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**ERRATUM**

Re: SAEM Annual Meeting Abstracts  1111
CME Information: A Multicenter Randomized Trial to Evaluate a Chemical-first or Electrical-first Cardioversion Strategy for Patients With Uncomplicated Acute Atrial Fibrillation

CME Editor: Corey Heitz, MD

Authors: Frank X. Scheuermeyer, MD, MHSc, Gary Andolfatto, MD, Jim Christenson, MD, Cristina Villa-Roel, PhD, and Brian Rowe, MD, MSc

If you wish to receive credit for this activity, please refer to the website: www.wileyhealthlearning.com/aem

Educational Objectives
After reading the article, participants should be able to discuss the effectiveness of chemical or electrical cardioversion-first strategies for patient in acute atrial fibrillation.

Activity Disclosures
This activity received no commercial support.

CME Editor Corey Heitz discloses no relevant financial relationships.

This activity underwent peer review in line with standards of editorial integrity and publication ethics. Conflicts of interest have been identified and resolved in accordance with John Wiley and Sons, Inc.’s Policy on Activity Disclosure and Conflict of Interest.

Accreditation
John Wiley and Sons, Inc. is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.
A Multicenter Randomized Trial to Evaluate a Chemical-first or Electrical-first Cardioversion Strategy for Patients With Uncomplicated Acute Atrial Fibrillation

Frank X. Scheuermeyer, MD, MHSc, Gary Andolfatto, MD, Jim Christenson, MD, Cristina Villa-Roel, PhD, and Brian Rowe, MD, MSc

ABSTRACT

Background: Emergency department (ED) patients with uncomplicated atrial fibrillation (AF) of less than 48 hours may be safely managed with rhythm control. Although both chemical-first and electrical-first strategies have been advocated, there are no comparative effectiveness data to guide clinicians.

Methods: At six urban Canadian centers, ED patients ages 18 to 75 with uncomplicated symptomatic AF of less than 48 hours and CHADS2 score of 0 or 1 were randomized using concealed allocation in a 1:1 ratio to one of the following strategies: 1) chemical cardioversion with procainamide infusion, followed by electrical countershock if unsuccessful; or 2) electrical cardioversion, followed by procainamide infusion if unsuccessful. The primary outcome was the proportion of patients discharged within 4 hours of arrival. Secondary outcomes included ED length-of-stay (LOS); prespecified ED-based adverse events; and 30-day ED revisits, hospitalizations, strokes, deaths, and quality of life (QoL).

Results: Eighty-four patients were analyzed: 41 in the chemical-first group and 43 in the electrical-first group. Groups were balanced in terms of age, sex, vital signs, and CHADS2 scores. All patients were discharged home, with 83 (99%) in sinus rhythm. In the chemical-first group, 13 of 41 patients (32%) were discharged within 4 hours compared to 29 of 43 patients (67%) in the electrical-first group ($p = 0.001$). In the chemical-first group, the median ED LOS was 5.1 hours (interquartile range [IQR] = 3.5 to 5.9 hours) compared to 3.5 hours (IQR = 2.4 to 4.6 hours) in the electrical-first group, for a median difference of 1.2 hours (95% confidence interval = 0.4 to 2.0).
hours, p < 0.001). No patients experienced stroke or death. All other outcomes, including adverse events, ED revisits, and QoL, were similar.

Conclusion: In uncomplicated ED AF patients managed with rhythm control, chemical-first and electrical-first strategies both appear to be successful and well tolerated; however, an electrical-first strategy results in a significantly shorter ED LOS.

Atrial fibrillation (AF) is the most common significant dysrhythmia encountered in the emergency department (ED)\(^1\) and in uncomplicated patients with symptoms less than 48 hours, the 2011 Canadian Cardiovascular Society (CCS) guidelines permit either rate or rhythm control.\(^2\) In Canadian academic centers, the proportion of patients with acute AF who undergo rhythm control ranges from 42% to 85%\(^3\) and emergency physicians typically employ one of two safe strategies.\(^4\)–\(^8\) Chemical cardioversion can be attempted first, typically with procainamide infusion; if this approach restores sinus rhythm, the patient is discharged. If unsuccessful, procedural sedation and electrical counter-shock are administered.\(^3\)–\(^6\),\(^8\) Alternatively, procedural sedation and electrical cardioversion may be attempted first; if successful, the patient is discharged home. If this fails to restore sinus rhythm, chemical conversion is attempted.\(^3\)–\(^8\) In both cases, if the patient converts to and maintains sinus rhythm, the patient is discharged home; otherwise the patient is typically consulted to cardiology.\(^3\)–\(^8\) Both strategies have been previously described and over a thousand patients have been collected for both electrical-first and chemical-first strategies with 30-day outcomes: no serious adverse events such as stroke, myocardial infarction, or death have been described to date.\(^3\)–\(^8\) Thus, although both strategies appear safe, comparative effectiveness data is lacking. As a result, Canadian management is variable: a chemical-first approach is used in 56% of patients and an electrical-first in 44%.\(^3\) To date, there has been one randomized trial comparing to an electrical-only versus chemical-only strategies demonstrated a shorter ED length of stay (LOS) for the former, but nearly one-fifth of patients were discharged home in AF, and one-third was lost to follow-up.\(^9\)

While both chemical-first and electrical-first cardioversion of uncomplicated AF appear very low risk,\(^3\)–\(^8\) we sought to determine if one strategy resulted in the achievement of sinus rhythm and resulting discharge more quickly. This could benefit patients by restoring normal physiology more quickly to minimize ED resource use. We conducted a randomized controlled trial focused on ED-based clinical outcomes and 30-day safety and patient-reported outcomes.

METHODS

Design and Oversight

This was a multicenter randomized study with concealed allocation involving ED patients with AF of less than 48 hours’ duration. The study protocol was registered at ClinicalTrials.gov (NCT01994070).

Setting

This trial was conducted at six urban EDs in western Canada and was approved by the ethics boards at all sites. All are university-affiliated teaching centers staffed by board-certified emergency physicians who generally only work at one site. The EDs ranged from small community hospitals with no on-site cardiologists to provincial referral centers with electrophysiology labs, 24-hour catheterization capability, and cardiac surgery including transplants and varied substantially in annual census, patient flow, case distribution, and overall admission rate. Recruitment took place during time blocks when research assistants were available. (Please see Data Supplement S1, Appendix S1 [available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13669/full], for a detailed description of settings including ED and hospital resources and times of enrollment.) All sites have trainees, mostly family medicine residents, although attending physicians made nearly all care decisions, including study eligibility, and timing of rhythm control.

Patients

While research assistants were on duty, consecutive potentially eligible patients between 18 and 75 years of age with episode of AF less than 48 hours’ duration as the primary diagnosis were screened by emergency physicians and referred for enrollment. Since > 90% of patients described in ED-based rhythm control studies\(^4\)–\(^8\) have a CHADS\(_2\) score\(^10\) less than 2 and little ED-based data on rhythm control in higher-risk patients exists, we stipulated that a CHADS\(_2\) score of 0 or 1 was required. Patients were required to be taking appropriate anticoagulation as per the 2011 CCS guidelines.\(^2,11\)
Patients who attended the ED for other reasons (for example, trauma or gout and were found to have incidental AF) were not included as the AF had likely been present for an unknown length of time. Hemodynamically unstable patients (those with altered mental status, acute chest pain or heart failure, or systolic blood pressure less than 90 mm Hg) were excluded as such patients are often treated with rapid electrical counter-shock.2 Patients with atrial flutter were ineligible since this dysrhythmia does not readily convert with procainamide.12 AF patients with an acute underlying medical illness were also excluded, since they respond poorly to rhythm control.13 Patients could not have had a cardiac procedure such as coronary artery bypass grafting, percutaneous coronary intervention, electrophysiological ablation, or pacemaker or defibrillation insertion within the prior 2 weeks, as such patients are typically managed by cardiologists or surgeons. Finally, patients who were acutely intoxicated or withdrawing from alcohol or illicit drugs were ineligible.

**Ethics**

Local research ethics boards approved the study at each site. Written informed consent was obtained from patients or a legal representative before enrollment.

**Study Treatments**

Prior to the study, and at regular intervals throughout the study, we informed all staff physicians regarding study protocol and patient eligibility. Approximately one-third of such patients may have an acute underlying illness, and this may be occult in many cases.13 To ensure that we did not mistakenly enroll such a patient, we encouraged physicians to obtain an electrocardiogram, complete blood count, electrolytes, serum creatinine, thyroid-stimulating hormone, cardiac troponin, and a chest radiograph on all patients. Using the RedCap (Vanderbilt University, Nashville, TN, licensed to the Women’s and Children’s Research Institute, University of Alberta, Edmonton, AB) online algorithm, consenting eligible patients were block randomized in groups of four at each site in a 1:1 fashion using concealed allocation. Patients were randomly assigned to receive one of two treatments: 1) chemical cardioversion, followed by electrical cardioversion if unsuccessful; or 2) electrical cardioversion, followed by chemical cardioversion if unsuccessful. Failure to achieve and maintain normal sinus rhythm after both treatments were completed mandated cardiologist consultation (please see Figure 1 for study groups). As per the 2011 Canadian guidelines periprocedural anticoagulation was discouraged. 2) Research assistants prospectively recorded all data directly into the online RedCap system, including patient demographics, vital signs, results of investigations, times and doses of medications, potential adverse events, and times of consultation and discharge.

**Chemical Cardioversion Rationale and Protocol**

Chemical cardioversion was attempted with procainamide since this has been well studied in North America.3–6,8 Although there are no specific ED-based guidelines, we recommended a dose of 17 mg/kg up to a maximum of 1500 mg infused over 1 hour. Furthermore, there is no current standardized time frame for chemical conversion, but prior research indicates that half of patients who convert do so within 1 hour and 90% convert within 2 hours.8 This information was conveyed to all physicians at the start of the study, at regular intervals throughout the study, and by research assistants at the bedside via the following standardized script: “Fifty percent of patients who convert will do so within one hour and 90% of patients who convert will do so within two hours” and no additional information was given.

**Electrical Conversion Rationale and Protocol**

For procedural sedation and analgesia, all sites required the attendance of at least one emergency physician, and a trained nurse and respiratory therapist. Although physicians could manage patients at their discretion, comfort level, and ED policy, the following regimen was recommended by the study team: propofol was to be administered with an initial bolus of 0.50 mg/kg, with further slow boluses of 0.25 mg/kg every minute thereafter if sedation depth was deemed inadequate by the attending physician.14 Electrical conversion was recommended as a synchronized biphasic waveform sequence of 100 to 150 to 200 J9 and a maximum of three shocks were allowed. Procainamide was initiated immediately after failure of the third shock.

**Outcomes**

The primary outcome was the proportion of patients discharged within 4 hours of ED arrival, which was defined as the time the patient registered at triage. (Prior to study commencement, the NCT primary outcome was defined as ED LOS. However, to ensure a parametric result and straightforward sample size calculation, the primary outcome was clarified as the proportion of patients...
discharged within 4 hours.) Prior retrospective studies have demonstrated that a chemical-first approach appears to have a median 5-hour ED LOS, while electrical-first approach appears to have a median 3-hour ED LOS. Confirming this, a two-center study found that 80% of electrical-first patients were discharged at 4 hours, while 50% of chemical-first patients were discharged at 4 hours. No attending physicians were aware of this outcome, since this could have biased the timing of any treatments. Instead, physicians were informed via standardized script that the study purpose was to assess the safety and efficiency of both methods.

Secondary outcomes included additional median time intervals, ED-based adverse events (AEs), and 30-day patient-centered outcomes. Regarding timing, the following patient care intervals were prespecified: registration to physician assessment, assessment to randomization, randomization to conversion, conversion to discharge, randomization to discharge, and registration to discharge. Regarding ED-based adverse events, prespecified AEs were based on the World Society of Intravenous Anesthesia guidelines (Table 1). Although these standards were developed for sedation, the main procainamide-related AEs—hypotension and arrhythmias—are also included. Research assistants familiar with these guidelines noted all potential AEs, and an independent safety committee of two emergency physicians blinded to allocation reviewed each to ascertain whether it was truly an AE.

Regarding 30-day outcomes, at 3 and 30 days, research assistants blinded to allocation telephoned patients and asked about further physician and hospital visits, as well as obtaining a quality-of-life (QoL) assessment based on the SF-8. The full questionnaire can be seen in Data Supplement S1, Appendix S2. If a patient could not be contacted by telephone, the family physician was contacted; if that failed, the regional ED databases were assessed for further visits to ensure stroke-free survival.

**Sample Size**

Based on previous data (80% patients discharged in the electrical-first group at 4 hours and 50% in the chemical-first group), 39 patients would be required in each group to have an 80% power to detect a difference of this magnitude or greater with a two-sided alpha of 0.05. An additional 10% enrollment was added to offset potential dropouts, resulting in a total sample size of 86 patients. No interim analysis was planned.

**Data Analysis**

The software package was STATA (StataCorp 2013, Stata Statistical Software, Release 13). Study variables are reported in terms of means with standard deviations (SDs) or medians with interquartile ranges (IQRs) where applicable. Patients with protocol violations were analyzed, but those who withdrew or were
Parametric outcomes were analyzed by a chi-square test (or Fisher’s exact test if there were five or less events per assessed outcome), while nonparametric outcomes were assessed by the Mann-Whitney U test. Significance was assumed at \( p < 0.05 \).

### RESULTS

#### Consort Diagram and Study Flow

The consort diagram and study flow can be seen in Figure 2. From December 1, 2013, to March 1, 2015, six sites had varying enrollment times (Data Supplement S1, Appendix S1) for a total of 42 site-months. Overall, we screened 222 patients less 75 years of age with AF less than 48 hours. Of the 135 eligible patients (approximately 3.2 patients per month per site) 86 were enrolled and randomized. Nonenrolled patients had ages, sex distribution, CHADS\(_2\) scores, and medication use similar to those of enrolled patients, but were more likely to have had prior AF, and nearly all had undergone prior cardioversion and already had a preferred method of management (Data Supplement S1, Appendix S3). Of the randomized patients, one patient withdrew from the chemical-first group prior to any treatment, and the investigators withdrew one patient from the electrical-first group for a troponin elevation prior to any treatment, leaving 84 subjects for analysis.
Baseline Characteristics
Baseline characteristics were balanced between the two groups, with 41 patients in the chemical-first group and 43 in the electrical-first group (Table 2). Four protocol violations occurred: A 77-year-old female with hypertension and 78- and 76-year-old males with hypertension were enrolled—all had a CHADS2 score of 2. A 68-year-old male who failed to achieve normal sinus rhythm with electrical conversion was referred to cardiology, rather than administered procainamide.

Main Results
In the chemical-first group, 13 of 41 patients (32%) were discharged within 4 hours compared to 29 of 43 patients (67%) in the electrical-first group (difference 36% [95% confidence interval {CI} = 16%–56%], p < 0.001) for a number needed to treat of 3 (95% CI = 2–6). In the chemical-first group, the median ED LOS was 5.1 hours compared to 3.5 hours in the electrical-first group, for a difference of 1.2 hours (95% CI = 0.4–2.0 hours, p < 0.001). The median LOS from randomization to conversion was 2.3 hours for the chemical-first group, and 0.6 hours for the electrical-first group, for a difference of 1.4 hours (95% CI = 0.8–1.9 hours) a 74% time reduction (Table 3).

In the chemical-first group, 22 of 41 (54%) patients converted with procainamide while the remainder required electrical countershock to attain normal sinus rhythm; all were discharged home. For patients who had unsuccessful procainamide attempts, physicians waited a median of 110 minutes (IQR = 80 to 149 minutes) prior to starting sedation for electrical conversion. In the electrical-first group, 38 of 43 (88%) converted, and four of the five remaining patients who also received procainamide reverted back to normal rhythm. One patient in each group received a cardiology consult and all patients were discharged home (Table 3). Breakdowns by individual treatments are given in Data Supplement S1, Appendix S4.

Figure 2. CONSORT diagram. *One patient declined to answer quality-of-life at 30 days, but the primary care confirmed that the patient was alive, not hospitalized, and stroke-free at 30 days. AF = atrial fibrillation.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Chemical-first (n = 41)</th>
<th>Electrical-first (n = 43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>15 (36.6)</td>
<td>17 (39.5)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58 (50–66)</td>
<td>60 (53–66)</td>
</tr>
<tr>
<td>Age range (range)</td>
<td>(21–77)</td>
<td>(28–78)</td>
</tr>
<tr>
<td>Canadian Triage and Acuity Score*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 2</td>
<td>36 (87.8)</td>
<td>37 (86.0)</td>
</tr>
<tr>
<td>Level 3</td>
<td>5 (12.2)</td>
<td>6 (14.0)</td>
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<tr>
<td>AF history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of AF</td>
<td>29 (70.7)</td>
<td>34 (79.1)</td>
</tr>
<tr>
<td>Prior cardioversion of any type</td>
<td>21 (53.9)</td>
<td>22 (51.2)</td>
</tr>
<tr>
<td>Number of chemical conversions</td>
<td>1 (0–2)</td>
<td>1 (0–2)</td>
</tr>
<tr>
<td>Number of electrical conversions</td>
<td>2 (1–5)</td>
<td>1 (1–3)</td>
</tr>
<tr>
<td>Initial vital signs</td>
<td></td>
<td></td>
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<tr>
<td>Pulse rate (beats/min)</td>
<td>117 (95–145)</td>
<td>116 (97–135)</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min)</td>
<td>17 (16–20)</td>
<td>16 (16–18)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>131 (124–139)</td>
<td>128 (120–138)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>80 (73–85)</td>
<td>80 (71–87)</td>
</tr>
<tr>
<td>Oxygen saturation on room air</td>
<td>99 (98–99)</td>
<td>98 (97–99)</td>
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<tr>
<td>Temperature in (°C)</td>
<td>36.6 (36.5–36.7)</td>
<td>36.6 (36.5–36.7)</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>10 (24.4)</td>
<td>14 (32.6)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (2.4)</td>
<td>2 (4.7)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0 (0.0)</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0.0)</td>
<td>0</td>
</tr>
<tr>
<td>CHADS2 score</td>
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<td></td>
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<tr>
<td>0</td>
<td>29 (70.7)</td>
<td>25 (58.1)</td>
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<td>1</td>
<td>12 (29.3)</td>
<td>15 (34.9)</td>
</tr>
<tr>
<td>2</td>
<td>0 (0.0)</td>
<td>3 (7.0)</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA</td>
<td>18 (43.9)</td>
<td>19 (44.2)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Coumadin</td>
<td>2 (4.9)</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>3 (7.3)</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Apixaban</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>2 (4.9)</td>
<td>5 (11.6)</td>
</tr>
<tr>
<td>Propafenone</td>
<td>3 (7.3)</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>0 (0.0)</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Sotalol</td>
<td>0 (0.0)</td>
<td>3 (7.0)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>3 (7.3)</td>
<td>2 (4.7)</td>
</tr>
<tr>
<td>Atenolol</td>
<td>0 (0.0)</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>2 (4.9)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Data are reported as n (%) or median (IQR).
AF = atrial fibrillation; ASA = aspirin; CHADS2 = stroke risk score composite of heart failure, hypertension, age > 75, diabetes (1 point each), stroke/TIA (2 points); IQR = interquartile range; TIA = transient ischemic attack.
*Canadian Triage and Acuity Score (CTAS) is a validated, reliable system used in Canada by triage nurses to determine in what time interval a patient should be seen. (The smaller the number the sicker the patient: CTAS 2 = 15 minutes to physician attendance; CTAS 3 = 30 minutes to physician attendance.)
Adverse Events
The chemical-first group had 10 adverse events (24%) while the electrical group had 11 (26%). All adverse events had minimal-risk outcomes (Table 4; please see Data Supplement S1, Appendix S5, for detailed vignettes, interventions, and outcomes).

