)</td>
<td>4.4%</td>
</tr>
<tr>
<td>Any readmission within 30 days of previous hospitalization</td>
<td>63.1%</td>
<td>$5.6$ ($-16.3$ to $5.1$)</td>
<td>63.2%</td>
</tr>
</tbody>
</table>

AIE = average incremental effect; TCN = transitional care nurse.

Percentage of ED visits resulting in readmission during ED visit (primary outcome), discharge during ED visit with subsequent readmission, and any readmission within 30 days of previous admission by intervention group and site. AIE of TCN intervention is expressed in percentage point difference from the comparison group.

*p < 0.05.

**Table 3**

Weighted Multivariable Regressions of TCN Intervention and Readmission Outcomes by Site

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mount Sinai Medical Center (n = 2,340)</th>
<th>Northwestern Memorial Hospital (n = 2,333)</th>
<th>St. Joseph’s Regional Medical Center (n = 2,165)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multinomial logistic regression, AIE of TCN vs. comparison, percentage point difference (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Readmission during ED visit</td>
<td>$-10.1$ ($-18.5$ to $-2.7$)*</td>
<td>$-17.3$ ($-23.1$ to $-11.5$)*</td>
<td>$-2.5$ ($-10.5$ to $5.5$)</td>
</tr>
<tr>
<td>Discharge during ED visit, but subsequently readmitted within 30 days of previous admission</td>
<td>$4.8$ ($0.4$ to $9.2$)*</td>
<td>$1.1$ ($-1.8$ to $4.0$)</td>
<td>$3.0$ ($-1.6$ to $7.5$)</td>
</tr>
<tr>
<td>Discharged from ED visit and never readmitted</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Logistic Regression, AIE of TCN vs. Comparison, Percentage Point Difference (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Readmission during or after index ED visit within 30 days of previous admission</td>
<td>$5.6$ ($-13.1$ to $1.8$)</td>
<td>$16.2$ ($-22.0$ to $-10.3$)*</td>
<td>$0.5$ ($-7.2$ to $8.2$)</td>
</tr>
</tbody>
</table>

AIE = average incremental effect; TCN = transitional care nurse.

Multinomial logistic regression comparing TCN group and comparison group with resultant AIE of the TCN intervention on readmission during the index ED visit (primary outcome), discharge from the ED with subsequent admission within 30 days of prior admission, or discharge from the ED without subsequent readmission.

Logistic regression comparing TCN group with comparison group and resultant AIE of any readmission during or after index ED visit occurring within 30 days of prior hospitalization.

*p < 0.05.
regardless of prior admission status, this study demonstrated a significant decrease in admissions on the day of evaluation by the TCN and at one hospital for 30 days after TCN evaluation. To our knowledge, this is the first study to demonstrate a significant decrease in hospital admissions during an ED visit for older adults who had a recent prior admission.

In 2014, a systematic review and meta-analysis of randomized controlled trials of programs designed to reduce 30-day readmissions found studies after 2002 were found to have less success than interventions prior to 2002. Successful programs were more likely to have a “consistent and complex strategy that emphasized the assessment and addressing of factors related to patient context and capacity for self-care (including the impact of comorbidities, functional status, caregiver capabilities, socioeconomic factors, potential for self-management, and patient and caregiver goals for care).” These interventions coordinated care across the inpatient-to-outpatient transition and involved multiple patient interactions; most involved patient home visits. Examples of successful programs include a study from Denmark that demonstrated a reduction in 30-day readmissions for older adults discharged from a geriatric ward with regular in-home follow-up visits for home rehabilitation, medical, and social support.

Two other studies from the United States in the 1990s demonstrated a reduction in readmissions at 24 weeks after admission for older adults discharged from medical or surgical wards by providing an advanced practice nurse-directed program stressing outpatient, in-home, and telephone follow-up. None of these studies were based in the ED or focused on patients who returned to the ED after an inpatient admission.

Like the inpatient-based programs above which were successful in decreasing 30-day readmissions above, our ED based TCN intervention is a program with a “consistent and complex strategy that emphasizes the assessment and addressing of factors related to patient context and capacity for self-care.” In the ED, TCNs may work with the primary ED clinical team, social workers, pharmacists, physical therapists, the patient’s outpatient clinicians, home care, and the patient’s family to identify and address risks of complications and adverse events. Admission for older adults carries significant risk such as infection, delirium, fall risk, and functional decline. Therefore, the successful discharge of high-risk older adults may decrease their risk for acquiring the adverse events associated with admission.

The Centers for Medicare & Medicaid Services emphasizes 30-day readmissions as a quality metric, and they are a focus of financial penalties for hospitals. Therefore, this administrative outcome is very important for hospitals financially. Bringing a robust and complex care coordination system to the ED, such as the TCN intervention, may be a way for hospitals to decrease 30-day readmissions. This may be especially true for hospitals where previous readmission reduction programs have not been successful for high-risk patients. It is, however, important to ensure that these high-risk older adults are discharged safely with appropriate follow-up, particularly as recent data on mortality have called into question the impact of the HRRP on patient safety. Additionally, longitudinal studies on patient-centered outcomes such as health-related quality of life are necessary to better understand the impact of TCN intervention on patients beyond administrative endpoints such as admission.

Differences in outcomes across sites may be related to differences in the intensity of intervention at each site or availability of other concurrent policies or programs to reduce 30-day readmissions. For example, patients who were in the ED after prior admission were automatically flagged for a TCN intervention at NMH. Because of this focus, the TCN team may have been more prepared to help patients with a recent hospital discharge by improving communication with the ED and inpatient social work teams or following up on home care or other services that were planned prior to hospital discharge. Alternatively, the automatic flag may have included some patients who were less likely to be readmitted at NMH compared to MSMC or SJRMC who did not have automatic flags for TCN intervention, but we guarded against this potential selection bias through entropy balancing.

Another potential cause of the differences between sites could be the duration and presence of prior geriatric ED interventions. SJRMC had a geriatric ED program for several years before the implementation of the study. The baseline opportunity for improvement may have already changed with earlier programs and thus the results from the comparison group may have been contaminated by the long history of GED improvements at that site.

LIMITATIONS

The primary limitation of this study is related to its observational design. Although entropy balancing is a
rigorous method to address selection bias from observed confounders, it does not account for the potential influence of unmeasured confounders that are associated with both the likelihood of receiving TCN intervention and the likelihood of readmission. Examples of possible unmeasured confounders include caregiver support or household income. It is also possible that patients could either have visited other EDs or have been readmitted at other hospitals that were not recorded in this study. To account for fact that a second TCN contact was likely to be different than an initial encounter, visits were excluded if the patient had prior TCN contact within 30 days of the index ED visit. This may have attenuated the results of this study as those patients with repeat TCN contact may be patients who are more likely to benefit from the TCN intervention. However, this accounted for less than 1% of the sample, so is unlikely to have significant impact on the results. In addition, the TCN intervention was implemented differently at each site to accommodate the availability of local resources and other programs and policies, which may have been in place during the study period. The details of any inpatient or outpatient interventions are not known and may impact the results for each site. For this reason, the sample populations from the three study sites were not pooled. Because the results were not pooled, the sample sizes at each individual site are low and may be susceptible to type II error. This study was not powered to determine a significant effect on readmission for patients hospitalized in the prior 30 days because it was a prospective observational study which was a subset of a larger study. Additionally, recent research has suggested that successful 30-day readmission programs are likely to represent a regression to the mean, rather than a true effect.\textsuperscript{39} Longer-term evaluation of the TCN program is needed to evaluate this possibility. Finally, within each site, the specifics of the TCN intervention may not have been applied uniformly, as TCNs were given latitude to make clinical decisions with the assistance of the rest of the multidisciplinary team including the ED physician team and the patient’s outpatient clinicians.

CONCLUSIONS

Care by transitional care nurses in the ED is associated with significantly decreased readmission at the index ED visit for older adults who returned to the ED within 30 days of a prior admission at two out of three studied hospitals. At one hospital this reduction was sustained for the entire 30-day readmission window. Programs such as the transitional care nurse intervention may be an effective way to decrease 30-day readmissions for geriatric patients in the ED. However, implementation of the program and availability of local resources likely has a significant impact on the effectiveness of the transitional care nurse intervention at decreasing 30-day readmissions.

We acknowledge "The GEDI WISE Investigators" to include (in addition to the named authors) the following for their contributions to the implementation and clinical care of the GEDI WISE program: Gallane Abraham, James Adams, Amer Aldeen, Cindy Amoko, Kevin Baumlín, Maria Christensen, Nicholas Genes, Corita R. Grudzen, Marianna Karounos, Sanjeev Malik, Barbara Morano, Denise Nassis, Gloria Nimo, Joanna M. Ortiz, Laura Rivera-Reyes, Martine Sanon, Richard Schulzt, Jason Shapiro, Debra Sumberg, and Gary Winkel.

References

Hyperkalemia is one of the most common and potentially life-threatening electrolyte disorders, particularly in patients with heart failure, chronic kidney disease (CKD), and diabetes mellitus.\textsuperscript{1,2} Prior studies estimate that hyperkalemia occurs in up to 10% of hospitalized patients and up to 2% to 3% of...
patients presenting to the emergency department (ED). Increased severity of hyperkalemia also correlates with increased risk of mortality even within 1 day of its occurrence, highlighting the importance of recognizing and treating this metabolic abnormality emergently.

Pharmacologic management to eliminate potassium from the body is limited to diuretics and potassium binders to excrete via the urinary and gastrointestinal tract, respectively. Although potassium shifting agents (i.e., albuterol and insulin) are commonly used, they are only temporizing agents. A binder that can quickly and reliably treat hyperkalemia may provide a clinically important alternative where dialysis is not readily available or an economically preferable model, and the need for emergent dialysis can be managed and transitioned to urgent dialysis.