Three- and Thirty-day Outcomes
Table 5 shows that all patients were contacted at 3 days, and 83 of 84 were contacted at 30 days. (One patient answered questions at 3 days, but when contacted at 30 days refused to answer; the primary care doctor was then contacted to confirm that this patient was alive and free from stroke or hospitalization.) At 30 days, there were no strokes or deaths in either group (95% CI = 0%–4.4%). All patients visited their family doctor; generally between 3 and 30 days after the ED visit. At 3 days, five of 41 chemical-first patients reattended the ED with one admission; one of 43 electrical-first patients reattended the ED with no admissions. At 30 days, nine of 41 chemical-first patients reattended the ED with two admission; three of 43 electrical-first patients reattended the ED with no admissions. All revisits were for recurrent AF and both admissions were for AF that was uncontrollable in the ED on the subsequent visit. QoL scores were similar for both groups across all domains.

DISCUSSION
In this multicenter randomized controlled clinical trial, a significantly greater proportion of ED patients with uncomplicated acute AF were discharged from the ED within 4 hours when managed with an electrical-first
cardioversion strategy, compared to a chemical-first cardioversion strategy. In addition, the median LOS was shorter by 1.2 hours for the electrical-first group, a significant difference. This was likely driven by the 74% reduction in median time from randomization to conversion for the electrical-first group. This is noteworthy and clinically sensible since “randomization time” in our study likely corresponds to the time an emergency physician would make the decision to manage a non-study AF patient with either a chemical- or electrical-first approach. Adverse events were minor, and all patients were discharged home at the index ED visit, with no strokes or deaths at 30 days. QoL scores were similar at three and 30 days. This demonstrates that, although both methods appear safe and are well tolerated in acute AF, patients undergoing an electrical-first approach have a far shorter ED LOS.

Emergency department–specific CCS guidelines emphasize that uncomplicated AF patients with symptom duration of less than 48 hours may undergo rate or rhythm control and ED-based rhythm control has been shown to be safe in thousands of patients over numerous retrospective and prospective analyses. Our study showed that, similar to prior findings, approximately half of patients undergoing chemical conversion alone converted to normal sinus rhythm. As a combination therapy, the Ottawa protocol (procainamide administration followed by electrical countershock if unsuccessful) has been well described and reports safe discharge of up to 97% of patients, with almost all in sinus rhythm. Likewise, the success rate of electrical conversion alone was approximately 90%, also similar to prior studies. In Canada, studies have shown that emergency physicians use each strategy approximately half the time, and this study may assist clinicians by demonstrating that the electrical-first strategy may restore sinus rhythm more quickly.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Chemical-first (n = 41)</th>
<th>Electrical-first (n = 43)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three-day outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients contacted</td>
<td>41 (100.0)</td>
<td>43 (100.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Saw a physician</td>
<td>8 (19.5)</td>
<td>5 (11.9)</td>
<td>0.381</td>
</tr>
<tr>
<td>ED revisit</td>
<td>5 (12.2)</td>
<td>1 (2.4)</td>
<td>0.109</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>1 (2.4)</td>
<td>0 (0.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Quality of health rated “excellent”</td>
<td>25 (61.0)</td>
<td>21 (50.0)</td>
<td>0.380</td>
</tr>
<tr>
<td>No limitations to physical activity</td>
<td>29 (70.7)</td>
<td>30 (71.4)</td>
<td>1.0</td>
</tr>
<tr>
<td>No difficulties doing daily work</td>
<td>31 (75.6)</td>
<td>29 (69.0)</td>
<td>0.625</td>
</tr>
<tr>
<td>No bodily pain</td>
<td>27 (65.9)</td>
<td>26 (61.9)</td>
<td>0.820</td>
</tr>
<tr>
<td>“Very much” energy</td>
<td>26 (63.4)</td>
<td>23 (54.8)</td>
<td>0.505</td>
</tr>
<tr>
<td>No limitations to social activities</td>
<td>35 (85.4)</td>
<td>30 (71.4)</td>
<td>0.182</td>
</tr>
<tr>
<td>30-day outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients contacted</td>
<td>41 (100.0)</td>
<td>42 (97.7)</td>
<td>1.0</td>
</tr>
<tr>
<td>Saw a physician</td>
<td>27 (65.9)</td>
<td>23 (54.8)</td>
<td>0.372</td>
</tr>
<tr>
<td>ED revisit</td>
<td>9 (22.0)</td>
<td>3 (7.1)</td>
<td>0.067</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>2 (4.9)</td>
<td>0 (0.0)</td>
<td>0.241</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Quality of health rated “excellent”</td>
<td>21 (52.4)</td>
<td>21 (51.2)</td>
<td>1.0</td>
</tr>
<tr>
<td>No limitations to physical activity</td>
<td>29 (70.7)</td>
<td>31 (73.8)</td>
<td>0.810</td>
</tr>
<tr>
<td>No difficulties doing daily work</td>
<td>34 (82.9)</td>
<td>37 (88.1)</td>
<td>0.548</td>
</tr>
<tr>
<td>No bodily pain</td>
<td>32 (78.0)</td>
<td>36 (85.7)</td>
<td>0.405</td>
</tr>
<tr>
<td>“Very much” energy</td>
<td>28 (68.3)</td>
<td>23 (54.8)</td>
<td>0.261</td>
</tr>
<tr>
<td>No limitations to social activities</td>
<td>32 (78.0)</td>
<td>37 (88.1)</td>
<td>0.254</td>
</tr>
</tbody>
</table>

Data are reported as n (%). One patient in the electrical group declined to answer follow-up questions at 30 days, but was confirmed by his primary care physician to be alive, stroke-free, and not hospitalized at 30 days.
In a single-center trial, Bellone and coworkers\textsuperscript{9} randomized patients to a chemical-only versus an electrical-only strategy and found the latter had higher conversion rates (89% vs. 74%) and shorter LOS (3 hours vs. 7 hours). However, all patients required ED-based echocardiography, 19% of patients were discharged home while still in AF, and 33% were lost to follow-up. Furthermore, there was no reported ascertainment of clinically relevant outcomes such as strokes, deaths, ED revisits, or rehospitalizations. We extend these findings by employing a sequential approach to conversion, not mandating specialized imaging, and providing complete follow-up on our cohort.

Importantly, the rates of stroke and death post-rhythm control have been very low.\textsuperscript{3–9} In a recent prospective Canadian six-ED study enrolling 1,091 patients with acute AF nearly exclusively managed with rhythm control, Stiell et al.\textsuperscript{17} described no 30-day deaths and a single stroke—an 81-year-old on coumadin with an ED INR of 2.3 who spontaneously converted and had an ischemic stroke on Day 23. While Canadian academic emergency physicians may be comfortable managing patients with acute AF with rhythm control, this may not extend internationally. Physicians in Australasia and the United Kingdom employ rhythm control approximately half the time, while American physicians employ rhythm control one-quarter of the time.\textsuperscript{19} However, there is evidence that emergency physicians might be able to facilitate safe early discharge, rather than admission, of AF patients: in a single center, Decker and coworkers\textsuperscript{18} randomized 153 patients to either cardiology admission or an ED-based strategy of rate, then rhythm control, resulting in a decrease in LOS from 25 to 10 hours; nearly all patients were discharged in sinus rhythm. There may be increasing appeal for similar ED-based AF pathways that could incorporate rhythm control and safe discharge for low-risk patients.\textsuperscript{20}

Of our patients receiving electrical countershock first, half were discharged within 1 hour of randomization, and some patients who received procainamide first were discharged in a similar time frame. The recent cohort of Stiell et al.\textsuperscript{17} had a median ED LOS of 5 hours, but our data suggest that far shorter times—perhaps 1 to 2 hours—may be routinely possible. Some of our extreme LOS likely resulted from other factors including the presence of multiple critically ill patients in the department, the unavailability of trained nurses or respiratory therapists at a particular time, or single-physician coverage, when a hemodynamically stable AF patient might be a lower priority.

Although ED-based outcomes such as LOS and adverse events have been described, the QoL in ED AF patients has been minimally investigated.\textsuperscript{21} Although AF in this group may not be “dangerous” in terms of death, stroke, or hospitalization,\textsuperscript{3–8} symptoms can be profoundly unpleasant and interfere with daily activities and enjoyment of life for both patients and families. It is important to note that the proportion of patients in the chemical-first group reattending the ED was substantially (though not significantly) higher than in the electrical-first group. While the QoL scores may have been similar, this may indicate that the electrical-first approach provides a long-term benefit a greater proportion of patients. Importantly, our findings add to the literature by comparing two accepted treatments, measuring important outcomes—including patient-reported results—and demonstrating that these patients, irrespective of initial management strategy, are safe; have minimal discomfort after their ED visit; and have an acceptable QoL at 3 and 30 days.

**LIMITATIONS**

The study took place in six urban Canadian EDs, where all physicians were experienced at managing chemical conversion, electrical countershock, and procedural sedation and analgesia, and our results may not be generalizable to other EDs without such experience. At two of the six sites, research assistants were only available during daytime hours. Screening logs may be unreliable and some eligible patients missed. LOS can be driven by many variables including department crowding, the presence of other critically ill patients in the department, physician coverage, and nurse or respiratory therapist availability. Neither clinicians nor patients could realistically be blinded. Despite the standardized instructions and script, the timing of procainamide administration, tolerance for conversion, and departmental protocols for sedation may vary as physicians were allowed to exercise clinical judgment. While this introduces variability, it may also enhance external validity. Intravenous procainamide is the most commonly used chemical agent in Canadian EDs,\textsuperscript{3–8} but is graded as level IIb evidence for rhythm control,\textsuperscript{22} although it is important to note that these recommendations did not arise from ED-based studies. Anticoagulation was based on the 2011 Canadian ED guidelines\textsuperscript{11} and we did not evaluate emergency
physicians’ anticoagulation decisions. Furthermore, these guidelines were not congruent with American recommendations and have been superseded several times in Canada.

Our study was not powered to assess such events, and given the very low rate of serious outcomes it would require a far larger trial to prove safety. Over one-third of eligible patients declined participation, and they were more likely have had prior AF with conversion attempts. This may bias results in favor of patients with infrequent or newly diagnosed AF. Our results cannot be extrapolated to patients with chronic AF, those at higher risk of stroke, those with acute underlying medical illnesses, or adults > 75 years of age, although such patients are not typically managed with rhythm control. Finally, the SF-8 is a general health systems questionnaire and has not been validated in this cohort of patients, although AF-specific QoL measures have been recently developed. Neither patient nor physician satisfaction was assessed, nor were costs. While Canada has universal health care, in different settings, it may potentially be less costly and provide better QoL to rapidly convert patients in the ED, rather administer than rate control and likely anticoagulation for eventual follow-up with a cardiologist.

CONCLUSION

In uncomplicated ED atrial fibrillation patients, chemical-first and electrical-first strategies both appear to be successful and well tolerated; however, an electrical-first strategy results in a significantly shorter ED length of stay. Our results should encourage clinicians to initially consider an electrical-first approach for such patients.

The authors are indebted to the patients who chose to participate in this study. The contributions of Natalie Runham and Pam Pang at the University of Alberta Hospital (UAH) and Pamela Chow at the Sturgeon Community Hospital (SCH) sites are much appreciated. Drs. Corinne Hohl (Vancouver General Hospital) and Brian Grunau (St. Paul’s Hospital) composed the safety committee. Finally, we thank the ED staff of UAH, SCH, Lions Gate Hospital, Mount St. Joseph’s Hospital, South Health Campus, and St. Paul’s Hospital for their efforts and enthusiasm.

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.13669/full

Data Supplement S1. Supplemental material.
“It Wasn’t Just One Thing”: A Qualitative Study of Newly Homeless Emergency Department Patients

Kelly M. Doran, MD, MHS, Ziwei Ran, MSW, Donna Castelblanco, MBE, Donna Shelley, MD, MPH, and Deborah K. Padgett, MA, PhD, MPH

ABSTRACT

Objectives: Emergency departments (EDs) frequently care for patients who are homeless or unstably housed. One promising approach taken by the homeless services system is to provide interventions that attempt to prevent homelessness before it occurs. Experts have suggested that health care settings may be ideal locations to identify and intervene with patients at risk for homelessness, yet little is known even about the basic characteristics of patients who might benefit from such interventions.

Methods: We conducted in-depth, one-on-one qualitative interviews with ED patients who had become homeless within the past 6 months. Using a semistructured interview guide, we asked patients about their pathways into homelessness and what might have prevented them from becoming homeless. Interviews were digitally recorded and professionally transcribed. Transcripts were coded line by line by multiple investigators who then met as a group to discuss and refine codes in an iterative fashion.

Results: Interviews were completed with 31 patients. Mean interview length was 42 minutes. Four main themes emerged: 1) unique stories yet common social and health contributors to homelessness, 2) personal agency versus larger structural forces, 3) limitations in help from family or friends, and 4) homelessness was not expected.

Conclusions: These findings demonstrate gaps in current homeless prevention services and can help inform future interventions for unstably housed and homeless ED patients. More immediately, the findings provide rich, unique context to the lives of a vulnerable patient population commonly seen in EDs.

Homelessness is a persistent and vexing problem throughout the United States. In many cities, the numbers of people who are homeless remain persistently high.1–3 In New York City, for example, the homeless shelter census has risen over the past 10 years—to more than 60,000 in 2017—despite tens of thousands of people being provided with permanent supportive housing or rental subsidies.4 As some people exit homelessness, however, others stream through the “front door” to take their place. Accordingly, policymakers have increasingly focused on homelessness prevention as a key strategy for reducing homelessness, from the Department of Emergency Medicine (KMD), the Department of Population Health (KMD, DS), and the Department of Emergency Medicine (DC), NYU School of Medicine; and the NYU Silver School of Social Work (ZR, DKP), New York, NY. Ms. Castelblanco is currently with The Center for Great Expectations, Somerset, NJ.

Received October 23, 2018; revision received December 17, 2018; accepted December 18, 2018.

Research reported in this publication was supported by the National Institute on Drug Abuse of the National Institutes of Health (K23DA039179, PI Doran), the United Hospital Fund (PI Doran), and the Doris Duke Charitable Trust—NYULMC (PI Doran). The content is solely the responsibility of the authors and does not represent the official views of any funder.

KMD received grant funding for this study from the NIH/NIDA, the United Hospital Fund, and the Doris Duke Charitable Trust—NYULMC as noted above. The other authors have no potential conflicts to disclose.

Author contributions: KMD, DS, and DKP conceived of the study and developed the interview guide; DC and KMD conducted the interviews; DC, ZR, and KMD conducted data analysis, including coding the interviews; KMD drafted the manuscript and all authors provided critical feedback and approved the final version.

Supervising Editor: Harrison J. Alter, MD, MS.

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ISSN 1553-2712 © 2019 by the Society for Academic Emergency Medicine doi: 10.1111/acem.13677
with growing proportions of homeless services budgets going toward efforts to prevent homelessness. While homelessness prevention services are generally provided in community-based settings, some experts have suggested that hospitals may be important sites to identify people at high risk for homelessness and refer them to services. Prior research has shown that emergency department (ED) patients have particularly high rates of housing instability and vulnerability for homelessness. EDs may therefore be promising sites for homelessness risk screening and prevention services. Hospitals and health systems may be interested in preventing homelessness since copious prior research has shown that homelessness is associated with negative health outcomes and higher than average use of hospital-based care including ED visits.

Understanding how to best prevent homelessness requires knowing about why people become homeless in the first place. Prior research has found that homelessness is associated with poverty, interpersonal conflict and abuse, job loss, substance use, mental health, “life shocks” such as birth of a child or illness, and criminal justice system involvement, among many other factors. Much of the past research on correlates of homelessness has been cross-sectional, limiting the ability to determine temporality and causality of the observed relationships. Given the complexity of interrelated factors that may lead to homelessness, qualitative research is particularly well suited to exploring pathways to homelessness. There has been little prior qualitative research, however, that has specifically examined reasons for and precipitants of homelessness in the words of people who have been affected by it. Further, to our knowledge no prior research has examined pathways to homelessness among ED patients, a potentially unique group. To fill this gap, we conducted a qualitative study using in-depth interviews with ED patients who had recently become homeless to explore their self-identified reasons for becoming homeless.

METHODS

We conducted one-on-one, in-depth, semistructured qualitative interviews with 31 ED patients who had recently become homeless. This study was part of a larger body of research aiming to develop homelessness prevention interventions for ED patients. Study methods and results are presented in accordance with the consolidated criteria for reporting qualitative research (COREQ).

Study Setting and Population

The study was conducted at an urban, public hospital ED and contiguous urgent care center. English-speaking patients 18 years or older with a new-onset homelessness (defined as living in a shelter or on the streets) episode in the past 6 months were eligible. We chose this time frame because we felt that patients would be most likely to remember details about how and why they became homeless when it was a relatively recent experience. Patients were eligible regardless of whether this was their first time ever homeless or if they had past experiences of homelessness. Patients were ineligible if they were too intoxicated to provide consent, otherwise medically unfit (e.g., critically ill), psychologically distressed, in police or prison custody, or could not understand study consent (e.g., dementia).

Participants were recruited in two ways. First, ED care providers (doctors, nurse practitioners, physician assistants, nurses) were informed of the study and asked to alert the study team for any patients whom they learned had become homeless in the past 6 months. The majority of participants were recruited in this manner. A smaller number of participants were recruited via direct screening of ED patients for eligibility by study staff. Because one of the overall study’s goals was to examine the relationship of homelessness and substance use, we used purposive sampling to ensure that patients with unhealthy alcohol or drug use were adequately represented in addition to patients without substance use.

Interview Procedures

One of two study authors (KD, DC) conducted the interviews. KD is an emergency physician with formal qualitative research training and experience and extensive past experience working on issues related to homelessness. DC was a study research coordinator with a background in bioethics. KD trained DC in qualitative research techniques and reviewed all interview transcripts to ensure interview quality. Neither interviewer was part of the participants’ medical care teams. All participants provided written informed consent. Participants received $20 to compensate them for their time. Each participant was interviewed only once. The study was approved by the NYU School of Medicine Institutional Review Board.

Interviewers used a semistructured interview guide (Table 1) to ensure that key concepts were covered
while allowing flexibility in question sequencing and probes to enhance interview flow. The interview guide was pilot tested with two ED patients prior to beginning the study. Interviewers also collected basic demographic information and recorded brief field notes immediately after the interview.

Interviewers took steps to ensure participant privacy and comfort in the ED setting. When possible, interviews were conducted in private treatment areas such as a single room or single curtained bay without other patients nearby. Interviews were conducted with only the participant present; visitors were asked to leave the area.

Interviews were digitally recorded. A professional transcription company transcribed all interviews. One of the study authors (DC) checked each transcription against the digital recording for accuracy, making any needed edits prior to analysis.

### Table 1

<table>
<thead>
<tr>
<th>Interview Guide Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can you tell me about the most recent time you became homeless?</td>
</tr>
<tr>
<td>Probe: How long have you been living [in the shelter, outside, etc.?]?</td>
</tr>
<tr>
<td>Probe: Where were you staying right before you became homeless?</td>
</tr>
<tr>
<td>Have you ever had other times in your life when you’ve been homeless? Can you tell me about those?</td>
</tr>
<tr>
<td>Probe: How were those past times you’ve been homeless resolved/ended?</td>
</tr>
<tr>
<td>What do you think led to your becoming homeless [this time]?</td>
</tr>
<tr>
<td>Probe: Different reasons like they lost a job, mental illness, etc.</td>
</tr>
<tr>
<td>Probe: Of the reasons you mentioned, what do you think was the most important? Why?</td>
</tr>
<tr>
<td>Probe: If they have been homeless before probe reasons for previous episodes of homelessness.</td>
</tr>
<tr>
<td>Before you became homeless did you turn to any organization, person, or place for help?</td>
</tr>
<tr>
<td>Probe: For example, did you use any homelessness prevention programs? Or speak to a social worker? Or go to an ER for help? Have you heard of homelessness prevention services offered by NYC called Homebase?</td>
</tr>
<tr>
<td>Probe: Did someone refer you to these services, or did anyone refer you to services that you did not use? Why or why not?</td>
</tr>
<tr>
<td>Probe: What were your experiences with these services? Were they able to help you or not? Why or why not?</td>
</tr>
<tr>
<td>Is there anything you can think of that might have prevented you from becoming homeless?</td>
</tr>
<tr>
<td>Probe: For example, any help that you might have received from friends or family, or from organizations designed to help people?</td>
</tr>
</tbody>
</table>

Not shown: interview guide questions on the relationship between homelessness and substance use and participant thoughts on ED-based homelessness prevention interventions, which were part of the larger research study and less central to the current paper.

### Data Analysis

We identified a list of seven key domains a priori based on the prior literature and our overall study goals, but allowed new codes and themes to emerge organically from the text in the grounded theory tradition. A core team of two to three researchers reviewed transcripts independently and then met to discuss differences in code interpretations. All interviews were coded by KD and ZR (a research assistant with a background in social work); DC also coded the majority of interviews. All coders had prior professional experience working with homeless populations or with other populations vulnerable to homelessness.

Interviews were conducted and coded in blocks of two to three interviews. We used the constant comparison method, identifying new codes, refining existing ones in an iterative manner, and adjusting the code structure accordingly for each early block of interviews. The codebook was solidified after the first 12 interviews had been coded and did not require further modification; the final codebook contained 27 codes. We continued interviews until theoretical saturation—the point at which no new major themes were emerging from subsequent interviews—had been achieved.

We used Dedoose (version 8.0.42) to assist in data management and organization.

In addition, we maintained a case summary matrix that collated demographic information; homelessness, substance use, work, and health history; and other interview notes for each participant. Following best practices for validity in qualitative research, we also maintained an audit trail including field notes taken after each interview, individually coded transcripts, and comments and revisions from group coding meetings.

### RESULTS

Interviews were conducted April 2017 through June 2018. Sixty-six patients were screened for eligibility; 33 were ineligible (primarily due to not having a new episode of homelessness in the past 6 months), two were eligible but refused to participate, and 31 agreed and completed interviews. Participants were primarily male, represented a mix of race and ethnicities, and had a mean age of 50 years (Table 2). The majority (67.7%) had at least one other episode of homelessness prior to the current episode.

Interviews lasted a mean of 42 minutes, with a range of 19 to 87 minutes. Four main themes emerged: 1) unique stories yet common social and...
health contributors to homelessness, 2) personal agency versus larger structural forces, 3) limitations in help from family or friends, and 4) homelessness was not expected. Table 3 summarizes the themes and provides illustrative quotes.

Theme 1: Unique Stories yet Common Social and Health Contributors to Homelessness

Participants recounted a wide array of life stories and recent events leading to homelessness. Yet despite the uniqueness of each individual’s situation, there was significant commonality in the broad underlying factors contributing to homelessness. These factors encompassed both “traditional” health issues (i.e., substance use and physical health problems), as well as a variety of social factors that—in addition to contributing to homelessness—are also known to contribute to ED visits and overall health.7 The most common contributors to homelessness mentioned by participants were job loss, not having enough money, not being able to live with family or friends, moving from another city or state, substance use, and other physical health problems. Less commonly endorsed were institutional discharge (e.g., jail/prison, hospital) and domestic or other violence.

More than half of participants reported job loss as a contributor to homelessness. Some described job loss as the main reason for their homelessness, including Participant 24 (woman in her 40s), who explained, “I had a job and an apartment and everything, and my employer lost their biggest client which was half their revenue. And they laid off like half the workforce and I was one of the people. After that I couldn’t pay my rent so I ended up having to lose my apartment.” Some participants had savings or could borrow money from friends or family, but those resources eventually waned. As Participant 3 (man in his 50s) explained, “I’ve been looking for work since the beginning of the year; it’s been very slow. What happened was, I went through my savings in January and mid-February and then I borrowed some financial help from family and friends and then that sort of ended and then by end of March-April, I had to find some other means of housing.” Other participants were already behind on rent and job loss was a “final straw.” Health conditions were common precipitants of job loss. Fewer participants reported being fired for lateness or interpersonal conflict. While job loss was the most common financial precipitant of homelessness, some participants reported other types of financial problems. A minority of participants noted trouble with spending or financial planning or having bills—including for medications/medical care and telephones—limiting the amount of money they had for rent.

Participants commonly reported living with family or friends and then becoming homeless when those arrangements ended. Sometimes this occurred when friends or family members died. For example, Participant 8 (man in his 40s) recounted, “I had an apartment in Jersey. So I gave that up. I moved back home. I was taking care of my grandmother and my mom. And then my mother passed. My grandmother went to my aunt’s house. And I had no place to go . . . .” In other cases, participants reported being “kicked out” by friends or family due to various disagreements or tensions. In some cases, participants seemed to have more choice in the matter, such as Participant 56 (man in his 60s), who was living with his mother and stepfather but reported that his stepfather “had all this plan also, that once I was there, he was gonna make my life miserable,” so eventually he chose to leave.
Several participants moved into homelessness in NYC from other states in pursuit of jobs, better health care (including substance use treatment), or public services/benefits or to get away from friends or family. In most cases, participants were not in particularly stable situations in their prior locations, however. For example, Participant 33 (man in his 20s) had been living with his mother in Florida but moved away because he was caught up in illegal activity there: “I’m in this predicament because I moved from and I was doing horrible things there and I wanted to change my life. . . . We kinda knew we’re gonna be homeless if we came up here but we didn’t think it was going to be like this.”

Participants recounted that substance use contributed to homelessness via pathways including job loss, severed relationships with friends and family, lack of money due to spending it on substances, and what they identified as poor decision making. Around half of participants expressed other health problems as contributors to their homelessness, including via job loss as noted above. For example, Participant 4 (man in his 30s) reported that after he started treatment for hepatitis C, his retail job “started noticing a difference in my look, how I look and acted, and they put me on medical leave.” He was on leave for 12 weeks—the maximum available time—and returned to work while still experiencing medication side effects and was subsequently fired. Participants noted inability to do certain types of work (e.g., construction) due to health conditions including back pain, vertigo, seizures, kidney disease, and partial paralysis. In some cases, participants wanted to work but were turned away. Participant 35 (man in his 30s) reported being told “you’re a liability” when looking for a job due to his seizure history. Other participants reported having been in accidents with injuries that either prevented them from working or—in two cases—led to opioid dependence, which ultimately contributed to homelessness. In a few cases, participants entered homelessness immediately after hospitalizations or nursing home stays. Overall, participants perceived little protection related to their health conditions in seeking and maintaining employment, even despite employment laws such as the Family Medical Leave Act (FMLA) that might be designed to provide certain protections.

When asked what caused their homelessness, participants often stated initially the one or sometimes two

Table 3
Summary of Themes

<table>
<thead>
<tr>
<th>Theme</th>
<th>Illustrative Quotes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theme 1: Unique stories yet common social and health contributors to homelessness</td>
<td></td>
</tr>
<tr>
<td>1A. Job loss/lack of money</td>
<td>“We had to leave [the apartment] because when I got injured I couldn’t work so we owed the landlord $1,200 for that month.” (Participant 33; man in his 20s)</td>
</tr>
<tr>
<td>1B. Could not live with friends/family</td>
<td>“I was living with my mother. And then she gave me the kick out and so I took the kick out ‘cause I’m not gonna argue or fight about it, so I had to go.” (Participant 9; woman in her 40s)</td>
</tr>
<tr>
<td>1C. Moves</td>
<td>“Jersey doesn’t have stuff that New York offers, you know?” (Participant 8; man in his 40s)</td>
</tr>
<tr>
<td>1D. Substance use</td>
<td>“The drugs is what drag me down.” (Participant 64; man in his 40s)</td>
</tr>
<tr>
<td>1E. Health conditions</td>
<td>“When they know that I’m [on dialysis], they’d be like, ‘Oh no. You got to get out. . . . You cannot work for me. Because I don’t want something to happen to you.'” (Participant 38; man in his 50s)</td>
</tr>
<tr>
<td>Theme 2: Personal agency versus larger structural forces</td>
<td></td>
</tr>
<tr>
<td>2A. Rent/housing market</td>
<td>“He locked me out illegally, totally illegally, everybody there. It wasn’t the proper eviction. There were so many things he did wrong and illegal but still here I am, he’s still renting the place to somebody else, he’s still cashing the public assistance rental system checks that they’ve been sending him.” (Participant 32; man in his 60s)</td>
</tr>
<tr>
<td>2B. Job market</td>
<td>“I get a security license and I’ve done security work for like a week and a half. But the guy wanted us to buy our own uniform and pay $1.00 less than the minimum wage.” (Participant 30; man in his 60s)</td>
</tr>
<tr>
<td>2C. Narratives emphasize personal choice</td>
<td>“I’m a grown man. I put myself in this situation.” (Participant 8; man in his 40s)</td>
</tr>
<tr>
<td>Theme 3: Limitations in help from family or friends</td>
<td>“[My daughter] had three kids, husband’s not working that much and she’s working and I don’t wanna put an entire burden on them . . .” (Participant 6; man in his 60s)</td>
</tr>
<tr>
<td>Theme 4: Homelessness was not expected</td>
<td>“So many people in those subways out there homeless and just—and I never thought I’d be like—join with these guys.” (Participant 56; man in his 60s)</td>
</tr>
<tr>
<td></td>
<td>“I should’ve been worrying about if things didn’t work out. And then things didn’t work out. . . I didn’t worry about that until it was too late.” (Participant 11; man in his 50s)</td>
</tr>
</tbody>
</table>
most prominent or proximal causes of their homelessness. In listening to their stories, however, it was clear that for most people homelessness resulted from a series of several different factors. Participant 12 (man in his 40s) explained, “It was a lot of factors. It was just hitting me all at once. I mean there was a million things.” Many participants described their homelessness as a rather sudden event, although careful analysis of their stories generally indicated that homelessness seemed at least several months or years in the making, with hardships sometimes beginning during childhood.

**Theme 2: Personal Agency Versus Larger Structural Forces**

We observed a tension between narratives that highlighted personal agency, choice, or self-determination yet which also underscored the role of larger external structural factors—over which an individual would have little control—in contributing to homelessness. Twenty-three participants mentioned contributors to their homelessness that could be considered structural factors, in particular high rental costs and employment challenges. Several participants commented on the high price of rent. Participant 29 (man in his 60s) recounted, “I started looking for a place and you know apartments are $1,500 [for a] studio.” Related to the rental market, some participants reported unscrupulous—and in some cases illegal—landlord practices. Participant 1 (woman in her 50s) summarized that when new management took over her building, “They finally tried to evict us [because] ... they want to raise the rent and move other people, tenants, in.” While she and other residents tried to fight for a while, she eventually “wound up leaving.” Other participants reported being forced out of their apartments after they complained about repair or safety issues, including Participant 56 (man in his 60s):

> When I call NYC, the city, to complain about my apartment then she [landlord] ... started eviction procedures. And it took over a year for her to get me out. But when she finally did, the marshal came and then they took me out.

Several participants reported living in informal “cash for room”—type arrangements, in which they paid to live in a room in an apartment belonging to someone unrelated to them. Such arrangements could be more affordable than having one’s own apartment, yet participants also felt they had few options in these unofficial arrangements when they could no longer pay the rent.

The job market was another structural factor commonly brought up by participants. Some participants noted a lack of available jobs for people like them, whether due to age, medical conditions, or lack of particular qualifications. Participants noted losing jobs because of layoffs due to changing technology, because employers found cheaper labor, or simply because their prior companies had shut down. Participants who did manage to find work reported low pay and lack of job security or benefits. For example, Participant 24 (woman in her 40s) noted having had a “temp” job in which “they can fire you anytime they wanted.” Once losing their jobs, some participants reported difficulty receiving unemployment benefits. Overall, much as with the rental market, the job market appeared to be stacked against participants, who had comparatively little power or recourse.

Less commonly mentioned structural factors that appeared contributive to participants’ homelessness included insufficient government benefits, bureaucracy of child protective service cases, lack of social services, lack of insurance or health care, and eligibility restrictions of housing subsidy programs.

Despite the role of these external structural factors, some participants emphasized their own choices in recounting the stories of how they became homeless. For example, Participant 27 (man in his 60s) said he chose to leave a nursing home because “I’m tired of sitting in there doing nothing all day.” Two participants reported moving from more stable living situations in other states because they preferred NYC; Participant 10 (man in his 50s) reflected, “I don’t think North Carolina is ever gonna be ready for me. ... The days are long and I’m a New Yorker.” As will be described with the next theme, several participants reported choosing not to live with friends or family even when such arrangements were available.

**Theme 3: Limitations in Help From Family or Friends**

While most participants reported receiving help—most commonly financial assistance or a place to stay—from family or friends, nearly all reported significant limitations in the amount of assistance they received. Commonly, these limitations resulted from family/friends themselves having limited resources. For example, Participant 38 (man in his 50s) had an older
sister who helped pay for him to move to NYC but could not provide other help “because she gotta pay her bills, you know?” Rarely, participants reported that family members had resources but did not want to help.

Some participants reported that they did not want to bother family members, whether because family members had their own struggles or, conversely, because they felt family members were doing well and they did not want to interfere. Participant 25 (man in his 50s) reported, “My nieces are doing great. I don’t need to be interrupting their lives.” Participant 65 (man in his 60s) had a sister nearby who he could stay with but “I don’t [want to] bother her,” which he explained was because she had children and he was also worried about her learning that he was HIV-positive. Some participants reported valuing their privacy over a place to stay. For example, Participant 64 (man in his 40s) said, “I got family all up in the Bronx, all over New York. It’s just that I don’t like having people all over my business.” Other participants expressed having too much pride or feeling embarrassment about their situation.

Several participants reported that they did not have family or friends to whom they could turn, sometimes due to deaths or because family lived in other states. Death of friends/family was described by approximately half of participants. In a few instances such death directly precipitated homelessness when a participant had been living with the person who died. In other cases, deaths of family/friends resulted in participants having fewer social connections upon whom they could draw for support. Participant 60 (man in his 40s) noted, “My mother is dead, my father is dead, my brother is gone, my other brother’s dead, my mom—my one brother’s, uh, moved up to Vermont like 12 years ago. I haven’t spoken to him in 12 years. I have no family. None.”

Interestingly, some participants who said initially that they had no family went on to describe multiple family members who actually lived nearby. Some participants may have felt that they functionally had no family given alienation from or other limitations in their relationships. As Participant 21 (man in his 40s) explained, he had family nearby but “They’re a bunch of creeps. Yeah, because if they got money and they doing good, they really don’t care about the next that’s messed up like me … so here I am.” Other participants reported being estranged from family, such as Participant 8 (man in his 40s) who said, “I’m the black sheep of the whole family, you know! I mean that’s on me too. I did 10 years in prison over heroin.”

Theme 4: Homelessness Was Not Expected
Participants often noted surprise at finding themselves homeless, such as Participant 33 (man in his 20s) who reflected, “I did not expect for this to happen, not at all.” Others commented on how quickly homelessness seemed to fall upon them, such as Participant 12 (man in his 40s): “If this happened so quick, this can happen to anybody.” Similarly, Participant 50 (man in his 30s) reflected, “I can’t tell the future—well, like see, my story is I wasn’t gonna know that I was gonna be homeless in a short period of time.”

In fact, while some participants had clearly spent time ruminating on the factors leading up to their homelessness, others commented that they had never before been asked about how they became homeless or even really thought about it. When asked what led to him becoming homeless, Participant 10 (man in his 50s) remarked, “you have damn good questions. I wish I could give you an answer. I don’t know. I’ve never seen this. I’ve lived pretty decently, responsibly, and then this happened.” Such responses were surprising because from the perspective of an outsider, all participants recounted life stories and recent situations rife with risk factors for homelessness. For example, Participant 10 had a history of substance use, chronic health problems, incarceration for assault, and poor family relationships. Further, two-thirds of participants had prior episodes of homelessness, which makes it additionally surprising that so many participants reported that their homelessness was unexpected.

Relatedly, when participants were asked what might have prevented their homelessness or homelessness for other people, they had difficulty conceptualizing the idea of homelessness prevention. Participant 29 (man in his 60s) struggled to reply to a question on preventing homelessness:

Help from becoming homeless? [pause]. Ah that’s a rough one because it just happens, you know? You don’t—these are things that, uh, people’s lives are not together in certain ways. So they would have to be able to see that they’re about to … not have a home … you’d have to be able to see that and a lot of times they don’t really know. It just happens, you know?

Similarly, Participant 24 (woman in her 40s) reflected, “I was back on my feet. I was doing all the right things and I ended up losing everything anyway. So, you know, I don’t know what to tell you about
how to help other people. I really don’t.” When asked how their homelessness might have been prevented, many participants reverted to providing critiques of existing shelters. Nearly universally, participants had not sought formal services available to help prevent their homelessness, either because they were unaware such services existed or because they had not expected to become homeless. Some participants noted, only in retrospect, that they saw signs that they might have been at risk for homelessness and wish they had been more prepared. Participant 7 (man in his 30s) admitted, “Yes and I kinda saw it. I just didn’t think it was gonna happen.”

**DISCUSSION**

Through in-depth interviews with recently homeless ED patients we identified four themes related to their pathways to homelessness: 1) unique stories yet common social and health contributors to homelessness, 2) personal agency versus larger structural forces, 3) limitations in help from family or friends, and 4) homelessness was not expected. Many of our findings affirmed prior qualitative research, which has suggested multifactorial contributors to homelessness including substance use, job loss, structural factors such as high rents, relationship breakdown or challenges, and health issues. Our study contributes to the literature by providing more in-depth context to these reasons—in participants’ own voices—than possible via survey or other quantitative research.

Participants’ stories revealed multiple contributors to their homelessness. When asked directly about what might have prevented their homelessness, however, most participants struggled to answer. This difficulty is perhaps not surprising considering that experts also debate about the best ways to prevent homelessness. It may also reflect a “present orientation” borne of immediate needs and an overall lack of awareness of homelessness prevention services. This speculation is supported by the fact that only a minority of people who enter shelters in NYC have previously accessed available homelessness prevention services. Prior research has suggested high rates of traumatic brain injury and cognitive impairment among people who are homeless, which may have also been somewhat contributory to our findings, although we did exclude patients who were not able to understand the study informed consent process.