However, evidence on oral potassium binders for treatment of hyperkalemia is limited, particularly in the acute setting. Patiromer is an oral potassium binder that exchanges potassium for calcium and is Food and Drug Administration (FDA) approved for treatment of chronic hyperkalemia. The binder is not absorbed systemically but stays in the gastrointestinal tract and binds to potassium, predominantly in the colon where potassium concentration is the highest. Under physiologic conditions, 1 g of patiromer can bind more than 8 mEq of K. The efficacy and safety of patiromer for treatment of chronic hyperkalemia has been demonstrated across four large randomized controlled trials totaling 666 patients. The FDA recommended dose for management of chronic hyperkalemia is between 8.4 and 25.2 g daily. Although infrequent, the most common adverse reactions are gastrointestinal symptoms and hypomagnesemia. Although one previous study reported that patiromer significantly lowered serum potassium within 7 hours of administration, there have been no clinical studies evaluating its efficacy for the management of acute hyperkalemia in the ED. We hypothesize that a single dose of patiromer will lower serum potassium when compared with standard therapy within 6 hours. Since a dosage of 25.2 g per day has been previously studied, we hypothesize that a single dose of 25.2 g of oral patiromer will be well tolerated in hyperkalemic patients in the ED setting. We chose to give the higher dose of patiromer to determine the maximal effect in a rapid manner.

**METHODS**

**Study Design and Setting**

This is a single-center, single-blinded, randomized, open-label, pilot study performed at a large inner-city academic ED. The study was approved by the institutional review board and registered with clinicaltrials.gov (NCT02933450).

**Selection of Participants**

Potential subjects were identified using an electronic track board. Patients ≥ 18 years of age with end-stage renal disease (ESRD), who had a serum potassium level of ≥ 6.0 mEq/L and anticipated to wait for hemodialysis for at least 4 hours, were eligible for enrollment. Exclusions were 1) a significant arrhythmia on initial electrocardiogram (ECG; determined by clinical provider), 2) known allergy to patiromer, 3) administration of any potassium binder other than the study drug, or 4) pregnancy.

**Interventions**

Patients were randomized to standard of care (SOC) or a single dose of 25.2 g of oral patiromer plus SOC (PAT) cohort using a block-randomization (size = 6) method. SOC is defined as intervention provided by clinical provider according to individual practice pattern or hospital protocol. Providers were blinded to treatment assignment; however, patients were aware that they were given a “study drug,” and data were gathered by research nurses. Research data were not shared with clinical providers, who followed ED protocols to recheck potassium and treat appropriately. Patients were observed with telemetry monitoring for up to 10 hours or until they received hemodialysis, whichever occurred first. Blood draws and ECGs were performed at enrollment and at 1, 2, 4, 6, and 8 hours thereafter.

**Outcomes**

The primary outcome was the difference in serum potassium between SOC and PAT groups at 6 hours. The secondary outcomes were the differences between groups in the amount and number of dosages of insulin and albuterol given over 2, 4, and 6 hours. Recorded adverse events included rates of new gastrointestinal symptoms, hypomagnesemia, and hypoglycemia.

**Data Analysis**

Demographic characteristics and baseline serum potassium were compared between the two treatment arms.
using the independent t-test, Wilcoxon rank-sum test, Fisher’s exact test, or chi-square test. A mixed-effect linear regression model with an unstructured covariance was used to model potassium levels over time, based on the assumption that the data are normally distributed. Residuals were analyzed to support the appropriate use of this model to estimate means and compare them between groups. The model included fixed effects for time, treatment group, the group–time interaction, baseline potassium, and whether a potassium lowering drug was given within 30 minutes of baseline. The adjusted means of potassium levels were compared between groups at each time point, between time points for each group, and for the change in potassium over time between the patiromer (PAT) and SOC groups. These comparisons were adjusted for multiple hypothesis testing using Bonferroni’s method. The amount of insulin and albuterol given and the number of interventions (treatments) within 2, 4, and 6 hours were compared using the Wilcoxon rank-sum test.

Adverse events were summarized by treatment arm and compared using Fisher’s exact test or chi-square test. Analyses were conducted on a per-protocol basis; patients who went for hemodialysis treatment before 4 hours of medical treatment were excluded from the analysis.

RESULTS

Baseline Characteristics

Of 43 patients randomized, 30 (15 in each group) completed 4 hours and 19 completed 6 hours of treatment (10 in the SOC group and nine in the PAT group) and were eligible for analysis (Figure 1). There were no differences in age, sex, baseline potassium, magnesium, or glucose between the two groups (Table 1).

Primary and Secondary Outcomes

There was no difference in adjusted mean serum potassium between SOC and PAT groups at 6 hours (6.32, confidence interval [CI] = 6.0 to 6.63 vs. 5.81, CI = 5.48 to 6.14). However, 2 hours posttreatment the serum potassium of the PAT group (5.90 mEq/L, 95% CI = 5.63 to 6.17 mEq/L) was lower than that of SOC (6.51 mEq/L, 95% CI = 6.25 to 6.78; Figures 2 and 3, Table 2). Mean potassium was significantly lower at 2 (0.52 mEq/L), 4 (0.69 mEq/L), and 6 hours (0.61 mEq/L) compared with baseline in the PAT group, but only at 4 hours (0.60 mEq/L) in the SOC group; Table 3). The rate of change of potassium at each time point versus baseline was not different between the groups. Further, there were no
differences in amount of insulin or albuterol used, and number of interventions between groups (Table 4; Figures 4 and 5). The median amount of albuterol used in the PAT cohort was less, but not significantly, than what that used in the SOC cohort (0 mg vs. 12.5 mg; \( p = 0.097 \)).

A linear mixed-effects regression model was used to estimate and compare means. A residual and a QQ plot (Figures S1 and S2, available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13868/full) were analyzed and found to support the use of this model to compare means.

### Adverse Events

Rates of new gastrointestinal symptoms and hypoglycemia were uncommon in both groups. One (7.1%) PAT and two (13.3%) SOC patients reported gastrointestinal symptoms (nausea, vomiting, or gastrointestinal discomfort). Three patients (20%) experienced hypoglycemia in each group, and no patient experienced hypomagnesemia in either group. Hypoglycemia was defined as blood glucose \(< 70 \text{ mg/dL}\) and only dextrose was given in to raise the glucose level.

### DISCUSSION

This is the first study that evaluates the efficacy of patiromer for the management of acute hyperkalemia in the ED. We found that a single oral dose of 25.2 g patiromer, together with standard treatment, significantly lowered serum potassium level as early as 2 hour but did not show a difference at 6 hours when compared with standard treatment alone. Although not significant, the patiromer group used less albuterol than the SOC group at 6 hours. Furthermore, the higher dose of patiromer was well tolerated.

While there is no previously published data on the use of patiromer for the acute management of hyperkalemia in the ED, a single phase I study by Bushinsky et al.\(^\text{17,18}\) has evaluated the onset of action of patiromer in CKD in a controlled inpatient research unit. This study included subjects with serum potassium between 5.5 and 6.5 mEq/L and administered only 8.4 g of patiromer with morning and evening meals for a total of four doses. Serum potassium was assessed at baseline, at 4 hours, and then every 2 to 4 hours thereafter, for up to 48 hours, while inpatient. Mean baseline potassium was 5.93 mEq/L and was significantly reduced by 7 hours after the first dose and at all subsequent times.

Our study is a real-world evaluation of patiromer in patients with hyperkalemia in the ED. It is different
from that of Bushinsky et al. on several accounts: 1) our study’s baseline potassium was higher in the PAT cohort (median potassium of 6.4 mEq/L) and, therefore, had the potential for a larger change; 2) we administered a 300% higher dosage of patiromer (25.2 g vs. 8.4 g) and thus maximized the potential for potassium binding in the intestinal tract; and 3) we monitored serum potassium more frequently to capture the earliest point when patiromer takes effect.

Table 2
Mean Potassium Over Time (Numerical Representation of Figure 1)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 hr</th>
<th>2 hr</th>
<th>4 hr</th>
<th>6 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOC</td>
<td>6.68</td>
<td>6.64</td>
<td>6.51</td>
<td>6.08</td>
<td>6.32</td>
</tr>
<tr>
<td>PAT</td>
<td>6.42</td>
<td>6.17</td>
<td>5.90</td>
<td>5.73</td>
<td>5.81</td>
</tr>
<tr>
<td>p-value</td>
<td>0.878</td>
<td>0.075</td>
<td>0.009</td>
<td>0.329</td>
<td>0.155</td>
</tr>
</tbody>
</table>

K = potassium; PAT = patiromer cohort; SOC = standard of care cohort.
p-values adjusted for multiple comparisons using Bonferroni method.

Table 3
Adjusted Mean Serum Potassium Change From Baseline

<table>
<thead>
<tr>
<th></th>
<th>SOC</th>
<th>PAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (0 hr)</td>
<td>6.68</td>
<td>6.42</td>
</tr>
<tr>
<td>1 hr</td>
<td>-0.04</td>
<td>-0.25</td>
</tr>
<tr>
<td>2 hr</td>
<td>-0.17</td>
<td>-0.52*</td>
</tr>
<tr>
<td>4 hr</td>
<td>-0.60*</td>
<td>-0.69*</td>
</tr>
<tr>
<td>6 hr</td>
<td>-0.36</td>
<td>-0.61*</td>
</tr>
</tbody>
</table>

*PAT = patiromer; SOC = standard of care.
*Means statistically significant change when compared with baseline. p-values adjusted for multiple comparisons using Bonferroni method.