A few prior studies have used qualitative research to examine pathways to homelessness among various subgroups of people. Padgett et al. published a series of papers based on qualitative interviews with homeless and formerly homeless adults with mental illness. Similar to the findings of our study, interview participants reported that family members had been able to offer only limited support because they were “in the same boat” themselves. Also similar to our findings and despite including only participants with mental health issues, Padgett et al. found a notable lack of direct discussion of mental illness in participant interviews, with themes around substance use and other health problems taking more prominence. For our study specifically, it is also possible that we found less prominence of mental illness among our sample of newly homeless patients than if we had focused on people who were chronically homeless.

In another qualitative study, Metraux et al. conducted interviews with post-9/11 era veterans and reported some similar findings to ours—including the centrality of unemployment and relationships—while also identifying specific challenges in postmilitary life and access to VA services. Similarly, focus groups with homeless women veterans identified a constellation of contributors to homelessness both related and not related to military service, including unemployment, relationship problems, and lack of social support. Qualitative research with homeless families in Canada and homeless adults in England also identified limitations in social support and relationship breakdown as central in pathways to homelessness. Another study, of drug users in Connecticut, found that personal factors including lack of social support and substance use interacted with structural factors such as lack of housing subsidies to contribute to homelessness.

We were interested in observing a tension between what participants identified as broader structural factors contributing to their homelessness and personal narratives that often emphasized the role of choice. Such emphasis on personal agency and self-determination may be an ego-protection mechanism and has been observed in prior research with homeless populations. In Sidewalk, an ethnography of NYC Street vendors, Mitchell Duneier observed that “the people I wrote about sometimes took complete responsibility for their own failures, unable to comprehend the obstacles and opportunities in their lives, the pressures and constraints they may have faced, and thus the probabilities of particular outcomes independent of
their own actions.”47 He therefore cautioned against taking participants’ stories solely “at face value.”47 In our paper we have attempted to balance portraying participants’ own explanations for their homelessness while also being attuned to the deeper messages evident when taking a broader, holistic view of their stories. Our research included only the perspective of ED patients experiencing homelessness themselves; future research could triangulate qualitative or other research with social service providers, for example, to further elucidate barriers in the human services sector that might contribute to homelessness.

To our knowledge, no prior research has examined pathways to homelessness among ED patients. McCormack et al.48 conducted in-depth life history interviews with chronically homeless, frequent visitors to the ED who also had alcohol dependence. This study was conducted among a very unique subpopulation of ED patients and did not specifically explore pathways to homelessness. Homelessness plays an oversized role in U.S. EDs, in part due to the ED’s role as a medical and social safety net and in part due to the greater than average health needs of people who are homeless.13,15,49,50 Research spanning multiple localities and types of EDs has found that a disproportionate number of ED patients are homeless.7,15 Other research has found that ED providers struggle to provide optimal care to patients who are homeless, which may lead to provider burnout.51,52

In addition to seeing large numbers of patients who are already homeless, EDs also serve many patients who are unstably housed and at risk for future homelessness.6,7 Some experts have proposed that EDs may, therefore, be important sites for homelessness risk screening and preventative interventions.5 Such interventions are well aligned with the health care system’s increasing emphasis on social determinants of health such as housing.53–55 The current study was designed in part to inform the development of such an intervention, which will be studied in future research. For example, the finding that patients were often surprised at becoming homeless may explain prior observations that most people who become homeless have not sought homelessness prevention services,4 and it speaks to the potential benefit of universal homelessness risk screening in the ED rather than relying on patients to self-identify a need for services. Also, we discovered in this sample of ED patients that health conditions were often strong contributors to homelessness; such cases may be particularly ripe for health system collaboration to help prevent homelessness. Our finding that patients had significant limitations in support from family or friends suggests that future interventions may need to provide material or other support to strengthen any existing relationships or provide new forms of social support such as through peer navigator or community health worker models. Finally, our finding that structural issues such as the job market and affordable housing availability were significant contributors to homelessness suggests that these issues must also be addressed in larger initiatives to prevent homelessness. While it may seem that such issues are outside the scope of health care, some health care institutions have actually attempted to change their communities by building affordable housing or providing employment opportunities to community residents.53,56

LIMITATIONS

Our study was conducted among patients at a single NYC ED and thus may not be generalizable to other populations. Women were underrepresented in our study, potentially due to the study hospital’s proximity to a large men’s shelter. As we did not intend to compare experiences of women versus men in our study, we did not attempt to oversample women. In addition to experiences shared with men, women may have additional reasons for homelessness including pregnancy24 and domestic violence;23 past qualitative research has specifically examined pathways to homelessness among women.45 Further, unlike for quantitative research, qualitative research does not seek to be generalizable as much as it seeks to produce information that readers might find transferable to other contexts.57 While we conducted our interviews in a busy ED, we took multiple steps to ensure participant comfort and generally were able to conduct interviews in a private manner. Finally, we did not perform participant checking of themes because we did not want to collect identifying or contact information given the sensitive nature of the interview questions; we did, however, follow multiple other best practices for rigor in qualitative research as described under Methods.34

CONCLUSION

In this qualitative study of recently homeless ED patients, we found multiple contributors to homelessness that can inform future homelessness prevention
interventions. More broadly, our findings may help ED providers to better understand the life experiences of their patients that contribute to their health and ED use.

References


Prehospital Double Sequential Defibrillation: A Matched Case–Control Study

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ABSTRACT

Objectives: The goal of our study was to determine whether prehospital double sequential defibrillation (DSD) is associated with improved survival to hospital admission in the setting of refractory ventricular fibrillation/pulseless ventricular tachycardia (VF/pVT).

Methods: This project is a matched case–control study derived from prospectively collected quality assurance/quality improvement data obtained from the San Antonio Fire Department out-of-hospital cardiac arrest (OHCA) database between January 2013 and December 2015. The cases were defined as OHCA patients with refractory VF/pVT who survived to hospital admission. The control group was defined as OHCA patients with refractory VF/pVT who did not survive to hospital admission. The primary variable in our study was prehospital DSD. The primary outcome of our study was survival to hospital admission.

Results: Of 3,469 consecutive OHCA patients during the study period, 205 OHCA patients met the inclusion criterion of refractory VF/pVT. Using a predefined algorithm, two blinded researchers identified 64 unique cases and matched them with 64 unique controls. Survival to hospital admission occurred in 48.0% of DSD patients and 50.5% of the conventional therapy patients (p > 0.99; odds ratio = 0.91, 95% confidence interval = 0.40–2.1).

Conclusion: Our matched case–control study on the prehospital use of DSD for refractory VF/pVT found no evidence of associated improvement in survival to hospital admission. Our current protocol of considering prehospital DSD after the third conventional defibrillation in OHCA is ineffective.

The optimal management strategy of prehospital refractory ventricular fibrillation/pulseless ventricular tachycardia (VF/pVT) is controversial. The Minnesota Resuscitation Consortium has implemented a management strategy of mechanical cardiopulmonary resuscitation (CPR) facilitated transport, extracorporeal membrane oxygenation (ECMO), and primary coronary intervention (PCI). Alternatively, some emergency medical services (EMS) systems are using prehospital beta-blockers based on limited emergency...
Another proposed management strategy is the prehospital use of double sequential defibrillation (DSD). However, in the setting of out-of-hospital cardiac arrest (OHCA), prehospital DSD is an unproven therapy.²,³

In DSD, the “double” refers to the use of two separate defibrillators on the same patient. The operator attempts to deliver simultaneous defibrillations from both devices. Human limitations result in “sequential” administration of the defibrillations. Other authors have also referred to the technique as “dual defibrillation,” “double simultaneous defibrillation,” and “dual sequential defibrillation” in the literature.⁶–⁸ DSD was first developed and tested in canine models of refractory VF.⁹–¹¹ Limited observational data suggest that DSD is efficacious in the setting of refractory VF/pVT during routine electrophysiology testing.¹² DSD continues to be used sporadically by electrophysiologists to treat refractory VF.⁸

Numerous hypotheses exist about the mechanism of action. Limited observational data suggest that delivering sequential shocks may lower the defibrillation threshold compared to a traditional single shock.¹³,¹⁴ Alternatively, others hypothesize that defibrillation is a weight-based treatment and larger individuals may require more joules.⁷,¹⁵ The last leading theory for the mechanism of action is that DSD changes the vector of the therapy and may result in more myocardium depolarization.¹²

Importance
There is one case report, three small case series, and two retrospective cohort analyses evaluating the use of DSD in the prehospital setting.¹⁶–²¹ However, to date, there have been no matched case–control studies to evaluate the efficacy of prehospital DSD for refractory VF/pVT.

Goals of This Study
The goal of our study was to determine if the San Antonio Fire Department (SAFD)’s current usage of prehospital DSD is associated with improving survival to hospital admission in the setting of refractory VF/pVT.

MATERIALS AND METHODS
Study Design and Setting
This project is a matched case–control study derived from prospectively collected quality assurance/quality improvement (QA/QI) data. The data set was obtained from the SAFD OHCA QA/QI database between January 2013 and December 2015. The study was designed to adhere to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.²² The University of Texas Health Science Center at San Antonio (UTHSCSA) Institutional Review Board approved our study as part of an ongoing cardiac arrest performance improvement initiative.

The SAFD is the sole 9-1-1 provider for a population of approximately 1.4 million people spread over a 460-square-mile area. The UTHSCSA Department of Emergency Health Sciences’ Office of the Medical Director (OMD) provides medical direction for the SAFD. EMS physicians and fellows provide all online medical direction. The SAFD deploys a four-person fire company and two dual-paramedic-staffed mobile intensive care ambulances to all OHCA calls. The SAFD staffs approximately 75% of its fire companies with at least one paramedic.

During the entire study period, the SAFD EMS VF/pVT protocol directed the lead paramedic to consider DSD after administering three 200-J conventional defibrillations (Zoll-X Series biphasic defibrillator). The OMD delegated the decision to administer DSD to the lead paramedic. In our system, we utilized anterolateral pad placement combined with anterior–posterior pad placement for DSD (Figure 1).
Selection of Participants
Our matched case–control study was derived from consecutive SAFD OHCA patients between January 2013 and December 2015. Our inclusion criterion was refractory VF/pVT, defined as the administration of at least three conventional 200-J defibrillations without conversion to a nonshockable rhythm. We excluded any patients with incomplete relevant data. The cases were defined as patients that survived to hospital admission. The matched controls were defined as OHCA patients that did not survive to hospital admission.

Exposure
The exposure was prehospital DSD.

Methods of Measurement
The UTHSCSA OMD utilizes an internal OHCA database as part of an ongoing QA/QI program. Our database captures a wide variety of variables including: patient demographic information, resuscitative efforts, and patient outcomes. The OMD reviews all SAFD OHCA electronic patient care reports (ePCRs). Relevant data elements are pulled from the ePCR and entered into the database. As soon as practicable after the event (typically within 24 hours), an OMD staff member will conduct a structured interview of the resuscitation team leader. SAFD EMS equipment can be interrogated to collect relevant data if required. The OMD collects patient outcome data for any patient transported to the hospital for further care. Hospital records, obituary reviews, and the Social Security Death Index are used to determine hospital survival.

One author (JGM) extracted the patients with refractory VF/pVT from our OHCA database. He was blinded to patient outcomes but not to the study hypothesis at the time of extraction. The two authors (AJH and AMD) responsible for performing the case–control matching were blinded to the study hypothesis and patient outcomes. The case–control matching team matched the cases following an internally derived algorithm that attempted to control for known confounders.23–26 First, the algorithm directed the two researchers to match the cases with controls within the same year of arrest to attempt to control for any changes in paramedic education and inpatient treatment modalities. After AJH and AMD segregated the patients by year of arrest, the matching occurred. The algorithm directed the two researchers to match the cases by the following categories: EMS-witnessed arrest, witnessed arrest, bystander CPR, age ± 5 years, race, and time of arrest. EMS-witnessed arrest was given the highest priority for matching and time of arrest was given the lowest priority. The two authors matched each unique case with the best available unique control. After the unique cases were matched with unique controls, one author (JGM) performed the data analysis.

Outcomes
The primary outcome of our study was survival to hospital admission. Secondary outcomes were prehospital return of spontaneous circulation (ROSC), survival to hospital discharge, and neurologically intact survival to hospital discharge (defined as Cerebral Performance Category [CPC] 1 and 2).

Data Analysis
Our team used Fisher’s exact test to examine the association between DSD and our identified outcomes. Statistical significance was defined as $p < 0.05$. We utilized an odds ratio (OR) to estimate the magnitude of the effect that DSD had on our identified outcomes. We used the Wilson/Brown method to determine the 95% confidence intervals (CIs) of proportions. Microsoft Excel was used to manage the data. We analyzed the data with Graph Pad Prism 7.

This study is retrospective in nature. Therefore, we used all years with finalized data in our registry to arrive at our initial cohort. We assumed that an OR equal to 3.47 correlates to a moderate effect size.27 Additionally we predicted that the percentage of the exposure (DSD) among the controls would be 20%. Our team opted for a 1:1 matched study design based on the size of our available sample. Give these factors our power analysis suggested that a minimum of 49 matched pairs (49 patients who survived to hospital admission and 49 patients who did not survive to hospital admission) would be needed to obtain statistical significance (80% power for a significance of 0.05).

RESULTS
Characteristics of Study Subjects
Of 3,469 consecutive OHCA patients during the study period, 205 OHCA patients met the inclusion criteria of refractory VF/pVT. Ten cases had incomplete outcome data and were excluded from analysis. Sixty-four unique cases of survival to hospital admission were
Figure 2. There were 205 cases from the cardiac arrest database that met inclusion criteria for refractory VF or pVT. Ten cases were excluded as they were missing outcome data. Of the 195 remaining cases of refractory VF/pVT, 64 survived to hospital admission. The matched controls did not survive to hospital admission. OHCA = out-of-hospital cardiac arrest; pVT = pulseless ventricular tachycardia; VF = ventricular fibrillation.

identified and matched with 64 unique controls (Figure 2). The demographics of the DSD and conventional therapy groups are reported in Table 1. A breakdown of the therapies administered to the DSD and conventional therapy groups are reported in Table 2.
Table 1
Demographic Information About the Two Groups, DSD and Those Receiving Conventional Therapy

<table>
<thead>
<tr>
<th></th>
<th>DSD</th>
<th>Conventional Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.3 (±10.6)</td>
<td>58.4 (±13.3)</td>
</tr>
<tr>
<td>Male</td>
<td>88 (70.0–95.8)</td>
<td>77.7 (68.7–84.6)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>16 (6.4–34.7)</td>
<td>16.5 (10.6–24.9)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>60 (40.7–76.6)</td>
<td>38.8 (30.0–48.5)</td>
</tr>
<tr>
<td>White</td>
<td>20 (8.9–39.1)</td>
<td>40.8 (31.8–50.4)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (0.2–19.5)</td>
<td>3.9 (1.5–9.6)</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>32 (17.2–51.6)</td>
<td>50.5 (41.0–59.9)</td>
</tr>
<tr>
<td>Public AED usage</td>
<td>8 (1.4–25.0)</td>
<td>3.9 (1.5–9.6)</td>
</tr>
<tr>
<td>Bystander-witnessed arrest</td>
<td>52 (33.5–70.0)</td>
<td>61.2 (51.5–70.0)</td>
</tr>
<tr>
<td>EMS-witnessed arrest</td>
<td>8 (1.4–25.0)</td>
<td>1.9 (0.3–6.8)</td>
</tr>
</tbody>
</table>

Data are reported as mean (±SD) or % (95% CI).
AED = automated external defibrillator; CPR = cardiopulmonary resuscitation; DSD = double sequential defibrillation.

Table 2
Treatment Information About the Two Groups, DSD and Those Receiving Conventional Therapy

<table>
<thead>
<tr>
<th></th>
<th>DSD</th>
<th>Conventional Therapy</th>
</tr>
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<tbody>
<tr>
<td>ALS response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dispatch to EMS arrival (minutes), median (IQR)</td>
<td>8 (6–12)</td>
<td>8 (6–10)</td>
</tr>
<tr>
<td>CPR augmentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical CPR, % (95% CI)</td>
<td>40.0 (23.4–59.3)</td>
<td>21.0 (14.6–30.3)</td>
</tr>
<tr>
<td>Drugs administered, median (IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone (mg)</td>
<td>450 (450–450)</td>
<td>450 (450–450)</td>
</tr>
<tr>
<td>Epinephrine (mg)</td>
<td>6 (4.5–6.5)</td>
<td>5 (4–6)</td>
</tr>
<tr>
<td>Defibrillations administered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BLS AED usage, % (95% CI)</td>
<td>28.0 (14.3–47.6)</td>
<td>40.8 (31.8–50.4)</td>
</tr>
<tr>
<td>Total EMS defibrillations, median (IQR)*</td>
<td>7 (6–8.75)</td>
<td>5 (4–5)</td>
</tr>
<tr>
<td>Defibrillations prior to DSD attempt, median (IQR)†</td>
<td>4.5 (4–6.75)</td>
<td></td>
</tr>
</tbody>
</table>

AED = automated external defibrillator; ALS = advance life support; BLS = basic life support; DSD = double sequential defibrillation; IQR = interquartile range.

*Includes fire department AED defibrillations, EMS defibrillations, and EMS DSDs.
†Data only available for 2014 and 2015.

Main Results
In our matched case–control study, survival to hospital admission occurred in 48.0% of DSD patients and 50.5% of the conventional therapy patients (p > 0.99; OR = 0.91, 95% CI = 0.40–2.1). Prehospital ROSC occurred in 20.0% of the DSD patients and 40.8% of the conventional therapy patients (p = 0.07; OR = 0.36, 95% CI = 0.14–1.06). Survival to hospital discharge occurred in 16.0% of the DSD patients vs 23.3% of the conventional therapy patients (p = 0.59) (OR = 0.63, 95% CI = 0.22–1.9). Neurologically intact survival to hospital discharge occurred in 12.0% of the DSD patients versus 19.4% of the conventional therapy patients (p = 0.56; OR = 0.57, 95% CI = 0.17–2.1; Table 3).

DISCUSSION
We found no association between the use of prehospital DSD for refractory VF/pVT and survival to hospital admission. Additionally, none of our secondary outcomes demonstrated a difference between the DSD cohort and the conventional therapy cohort. This analysis of the effectiveness of our prehospital DSD protocol had sufficient power to detect a moderate effect on the patient-centered outcome of survival to hospital admission. Currently, we believe that this study is the largest to date that compares prehospital DSD with conventional therapy in refractory VF/pVT management. Additionally, using a matched case–control design allowed us to mitigate some confounding variables from our cohort.
Previously, we reported our experience with DSD in recurrent and refractory shockable rhythms OHCA. Among the authors, there was disagreement over whether or not recurrent and refractory shockable rhythms should be analyzed together. Our previous study did not attempt to control for differences between the two populations. This matched case–control study was designed to alleviate these concerns.

The three case series on the prehospital use of DSD found neurologically intact survival rates of 0, 16.6, and 28.6%, respectively.17,19,20 The London-based retrospective cohort analysis found a 7.0% survival to hospital discharge.21 Our finding of 12% neurologically intact survival to hospital discharge is in line with these publications.

Our study suggests that there is no benefit to our current protocol of considering prehospital DSD after the third conventional defibrillation for refractory VF/pVT. One hypothesis for our findings is that we deployed the DSD therapy too late in the patient’s clinical course to make a significant difference in their outcome. The fact that we typically deploy DSD after the fourth shock in our system supports this hypothesis. By deploying DSD as a salvage therapy in our system, we selected for the most refractory electrical storm cases. The interquartile range of the total EMS defibrillations of the DSD cohort (6–8.75) and the standard therapy cohort (4–5) supports the assertion that patients in the DSD cohort were more “refractory” than the standard therapy cohort. If one extends this theory to its ultimate conclusion, the fact that there was no difference in the DSD cohort versus conventional therapy cohort may be indicative of DSD having some clinical effect. Alternatively, it is equally plausible that DSD is no more effective than conventional defibrillation. The primary endpoint of survival to hospital admission is merely a step to the ultimate objective of neurologically intact survival to hospital discharge. To make a significant impact on the real objective, the effect size on the intermediate step of survival to hospital admission needs to be significant. The 95% CI of our OR (0.40 to 2.1) is not consistent with the required effect size that would make DSD an essential link in the chain of survival for electrical storm patients.

As a result of these data, we critically examined our policy. In our system, two defibrillators will be present at all of our OHCA resuscitations. Therefore, implementing DSD requires no change in how we allocate our resources. We modified our treatment strategy to include more aggressive DSD implementation in combination with a plan to screen these electrical storm patients for a combination of mechanical CPR-facilitated transport, ECMO, and PCI.

Future studies are needed from other large-volume EMS systems. Researchers should attempt to compare DSD outcomes with conventional therapy outcomes in those systems. Due to the low incidence of the disease process and lack of clear benefit of the therapy, a prospective multisystem cohort analysis is the best option for determining if DSD is a beneficial prehospital therapy.

**LIMITATIONS**

Our study has limitations. First, matched case–control studies are inherently vulnerable to selection bias. We attempted to mitigate this by blinding the individuals responsible for matching cases and controls. Additionally, our predefined matching algorithm was designed to minimize the subjective nature of matching cases with controls. Second, our protocol leaves the decision to administer DSD to the lead paramedic. This protocol structure increases the possibility of an unknown confounding variable causing bias. In our system, the data suggest that DSD was employed as a salvage therapy for refractory VF patients. Third, a matched case–control study is only generalizable to a similar target

<table>
<thead>
<tr>
<th>Outcome</th>
<th>DSD</th>
<th>Conventional Therapy</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival to hospital admission</td>
<td>48% (12/25)</td>
<td>50.5% (52/103)</td>
<td>1.00</td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prehospital ROSC</td>
<td>20% (5/25)</td>
<td>40.8% (42/103)</td>
<td>0.07</td>
</tr>
<tr>
<td>Survival to hospital discharge</td>
<td>16% (4/25)</td>
<td>23.3% (24/103)</td>
<td>0.59</td>
</tr>
<tr>
<td>CPC 1 or 2 survival to hospital discharge</td>
<td>12% (3/25)</td>
<td>19.4% (20/103)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

CPC = Cerebral Performance Category; DSD = double sequential defibrillation; ROSC = return of spontaneous circulation.
population. This data set was derived from a large, highly resourced advanced life support EMS system. Additionally, the source of our refractory VF/pVT cohort is QA/QI data. Therefore, it is not generalizable. Fourth, we were not able to control for quality of CPR. Although we do use a standard CPR feedback device during our resuscitations, that data point is not imported into the ePCR. The UTHSCSA OMD lacks the workforce to manually download CPR quality data for all of our OHCA patients. Previous data sets that yielded negative results after analysis have subsequently yielded positive results on reanalysis after controlling for CPR quality. Finally, data fidelity was not complete in the existing OHCA database for some of the relevant data elements. As a result of the omitted data, 4.8% of the relevant patient population was not eligible for inclusion. These missing data points are a source of information bias.

CONCLUSION

Our matched case–control study on the prehospital use of double sequential defibrillation for refractory ventricular fibrillation/pulseless ventricular tachycardia found no evidence of associated improvement in survival to hospital admission. Our current protocol of considering prehospital double sequential defibrillation after the third conventional defibrillation in out-of-hospital cardiac arrest is ineffective.

We thank the San Antonio Fire Department, the Office of the Medical Director for the San Antonio Fire Department, and Joan Petty Polk for their significant contributions to this work.

References

19. Cortez E, Krebs W, Davis J, Keseg DP, Panchal AR. Use of double sequential external defibrillation for refractory
Changes in Pain Score Associated With Clinically Meaningful Outcomes in Children With Acute Pain

Daniel S. Tsze, MD, MPH, Gerrit Hirschfeld, PhD, Carl L. von Baeyer, PhD, Leonor E. Suarez, MFA, and Peter S. Dayan, MD, MSc

ABSTRACT

Background: Identifying changes in pain score associated with clinically meaningful outcomes is necessary when using self-report measures to assess pain in children. We aimed to determine the changes in pain score associated with a minimum clinically significant difference (MCSD), ideal clinically significant difference (ICSD), and patient-perceived adequate analgesia (PPAA) and to evaluate for differences based on initial pain intensity and patient characteristics.

Methods: This was a cross-sectional study of children 6 to 17 and 4 to 17 years old who were assessed using the Verbal Numerical Rating Scale (VNRS) and Faces Pain Scale–Revised (FPS-R), respectively. Children qualitatively described any endorsed change in pain score; those who received an analgesic were asked if they wanted additional analgesics to decrease their pain intensity. We used a receiver operating characteristic curve–based methodology to identify changes in pain score associated with “a little less” and “much less” pain (MCSD and ICSD, respectively) and patients declining additional analgesics because of adequate analgesia (PPAA).

Results: We enrolled 431 children with painful conditions. For the VNRS, raw change and percent reductions in pain scores associated with MCSD, ICSD, and PPAA were 2/10 and 20%, 3/10 and 44%, and 2/10 and 29%, respectively, and for the FPS-R, 2/10 and 33%, 4/10 and 60%, and 4/10 and 40%, respectively. Raw change in pain scores increased with increasing initial pain intensity, but percent reductions remained stable. There were no significant differences based on patient characteristics such as age, sex, and race/ethnicity.

Conclusion: Our findings provide patient-centered outcomes in children that are suitable for designing trials and are generalizable across patient characteristics.

Pain scales such as the Verbal Numerical Rating Scale (VNRS) and Faces Pain Scale–Revised (FPS-R) are frequently used to assess changes in pain intensity in children with painful conditions. These self-report measures of pain have strong validity and reliability in children with acute pain.1,2 To properly
use these measures to assess pain in children, it is necessary to identify changes in pain score associated with clinically meaningful outcomes. These changes in pain score can be used by researchers to design trials based on outcomes and effect sizes that are clinically meaningful to patients and may be one way for clinicians to determine whether their treatment had a clinically meaningful effect on their patients.1–4

Previously reported clinically meaningful outcomes include the minimum clinically significant difference (MCSD) and ideal clinically significant difference (ICSD), which typically represent a change in pain score that a child reports to be “a little less” and “much less,” respectively.5–7 However, these outcomes have not been consistently defined across different self-report measures in children presenting with acute pain, which is necessary prior to their implementation in practice. The generalizability of any clinically meaningful outcome also needs to be evaluated across patients with different initial pain intensities and differing characteristics. A decrease in pain score considered to be meaningful has been shown to vary based on a patient’s initial pain intensity, and a child’s age, sex, and race/ethnicity are related to their ability to describe and quantify pain, as well as their perception of and sensitivity to pain.5,8–15

In addition, a limitation of the MCSD and ICSD is that they do not explicitly address a clinically important goal for children with pain—namely, whether the child feels that his/her pain has been adequately treated. We define the clinically meaningful outcome of “patient-perceived adequate analgesia” (PPAA) as the change in pain score associated with a child declining additional analgesia to make his/her pain intensity less after an initial treatment is administered because he/she feels that his/her pain has been adequately treated. The change in pain score representing PPAA is an outcome measure and has not been previously described and may be a more patient-centered outcome than the MCSD and ICSD. It is unknown if changes in pain score representing an MCSD or ICSD are the same as the change in pain score representing PPAA.

We aimed to determine the changes in pain score in children with acute pain associated with the MCSD, ICSD, and PPAA, when using the VNRS and FPS-R. Our secondary aim was to determine and compare the MCSDs, ICSDs, and PPAA based on initial pain intensity and patient characteristics such as age group, sex, and race/ethnicity. Our exploratory aim was to determine and compare these clinically meaningful outcomes based on primary language and etiology of pain.

**METHODS**

**Study Design**

We conducted an observational cross-sectional study. The institutional review board approved this study with verbal informed consent.

**Study Setting and Population**

We conducted this study in an urban pediatric emergency department (ED) with an annual census of approximately 55,000 visits. This study was part of a larger pain scale validation study that included children with both painful and nonpainful conditions.1 This planned secondary analysis only included children with painful conditions. We enrolled a convenience sample of children aged 4 to 17 years with painful conditions as identified by the triage nurse and confirmed by the study team by asking children themselves whether they had “any pain” or “any hurt.” Children who responded affirmatively were considered to have a painful condition. We excluded children if they had developmental delay or neurologic impairment, intoxication, altered mental status, a medical condition necessitating multiple painful procedures (e.g., malignancy), or a chronic disease associated with pain (e.g., sickle cell disease) or if they did not speak English or Spanish.

**Measurements**

The VNRS has demonstrated strong convergent validity, known-groups validity, responsivity, and test–retest reliability in children 6 to 17 years old with acute pain.1 The VNRS was administered by asking, “On a scale from zero to ten, where zero means no pain and ten means the most or worst pain, how much pain do you have right now?” The interaction was verbal, using no materials or equipment. The FPS-R (Figure 1) has demonstrated strong convergent validity, known-groups validity, responsivity, and test–retest reliability in children 4 to 17 years old with acute pain.2 The FPS-R was administered by showing the child a picture of the pain scale and reading standardized instructions in English or Spanish (www.iasp-pain.org/FPSR). For both the VNRS and the FPS-R, the word “hurt” was used interchangeably with “pain,” depending on what seemed most understandable for each child. Children were
documented as not understanding the VNRS if they did not respond or responded with a nonnumeric response or a number outside the 0 to 10 range, when asked twice. Children were considered as not understanding the FPS-R if they did not respond or select a face when asked twice.

**Procedures**

We performed two serial assessments of pain intensity in each child’s primary language. Children were not provided with the pain intensity score reported during the first assessment when the second assessment was performed. For both the first and the second assessments, the child was asked to report his/her pain intensity first on the VNRS and then on the FPS-R. An analgesic was administered at the treating physician’s discretion after the first assessment. If the child had received an analgesic, the second assessment was conducted 30 to 60 minutes after analgesic administration. During the second assessment, the child was asked: “Is your pain much less, a little less, about the same, a little worse, or much worse compared to before you got your medicine?” The child was then asked, “Do you want more medicine to make your pain less?” The word “hurt” was used interchangeably with “pain,” and the word “smaller” was used interchangeably with “less,” depending on what seemed most understandable for each child. If the child responded that he/she did not want more medicine, he/she was asked for the reason why. If the child stated it was because his/her pain was adequately relieved, then his/her response was documented as “no” (i.e., not wanting more medicine to make his/her pain less). If the child declined medicine for reasons unrelated to pain relief (e.g., medication tasted bad, did not want a needle, afraid of side effects), the study team member would attempt to address and alleviate these concerns and then revisit the child’s desire for additional analgesia. Specifically, the study team member would ask if the child would want any additional medicine to make his/her pain less if there was an analgesic available that did not have any of the specifically disclosed issues, or any other anticipated negative effects. This was repeated until all endorsed concerns were addressed. If the child still declined after having addressed all endorsed concerns, his/her response was documented as no (i.e., not wanting more medicine to make his/her pain less). This interaction was conducted in such a way as to elicit the preferences of the child rather than the caregiver present with the child.

If the child did not receive an analgesic, the second assessment was conducted 30 to 60 minutes after the first assessment was performed. During the second assessment, the child was asked, “Is your pain much less, a little less, about the same, a little worse, or much worse compared to how you felt about [number of minutes since last assessment] ago?” or “... compared with how you felt the last time I asked you how much pain or hurt you had?” depending on what was most understandable for each child. Children who did not receive an analgesic were not asked if they wanted additional analgesia to make their pain less.

**Outcome Measures**

The MCSD and ICSD are the changes in pain score associated with a child reporting that his/her pain intensity is a little less or much less, respectively.5–7 PPAA is an outcome measure developed by the authors and described here for the first time. We defined PPAA as the change in pain score associated with a child declining additional analgesia to make his/her pain intensity less after an initial treatment is administered because he/she feels that his/her pain has been adequately treated (as opposed to declining additional analgesia for other reasons such as fear of side effects). A child was determined to have experienced PPAA if they responded no when asked, “Do...
you want more medicine to make your pain less?” using the specified procedure described above. PPAA is conceptually similar to the previously described “perceived need for medicine,” which is the pain score at which a child answers “yes” to questions such as, “Do you feel the need for more pain medicine right now?” or the pain score which a child reports when asked what pain score the minimum would be to warrant treatment. However, PPAA is a change in pain score while perceived need for medicine is a single pain score.

Data Analyses
Descriptive statistics were used to describe the characteristics of patients enrolled, and the changes in pain scores endorsed by children who reported a MCSD, ICSD, and PPAA. For the VNRS, children aged 6 to 17 years old were analyzed. For the FPS-R, children aged 4 to 17 years old were analyzed. For both pain scales, patients were removed if they did not provide a response consistent with the valid options available for each scale (e.g., for the FPS-R, selecting the space in between two faces, instead of selecting a face itself). For the MCSD and ICSD determination, patients were removed from analysis if they did not understand, or did not respond to, the question asked at the second assessment to qualitatively describe their change in pain. For the PPAA determination (which is relevant only to patients who have received an analgesic), patients were removed from analysis if 1) they did not receive an analgesic or 2) they did not understand, or did not respond to, the questions asked regarding whether they wanted additional analgesia.

To determine the change in pain score with the best test characteristics associated with MCSD, ICSD, and PPAA, we used a method based on the receiver operating characteristic (ROC) curve. ROC-based methods use dichotomous reference criteria to determine cut points for continuous measures that optimally differentiate between the two classes of the criteria. Specifically, we determined the sensitivity, specificity, and area under the curve (AUC) of all possible cut points and determined the cut point as optimal that had the lowest absolute difference between sensitivity and specificity (and therefore the highest AUC). We used three different reference criteria: First, for MCSD we compared children who reported that their pain was much less, to those whose pain was a little less, about the same, a little worse, or much worse. Third, for PPAA we compared children who answered no when asked if they wanted additional analgesia to make their pain less (which represented PPAA) to those who answered yes to the same question. To guard against finding spurious differences, we used bootstrapping to determine the magnitude of the variability of each cut point. We reported the change in pain score for the MCSD, ICSD, and PPAA as both a raw change and a percent reduction in pain score.

To evaluate for differences in MCSD, ICSD, and PPAA based on initial pain intensity, we determined each within categories of initial pain intensity (i.e., mild, moderate, and severe) for both pain scales using the same ROC-based methods described earlier. We defined the categories of initial pain intensity using conventionally accepted thresholds (i.e., 1–3 = mild, 4–6 = moderate, and 7–10 = severe). Similarly, to evaluate for differences based on patient characteristics, we determined and compared the MCSD, ICSD, and PPAA for subgroups based on age group (younger, 6 to 7 years for VNRS and 4 to 7 years for FPS-R; older, 8 to 17 years); sex (female and male); race/ethnicity (Hispanic, black, and white); primary language (English and Spanish); and etiology of pain (traumatic and nontraumatic). The age categories were selected to stratify younger patients into age groups that have been shown to demonstrate more variability in their accuracy and responses when describing pain.

The sample size was based on the parent study for which this study was a planned secondary analysis. We conducted statistical analyses using SPSS (version 24, IBM Corp.) and R (version 3.5, R Foundation for Statistical Computing).

RESULTS
Characteristics of Study Subjects
From April 2014 to March 2016, we enrolled 431 children with painful conditions (Figure 2), with Table 1 showing the characteristics of the patients analyzed for each clinically meaningful outcome when using the VNRS and FPS-R. There were more patients reporting an initial pain score representing severe pain intensity (i.e., 7–10) when using the VNRS compared to the FPS-R, with the understanding that the VNRS has more pain score options to choose from that
represent severe pain intensity (i.e., 7, 8, 9, or 10 for the VNRS, compared to 8 or 10 for the FPS-R).

**Main Results**

Tables 2 and 3 show the MCSD, ICSD, and PPAA as raw change and percent reduction in pain score and the associated test characteristics for the VNRS and FPS-R, respectively. The raw change in pain score representing PPAA was similar to the MCSD when using the VNRS and similar to the ICSD when using the FPS-R. The percent reduction changes in pain score representing PPAA for both pain scales were greater than the MCSD and less than the ICSD.

Tables S1 and S2 in Data Supplement S1 (available

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**Figure 2.** Patient enrollment. FPS-R = Faces Pain Scale–Revised; ICSD = ideal clinically significant difference; MCSD = minimum clinically significant difference; PPAA = patient-perceived adequate analgesia; VNRS = Verbal Numerical Rating Scale.
Table 1
Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Analyzed for VNRS</th>
<th>Analyzed for FPS-R</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>MCSD/ICSD (n = 342)</td>
<td>PPAA (n = 239)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>172 (50.3)</td>
<td>121 (50.6)</td>
</tr>
<tr>
<td>Male</td>
<td>170 (49.7)</td>
<td>118 (49.4)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
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<td>N/A</td>
</tr>
<tr>
<td>5</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>6</td>
<td>46 (13.5)</td>
<td>25 (10.5)</td>
</tr>
<tr>
<td>7</td>
<td>47 (13.7)</td>
<td>19 (7.9)</td>
</tr>
<tr>
<td>8</td>
<td>17 (5)</td>
<td>10 (4.2)</td>
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<td>9</td>
<td>27 (7.9)</td>
<td>17 (7.1)</td>
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<td>10</td>
<td>18 (5.3)</td>
<td>14 (5.9)</td>
</tr>
<tr>
<td>11</td>
<td>30 (8.8)</td>
<td>25 (10.5)</td>
</tr>
<tr>
<td>12</td>
<td>29 (8.5)</td>
<td>24 (10)</td>
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<td>13</td>
<td>24 (7)</td>
<td>21 (8.8)</td>
</tr>
<tr>
<td>14</td>
<td>33 (9.6)</td>
<td>28 (11.7)</td>
</tr>
<tr>
<td>15</td>
<td>29 (8.5)</td>
<td>25 (10.5)</td>
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<tr>
<td>16</td>
<td>24 (7)</td>
<td>20 (8.4)</td>
</tr>
<tr>
<td>17</td>
<td>18 (5.3)</td>
<td>11 (4.6)</td>
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<tr>
<td><strong>Race/ethnicity</strong></td>
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<tr>
<td>Hispanic</td>
<td>271 (79.2)</td>
<td>188 (78.7)</td>
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<tr>
<td>Black</td>
<td>44 (12.9)</td>
<td>32 (13.4)</td>
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<tr>
<td>White</td>
<td>19 (5.6)</td>
<td>13 (5.4)</td>
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<tr>
<td>Other*</td>
<td>8 (2.3)</td>
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<tr>
<td><strong>Primary language</strong></td>
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<tr>
<td>English</td>
<td>312 (91.2)</td>
<td>225 (94.1)</td>
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<tr>
<td>Spanish</td>
<td>30 (8.8)</td>
<td>14 (5.9)</td>
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<td><strong>Painful condition</strong></td>
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<tr>
<td>Soft tissue injury</td>
<td>93 (27.2)</td>
<td>79 (33.1)</td>
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<tr>
<td>Abdominal pain</td>
<td>79 (23.1)</td>
<td>48 (20.1)</td>
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<tr>
<td>Headache</td>
<td>42 (12.3)</td>
<td>34 (14.2)</td>
</tr>
<tr>
<td>Ear/throat pain</td>
<td>41 (12)</td>
<td>24 (10)</td>
</tr>
<tr>
<td>Fracture</td>
<td>20 (5.8)</td>
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<td>Back pain</td>
<td>14 (4.1)</td>
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<td>Chest pain</td>
<td>12 (3.5)</td>
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<td>Laceration</td>
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<tr>
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<tr>
<td><strong>Initial pain score reported</strong></td>
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<tr>
<td>0</td>
<td>4 (1.2)</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>1–3</td>
<td>45 (13.2)</td>
<td>14 (5.8)</td>
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<tr>
<td>4–6</td>
<td>112 (32.7)</td>
<td>71 (29.7)</td>
</tr>
<tr>
<td>7–10</td>
<td>181 (52.9)</td>
<td>151 (63.2)</td>
</tr>
<tr>
<td><strong>Reported change in pain</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Much less</td>
<td>73 (21.3)</td>
<td>57 (23.8)</td>
</tr>
<tr>
<td>A little less</td>
<td>146 (42.7)</td>
<td>124 (51.9)</td>
</tr>
<tr>
<td>About the same</td>
<td>87 (25.4)</td>
<td>44 (18.4)</td>
</tr>
<tr>
<td>A little more</td>
<td>23 (6.7)</td>
<td>7 (2.9)</td>
</tr>
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(Continued)
as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13683/full) show, for both the VNRS and FPS-R, a trend of increasing raw change score associated with increasing initial pain intensity for MCSD, ICSD, and PPAA, respectively. The percent reduction in pain score remained similar across all three categories of initial pain intensity for the VNRS, but only across categories of moderate and severe initial pain intensity for the FPS-R. For both pain scales, raw change and percent reduction in scores associated with MCSD, ICSD, and PPAA appeared to be similar between subgroups based on age, sex, race/ethnicity, primary language, or etiology of pain (Data Supplement S1, Tables S3 and S4).