Figure 3 Change in potassium (K) from baseline at different time points for individual patients. n = 30 at 1, 2, and 4 hours; n = 19 at 6 hours.

Table 4
Secondary Outcomes

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Median (IQR)</th>
<th>N (%)</th>
<th>Median (IQR)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin given (IU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 hr</td>
<td>15 (33)</td>
<td>0 (0.0–5.0)</td>
<td>15 (40)</td>
<td>0 (0.0–5.0)</td>
</tr>
<tr>
<td>4 hr</td>
<td>15 (60)</td>
<td>5 (0.0–5.0)</td>
<td>15 (47)</td>
<td>0 (0.0–5.0)</td>
</tr>
<tr>
<td>6 hr</td>
<td>10 (70)</td>
<td>5 (0.0–10.0)</td>
<td>9 (44)</td>
<td>5 (0.0–7.0)</td>
</tr>
<tr>
<td>Albuterol given (mg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 hr</td>
<td>15 (27)</td>
<td>0 (0.0–2.5)</td>
<td>15 (20)</td>
<td>0 (0.0–0.0)</td>
</tr>
<tr>
<td>4 hr</td>
<td>15 (53)</td>
<td>2.5 (0.0–15.0)</td>
<td>15 (33)</td>
<td>0 (0.0–2.5)</td>
</tr>
<tr>
<td>6 hr</td>
<td>10 (70)</td>
<td>12.5 (0.0–17.5)</td>
<td>9 (56)</td>
<td>0 (0.0–10.0)</td>
</tr>
<tr>
<td>Number of interventions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 hr</td>
<td>15 (40)</td>
<td>0 (0.0–1.0)</td>
<td>15 (40)</td>
<td>0 (0.0–1.0)</td>
</tr>
<tr>
<td>4 hr</td>
<td>15 (67)</td>
<td>1 (0.0–2.0)</td>
<td>15 (47)</td>
<td>0 (0.0–2.0)</td>
</tr>
<tr>
<td>6 hr</td>
<td>10 (80)</td>
<td>2 (1.0–3.0)</td>
<td>9 (56)</td>
<td>1 (0.0–2.0)</td>
</tr>
</tbody>
</table>

N = total number of patients in the cohort; % = percentage of patients receiving respective medication or intervention.
*IQR = interquartile range; PAT = patiromer; SOC = standard of care.

for potassium binding in the intestinal tract; and 3) we monitored serum potassium more frequently to capture the earliest point when patiromer takes effect. We believe that these differences explain why we see a unique effect at 2 hours. However, since it was a small study and allowed coadministration of other potassium-lowering agents, it was difficult to show a consistent statistical difference between the groups.
LIMITATIONS

As a small pilot, no power analysis was done a priori, and so our outcomes are limited to those findings with large effects. First, our open-label design, convenience sampling, and the lack of generally accepted hyperkalemia management guidelines\(^\text{19}\) allowing multiple SOC interventions create challenges to identifying longer-term impact of patiromer after its initial 2-hour effect. Second, as it would be unethical to withhold therapy in patients with severe hyperkalemia, three PAT patients received SOC before enrollment and treatment with patiromer. Although both comparator groups received SOC it will require a blinded study to more precisely determine time dependent outcomes with patiromer. Last, as part of the SOC at our institution, a lower dose (5 units) of insulin was administered to treat hyperkalemia, given its hypoglycemic effect in ESRD patients.\(^\text{20}\) It is conceivable that the difference between the two groups would have been different had we used a higher dose. Future studies should use our findings to perform an appropriate power calculation and conduct a multicenter randomized double-blind controlled study to address some of the limitations of this study. Further, it would be helpful to enroll hyperkalemia from all etiologies to make the results more generalizable.

CONCLUSIONS

In this pilot study on the management of ED patients with acute severe hyperkalemia, a single dose of 25.2 g oral patiromer lowered the serum potassium within 2 hours but did not have a sustained effect at 6 hours compared to standard care. Our results are encouraging and support the need for a larger, definitive, multicenter study to establish the role of patiromer in the acute management of hyperkalemia.

References


Supporting Information

The following supporting information is available in the online version of this paper available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13868/full

Figure S1. Residuals from the linear mixed effects regression model that was used to compare serum potassium.

Figure S2. Q-Q plot of residuals from the linear mixed effects regression model that was used to compare serum potassium.
Supraventricular tachycardia (SVT) is a potentially life-threatening disease state which accounts for 50,000 emergency department (ED) visits annually. SVT encompasses a variety of rhythm disturbances including atrial fibrillation, atrial flutter, sinus tachycardia, atrioventricular nodal reentrant tachycardia, and atrioventricular reciprocating tachycardia. The American Heart Association 2015 guidelines for Adult Advanced Cardiac Life Support recommends adenosine in nonhypotensive patients in regular narrow-complex SVT. Adenosine is an endogenous purine nucleoside that blocks atrioventricular nodal conduction via the A1 receptors in the cardiac tissue. These in turn act on Gi-cAMP to stimulate potassium channels yielding hyperpolarization of cardiac myocytes thus returning the heart to a normal sinus rhythm (NSR).

The pharmacokinetic profile of adenosine makes it an ideal agent to treat SVT. With a rapid onset and a half-life less than 10 seconds, cardioversion can be performed quickly with limited adverse effects. Due to these unique kinetics, a large-volume flush of saline is concomitantly administered to ensure adequate delivery to the myocardium. Adenosine is commonly administered as a 6-mg rapid intravenous bolus over 1 to 2 seconds followed by a rapid 20-mL saline flush. If the first dose does not result in termination of SVT to NSR within 1 to 2 minutes, a repeat dose of 12 mg can be given and the dose may be repeated one additional time if required for a total of three doses. A decrease in the initial adenosine dose to 3 mg is recommended for administration through a central line.

Typically, adenosine is administered via a two-way stopcock, where drug and a 20-mL saline flush are administered in tandem. This method suffers from physical logistic issues. For example, locating a two-way stopcock may cause a delay in therapy and certain emergency medicine transport services may not stock such a device. This method also requires the nursing staff to precisely coordinate their actions delivering the drug and flush simultaneously. An alternative method of combining the drug and the flush in a single syringe may offer higher rates of conversion, lower the need for repeat doses, eliminate the need for a stopcock, and limit peripheral IV extravasations. Combining medication and flush has been popularized by free open-access medical education in recent years. Hayes reviewed the benefits, methodology, and available literature in 2012, with an update in 2018. EMcrit.org post from Weingart in 2015 also endorsed a one-syringe method. Adenosine is compatible and stable in 0.9% sodium chloride. Currently, minimal evidence exists surrounding this method of administration. The objective of this study was to evaluate the administration technique of adenosine delivered as a single-syringe diluted with saline compared to the two-syringe method for conversion of SVT to NSR.

This single-center, prospective, observational study was conducted from November, 1, 2016, through February 28, 2018. This was an institutional review...
board–approved study, with a waiver to consent as the process is standard practice at our institution.

Patients above the age of 18 presenting to the ED with stable narrow-complex regular rhythm tachycardia requiring adenosine administration were included. Patients were excluded if systolic blood pressure was below 90 mm Hg, had evidence of poor perfusion, or had a history of bronchospasm. The physician would identify patients with SVT and would inform the pharmacist of his or her preferred adenosine administration method. Selection of administration method was solely up to the provider regardless of admission into the study.

The pharmacist would prepare adenosine as either a single-syringe containing both 6 mg of adenosine and 18 mL of 0.9% sodium chloride or two separate syringes of adenosine and 20 mL 0.9% sodium chloride flush. Nursing staff would administer the syringe(s) using the largest IV available.

A medical technician would collect a continuous EKG during and immediately after administration of the medication. If conversion to NSR was not achieved, as determined by the physician, the dose of adenosine was increased to 12 mg in both groups and given via the same administration method previously used. A total of three doses could be provided to each patient.

The primary endpoint was the percentage of patients with successful conversion of SVT to NSR after the first dose. Secondary endpoints included achievement of NSR up to three doses and adverse effects secondary to the administration techniques. We assumed the efficacy of the single-syringe treatment group (SS) would be at least 80% as effective as the two-syringe method (TS) and set the noninferiority margin to 20%. To achieve a power of 80% with an alpha set at 0.05, it was determined that 75 patients were needed in each group. If no difference was detected between groups, we would be able to reject the null hypothesis. Descriptive statistics were utilized for demographic data, presented as medians and interquartile ranges for continuous data and as percentages for dichotomous and categorical data. A noninferiority test of proportions was utilized to compare the percent of conversion from SVT to NSR between the two methods of administration. The data analysis for this paper was generated using SAS software (Version 9.4) of the SAS System for Unix.

Across the study period, a total of 53 patients were enrolled in the study. The median age of patients was relatively similar in both arms, 55 and 58 years old, respectively. The SS arm was predominately female, 62%, while the TS arm was 48% female (Table 1). Successful conversion to NSR with the first dose was higher in the SS arm 73.1% (95% CI = 0.55 to 0.91) to 40.7% (95% CI = 0.21 to 0.61); noninferiority, p = 0.0176). Successful conversion to NSR with up to three doses was also higher in the SS arm 100% (95% CI = 1.0 to 1.0) to 70.4% (95% CI = 0.52 to 0.89; noninferiority, p = 0.0043). One patient in the conventional TS arm suffered extravasation and phlebitis compared to none in the SS arm.