Figure 3 shows the distribution of pain scores reported that were associated with a MCSD, ICSD, and PPAA for the VNRS and FPS-R. A large proportion of children endorsed a change in pain score that was greater than the changes in pain score representing MCSD, ICSD, and PPAA that we identified in this study (Tables 2 and 3). For the VNRS, 51 (34.9%), 45 (61.6%), and 71 (52.5%) children endorsed a change in pain score representing a MCSD, ICSD, and PPAA, respectively, that was higher than the estimates we identified. For the FPS-R, 57 (34.8%), 39 (41.1%), and 46 (29.3%) children endorsed a change in pain score representing a MCSD, ICSD, and PPAA, respectively, that was higher than the estimates we identified. There were a

Table 1 (continued)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Analyzed for VNRS</th>
<th>Analyzed for FPS-R</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>MCSD/ICSD (n = 342)</td>
<td>PPAA (n = 239)</td>
</tr>
<tr>
<td>Much more</td>
<td>13 (3.8)</td>
<td>7 (2.9)</td>
</tr>
<tr>
<td>Analgesics administered</td>
<td>Ibuprofen</td>
<td>Parenteral opioid</td>
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<td></td>
<td>124 (36.3)</td>
<td>53 (15.5)</td>
</tr>
<tr>
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<td>144 (34.9)</td>
<td>57 (13.8)</td>
</tr>
<tr>
<td></td>
<td>144 (52.4)</td>
<td>57 (20.7)</td>
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</tbody>
</table>

Data are reported as n (%).
*Other = American Indian or Alaska Native, Asian, more than one, and “don’t know”
†Includes both pharmacologic and nonpharmacologic (e.g., ice packs) analgesics
FPS-R = Faces Pain Scale–Revised; ICSD = ideal clinically significant difference; MCSD = minimum clinically significant difference; PPAA = patient-perceived adequate analgesia; VNRS = Verbal Numerical Rating Scale.

Table 2
Changes in VNRS Pain Scores Representing MCSD, ICSD, and PPAA and Associated Test Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Change in Pain Score (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCSD*</td>
<td>Raw change score 2 (1–2)</td>
<td>0.74 (0.69–0.92)</td>
<td>0.89 (0.71–0.93)</td>
<td>0.88 (0.84–0.91)</td>
</tr>
<tr>
<td></td>
<td>Percent reduction 20 (14–22)</td>
<td>0.82 (0.75–0.86)</td>
<td>0.81 (0.76–0.86)</td>
<td>0.84 (0.79–0.89)</td>
</tr>
<tr>
<td>ICSD†</td>
<td>Raw change score 3 (3–3)</td>
<td>0.74 (0.63–0.84)</td>
<td>0.78 (0.73–0.83)</td>
<td>0.83 (0.76–0.88)</td>
</tr>
<tr>
<td></td>
<td>Percent reduction 44 (40–50)</td>
<td>0.77 (0.72–0.85)</td>
<td>0.80 (0.74–0.83)</td>
<td>0.82 (0.77–0.87)</td>
</tr>
<tr>
<td>PPAA‡</td>
<td>Raw change score 2 (2–3)</td>
<td>0.74 (0.53–0.80)</td>
<td>0.59 (0.52–0.78)</td>
<td>0.70 (0.63–0.77)</td>
</tr>
<tr>
<td></td>
<td>Percent reduction 29 (25–33)</td>
<td>0.69 (0.61–0.74)</td>
<td>0.67 (0.62–0.74)</td>
<td>0.72 (0.66–0.78)</td>
</tr>
</tbody>
</table>

Sensitivity, specificity, and AUC reflect the ability of the determined change in pain score to identify those who have or have not experienced a specific clinically meaningful outcome (i.e., MCSD, ICSD, or PPAA).
AUC = area under the curve; ICSD = ideal clinically significant difference; MCSD = minimum clinically significant difference; PPAA = patient-perceived adequate analgesia; VNRS = Verbal Numerical Rating Scale.
*Number of patients endorsing MCSD = 146
†Number of patients endorsing ICSD = 73
‡Number of patients endorsing PPAA = 136
small number of children who reported an increase (rather than decrease) in pain score, despite endorsing a clinically meaningful decrease in pain: for the VNRS, there were five (2.3%) children who did so when endorsing an MCSD or ICSD and six (4.4%) children who did so when reporting PPAA; for the FPS-R, there was one (0.4%) child who did so when endorsing an MCSD and six (3.8%) children who did so when reporting PPAA. There were children of both younger and older ages in this cohort that reported an increase in pain score.

**DISCUSSION**

We have identified raw change and percent reduction in pain scores associated with clinically meaningful outcomes in children with acute pain with the use of the VNRS and FPS-R. These changes in pain score appear to be similar across most patient characteristics, although we observed higher raw changes in pain score associated with higher initial pain intensity. Although we have determined the estimates that best identify the MCSD, ICSD, and PPAA for most patients, we observed a wide range of scores reported by children associated with each outcome.

The changes in pain score we identified allow researchers to design trials based on clinically meaningful outcomes using two of the most commonly used self-report measures of pain in children. The PPAA, in particular, may be preferable to the MCSD or ICSD, neither of which necessarily represents a patient’s desired goal when seeking treatment for their pain. Our findings demonstrate that the raw change and percent reduction in pain scores representing PPAA are not consistently the same as those representing either the MCSD or the ICSD when using the VNRS or FPS-R. In particular, the percent reduction in pain score representing PPAA was greater than the MCSD and less than the ICSD when both pain scales were used. This highlights the importance of asking a child a question that specifically addresses their own perception of whether they experienced adequate analgesia, rather than assuming that they experienced adequate analgesia just because they reported a change in pain score that was associated with a subjective decrease in pain that was a little less or much less.

Researchers may prefer to choose the percent reduction instead of raw change in pain score as a desired effect size for trials, given the variability in the raw change in pain score across different categories of initial pain intensity. The change in pain score required to experience a meaningful decrease in pain has been shown to differ based on a patient’s initial pain intensity; a higher initial pain intensity usually requires a greater decrease in pain to achieve a meaningful improvement.5,14,15 We observed a similar finding in our study, with the raw change scores required to achieve a MCSD, ICSD, or PPAA increasing with increasing initial pain intensity. However, the percent reductions in pain score associated with MCSD, ICSD, and PPAA appear to be more consistent and

<table>
<thead>
<tr>
<th>Change in Pain Score (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MCSD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw change score</td>
<td>2 (2–2)</td>
<td>0.85 (0.81–0.89)</td>
<td>0.87 (0.83–0.90)</td>
</tr>
<tr>
<td>Percent reduction</td>
<td>33 (25–33)</td>
<td>0.81 (0.77–0.88)</td>
<td>0.82 (0.75–0.86)</td>
</tr>
<tr>
<td><strong>ICSD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw change score</td>
<td>4 (4–4)</td>
<td>0.63 (0.53–0.73)</td>
<td>0.79 (0.74–0.83)</td>
</tr>
<tr>
<td>Percent reduction</td>
<td>60 (60–67)</td>
<td>0.80 (0.71–0.84)</td>
<td>0.77 (0.74–0.82)</td>
</tr>
<tr>
<td><strong>PPAA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw change score</td>
<td>4 (2–4)</td>
<td>0.51 (0.44–0.84)</td>
<td>0.78 (0.49–0.84)</td>
</tr>
<tr>
<td>Percent reduction</td>
<td>40 (40–50)</td>
<td>0.71 (0.63–0.76)</td>
<td>0.70 (0.65–0.78)</td>
</tr>
</tbody>
</table>

Sensitivity, specificity, and AUC reflect the ability of the determined change in pain score to identify those who have or have not experienced a specific clinically meaningful outcome (i.e., MCSD, ICSD, or PPAA). AUC = area under the curve; ICSD = ideal clinically significant difference; MCSD = minimum clinically significant difference; PPAA = patient-perceived adequate analgesia; VNRS = Verbal Numerical Rating Scale.

*Number of patients endorsing MCSD = 164
†Number of patients endorsing ICSD = 95
‡Number of patients endorsing PPAA = 157.
stable across the categories of moderate and severe pain intensity for both the VNRS and the FPS-R. This would suggest that using a percent reduction in pain score might be a more generalizable estimate for effect size when studying the treatment of pain in children presenting with moderate to severe initial pain intensity.

We did not find any significant differences based on patient characteristics in our identified estimates of clinically meaningful outcomes. The changes in pain score representing each outcome were similar between the subgroups based on patient characteristics, suggesting that the estimates determined for MCSD, ICSD, and PPAA are generalizable across most populations.
There were some variations noted in subgroups based on race/ethnicity and primary language, but these differences were not consistently observed in both pain scales, nor were they consistently present in both raw change and percent reductions in pain score within each subgroup or between each clinically meaningful outcome. The relatively smaller number of individuals available for analyses in some of these subgroups may have resulted in larger variability in these estimates and the observed differences in estimates identified.

The PPAA has not been previously described, but the MCSD and ICSD for the VNRS and FPS-R have been previously reported in similar populations of children with acute pain presenting to the ED. For the VNRS, Bailey et al. studied 202 children between the ages of 8 and 17 years and identified an MCSD of 1/10 and an ICSD of 2.5/10. These estimates are lower than those identified in this study. The difference may be due to differing analysis methods, with Bailey et al. using a distribution-based method to identify the median score associated with MCSD and ICSD, rather than the ROC-based methodology that we used. A ROC-based methodology may be preferable, as it allows one to select an estimate with optimal test characteristics, rather than being committed to whatever test characteristics are associated with a measure of central tendency. For the FPS-R, we previously studied 314 children between the ages of 4 and 17 years and identified a raw change and percent reduction in pain score of 2/10 and 25%, respectively, for MCSD and a raw change and percent reduction in pain score of 3/10 and 60%, respectively, for ICSD. We used the same ROC-based methodology in this prior study, the results of which are similar to those observed in this study.

Although these changes in pain score associated with clinically meaningful outcomes are useful for research, they are not useful on an individual patient basis. We observed a wide range of changes in pain scores associated with each outcome (Figure 3). A small number of patients even reported an increase, rather than decrease, in pain score to represent a MCSD, ICSD, or PPAA. If we were to use any of the changes in pain score identified in our study as a goal for treating individual patients, as many as 30% to 60% of them could potentially be inadequately treated for their pain. Therefore, our findings suggest that these changes in pain score associated with MCSD, ICSD, and PPAA may be useful as population-based estimates for research but should not be used to guide treatment decisions for individual patients. What a patient perceives to be clinically meaningful and whether a patient desires additional analgesia are multifactorial: it is more complex than a single number and is influenced by each patient’s individual pain temperament or sensitivity, proclivity toward medications, and degree of aversion regarding adverse events. Rather than providing additional analgesia based solely on whether a certain change in pain score was achieved, it may be more appropriate for clinicians to ask whether or not the child desires additional analgesia, while taking into consideration the child’s personal preferences and perceptions and the clinical context.

LIMITATIONS

Our study has several limitations. We enrolled a convenience sample rather than consecutive patients, although our sample included a diverse representation of painful conditions, analgesics administered, and distribution of pain intensities. Changes in pain scores were reported to a member of the study team and not recorded in a blinded fashion, so subjects could have been subtly influenced to respond in ways that were consistent with the study team member’s expectations. We only studied children with acute pain and did not include children with chronic or recurrent pain states, such as sickle cell disease. Our findings may not be generalizable to these children due to differences in how they perceive and respond to pain. We did not document the reason why a child did not receive an analgesic and do not know if it was because the child declined an analgesic, because the clinician chose not to administer an analgesic, or for some other reason.

CONCLUSIONS

We have determined changes in pain score associated with a minimum clinically significant difference, ideal clinically significant difference, and patient-perceived adequate analgesia. Patient-perceived adequate analgesia may be a preferable and more patient-centered outcome than a minimum clinically significant difference and ideal clinically significant difference, and a percent reduction is more stable than a raw change in pain score across different categories of pain intensity. These population-based estimates of clinically meaningful outcomes are generalizable across different
subgroups based on patient characteristics and may be useful when selecting a desired effect size when designing trials. However, these changes in pain score are not appropriate for making treatment decisions at the level of the individual patient.

We thank Vartan Pahalyants, Allison Hyland, Jeffrey Sung, and Caitlin Oldenkamp for their assistance with patient enrollment.

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.13683/full

Data Supplement S1. Supplemental material.
ABSTRACT

Background: The optimal order of drug administration (sedative first vs. neuromuscular blocking agent first) in rapid sequence intubation (RSI) is debated.

Objective: We sought to determine if RSI drug order was associated with the time elapsed from administration of the first RSI drug to the end of a successful first intubation attempt.

Methods: We conducted a planned secondary analysis of a randomized trial of adult ED patients undergoing emergency orotracheal intubation that demonstrated higher first-attempt success with bougie use compared to a tracheal tube + stylet. Drug choice, dose, and the order of sedative and neuromuscular blocking agent were not stipulated. We analyzed trial patients who received both a sedative and a neuromuscular blocking agent within 30 seconds of each other who were intubated successfully on the first attempt. The primary outcome was the time elapsed from complete administration of the first RSI drug to the end of the first intubation attempt, a surrogate outcome for apnea time. We performed a multivariable analysis using a mixed-effects generalized linear model.

Results: Of 757 original trial patients, 562 patients (74%) met criteria for analysis; 153 received the sedative agent first, and 409 received the neuromuscular blocking agent first. Administration of the neuromuscular blocking agent before the sedative agent was associated with a reduction in time from RSI administration to the end of intubation attempt of 6 seconds (95% confidence interval = 0 to 11 sec).

Conclusion: Administration of either the neuromuscular blocking or the sedative agent first are both acceptable. Administering the neuromuscular blocking agent first may result in modestly faster time to intubation. For now, it is reasonable for physicians to continue performing RSI in the way they are most comfortable with. If future research determines that the order of medication administration is not associated with awareness of neuromuscular blockade, administration of the neuromuscular blocking agent first may be a logical default administration method to attempt to minimize apnea time during intubation.

Rapid sequence intubation (RSI) traditionally involves the sequential administration of a sedative and neuromuscular blocking agent. The sedative agent renders the patient unconscious; the neuromuscular blocking agent produces muscle relaxation, which improves laryngeal view, reduces intubation-associated complications, and improves the likelihood of intubation success. RSI is the most common method of emergency intubation, used in approximately 85% of ED intubations and 75% of intensive care unit intubations. Although both drugs are administered in quick succession, to our knowledge the order of drug administration is not based on empiric data.

Safe apnea time, the interval between apnea and hypoxemia, is difficult to anticipate for an individual patient. Safe apnea time can be as short as several seconds and as long as several minutes, depending on patient characteristics (e.g., age, body mass index, underlying illness, metabolic rate, acid/base status, shunt physiology, among others) and the method of...
preoxygenation. Because safe apnea time cannot be known prospectively, minimizing total apnea time, the interval from apnea to initial ventilation after intubation, is a goal of RSI when performing intubation in critically ill patients. Drug order in RSI could potentially affect apnea time.

While administration of the sedative agent first is common and increases the likelihood of adequate sedation prior to neuromuscular blockade, sedatives can cause hypoventilation and apnea. If hypoventilation or apnea precede the onset of neuromuscular blockade, the patient incurs both an increased risk of hypoxemia and a potential delay between apnea onset and optimal intubating conditions (i.e., full muscle relaxation). In contrast, administration of the neuromuscular blocking agent first may better align the onset of apnea caused by the sedative agent with the onset of optimal intubating conditions, thereby minimizing unnecessary apnea time. While some advocate against this approach for fear of patient awareness while under neuromuscular blockade, it has been studied in the operating room setting.

We sought to determine if RSI drug order was associated with the time elapsed from administration of the first RSI drug to the end of a successful first intubation attempt. This interval was chosen as a pragmatic surrogate for apnea time.

Selection of Participants
From September 2016 through August 2017 we enrolled consecutive patients undergoing endotracheal intubation with a Macintosh laryngoscope blade, excluding prisoners, pregnant women, and those with known distortion of upper airway or glottic structures.

For this secondary analysis, as we were interested in RSI drug order, we analyzed only those patients who received both a sedative (including ketamine or etomidate) and a neuromuscular blocking agent (with succinylcholine or rocuronium). We excluded those with missing data for the timing of drug administration. We excluded other pharmacologic agents used for RSI (e.g., propofol, midazolam, atracurium) because they are used infrequently in our ED and nationally.

Both sedative and neuromuscular blocking agents should be administered near simultaneously in RSI, a delay of greater than 30 seconds between drug administrations seems unreasonable for RSI, so we chose to exclude those cases. We excluded those not intubated successfully on the first attempt because patient, intubator, and device characteristics are more likely than drug order to influence first attempt success. Conversely, drug order is more likely to influence the time elapsed from drug administration to successful intubation than it is to influence intubation success. Additionally, attempt duration likely varies between failed and successful intubation attempts, potentially confounding the association of interest in this study.

Interventions
In the main trial, we randomized patients to bougie or tracheal tube + stylet for the first attempt at orotracheal intubation. Drug choice, dose, and the order of sedative and neuromuscular blocking agent were at the discretion of the intubating physician. In both groups (bougie or tracheal tube + stylet), the laryngoscope blade was kept in the mouth until the endotracheal tube was successfully placed into the trachea.

Methods of Measurement
Trained research associates prospectively collected detailed process and outcome data beginning at randomization and ending 1 minute following the end of the first intubation attempt. Key process data captured by manual timing with a stopwatch included time of drug administration (defined as when the drug syringe was completely empty) and when the intubation attempt began and ended. Intubation attempts began
when the laryngoscope was placed in the mouth and ended when the laryngoscope was removed from the mouth, regardless of whether bougie or tube passage was attempted. After the procedure, the intubating physician completed a structured data collection form to gather additional information about the patient and intubation attempts, including whether any difficult airway characteristics were present, including body fluid(s) obscuring the laryngeal view, airway obstruction or edema, obesity, short neck, small mandible, large tongue, facial trauma, or cervical spine immobilization.

Outcome Measures
We defined the primary outcome, intubation time, as the time elapsed from administration of the first RSI drug to removal of the laryngoscope blade (end of the attempt). This represents a pragmatic surrogate for apnea time, as there was no way to reliably record the onset of hypopnea, bradypnea, or actual apnea during emergency intubation. Secondary outcomes included first-attempt duration, hypoxemia, and first-attempt success (this final outcome analyzed patients who met other inclusion criteria, regardless of whether the first attempt was successful, \[N = 610\]).

Primary Data Analysis
Patients were classified based on which drug they received first (neuromuscular blocking agent or sedative). We present baseline characteristics and intubation process measures stratified by RSI drug order. We describe the outcomes stratified by drug order and neuromuscular blocking agent used, with medians and interquartile ranges (IQR) or proportions and 95% confidence intervals (CIs), as appropriate. Differences in proportion or median differences are reported.

Because this secondary analysis was observational we performed a multivariable analysis to control for potential confounding. We constructed a mixed-effects generalized linear model for the outcome of elapsed time from the end of complete administration of the first RSI drug until the end of the first intubation attempt (intubation time). The independent variable of interest was RSI drug order. We selected other independent variables a priori that could potentially affect the intubation time, including specific neuromuscular blocking agent (succinylcholine or rocuronium), first device passed (bougie or tracheal tube + stylet), whether the video laryngoscope screen was ever viewed during the attempt, presence of any difficult airway characteristics, and Cormack-Lehane grade. A variable identifying each unique intubating physician was included as a random-effect term.

The specific neuromuscular blocking agent was included because, at recommended doses, succinylcholine has a slightly faster onset than rocuronium. Screen viewing was included because intubations requiring screen usage may last longer. We did not include the laryngoscope type as a covariate because in the trial more than 95% of patients were intubated using a C-MAC Macintosh blade. To assess goodness of fit we plotted the deviance residuals against the estimated linear predictor.

We did not perform any sample size calculations for this analysis as the size of this trial because no estimates of intubation time stratified by RSI medication order exist; additionally, the sample size was determined by the parent trial. As the standard deviation for intubation time was 23 seconds, we estimated that the parent trial size of 757 would provide 80% power to detect an absolute difference of 6 seconds between the two groups, a difference that could have clinical relevance in certain patient populations. We used Stata (Version 15, StataCorp) for all data analyses.

Sensitivity Analyses
We performed two sensitivity analyses to account for patients excluded in the main analysis. The first relaxed our requirement that the first intubation attempt be successful. The second sensitivity analysis additionally relaxed our requirement RSI drugs needed to be administered within 30 seconds of each other. In both sensitivity analyses we used the same mixed-effects generalized linear model with the same covariates as the primary analysis.

RESULTS

Characteristics of Study Subjects
Of 757 patients enrolled in the BEAM trial, 562 were eligible for inclusion in the main analysis, 153 (27%) with the sedative agent administered first and 409 (73%) with the neuromuscular blocking agent administered first (Figure 1). Baseline characteristics and intubation process measures are presented in Tables 1 and 2, respectively.

Outcomes
In the unadjusted analysis of the primary outcome, the median (IQR) intubation time for the neuromuscular blocking agent group first was 80 (66–99)
seconds and the median (IQR) intubation time for the sedative group first was 84 (66–99) seconds (median difference = 5 seconds [95% CI = 0–10 seconds]). Subject-level data for the time to intubation are presented in Figure 2. Unadjusted analysis of secondary outcomes (attempt duration, rates of hypoxemia, and first-attempt success) were not significantly different (Table 3). Outcomes by specific neuromuscular blocking agents were not different from the unstratified analysis (Data Supplement S1, Table S1, available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13723/full).

Results of the multivariable analysis are displayed in Table 4. Administration of the neuromuscular blocking agent before the sedative agent was associated with a reduction in time from RSI administration to the end of intubation attempt of 6 seconds (95% CI = 0 to 11 seconds). Not viewing the video screen and more operator experience were associated with shorter intubation times; worsening laryngoscopic view (Cormack-Lehane grade) was associated with longer intubation times (Table 4).

**Sensitivity Analyses**

Results of the sensitivity analyses, which performed identical analyses on an expanded group of patients (including those with first attempt failure and additionally those with elapsed times between RSI agents of ≥30 seconds) are displayed in Data Supplement S1, Table S2. The direction of the coefficients was unchanged from the main analysis.

**DISCUSSION**

Limiting apnea time during orotracheal intubation in critically ill patients is of fundamental importance. Some have postulated that administration of the neuromuscular blocking agent before the sedative agent in RSI may shorten the apnea time.\(^8\) In this secondary analysis of a single-center, randomized trial of ED patients undergoing emergency intubation, the neuromuscular blocking agent was administered before the sedative in 73% of cases using RSI. In this study, administration of the neuromuscular blocking agent first was associated with a 6-second reduction in the elapsed time from RSI administration to the end of intubation, a surrogate for apnea time (95% CI = 0 to
Table 2
Intubation Process Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Sedative First (n = 153)</th>
<th>Neomuscular Blocking Agent First (n = 408)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preintubation sedative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etomidate</td>
<td>151 (99)</td>
<td>406 (99)</td>
</tr>
<tr>
<td>Ketamine</td>
<td>2 (1)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Preintubation neuromuscular blockade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>95 (62)</td>
<td>248 (61)</td>
</tr>
<tr>
<td>Rocuronium</td>
<td>58 (38)</td>
<td>161 (39)</td>
</tr>
<tr>
<td>Elapsed time between administration of first and second RSI drug (seconds)</td>
<td>10 (5–13)</td>
<td>10 (7–14)</td>
</tr>
<tr>
<td>Elapsed time between administration of first drug and insertion of laryngoscope blade (seconds)</td>
<td>45 (36–53)</td>
<td>43 (35–53)</td>
</tr>
<tr>
<td>Elapsed time between administration of second RSI drug and insertion of laryngoscope blade (seconds)</td>
<td>35 (28–43)</td>
<td>32 (24–41)</td>
</tr>
<tr>
<td>Intubating position</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sniffing position</td>
<td>99 (65)</td>
<td>252 (62)</td>
</tr>
<tr>
<td>Neutral cervical spine</td>
<td>35 (23)</td>
<td>120 (29)</td>
</tr>
<tr>
<td>Cervical spine extension without sniffing</td>
<td>19 (12)</td>
<td>35 (9)</td>
</tr>
<tr>
<td>Oxygen saturation at the beginning of the intubation attempt (%)</td>
<td>100 (98–100)</td>
<td>100 (98–100)</td>
</tr>
<tr>
<td>Apneic oxygenation used</td>
<td>97 (63)</td>
<td>247 (60)</td>
</tr>
<tr>
<td>Operator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency medicine senior resident or fellow (PGY-3 or higher)</td>
<td>118 (77)</td>
<td>356 (87)</td>
</tr>
<tr>
<td>Emergency medicine junior resident (PGY-2 or lower)</td>
<td>33 (22)</td>
<td>43 (11)</td>
</tr>
<tr>
<td>Emergency medicine faculty</td>
<td>2 (1)</td>
<td>10 (2)</td>
</tr>
<tr>
<td>C-MAC Macintosh blade used*</td>
<td>148 (97)</td>
<td>396 (97)</td>
</tr>
<tr>
<td>Video screen use†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screen never used</td>
<td>85 (56)</td>
<td>247 (60)</td>
</tr>
<tr>
<td>Screen viewed for the entire attempt</td>
<td>35 (23)</td>
<td>70 (17)</td>
</tr>
<tr>
<td>Screen viewed during passage of the tube or bougie into the glottis</td>
<td>33 (22)</td>
<td>92 (23)</td>
</tr>
<tr>
<td>Best Cormack-Lehane laryngeal view</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1 (best view)</td>
<td>116 (76)</td>
<td>301 (74)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>27 (18)</td>
<td>66 (16)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>7 (5)</td>
<td>22 (6)</td>
</tr>
<tr>
<td>Grade 4 (worst view)</td>
<td>2 (1)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>First device entered into the mouth after the laryngoscope</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bougie</td>
<td>85 (56)</td>
<td>216 (53)</td>
</tr>
<tr>
<td>Endotracheal tube + stylet</td>
<td>68 (44)</td>
<td>193 (47)</td>
</tr>
</tbody>
</table>

Data are reported as n (%) or median (IQR). IQR = interquartile range; PGY = postgraduate year; RSI = rapid sequence intubation.

*The remaining patients were intubated using a hyperangulated blade (five in sedative group, seven in neuromuscular blocking agent group) or with a direct Macintosh laryngoscope (six in neuromuscular blocking agent group).

†Patients intubated with nonvideo Macintosh laryngoscope were coded as “screen never used.”

11 seconds). The trend toward shorter intubation times when neuromuscular blocking agents are administered first, if true, is not likely to be clinically significant except in the most critically ill patients requiring endotracheal intubation (i.e., those with the least physiologic reserve, e.g., severe metabolic acidosis, asthma, acute respiratory distress syndrome, among others). However, apart from the theoretical, albeit unlikely, concern of awareness of neuromuscular blockade, it is difficult to think of a compelling reason to administer the sedative agent before the neuromuscular blocking agent.

Administration of a nondepolarizing neuromuscular blocking agent before sedation has been described in the operating room setting. In this practice, termed “the timing principle,” the neuromuscular blocking agent is administered and the patient is monitored for weakness or paralysis; when weakness is detected the sedative agent is administered.15–18,23,24 This technique is performed so that the peak effect of the sedative agent occurs near the onset of paralysis to avoid sedative-induced hypoventilation or apnea before the neuromuscular blocking agent takes full effect. This “timing principle” practice delays sedative administration after neuromuscular blocking agent administration longer than any delay inherent in RSI.

Administration of the neuromuscular blocking agent first ostensibly allows earlier insertion of the laryngoscope blade from the time of RSI medication administration. In this study, however, the elapsed time from administration of the first RSI medication and insertion of the laryngoscope blade was similar in both groups (2-second difference, Table 2). However, the total intubation time, the time from first RSI medication to the end of the intubation attempt, was 6 seconds shorter when the neuromuscular blocking agent was administered first. This suggests that the difference between the two approaches depends not only on earlier laryngoscope insertion, but additionally on earlier complete muscle relaxation, allowing more facile laryngoscopy and tube delivery.

An objection sometimes proffered against administration of the neuromuscular blocking agent first is the possibility of losing intravenous access between RSI agents or delayed administration of the sedative. This current study cannot answer this query. In emergency intubation, successful first-attempt intubation may be a higher priority than patient experience, especially because if venous access is lost a benzodiazepine can be administered to cause amnesia to the event.25 In
Figure 2. Subject-level data for the time elapsed between the complete administration of the first RSI medication and the start and end of the intubation attempt, by group, sorted in order of elapsed time until the attempt ended. Each participant is displayed as a single vertical line connecting the starting and ending times of the attempt. The attempt began when the laryngoscope was inserted into the mouth and ended when the laryngoscope was removed. Box-and-whisker plots for the elapsed time from the complete administration of the first RSI medication to the end of intubation are displayed on the right side of the graph for the two study groups. N = neuromuscular blocking agent first group; S = sedative first group.

Table 3
Unadjusted Study Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Sedative First (n = 153)</th>
<th>Neuromuscular Blocking Agent First (n = 409)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation time (seconds)†</td>
<td>84 (69–108)</td>
<td>80 (66–99)</td>
<td>5 (0 to 10)</td>
</tr>
<tr>
<td>Attempt duration (seconds)‡</td>
<td>38 (27–55)</td>
<td>35 (25–47)</td>
<td>3 (-1 to 6)</td>
</tr>
<tr>
<td>Hypoxemia†</td>
<td>12/151 (8)</td>
<td>51/404 (13)</td>
<td>-5% (-10% to 1%)</td>
</tr>
<tr>
<td>First-attempt success§</td>
<td>153/161 (95; 90–98)</td>
<td>409/449 (91; 88–94)</td>
<td>4% (0% to 8%)</td>
</tr>
</tbody>
</table>

Data are reported as median (IQR), n (%), or n (%; 95% CI). Positive values in the difference column indicate longer duration or higher proportion for the sedative first group.

IQ = interquartile range.
†Defined as elapsed time from complete administration of the first RSI drug to removal of the laryngoscope blade.
‡Defined as the time elapsed between insertion and removal of the laryngoscope blade.
§Defined as an oxyhemoglobin saturation < 90% (or, if the attempt began with a saturation < 90%, an absolute decrease in saturation of >10%) during or within 1 minute after completion of the intubation attempt. Data not available for seven patients.
§This includes patients regardless of first intubation attempt success (n = 610).

these situations, if a sedative were the only agent administered, intubation is likely to be more difficult and prone to complications, including first-attempt failure and vomiting and aspiration.2-4,7 It would be difficult for any study to definitively answer this specific question.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Coefficient (s)</th>
<th>95% CI (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuromuscular blocking agent</td>
<td>-6</td>
<td>-11 to 0</td>
</tr>
<tr>
<td>Rocuronium†</td>
<td>4</td>
<td>-2 to 9</td>
</tr>
<tr>
<td>First device: tracheal tube + stylet‡</td>
<td>-6</td>
<td>-10 to 0</td>
</tr>
<tr>
<td>Video screen not used§</td>
<td>-10</td>
<td>-16 to -4</td>
</tr>
<tr>
<td>Difficult airway characteristic</td>
<td>3</td>
<td>-2 to 8</td>
</tr>
<tr>
<td>Cormack-Lehane grade</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 4
Mixed-effects General Linear Model Results for Time From RSI Administration to End of Intubation Attempt

This table displays results from the mixed-effects generalized linear model for the outcome of time from complete administration of the first RSI agent until removal of the laryngoscope blade. The coefficient column displays the amount of time (in seconds) associated with each variable, compared to its reference counterpart. Negative coefficients indicate shorter intubation times.

Based on the limited available literature, including the current observational study, it is acceptable to administer the sedative and neuromuscular blocking agent in either order. Administration of the neuromuscular blocking agent first, if beneficial at all, is most likely to influence outcomes for patients at the extremes of critical illness where mitigating unnecessary apnea time is of the utmost importance. More important factors are probably the devices used and operator experience. However, because the theoretical downside of administering the neuromuscular blocking agent first is small (i.e., awareness of neuromuscular blockade that is not likely to be remembered if a sedative is administered in a timely fashion), it might be sensible for the default method to be administration of the neuromuscular blocking agent first, potentially shortening apnea time. Future research should determine if the order of medication administration is associated with awareness of neuromuscular blockade or patient memories of intubation. If no association exists, a strong case can be made for administration of the neuromuscular blocking agent before the sedative.

LIMITATIONS

In this analysis we used the outcome of the elapsed time from RSI administration to end of the intubation...
attempt; this served as a surrogate for apnea time, a more patient-important outcome. Depending on the actual effect of sedatives on ventilatory effort, an analysis of apnea time could differ from the present analysis. Although we analyzed 562 patients, only 153 had the sedative agent administered first. This relatively small sample size caused imprecision in the model; a larger, more balanced trial would be required to confirm the modest difference of 6 seconds between groups. In this study we did not record patient memories of intubation and cannot know if administering the neuromuscular blocking agent first has adverse effects such as awareness of paralysis, though this is unlikely given the rapidity of sedation administration. Finally, drug order could theoretically be associated with first-attempt success if the intubating physician attempts intubation before complete muscle relaxation. While this study was not designed to answer this question, future studies should record this outcome.

**CONCLUSION**

In conclusion, administration of either the neuromuscular blocking or the sedative agent first are both acceptable. Administering the neuromuscular blocking agent first may result in modestly faster time to intubation. For now, it is reasonable for physicians to continue performing RSI in the way they are most comfortable with. If future research determines that the order of medication administration is not associated with awareness of neuromuscular blockade, administration of the neuromuscular blocking agent first may be a logical default administration method to attempt to minimize apnea time during intubation.

We thank the Hennepin County Medical Center residents and Research Associate Program for their contribution to research in emergency medicine.

**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.13723/full
Data Supplement S1. Supplemental material.
Acceptability, Usability, and Effectiveness: A Qualitative Study Evaluating a Pediatric Telemedicine Program

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ABSTRACT

Background: Pediatric emergency telemedicine consultations have been shown to provide support to community emergency departments treating critically ill pediatric patients. However, despite the recognized value of telemedicine, adoption has been slow. To determine why clinicians frequently do not use telemedicine when it is available for pediatric patients, as well as to learn how to improve telemedicine programs, we conducted a qualitative study using stakeholder interviews.

Methods: We conducted a qualitative study using grounded theory methodology, with in-depth interviews of referring and accepting physicians and referring, transport, and transfer center nurses. We analyzed data iteratively and adapted the interview guide based on early interviews. We solicited feedback from the participants on the conceptual model.

Results: Sixteen interviews were conducted; all respondents had been involved in a telemedicine consultation at least five times, with some having used telemedicine more than 30 times. Analysis resulted in three themes: 1) recognizing and addressing telemedicine biases are central to gaining buy-in; 2) as technology advances, telemedicine processes need to adapt accordingly; and 3) telemedicine increases collaboration among health care providers and patients/families in the patient care process.

Conclusions: To improve patient care through increased use of telemedicine for pediatric emergency consultations, processes need to be modified to address provider biases and end-user concerns. Processes should be adapted to allow users to utilize a variety of technologies (including smartphones) and to enable more users, such as nurses, to participate. Finally, telemedicine can be used to improve the patient and family experience by including them in consultations.

Few emergency departments (EDs) are fully equipped to manage pediatric emergency conditions.¹ Pediatric emergency telemedicine consultations can address this issue by providing on-demand, synchronous videoconferencing between community ED clinicians and specialty hospital pediatricians.² ³ Such
Telemedicine has been available at our center for pediatric emergency consultations since 2003. Our 121-bed children’s hospital, a quaternary care center located in Northern California, is the referral center for many children across a 33-county region covering 65,000 square miles and serving approximately 6 million people. The children’s hospital receives transfers from over 130 EDs and hospitals in the region and accepted over 2,500 patients as transfers in 2017. To begin the transfer process, or request a telemedicine consultation, referring ED providers contact the transfer center. The transfer center collects basic information about the patient and then determines the appropriate provider to complete the transfer/telemedicine consultation. While these consultations are primarily completed by pediatric critical care physicians or neonatal critical care physicians, consultations can be completed by any pediatric provider, including pediatric hospitalists and pediatric surgeons.