This study suffers from several limitations. We were unable to recruit 75 patients in each arm due to time constraints thus limiting the power of the study. Additionally, our noninferiority margin was quite large. As we observed more conversion to NSR in the SS arm, the probability that SS is 20% inferior is low. Although the difference between the groups was stronger than initially assumed, our results should be interpreted as pilot data and referenced for future studies. The location of IV access was not recorded, and more distal lines could potentially confound the rates of NSR conversion. The administration technique for the TS method was not recorded and was not standardized. There could have been a difference in administration success depending on the equipment used: stopcock, single-port IV, two-port IV. We can only draw limited conclusion in regards to safety, as the study was not powered to measure this endpoint and event rates were incredibly low in both groups. We did not exclude patients who may have received additional rate controlling medications prior to adenosine administration. Our patients were not randomized and limits the strength of the study. Most importantly, observational studies can provide erroneous conclusions. As such, our current results merit confirmation in a randomized trial. However, this study represents real-world practices thus lends credit to external validity.

Table 1
Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Single Syringe (n = 26)</th>
<th>Two Syringe (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55 (46–72)</td>
<td>58 (47–68)</td>
</tr>
<tr>
<td>Female</td>
<td>16 (62)</td>
<td>13 (48)</td>
</tr>
<tr>
<td>Baseline HR</td>
<td>184 (151–198)</td>
<td>169 (152–189)</td>
</tr>
<tr>
<td>Baseline sBP</td>
<td>133 (109–141)</td>
<td>120 (111–136)</td>
</tr>
<tr>
<td>Baseline MAP</td>
<td>96 (86–112)</td>
<td>83 (66–98)</td>
</tr>
</tbody>
</table>

Data are presented as median (interquartile range) or n (%).
HR = heart rate; MAP = mean arterial pressure; sBP = systolic blood pressure.
There has been provider concern that diluting adenosine prior to administration could reduce the drug’s efficacy. Our results counter this argument and show that the SS method is highly effective with a 73% chance of successful NSR conversion with first dose of adenosine and 100% chance with repeat doses. The differences between the groups were so striking that an ad hoc superiority analysis was performed to determine if only the SS administration method should be recommended. Unfortunately, due to the limited sample size, superiority was not demonstrated.

Our results are comparable to those of Choi et al. who conducted a similar study comparing a TS method to a SS administration method using only 15 mL of saline to dilute the adenosine. Choi et al. reported no difference in successful termination of paroxysmal SVT, with 80 and 85.7% success rates using the SS and TS method (chi-square test, p = 0.39). While they did not report first-dose success rates, total dose used in each group was similar 10.3 mg SS versus 11 mg TS arm suggesting repeat dosing was common in both groups. Similarly, our cohorts had a decrease in mean total dose of adenosine administered. Our data showed a higher chance of successful conversion to NSR in the SS group with repeated doses of adenosine compared to the TS group, 100% versus 70.4%. These data suggest that regardless of dose the SS method may be a superior technique. Adverse events were limited in each group with no reports of dyspnea, bradycardia, or asystole.

In conclusion, the SS administration method is simple and no less effective than the TS method. Physicians should consider using the SS method particularly if no stopcock is available or if only a single-port IV can be used for drug administration. Further randomized control studies should be completed to validate these results.

References
HOT OFF THE PRESS

Hot Off the Press: SGEM #257—EMTALA: It's the Law of the Land

Corey Heitz, MD†, Justin Morgenstern, MD‡, Christopher Bond, MD§, and William K. Milne, MD¶

ABSTRACT
The Office of the Inspector General has the authority to levy fines relating to violations of the Emergency Medicine Treatment and Labor Act (EMTALA) for both medical and psychiatric care. Terp et al. have described the incidence of violations and penalties levied for psychiatric cases and compared them to that for medical. This article reviews that article and the podcast recorded with Dr. Terp and the ensuing discussion in the podcast and online.

BACKGROUND
The Emergency Medicine Treatment and Labor Act (EMTALA) was passed into law in the United States in 1986 to prevent patient dumping and inadequate initial care of emergency department (ED) patients who were uninsured.1 Under EMTALA, patients presenting to an ED must have a medical screening evaluation, stabilization of emergency conditions, and timely transfer to a hospital with adequate services.2 In recent years, the Center for Medicare and Medicaid Services has confirmed that EMTALA applies not only to medical but also psychiatric cases.3

ARTICLE SUMMARY
The study described is a retrospective observational study evaluating EMTALA-related civil monetary penalties between 2002 and 2018. The authors obtained case descriptions from the Office of the Inspector General (OIG) relating to the EMTALA law. Psychiatric cases were identified and described and then compared with medical cases for the same time period. Psychiatric emergencies were involved in 44 (19%) of cases, with a mean settlement value of $85,488. Cases with medical emergencies had a mean settlement value of $32,004. No psychiatric cases were settled against the physician individually. Five of the six largest EMTALA-related settlements were for psychiatric cases, with the three largest being $1,295,000, $260,000, and $200,000. A total of 84% of the EMTALA violations for psychiatric cases were for failure to provide an adequate screening evaluation.

QUALITY ASSESSMENT
This was a well-done retrospective study. Cases were adequately identified and described in sufficient detail. Comparisons between medical and psychiatric cases were performed and accurate. A detailed case study was provided to highlight what occurs when an EMTALA violation is suspected and investigated. Any retrospective study is limited by the nature of the database from which it gets its data. While the presumption is that the information from the OIG is complete, we have no measurement of this. Cases may have been missed due to search strategy or due to data
entry errors. In addition, this is a subset of all EMTALA violations and includes only those with financial penalties levied. As such, there may be other areas for improvement not identified in this data. Finally, EMTALA is a U.S. federal law, and a distinction exists between good legal practice (as defined in one country) and good medical practice overall.

**KEY RESULTS**

A total of 230 civil monetary penalties relating to EMTALA were levied between 2002 and 2018, with 222 (97%) levied against facilities and eight (3%) against individual physicians. A decline in settlements related to nonpsychiatric emergencies was noted, with an increase in those related to psychiatric emergencies.

- Five (83%) of the six settlements more than $100,000 were for psychiatric complaints;
- The three largest settlements were $1,295,000, $260,000, and $200,000;
- Psychiatric cases: mean = $85,488.64 (95% CI = $25,766.07 to $145,211.20);
- Nonpsychiatric cases: mean = $32,004.45 (95% CI = $28,802.75 to $35,206.16).

**AUTHORS’ COMMENTS**

Civil monetary penalties for EMTALA violations involving psychiatric patients are increasing and are very expensive for hospitals. Institutions need to have protocols in place to avoid inadequate stabilization, screening, and inappropriate transfer of patients.

**Twitter Poll**

**Paper-in-a-pic from Kirsty Challen, @EMOttawa**

**EMTALA penalties for psychiatric emergencies.**

<table>
<thead>
<tr>
<th>230 settlements from Office of the Inspector General 2002-18</th>
</tr>
</thead>
<tbody>
<tr>
<td>44 (19%) psychiatric emergencies</td>
</tr>
<tr>
<td>All against hospital</td>
</tr>
<tr>
<td>Mean settlement</td>
</tr>
<tr>
<td>$32,004</td>
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</tbody>
</table>

**TAKE-TO-WORK POINTS**

Patients with psychiatric emergencies are a high-risk population. Physicians and institutions need to ensure that medical screen evaluations are adequate, and resources are in place to provide appropriate care or timely transfer of these patients.

**References**

Rocuronium Versus Succinylcholine for Rapid Sequence Intubation

Abdullah Bakhsh, MBBS, FAAEM

NARRATIVE

Rapid sequence intubation (RSI), placing a tube into the trachea facilitated by rapid sedation and paralysis to improve ventilation and oxygenation, is a common procedure in emergent, critical care, and operating room settings. There is great interest in drugs that improve the process. The two most commonly used paralytic agents in the emergency department (ED) are succinylcholine (depolarizing) and rocuronium (nondepolarizing). Traditionally succinylcholine has been the preferred muscle relaxant for RSI because of its rapid onset of 40 to 60 seconds and a short duration of action lasting 6 to 10 minutes. However, succinylcholine’s depolarizing action may lead to hyperkalemia, possibly inducing fatal cardiac arrhythmia. As a result, it is contraindicated in patients with known hyperkalemia, severe burns (beyond 48 hours), major crush injuries (beyond 48 hours), denervation syndromes, and muscular dystrophy. Rocuronium, however, is a steroid-based nondepolarizing muscle relaxant, which has been proposed for creating intubating conditions similar to those of succinylcholine. The duration of action is longer, lasting 37 to 72 minutes, and has an antidote, while the only contraindication is allergy.

The Cochrane review summarized here determines whether rocuronium creates intubating conditions comparable to those of succinylcholine, by comparing the Goldberg scale (Table 1). This scale allocates a score (1 through 4) for each of the following items: ease of intubation, vocal cord movement, and patient response to intubation. This scale gives a total point value of 12, in which 3 represents excellent, 4 to 6 represents good, 7 to 9 represents poor, and 10 to 12 represents inadequate intubating condition.

The Cochrane review included randomized controlled trials and controlled clinical trials meeting the following inclusion criteria: 1) score of intubation was reported as the main outcome, 2) compared succinylcholine with rocuronium, and 3) dose of rocuronium was at least 0.6 mg/kg (0.6–1.2 mg/kg) and dose of succinylcholine was at least 1 mg/kg. The sedative agents used for induction were thiopental,
benzodiazepines, propofol, etomidate, or ketamine. It is important to note that the majority of included trials were conducted in nonemergent settings and rocuronium was used at low doses (0.6–0.7 mg/kg) in most trials.

Overall, the meta-analysis revealed that succinylcholine was superior to rocuronium for achieving excellent intubating conditions (relative risk [RR] = 0.86, 95% confidence interval [CI] = 0.8 to 0.92, absolute risk reduction [ARR] = 12%, number needed to treat [NNT] = 8) and for clinically acceptable conditions (RR = 0.97, 95% CI = 0.95 to 0.99, ARR = 5%, NNT = 19). Heterogeneity among trials for both endpoints was very high. However, when dosing of the medication was analyzed, succinylcholine was superior only to low-dose (0.6–0.7 mg/kg) rocuronium and there was no difference in outcome between the groups when the recommended higher dose (0.9–1.0 mg/kg) of rocuronium was used. Since the recommended dose for rocuronium in RSI is higher than the dose used in the Cochrane’s main analysis, we did not include the efficacy endpoints for the low-dose rocuronium in the summary table.

### CAVEATS

The safety of RSI is sought by providers who have long dealt with periprocedural complications and general instability with this high-stakes procedure. It is important to note that the Cochrane review included only five studies (1,073 participants) occurring in the emergency setting. Therefore, the findings of the systematic review might not be applicable to ED. Additionally, measuring the endpoint of “excellent” and “clinically acceptable” intubating conditions has an uncertain clinical relevance to emergency physicians due to its subjectivity and potential for bias. A more important outcome is first-pass success along with peri-intubation adverse events, such as hypoxia, hypotension, and esophageal intubation.

The vast majority of studies in the Cochrane review compared succinylcholine with low-dose rocuronium (0.6–0.7 mg/kg). When using rocuronium, quality intubating conditions are achieved with higher doses (>0.9 mg/kg), whereas lower doses may take a longer onset of action resulting in the possibility of delayed/failed endotracheal tube placement or compromising the quality.

Since the publication of this Cochrane review in 2015, another study by April et al. based on registry data, has been published in 2018. This study included 4,275 intubations from the National Emergency Airways Registry (NEAR) comparing first-pass success rates and adverse events between succinylcholine and rocuronium. This analysis showed no difference in first-pass success (87.0% vs. 87.5%) or adverse events (14.7% vs. 14.8%) between succinylcholine and rocuronium groups. Moreover, the mean dose of succinylcholine was 1.8 mg/kg, whereas the mean dose of rocuronium was 1.2 mg/kg. These findings confirm the results in the subgroup analysis of the Cochrane review that compared succinylcholine with high-dose rocuronium.

Preferring one agent based on time of onset and duration of action is common and debated. Rocuronium is longer acting and has a reversal agent. Many ED physicians have more experience using succinylcholine, which is shorter acting, making a reversal agent less often helpful. Some clinicians opt for rocuronium to avoid adverse reactions (e.g., hyperkalemia) and to have the option of reversal on demand. Others recommend succinylcholine, preferring shorter paralysis.

Notably, heterogeneity in the primary and secondary outcome analyses was very high. This suggests these results should be interpreted with caution.

In summary, we believe that comparing succinylcholine with suboptimal low doses of rocuronium is inappropriate. We have based our finding of no difference and our color assignment (Yellow—further research needed) on the results of the proper comparison. We look forward to clinical trials comparing high-dose rocuronium (>0.9 mg/kg) with succinylcholine for RSI in the ED setting, while focusing on

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**Table 1**

<table>
<thead>
<tr>
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<tbody>
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<td>Difficult</td>
<td>Poor</td>
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<td>Open</td>
<td>Movement</td>
<td>Closed</td>
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<td>None</td>
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<td>Moderate coughing</td>
<td>Severe coughing</td>
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</table>
relevant outcomes of first-pass success rates and adverse outcomes.

References
Utility of Spinal Immobilization in Patients With Penetrating Trauma

Brit Long, MD1, Alex Koyfman, MD2, and Michael Gottlieb, MD3

<table>
<thead>
<tr>
<th>NNT color recommendation</th>
<th>Red (harm &gt; benefit)</th>
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<tr>
<td>Summary heading</td>
<td>Spinal immobilization for penetrating trauma is associated with increased mortality and does not mitigate neurologic deficits</td>
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<tr>
<td>Benefits in NNT</td>
<td>No one benefitted</td>
</tr>
<tr>
<td>Benefits in percentages</td>
<td>No one benefitted</td>
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<tr>
<td>Harms in NNT (NNH)</td>
<td>1 in 10 were harmed (died)</td>
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<td>Harms in percentages</td>
<td>10% higher risk of mortality</td>
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<td>Efficacy endpoints</td>
<td>Mitigation of neurologic deficit and potentially reversible deficit</td>
</tr>
<tr>
<td>Harm endpoints</td>
<td>Mortality</td>
</tr>
<tr>
<td>Who was in the studies?</td>
<td>24 studies comprising 155,089 total patients</td>
</tr>
</tbody>
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NARRATIVE

Spinal precautions are a key component of many emergency medical services (EMS) protocols.1,2 However, there is limited evidence regarding the ability of spinal immobilization (i.e., cervical collars and/or longboards) to improve patient outcomes among those with penetrating trauma, and spinal immobilization may increase complications.3,4 These complications include increased intracranial pressure, local pressure injury, missed penetrating injury, and delay in the successful performance of vital procedures (e.g., endotracheal intubation).1,3,4 Moreover, even if a cervical spine collar or longboard is properly applied, patients are often not adequately immobilized.1 While prior evidence suggested that few EMS and emergency department providers were aware of the potential harms with spinal immobilization in penetrating trauma,5 it has not been established that this potentially harmful intervention actually improves patient-relevant outcomes.

Investigators for the Eastern Association for the Surgery of Trauma (EAST) conducted a systematic review and meta-analysis that included randomized controlled trials, prospective observational or retrospective studies, and case–control studies evaluating the effects of spinal immobilization in adults with penetrating trauma (gunshot or stab wounds).1 Patients ≥ 13 years were considered to be adults, as these patients are typically treated as adults in many centers. Spinal immobilization was defined as the use of a cervical collar and/or longboard. The primary outcomes were mortality, neurologic deficits, and potentially reversible neurologic deficits (defined as deficit that could be either improved or reversed with definitive spinal immobilization). Secondary outcomes included missed injury and failed intubation. If pooling of data was inappropriate (moderate to high heterogeneity), the authors conducted a qualitative instead of quantitative analysis.

The systematic review included studies (n = 155,089) that met the inclusion criteria for qualitative analysis,
and five studies (n = 46,092) were suitable for quantitative analysis. All included studies were retrospective. No study demonstrated a benefit of spinal immobilization for mortality and neurologic injury. The incidence of neurologic injury was low, ranging from two to 76 per 1,000 patients. Studies focusing on patients with head and neck injuries found a higher incidence of neurologic injury, with 136 to 204 per 1,000 patients. Rates of potentially reversible neurologic injury were consistently very low as well. Quantitative analysis (meta-analysis) of the five appropriate studies found an increased risk of harm with regard to mortality (relative risk [RR] = 2.4, 95% confidence interval [CI] = 1.07 to 5.4; absolute risk difference [ARD] = 10.1%, 95% CI = 0.5% to 31.7%; and number needed to harm [NNH] = 10). There was no statistically significant difference for neurologic deficit (RR = 4.16, 95% CI = 0.56 to 30.89) or potentially reversible deficit (RR = 1.19, 95% CI = 0.83 to 1.70), although the point estimates favored no immobilization. There were insufficient data to perform quantitative analysis regarding failed intubation or missed injury.

CAVEATS

While this meta-analysis suggests that spinal immobilization in penetrating trauma is associated with increased mortality and does not reduce the risk of neurologic injuries, several limitations should be noted. All the included studies were retrospective and thus subject to the limitations inherent in this study design. The majority of studies assumed that spinal immobilization was performed based on protocol, but few studies described the type or extent of immobilization. Many studies evaluated only the projected risk versus benefit through assessment of the presence of true injury. The studies varied in their definition of the “potential benefit” of spinal immobilization, especially in regard to potentially preventable neurologic deficits. Additionally, the meta-analysis did not analyze penetrating head injury and penetrating neck injury separately. Some studies utilized surgical fixation as a surrogate outcome for reversible neurologic deficit, but these studies found that fixation may have prevented worsening of injury that had already occurred, rather than reversing it. Only five studies were designated for quantitative analysis. For mortality, the pooled estimate relied heavily on two studies, one of which (n = 45,284 patients) contributed most of the events. Moreover, a disproportionate number of patients were in the no-immobilization group versus the immobilization group. While the data suggest a NNH of 10, this may be related to bias in the single large retrospective study comprising the majority of the included patients. For mortality, the risk of bias was judged to be low and the quality of evidence moderate. For potentially reversible neurologic deficit, the risk of bias was low but the included studies varied widely in the definition of “potentially reversible,” which, given the rarity of injury, resulted in imprecision and wide CIs.

Nevertheless, this analysis suggests that spinal immobilization in adults with penetrating trauma is associated with an increase in mortality and not only no benefit but also apparent actual harm in terms of neurologic deficit or potentially reversible neurologic deficits. We have thus assigned a color recommendation of red (harm > benefits). Spinal immobilization is not recommended for routine use in penetrating trauma.

REFERENCES

Stressing Out About the Heart: A Narrative Review of the Role of Psychological Stress in Acute Cardiovascular Events

Paul I. Musey Jr., MD, Katharina Schultebraucks, PhD, and Bernard P. Chang, MD, PhD

ABSTRACT

Objectives: Survivors of acute cardiovascular disease (CVD) events, such as acute coronary syndrome (ACS) and stroke, may experience significant psychological distress during and following the acute event. Long-term adverse effects may follow, including the development of posttraumatic stress disorder (PTSD), increased overall all-cause mortality, and recurrent cardiac events. The goal of this concepts paper is to describe and summarize the rates of adverse psychological outcomes, such as PTSD, following cardiovascular emergencies, to review how these psychological factors are associated with increased risk of future events and long-term health and to provide a theoretical framework for future work.

Methods: A panel of two board-certified emergency physicians, one with a doctorate in experimental psychology, along with one PhD clinical psychologist with expertise in psychoneuroendocrinology were co-authors involved in the paper. Each author used various search strategies (e.g., PubMed, Psycinfo, Cochrane, and Google Scholar) for primary research and reviewed articles related to their section. The references were reviewed and evaluated for relevancy and included based on review by the lead authors.

Results: A meta-analysis of 24 studies (N > 2,300) found the prevalence of ACS-induced PTSD at nearly 12%, while a meta-analysis of nine studies (N = 1,138) found that 25% of survivors of transient ischemic attack and stroke report PTSD symptoms. The presence of PTSD doubles 3-year risk of CVD/mortality risk in ACS survivors. Cardiac patients treated during periods of ED overcrowding, hallway care, and perceived poor clinician-patient communication appear at greater risk for subsequent PTSD.

Conclusions: Psychological stress is often present in patients undergoing evaluation for acute CVD events. Understanding such associations provides a foundation to appreciate the potential contribution of psychological variables on acute and long-term cardiovascular recovery, while also stimulating future areas of research and discovery.

INTRODUCTION

Cardiovascular diseases (CVD), including coronary heart disease, heart failure, and stroke, remain the leading cause for morbidity and mortality worldwide, leading to millions of hospitalizations and accounting for approximately one-third of deaths in the United States. Emergency clinicians serve on the...
While most acute care resources and efforts appropriately focus on the detection and stabilization of acute CVD events, like acute coronary syndrome (ACS), the psychological experience of patients during medical events may also play an important role in the assessment and recovery of these patients. An emerging body of literature has found that for some patients, the psychological stress experience during CVD events may be durable and may even be associated with the development of adverse long-term anxiety symptoms, such as posttraumatic stress disorder (PTSD). While these psychological outcomes are important in and of themselves, they have also been associated with impaired cardiovascular recovery and increased risk for the development of new and recurrent CVD events. The interplay of psychological stress with personality and emotion is multidimensional and complex. Further, the psychological experience of acute illness may impact CVD patients on multiple levels, from autonomic stress to secondary cardiovascular behavior (e.g., medication adherence, emergency department (ED) recidivism, and rehospitalization). The goal of this concepts paper is to describe and summarize, for emergency clinicians, the rates of adverse psychological outcomes, such as PTSD, following cardiovascular emergencies and to review how these psychological factors are associated with increased risk of future events and long-term health. In doing so, we seek to introduce a theoretical framework for understanding the relationship between psychological variables and acute CVD, while also establishing future areas of research.

**METHODS**

A panel of two board-certified emergency physicians, one with a doctorate in experimental psychology, along with one PhD clinical psychologist with expertise in psychoneuroendocrinology, were co-authors involved in the paper. Each author used various search strategies (e.g., PubMed, Psycinfo, Cochrane, and Google Scholar) for primary research and reviewed articles related to their section. The references were reviewed and evaluated for relevancy and included based on review by the lead authors. This was a nonsystematic research synthesis and narrative review to evaluate the evidence regarding the contribution of psychological variables to acute CVD events and sequelae.

**RESULTS**

The Psychological Stress Experienced by Some Patients Undergoing A CVD Event May Lead to the Development of Sustained Adverse Psychological Outcomes

Past work has found that psychological contributors, such as anxiety and depression, may be associated with acute presentations of nonpsychiatric somatic complaints such as chest pain. However, distinct from this psychosomatic literature, the anxiety and stress experienced by individuals undergoing an acute evaluation of a CVD event may lead to the development of longer-term psychological morbidity, including posttraumatic stress disorder (PTSD). According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), PTSD is a psychiatric condition which can develop after an individual experiences or witnesses a traumatic event. Triggers may include physical or sexual assault, natural disaster, combat, and other forms of threatened death. The resulting symptoms cause a significant amount of distress and impair the individual’s ability to function. In addition to symptoms lasting more than 1 month, there are four criteria that are required: 1) intrusive thoughts of the traumatic event through flashbacks or dreams; 2) avoidance—individuals will avoid situations, people, and places that bring on reminders of the traumatic event; 3) negative cognitions and mood—distorted beliefs regarding blame or shame around the event; and 4) arousal—sleep disturbance, hypervigilance, and aggressive or self-destructive behavior.

In a meta-analysis of 24 studies (N > 2,300), the prevalence of ACS-induced PTSD worldwide was nearly 12%. Additionally, evidence suggests that the subjective psychological experience of having a “perceived” life-threatening event may play an important role, regardless of whether there was an actual CVD diagnosis. In a cohort of 1,000 ED patients, there was essentially no difference in the rate of 1-month positive PTSD screens in the two-thirds of patients who ruled out for acute ACS (19%) versus those who ruled in (17%). Interestingly, in a study of 143 patients with either non-ST elevation myocardial infarction or unstable angina, patients who were managed medically had higher rates of ACS-induced PTSD than those who underwent catheterization regardless of whether they were revascularized. The presence of sustained psychological outcomes exists along the spectrum of CVD, including transient ischemic attack (TIA) and
stroke survivors, where approximately 25% are found to have developed significant PTSD symptoms within one year of the event according to a meta-analysis of more than 1,100 patients. Unfortunately, these PTSD symptoms are long-lasting and not only associated with worse overall health status including poor quality of life but also adverse effects on overall cardiovascular well-being.\textsuperscript{19,20} Along with PTSD, anxiety and depression post-CVD event are also prevalent at a rate of approximately 15\%\textsuperscript{21,22} and associated with a high risk for poor outcomes at 1 year including impaired quality of life, recurrent chest pain, health care resource utilization, and lifestyle behavioral changes.\textsuperscript{23} One meta-analysis of approximately 25,000 patients placed the pooled proportion of depression at 25\% (95\% confidence interval [CI] = 16\% to 33\%) in the 1- to 5-year period after stroke.\textsuperscript{24}

This development of PTSD and other psychological sequelae after CVD evaluation or events may be due to a number of a diverse range of preexisting trait, state, neurophysiological, and environmental factors.\textsuperscript{25} Given the subjective experience of fear, cognitive factors, including a sense of loss of control, may help drive the development of PTSD.\textsuperscript{26} Unsurprisingly, patients who perceived more threat (e.g., a sense of danger, risk of serious medical harm due to their symptoms) during their ED evaluation had higher threat recall and were more vulnerable to developing posttraumatic psychological problems.\textsuperscript{27} Additionally, factors of the ED environment itself may also contribute to the development of adverse psychological outcomes during acute medical events. ED crowding has been associated with outcomes, ranging from delays in antibiotic administration to decreased patient satisfaction.\textsuperscript{28,29} ED crowding has also been shown to affect the development of psychological distress medically ill patients. In a study of 912 patients undergoing ACS evaluation, as objective measures of ED crowding increased, patients with prior depression reported the perceptions of the ED being more stressful and of receiving poorer care.\textsuperscript{30} Other work by Edmondson et al.\textsuperscript{31} found that increased tertiles of ED crowding (as operationalized by EDWIN scores), were associated with increased 1-month PTSD symptoms at follow-up.\textsuperscript{32}

Adding to the complexity of these environmental factors is the element of social interactions in the ED. In 763 ED patients evaluated for ACS, significantly higher 1-month PTSD symptoms were found in the 12\% of patients who perceived a high likelihood that a “nearby” patient would die.\textsuperscript{33} Additionally, in a cohort of 484 ED patients, negative social support in the ED (needing to comfort their social support person and/or their social support person making them anxious) was associated with developing posttraumatic stress symptoms after evaluation in the ED.\textsuperscript{34} Moreover, simply bringing close others (spouse/partner or child) to the ED during these evaluations is associated with increase recall of threat during the ED evaluation and ultimately correlated with subsequent PTSD symptoms.\textsuperscript{35} Whatever the ultimate mechanism may be, the fact that PTSD and these other psychological comorbidities are so prominent after CVD evaluation or event is notable because PTSD is often associated with an external traumatic stimulus (motor vehicle accident, combat, assault, etc.). The enduring somatic threat (EST) model proposed by Edmonson suggests that the evaluation and experience of life-threatening medical events, i.e., myocardial infarction or stroke leads to the development of PTSD-like symptoms which is unique and goes beyond what is traditionally accepted as an adjustment disorder.\textsuperscript{6,36} In the appraisal of this EST model, interestingly, for patients undergoing ACS evaluation, threat perception levels were not significantly different between patients who were ultimately diagnosed with ACS versus those without ACS.\textsuperscript{37} Additionally, those with higher peritraumatic ED cardiac threat had higher ongoing cardiac threat levels at 1-month follow-up evaluations which were associated with ACS-induced PTSD.\textsuperscript{38} In this model, younger patients appear to be more vulnerable to the effects of threat perception and developing posttraumatic stress symptoms after ACS evaluation.\textsuperscript{39} These findings are especially important as they suggest that the adverse psychological outcomes associated with ACS-induced PTSD may be associated with not only psychological, but also cardiovascular outcomes, such as major adverse cardiovascular events (MACE).

### Psychological Outcomes Such as PTSD Following Acute CVD Are Associated With Adverse CVD Outcomes in Survivors

The negative effects of psychological stress such as PTSD experienced by some CVD survivors may not be limited to behavioral outcomes, but may also have adverse effects on broader health outcomes such as recurrent CVD risk and mortality.\textsuperscript{4,7,22,40} Past work has found that preexisting psychiatric disease is associated with increased odds of death after ED discharge compared with those who do not have any known...
psychiatric comorbidity; notably, these deaths were largely medical in nature, with ACS being the most common cause.\(^5\) In a prospective cohort study (\(N > 220,000\)), psychological distress displayed a dose–response association with increased risk of ACS (30 and 18% in men and women, respectively) as well as stroke (24 and 44%, respectively, in men and women) even when controlling for traditional sociodemographic covariates.\(^4\) In the case of patients developing PTSD symptoms following CVD evaluation, recent evidence has found a significant increase in cardiovascular mortality and recurrent events, even after adjusting for depression and other covariates.\(^42\) A meta-analysis of three studies and 609 patients found that ACS survivors who developed PTSD following ACS had a doubling of ACS recurrence or mortality in the subsequent 1 to 3 years (risk ratio \(= 2.20\), 95% CI = 1.69 to 2.37) relative to patients with no PTSD symptoms.\(^4\) Intrusive symptoms (nightmares, flashbacks, and intrusive thoughts or images) have been associated with an adjusted hazard ratio of <3 for the combined outcome of MACE and all-cause mortality even when controlling for clinical characteristics in addition to age, sex, and depression.\(^43\) Similarly, among a cohort of more than 800 patients followed after their ACS presentation, patients who screened positive for major depressive disorder or generalized anxiety disorder were at greater risk for MACE in the 2 years following their event compared to those who did not screen positive.\(^44\) This is consistent with Shibeshi et al.,\(^45\) who also showed that the hazard ratio of high anxiety with relation to MACE was 1.97. Likewise, PTSD is associated with increased stroke risk with a hazard ratio of 3.47 for ischemic stroke.\(^46\)

Comparable to PTSD, anxiety has been associated with a 71% higher risk for stroke and a 41% increased risk of cardiovascular mortality in a meta-analysis of 28 studies (\(N > 222,000\)).\(^47\) With regard to depression, in a cohort of 3,600 patients who survived stroke, depression was associated with a mortality hazard ratio of 1.41.\(^48\) Further, in a recent meta-analysis including seven studies looking at poststroke depression in patients early after the CVD event (\(N > 119,000\)), depression was associated with a short-term mortality relative risk of 1.50.\(^49\) Similar findings were found in a 2019 meta-analysis of 15 prospective cohort studies (\(N > 250,000\)) showing a poststroke depression-related all-cause mortality hazard ratio of 1.59.\(^50\) These results mirror the all-cause mortality hazard ratio of 1.9 at 2 years seen in a meta-analysis of over 30 studies of post-ACS depression.\(^51\)

### Psychological Outcomes in Patients Evaluated for CVD May Also Impact Health Care Utilization and Recidivism (e.g., Rehospitalization) in CVD Survivors

Psychological variables among patients evaluated for potential CVD may also impact other health care measures such as ED recidivism and health care utilization. In a cohort of 167 patients presenting to the ED with “low-risk” chest pain, 47% screened positive for abnormally high-anxiety symptoms and these patients displayed a relative risk for two or more return ED visits of 9.1.\(^12\) Similarly, in a longitudinal analysis of 196 seeking evaluation for chest pain, anxiety, and interpretive fear at evaluation were associated with increased health care utilization.\(^52\) Furthermore, acute stress disorder symptoms or “early PTSD” in a sample of 974 patients evaluated for ACS was associated with 30-day ED and hospital (all-cause) readmissions with an adjusted odds ratio of 1.24.\(^7\)

Likely contributing to the recidivism, morbidity, and mortality outlined above, CVD-related PTSD may be associated with medication nonadherence.\(^53\) Kronish et al.\(^54\) showed that in a cohort of 535 poststroke patients, 18% screened positive for PTSD and had a relative risk of medication nonadherence of 2.7 compared to patients without PTSD. This nonadherence may be due in part to stroke survivors’ concerns and worry regarding their medications including long-term effects.\(^8\) One theory is that the medications themselves serve as a “traumatic reminder” as shown in a cohort of 424 patients evaluated in the ED for suspected ACS, higher PTSD scores were correlated with an increased likelihood of missing doses of cardiovascular medications to avoid reminders of the interaction, anxiety, and thoughts of future risk.\(^55\) This is significant as medication nonadherence has been shown to be associated with worse adverse events and even mortality in myocardial infarction survivors.\(^56\)

### An Opportunity to Develop a Multidisciplinary Approach to Understand Biopsychosocial Systems in the Management of CVD

The concept of a nosocomial associated psychological stress model may help frame our understanding of psychological stress during life-threatening conditions, such as ACS.\(^57\) Similar to established evidence
suggesting the presence of nosocomial risks during hospitalization, ranging from multidrug-resistant infections to delirium in the hospital setting, there may be nosocomial psychological effects associated with the ED and acute CVD events, ranging from increased anxiety during hospitalization, to dysregulations in sleep/wake cycles, and nutrition habits, leading to increased affective symptoms such as depression. Additionaly, is screening for anxiety, work in other patient samples and disease processes is validated in a cohort of ED patients treated for ACS brief ED-based self-report seven-item screening tool for of life threat during medical evaluation. Recently, a bedside assessments to be used at the time of patient inclusion for risk stratification. Along these lines, there have been multiple bedside screening tools for mood disorders used previously in the outpatient setting including the Hospital Anxiety and Depression Scale (HADS), the Generalized Anxiety Disorder 7-item scale (GAD-7), Patient Health Questionnaire 9-item (PHQ-9), scale for depression, or the four-item screener for anxiety and depression (PHQ-4). However, few such tools have been developed explicitly for the acute care setting with a focus on the perception of life threat during medical evaluation. Recently, a brief ED-based self-report seven-item screening tool for acute psychological stress (e.g., threat perception) was validated in a cohort of ED patients treated for ACS events, which may show promise, although future work in other patient samples and disease processes is required. Additionally, is screening for anxiety, depression, or threat perception sufficient as single domains to be used as predictive tools or should they be paired sequentially with posttraumatic screening tools such as the Posttraumatic Adjustment Scale (PAS), which has demonstrated specific utility in the ED for the identification of patients at risk for developing PTSD after evaluation. Moreover, how does this approach compare with multidomain assessment in the ED using computer adaptive screening tools such as the Computerized Adaptive Test for Mental Health (CAT-MH), which can assess multiple domains such as anxiety, depression, substance abuse, and PTSD simultaneously?

After optimizing bedside assessments and identification of at-risk ED patients, the next major research questions should focus on how best to assess acute and chronic psychological stress on the development of CVDs? Areas for further investigation may include secondary cardiovascular behaviors (tobacco abuse, poor diet, inadequate physical activity, and medication non-adherence), acute on chronic systemic inflammation, vascular endothelial dysfunction, and persistent autonomic dysfunction as pathophysiologic mechanisms whereby psychological stress influences CVD event. Additionally, further investigation is needed regarding the relative contributions of both patient-centered and environmental factors, such as ED crowding and length of stay to CVD outcomes. There may also be significant differences among the diverse demographics of patients with cardiac disease. Factors such as age, sex, gender, ethnicity, and race may all have some moderating factors in the development of psychological stress during and following an acute cardiac event. Future work should be aimed at exploring any potential subgroup differences and processes.

Finally, the end-goal of this work should be to develop ED interventions and processes of care that help to mitigate these adverse CVD outcomes. Accessible options include scripted communication and shared decision-making discussions initiated by the ED provider or support staff such as social workers as a part of a screening intervention and referral to treatment (SBIRT) model. Existing evidence has found that bedside communication between emergency clinicians
and patients is an important contributor of ED-based threat perception and threat. For example, a sample of 474 patients treated for ACS found that perceived positive clinician–patient communication was associated with lower acute stress/posttraumatic stress symptoms at 30-day follow-up. Other recent work has found that patient perception of provider compassion was associated with decreased subsequent PTSD symptoms at follow-up. Taken together, such bedside interventions may help reduce the development of such adverse psychological outcomes following acute illness in the ED setting. Beyond bedside communication, there should be exploration of multidisciplinary treatment options such as early behavioral health consultation for a subset of high-risk patients being treated for CVD. Further, the feasibility of referral of atrisk patients, particularly without a CVD diagnosis, directly to cognitive behavioral therapy or mindfulness-based stress reductions either in-person or app-based options should be examined.

LIMITATIONS

Given the scope of our topic, our narrative review was necessarily broad in scope and attempted to encompass literature from a diverse group of fields both within emergency medicine as well as behavioral medicine and psychology. Unlike a systematic review, where we had a single focused question with outcome, our concepts paper drew on multiple questions and processes to succinctly summarize for readers several key points. While we had three separate searches for this study, articles may have been overlooked or not included in this narrative review.

CONCLUSIONS

Being evaluated and treated for life-threatening events such as cardiovascular disease is frightening for many patients, which may have significant adverse effects on physiological and psychological recovery. An increased awareness of the presence of such psychological effects during cardiovascular disease is an important first step to identifying and assessing patient risk during cardiovascular events. Building on this evidence, an interdisciplinary program of work aimed at supporting cardiovascular disease in the context of acute medical stabilization and psychological support may ultimately lead to improvements in both patient psychological and cardiovascular well-being.

REFERENCES


News From Lake Wobegon . . . Clinician Gestalt Debunked?

In Garrison Keillor’s Lake Wobegon, “all the women are strong, all the men are good-looking, and all the children are above average.” In this fictional place of statistical impossibility, everyone is “better” than his neighbor. This fantasy world is akin to the house of medicine where we each have the tendency to believe that we are the “above average” clinician with superior insight, judgment, and reasoning. This “self-enhancement” bias empowers our gestalt far beyond its limits.

As emergency care providers we are frequently tasked with the challenge of risk stratifying patients with acute chest pain. In these high-stakes patient encounters, clinician gestalt is often used as the primary determinant of treatment and disposition decisions. Gestalt is defined as a provider’s impression of a patient’s risk following completion of history taking, physical examination, and review of initial diagnostic testing. Studies suggest that we often overestimate the risk of acute coronary syndrome (ACS) occurring in our patients, leading to unnecessary, expensive, and potentially harmful cardiac testing.1–3 Each year we spend billions of dollars evaluating patients for potentially emergent cardiac conditions,4,5 but the yield of these evaluations remains low.3,5,6 On the other hand, sometimes we underestimate a patient’s risk, which can result in mortality or significant morbidity. Unfortunately, studies estimate that emergency physicians miss 2% to 4% of patients with ACS.7,8 Patients discharged with missed ACS have a mortality rate twice that of patients admitted for ACS.8 Furthermore, missed ACS is a top cause of malpractice claims against ED clinicians, with payouts typically in excess of $100,000.9,10 Thus, our current practice patterns are not worthy of our Lake Wobegon mentality.

As clinicians, our patient evaluations naturally begin at the bedside. However, multiple studies suggest that the history and physical examination are insufficient to diagnose or exclude ACS. Less than 30% of patients with ACS report the classic or “typical” symptoms, such as radiating pain, left-sided chest pain, and vomiting.11,12 A large meta-analysis demonstrated that signs and symptoms alone are unable to rule in or rule out the diagnosis of ACS.13 Furthermore, a patient’s initial electrocardiogram (ECG) is normal in up to 25% of patients with ACS.12 Given the limited utility of a patient’s history, physical examination, and ECG for detecting ACS, it is not surprising that clinician gestalt performs poorly in most clinical trials. In a study of 912 patients with chest pain and a nonischemic ECG, gestalt was about as effective as a coin toss.14 A study by Hess and colleagues12 found that gestalt missed nearly one-quarter of patients with ACS. Body et al. assessed gestalt in 458 patients with acute chest pain, demonstrating that gestalt identifies less than 25% of patients as low-risk and safe for ED discharge. Additionally, the sensitivity and negative predictive value of gestalt were unacceptably low. Mokhtari et al. found that gestalt had a 6% ACS miss rate, far above what clinicians are willing to accept.7,15 Other studies have similar results, each demonstrating that gestalt has poor sensitivity and negative predictive value for the exclusion of ACS in the ED setting.16–18 In addition, a study comparing accelerated diagnostic protocols to gestalt assessments with serial troponins found that gestalt underperformed the HEART Pathway in both sensitivity for ACS and proportion of patients identified as low risk.18

Despite these numerous studies documenting the inadequacy of clinician gestalt, the viewpoint that it can be used to safely identify ED patients with acute chest pain for early discharge is recalcitrant and continues to be promulgated by some thought leaders in

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emergency cardiovascular care. They frequently point out that previous gestalt studies were small single-site studies and that many were not designed a priori to assess gestalt. Oliver et al.\textsuperscript{19} have closed this evidence gap by conducting the largest and perhaps best designed evaluation of gestalt to date. The results, as expected, are similar to prior evaluations of gestalt. In nearly 1,400 patients across 18 sites, gestalt was unable to accurately “rule in” or “rule out” ACS. Among patients deemed low risk with gestalt assessments of “definitely not” or “probably not” ACS, 5% of them were ultimately diagnosed with ACS. While adding objective measures such as ECG and troponin to gestalt improved diagnostic accuracy, sensitivity for the detection of ACS remained unacceptably low. Even when clinicians thought that the diagnosis was “definitely ACS,” they were correct < 75% of the time. Thus, without further objective measures, emergency care providers should neither feel comfortable discharging patients home based on low-suspicion gestalt nor should they feel confident initiating aggressive therapies on those with high-suspicion gestalt.

While some clinicians remain convinced of their own superior diagnostic skills and are opposed to protocols and pathways, labeling their use as cookbook medicine, the evidence regarding gestalt is clear. When it comes to chest pain risk stratification, if we ignore protocolized care, then we are doing so at our own and our patients’ peril. Oliver et al. demonstrate that relying on gestalt alone is a dangerous practice that no longer meets the standard of care. Recent studies have demonstrated the safety and effectiveness of accelerated diagnostic protocols for patients with acute chest pain.\textsuperscript{20–22} Thus, providing the highest-quality care for our patients requires humility, because we are forced to negate our “self-enhancement” bias and rely on protocols that help standardize chest pain risk stratification. Embracing accelerated diagnostic protocols may carry us to a Lake Wobegon after all, where “all the evaluations are strong, all the risk assessments are objective, and all the dispositions are safe.”

\textbf{References}


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To the Editor:

We read with interest, “Can Emergency Physician Gestalt ‘Rule In’ or ‘Rule Out’ Acute Coronary Syndrome: Validation in a Multicenter Prospective Diagnostic Cohort Study” by Oliver et al. In this large multicenter, prospective diagnostic accuracy study, the investigators conclude that gestalt (including electrocardiogram [ECG] interpretation) is not sufficient to exclude acute myocardial infarction (AMI) in patients who present to ED with suspected ACS. However, we feel the need to call attention to some issues in the study methods that may limit the strength of its findings.

First, Oliver et al. did not uniformly blind clinicians to the initial troponin level reasoning that this method may be a more pragmatic representation of gestalt in practice. However, an elevated troponin level was included in the diagnostic criteria for AMI, so physician knowledge of the troponin level will significantly bias gestalt (incorporation bias). If data were available, it would be useful to calculate the accuracy of gestalt from assessments during which clinicians were appropriately blinded to the initial troponin result. The accuracy of gestalt with an ECG only (without troponin result) would be informative considering the nonspecificity of troponin assays and the downstream consequences of positive results in patients in whom no acute coronary occlusion is ultimately identified.

Second, Oliver et al. did not consider (or adjust for) physician experience in their analysis, yet sufficient clinical experience is necessary to develop gestalt cognition. This may have had a number of consequences. The authors appropriately state that “our findings do not apply to patients who did not pass the clinicians’ pretest probability threshold for warranting investigation for ACS.” However, the experience of the clinician may impact his or her pretest probability threshold. This threshold may be based on confidently identifying an alternative diagnosis, and less experienced clinicians may be less equipped to do so. For example, in a similar study that did stratify the relationship of gestalt to AMI prevalence by clinician experience (and also blinded clinicians to initial troponin level), Body et al. reported that only less experienced (<7 years) physicians initiated testing despite recording their gestalt as “definitely not ACS.” This relatively lower threshold for testing would result in the inclusion of a proportion of patients with a lower overall AMI prevalence and thus limit clinical applicability. In the study by Oliver et al., it is possible that a number of less experienced clinicians may have similarly overestimated pre-test probability for AMI consequently inflating the Likert scale assessments. On the other end of the spectrum, Body et al. reported that experienced physician gestalt (gestalt of physicians with at least 7 years of postgraduate experience) may be relatively more specific for diagnosis of AMI, although notably, their data in each “years of experience” stratum was limited. Therefore, the participation of less experienced clinicians in both trials may have resulted in a lower AUROC and diminished the reported accuracy of gestalt to predict acute AMI.

So the available evidence remains limited when addressing the question: Can a clinician with sufficient clinical experience use gestalt and an ECG alone to
accurately exclude AMI in a patient with suspected ACS?

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We thank Dr. de Souza and Dr. Sinert for their comments regarding our study. Indeed we heartily concur that our study took an entirely pragmatic approach, allowing all doctors of sufficient seniority to make clinical decisions to participate. We also acknowledge that doctors were not blinded to initial cardiac troponin or electrocardiogram results. As the study took place in real time involving real patients, we realized in advance that it would have been unethical to blind physicians to such important clinical information. It would be challenging to conduct a study in which only senior emergency physicians could assess patients (while still avoiding selection bias) and in which those senior physicians were blinded to the ECG and cardiac troponin results. While that ideal remains impractical, our pragmatic approach does provide some fascinating insights to inform our clinical practice.

Interestingly, studies that have reported some data on the relationship between clinician experience and gestalt accuracy have not demonstrated any statistically significant benefit of experience.\textsuperscript{1,2} For example, the study by Body et al.,\textsuperscript{1} referred to by the authors, suggested that the judgment of senior emergency physicians may actually be less sensitive for acute coronary syndromes (ACS). The small sample size unfortunately limits any meaningful conclusion being drawn.

It is quite possible, however, that increasing experience tends to lead to overconfidence. It would be reasonable to speculate that more experienced clinicians could place greater reliance on the typicality of symptoms or the presence of Framingham risk factors for cardiovascular disease. Neither has been shown to be predictive of AMI in the acute setting.\textsuperscript{2-4} Perhaps, as Sir William Osler once noted, we should acknowledge that:

One must be a professional Ulysses in craft and wisdom not to sometimes err in estimating the nature of an attack of severe heart pain. There is no group of cases so calculated to keep one in a condition of wholesome humility.\textsuperscript{5}

Dr. de Souza and Dr. Sinert also note that some patients may not have been included in our study because their physician did not suspect an ACS. This observation is entirely correct: we set out to evaluate the accuracy of clinician judgment in patients for whom the clinician believed further investigation was warranted. Including all patients (regardless of clinical suspicion of ACS) would have meant subjecting patients to reference standard investigations that were not clinically indicated. It would again be unethical to blind clinicians to the results of those investigations, rendering the study both impractical (from a resource perspective) and potentially unethical (exposing patients to unnecessary risk).

In summary, our study cannot inform us whether we are currently underinvestigating patients for ACS (i.e., missing ACS in patients in whom the diagnosis was never suspected). However, our work shows convincingly that there are important limitations to clinician gestalt. Our pragmatic, real-world observational data strongly suggest that (contrary to many of our fears) we are not actually overinvestigating for ACS in patients with a primary complaint of pain or discomfort in or around the chest.

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