Despite its recognized value and availability, telemedicine is not universally employed during hospital-to-hospital transfers, suggesting that barriers exist that prevent its adoption and uptake. Prior studies have explored the acceptability of telemedicine; however, these studies have included mostly participants with little to no pediatric telemedicine experience, have explored telemedicine use for nonemergency settings, or have used survey data collection methods rather than in-depth interviews. Identified barriers to telemedicine use from these prior studies include technology challenges, workflow integration, perceived usefulness, regulatory issues, and costs. Participatory design methods ensure that systems are usable, acceptable, and effective. Unfortunately, such approaches are often not integrated into telemedicine interventions. The objective of this qualitative study was to understand facilitators and barriers to using telemedicine for pediatric ED transfer consultations from the perspectives of health care providers.

**METHODS**

**Study Design**

We conducted a qualitative study using in-depth interviews and grounded theory methodology. Prior to our qualitative study, there was a period of 3 years where the use of telemedicine (as opposed to telephone) was strongly encouraged for transfer consultations from community EDs to our pediatric critical care unit. The physician who conducted the consultation was usually the physician who accepted the patient; occasionally, due to shift change, severity of illness, or bed availability, the patient would be accepted by another provider or another hospital. To inform development of the interview guide, we reviewed 139 free-text responses that were collected during the 3-year period regarding patients who had a telephone consultation as opposed to a telemedicine consultation; telemedicine coordinators asked the pediatric critical care physicians why telemedicine was not used for these patients. Four researchers (JR, MG, HSF, GW) independently performed open-coding of the free-text responses, discussed the results, and formulated initial categories from the open-coding process. These categories were used to develop an initial interview guide with the following main topics: 1) experiences with using telemedicine for transfer consultations and 2) decision-making process regarding using telemedicine.

The initial interview guide was revised as data were analyzed and new categories of findings were developed. Exact wording of the interview guide questions was adapted based on the provider type being interviewed; the version for the referring physicians is provided in 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.13763/full). Specifically, based on preliminary analyses, interviewers (JR, MG, HSF, GW) probed more into two topics: 1) suggested changes to the telemedicine system or process and 2) specific patient types/diagnoses who should receive telemedicine. Interviews were conducted in person or by phone and were audio recorded and transcribed. Interviewers maintained field notes with contextual observations. Each participant provided verbal informed consent and received a $50 gift card. The University of California Davis Institutional Review Board approved the study.
Study Population
To identify the scope of the phenomenon and overall trajectory of the study, we initially used convenience sampling\(^\text{21}\) to identify referring physicians (physicians working in community EDs) and accepting physicians (pediatric critical care physicians) who had used telemedicine during the prior 3-year period in which telemedicine use was strongly encouraged. We subsequently used purposive sampling\(^\text{22}\) to identify referring ED nurses, transfer center nurses, and transport nurses to further explore topics that arose in the initial interviews. Sampling continued until thematic saturation was reached. Interviews were conducted in August and September 2018. Participants were identified through suggestions from accepting providers and community hospital site leads and were recruited via e-mail. Eligible participants were aged 18 years and older and English speaking. Eligible participants had experience using or coordinating telemedicine for transfer consultations for pediatric patients. Demographic information, including sex, age, occupation, years’ experience, and frequency of telemedicine use, was collected during interviews.

Data Analysis
Data were analyzed in an iterative process; analysis used a constant comparative approach.\(^\text{20,23}\) The process included the following steps: 1) open-coding of the first four interviews by each investigator; 2) full group meeting to discuss findings, distill open coding results into categories, and generate a codebook; 3) adapting of the interview guide based on the initial codes; 4) individual memo-writing and focused coding of next four interviews using categories; and 5) full group meeting to compare codes, discuss discrepancies to ensure consensus on application of codes, refine dimensions of existing codes, add new codes, develop tentative categories, and identify theoretical direction. The process was repeated twice for each following group of four transcripts and ended when the full group agreed thematic saturation was reached.

Interviews were conducted until theoretical saturation was reached; at this point the categories were fully developed and demonstrated conceptual coherence. The team then reviewed the final coded data to identify major themes and reviewed relationships between themes to develop a conceptual model. We performed member checking by soliciting feedback from the interviewed participants on the preliminary conceptual model and themes.\(^\text{24}\) Additional data validation occurred through investigator triangulation.\(^\text{25}\) The research team consisted of two inpatient pediatricians with some telemedicine experience (JR, MH), a sociologist (MG), a qualitative research analyst (GW), and a clinical research associate (HSF). Two investigators (JR, MG) had extensive qualitative research experience. An additional inpatient provider with telemedicine and qualitative research experience (LK) and the director of the pediatric telemedicine program (JM) were brought in to review the data and assist with the interpretation. We used ATLAS.ti to organize and store coding and data analysis.\(^\text{26}\)

**RESULTS**
We conducted 16 approximately 60-minute interviews with referring physicians working in community hospital EDs (\(n = 5\)), accepting pediatric critical care physicians (\(n = 5\)), referring ED nurses (\(n = 2\)), transfer center nurses (\(n = 2\)), and transport nurses (\(n = 2\)). One referring provider declined to participate but suggested their colleague, who participated; no other providers declined. Characteristics of participants are provided in Table 1. We identified three overarching analytic themes and six main categories across the transcripts that pertained to use of telemedicine for transfer consultations. Major themes included: 1)

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Participant Demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5 (31)</td>
</tr>
<tr>
<td>Female</td>
<td>11 (69)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>35–44</td>
<td>10 (63)</td>
</tr>
<tr>
<td>45–55</td>
<td>6 (38)</td>
</tr>
<tr>
<td>Role</td>
<td></td>
</tr>
<tr>
<td>Referring ED physicians</td>
<td>5 (31)</td>
</tr>
<tr>
<td>Accepting pediatric critical care physicians</td>
<td>5 (31)</td>
</tr>
<tr>
<td>Referring nurse</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Transport nurse</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Transfer center nurse</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Years in profession</td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>3 (19)</td>
</tr>
<tr>
<td>6–10</td>
<td>6 (38)</td>
</tr>
<tr>
<td>11–20</td>
<td>5 (31)</td>
</tr>
<tr>
<td>21+</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Number of times telemedicine used</td>
<td></td>
</tr>
<tr>
<td>5–10</td>
<td>3 (19)</td>
</tr>
<tr>
<td>11–20</td>
<td>5 (31)</td>
</tr>
<tr>
<td>21–30</td>
<td>5 (31)</td>
</tr>
<tr>
<td>31+</td>
<td>3 (18)</td>
</tr>
</tbody>
</table>

Data are reported as \(n\) (%).
acceptability—recognizing and addressing telemedicine biases are central to gaining buy-in; 2) usability—as technology advances, telemedicine processes need to adapt accordingly; and 3) telemedicine increases collaboration among health care providers and patients/families in the patient care process. Main categories included overlooking the benefits of telemedicine, conditionally buying in to telemedicine, technology barriers extending beyond the equipment, expanding roles and clarifying processes, communicating with more collaboration, and strengthening the involvement of the consultant. These are explored in more detail below with representative quotes in Tables 2 through 4. Respondent validation demonstrated that participants agreed with the conceptual model (Figure 1) and description of the themes.

**Theme 1: Acceptability—Recognizing and Addressing Telemedicine Biases Are Central to Gaining Buy-in (Table 2)**

**Category 1: Overlooking the Benefits of Telemedicine.** Almost every participant reported biases against telemedicine despite also acknowledging numerous benefits of using this technology for consultations; those with the strongest or most extreme negative perceptions were all accepting physicians. Multiple accepting and referring physicians began the interview discussing their resistance to using telemedicine, stating that it took too long, that it did not change their care plans, or that the technology was frustrating. However, as the interviews proceeded, many providers acknowledged that their negative perceptions may not be based in reality. One accepting provider specifically acknowledged that they perceived telemedicine to take a long time, but that it did not take much more time than a phone call. When asked about specific cases or instances where they had used telemedicine, interviewees acknowledged the benefits of telemedicine they had experienced. Benefits included allowing accepting providers to provide more tailored recommendations after visually assessing the patient, expediting patient disposition, improving family experience, increasing knowledge and confidence for referring physicians, and increasing comfort for accepting physicians.

**Category 2: Conditionally Buying In to Telemedicine.** Almost every participant stated that telemedicine was only or mostly useful for certain clinical circumstances. Participants shared diagnoses or illness severities that did or did not benefit from telemedicine consultations. However, there was no consensus among participants for when telemedicine should be used. For some, including all referring physicians, the most beneficial circumstance for using telemedicine was for severely ill patients. However, many accepting physicians and one referring physician believed that telemedicine was also useful for patients who were stable or whose presentation was unclear; for these patients, telemedicine was useful in preventing some transfers or avoiding unnecessary intensive care utilization. Some participants stated that telemedicine was most beneficial for patients with respiratory illnesses. Multiple participants used the example of diabetic ketoacidosis as a diagnosis for which telemedicine was particularly not useful. However, one accepting physician shared a story that involved benefits to family satisfaction when telemedicine was used in the care of a child with diabetic ketoacidosis.

Time limitations and competing demands were other components of providers’ conditional telemedicine buy-in. Many participants stated that providers wanted to use telemedicine and appreciated this technology, when there was adequate time to use it. However, there was limited time and competing demands, telemedicine was perceived to be less acceptable. Also, for very sick patients at referring hospitals, telemedicine can be seen as a barrier to efficient transport.

**Theme 2: Usability—As Technology Advances, Telemedicine Processes Need to Adapt Accordingly (Table 3)**

**Category 3: Technology Barriers Extending Beyond the Equipment.** Every participant, even those who had strong buy-in, mentioned equipment issues. Referring EDs often had only a few telemedicine “experts” who knew how to find the cart and turn it on, but these were often nurses who had more pediatric experience, so they were wanted at the bedside instead of troubleshooting telemedicine equipment. Equipment issues were not solely related to the hardware, but also related to the inability to integrate interpreter services and the limitations with where the telemedicine equipment was located. Some participants stated that smartphones were a ubiquitous, more user-friendly technology that providers often used to communicate during transfer consultations. Providers used smartphones as a workaround to transmit images and videos instead of using the formal telemedicine equipment.
### Table 2

**Theme 1: Acceptability—Recognizing and Addressing Telemedicine Biases Are Central to Gaining Buy-in**

<table>
<thead>
<tr>
<th>Category/Subcategory</th>
<th>Representative Quotations</th>
<th>Participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overlooking benefits of telemedicine Resistance to using telemedicine</td>
<td>Our physicians, the PICU docs would offer it . . . “Do you mind if I log onto the system and look at the kid?” And sometimes they would be willing and sometimes they would not. But a lot of those times the physicians just wanted to get our PICU doc on the phone.</td>
<td>Transfer center nurse</td>
</tr>
<tr>
<td></td>
<td>I’d ask, ‘Would you like me to telemedicine?’ And—because I wanted to, actually, and the other side was like, ‘No, we’re running the code, and, we’re you know doing things.’ Or, ‘I can’t do that right now.’</td>
<td>Accepting physician</td>
</tr>
<tr>
<td></td>
<td>People get frustrated and they don’t, like, it’s a sigh, we go, ‘Oh, God, I’ve got to get the telemed.’ Because it’s always like, is it going to work this time or is it not? So, if it worked better, it’d be one of those things we wouldn’t be so dreading when it comes up . . . I think if it was a little more streamlined, in that sense, it would be amazing all the time.</td>
<td>Referring nurse</td>
</tr>
<tr>
<td>Negative telemedicine perceptions that might not be based on reality</td>
<td>I think the level of care we provide is not different [with telemedicine] . . . It helps us give more precise recommendations; it’s always good to have more information. So, I think, in that regard, it’s better [than telephone].</td>
<td>Accepting physician</td>
</tr>
<tr>
<td></td>
<td>I think that it actually doesn’t take as much time as what we think it does and that even though we think it’s a barrier the time and busyness even though we think it’s a barrier to using it, I’m not so sure that it actually takes that much more time.</td>
<td>Accepting physician</td>
</tr>
<tr>
<td>Benefits of telemedicine</td>
<td>I’ve been in those situations and said, ‘Gosh, I’d feel better about all this if I could take a peek at this kid before he came.’ I do think that I’ve come to appreciate some of the benefits of it . . . I think it makes for safer transport and for less anxiety on my end because I’ve got to see the kid.</td>
<td>Accepting physician</td>
</tr>
<tr>
<td></td>
<td>Before we had telemedicine, you were kind of making guesses about how sick the patient is and you learn a lot by seeing them. So, not having the opportunity to see them, I felt like that would put me at a disadvantage sometimes, which meant the child was at a disadvantage.</td>
<td>Accepting physician</td>
</tr>
<tr>
<td></td>
<td>I actually think it speeds up our disposition and the patient getting to the higher level of care, faster. So, while it might sometimes seem to take a few minutes more, I actually think the overall decision about disposition, definitive treatment, occurs faster by taking the possible few extra minutes to initiate the telemedicine.</td>
<td>Referring physician</td>
</tr>
<tr>
<td></td>
<td>For parental benefit, and that feeling of communication and understanding what’s going on for parent’s sake . . . to encourage its use, even though maybe physician to physician you don’t feel like you need it. But to encourage its use for families.</td>
<td>Referring physician</td>
</tr>
<tr>
<td>Conditionally buying in to telemedicine Telemedicine felt to be useful for certain circumstances</td>
<td>You may get a call about a patient who maybe you’re really worried about and you really want to see what they look like so you can offer more directed intervention. Telemedicine is great. On the other hand, sometimes, you have a patient that you’re hearing about, but they don’t actually sound too sick for an ICU. And then you see them. It’s like, hmm, I really don’t think they are that sick and therefore, I can divert that patient to another level of care. For either patient because it helps you treat that patient more efficiently and effectively.</td>
<td>Accepting physician</td>
</tr>
<tr>
<td></td>
<td>More a complex, complicated code, like an extremely premature newborn, I would use telemedicine . . . The more severe the more likely I am to use telemedicine.</td>
<td>Referring physician</td>
</tr>
<tr>
<td>Competing demands and time constraints/sense of urgency limited telemedicine acceptability</td>
<td>In a situation where they feel like they have to intubate, there’s been a drowning, there’s something kind of urgent, they don’t want to take the time to do it. They want to speak with the physician, they want to get the kid here. They want to get the kid out of ER.</td>
<td>Transfer center nurse</td>
</tr>
<tr>
<td></td>
<td>Telemedicine, it actually doesn’t take that long, but it feels like a time constraint, and it’s actually something that you can’t multitask during. You have to be, you know, in one place, and you can’t be talking to other people and stuff. And it’s a period of time where people also feel like they can’t interrupt you. So, it definitely feels like you kind of have to set everything aside and do this thing for a few minutes. And especially overnight or when things are very busy in the afternoon in the ICU, it definitely feels like a huge thing—distraction if it needs to happen. And it makes it less likely to wanna do it.</td>
<td>Accepting physician</td>
</tr>
<tr>
<td></td>
<td>When we’re busy here doing—you know, telemedicine consults, they’re not particularly quick. They don’t feel like they’re quick . . . You have to find the computer, and you’ve gotta log in and get all set up . . . I think balancing those with what we felt were our immediate responsibilities here was a little bit kind of annoying for lack of better words.</td>
<td>Accepting physician</td>
</tr>
</tbody>
</table>
Technology barriers also included issues related to impression management between accepting and referring physicians. Many accepting physicians thought that they had to respond immediately to telemedicine consultation requests. Some accepting physicians thought that telemedicine did not permit the flexibility to multitask and simultaneously address competing demands. Accepting physicians shared that they could not reference online resources during telemedicine consultations, whereas telephone communication permitted that without compromising the impression of being the knowledgeable expert. Although telemedicine left some accepting physicians navigating feelings of vulnerability and anxiety, telemedicine gave some referring physicians and nurses a way to demonstrate their skill set. With telemedicine, accepting physicians could watch referring providers deliver care at the bedside, which fostered trust and built relationships.

Category 4: Expanding Roles and Clarifying Processes. Most physicians and nurses described a lack of clarity about who could use telemedicine and when it would be most appropriate to use. While nurses explained that they sometimes wanted to activate telemedicine, most believed that physicians were the only ones who could activate telemedicine. There was also a disconnect with physician expectations; accepting physicians thought that the role of the referring provider during telemedicine consultations was to be physically at the patient’s bedside, but that frequently did not happen—not that the nurse and family participated in the consult.

Telemedicine also duplicated processes. Transfer center nurses, transport nurses, and physicians expressed frustrations that information was first communicated by telephone and then repeated via telemedicine. Because transport nurses and transfer center nurses were not on telemedicine consultations, but otherwise would be on a bridged telephone line, telemedicine consultations were followed with another phone call to loop the nurses into the conversation. This process duplicated work and left the nurses receiving secondhand information. All transport and transfer center nurses wanted to expand their roles to be included on telemedicine consultations.

Theme 3: Effectiveness—Telemedicine Increases Collaboration Among Health Care Providers and Patients/Families in the Patient Care Process (Table 4)

Category 5: Communicating With More Collaboration. Telemedicine brought more individuals into the transfer communication process. It
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<th>Representative Quote</th>
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<tr>
<td>Technology barriers extending beyond the equipment</td>
<td>Technology interface limiting mobility or availability</td>
<td>In order to do telemedicine, you have to be near a telemedicine machine. Because we don’t have it on our laptops or desktops here in our offices. So, in the mornings, there’s a backup person that takes the transport calls so that the people on service can round and do everything they need to get done.</td>
<td>Accepting physician</td>
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<td>I would try to improve the hardware that is utilized so it is handheld or goes into the room on a tripod . . . whether it’s on an iPhone or a tablet or an iPad so that I can, even if I’m not in that patient’s room, I can coordinate with the telemedicine physician back at my workstation or have an ongoing discussion. Because as of now, you have to be in the room with the patient, with the telemedicine equipment available.</td>
<td>Referring physician</td>
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<td>Technology issues occurring and not being adequately solved</td>
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<td>[T]o be able to see X-ray images on the telehealth side. So, finding a way to actually be able to access those without, like, pulling the robot next to my PACS, for instance. And again, that’s where that communication tool [secure messaging tool via smartphone app] really helps, because I can take a quick photo and send it over.</td>
<td>Referring physician</td>
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<td>Wanting or expecting the technology to advance</td>
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<td>I just think the technology is difficult and it doesn’t always work. I mean, it seems like 50 percent of the time, they can’t get the machines on. That’s the frustrating part for me . . . We don’t know whether they’ve got the machine on. Is it them, the referring hospital, or is it our own docs that are not doing it right. Maybe they’re doing everything right and it’s just not working.</td>
<td>Transfer center nurse</td>
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<td>I still, to this day, feel like it’s very confusing . . . it’s always like this waiting game and you sit in the room and you’re waiting, you’re waiting . . . we’ll run and get the telemed and then we wait 45 minutes to get them on there . . . I think it’s kind of on both ends, we need to have a better process on our end to know how to get it in the room quickly and be ready.</td>
<td>Referring nurse</td>
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<td>End-users not knowing how to use the telemedicine equipment</td>
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<td>I think it’s about the ease of the process and how much equipment can make a big difference . . . telemedicine just seems so cumbersome from a physical process standpoint of connecting and all that. In today’s age, it just seems silly with cell phones and iPads and all that to then have this big cart and it looks like it’s from the 1990s sort of a thing . . . the cumbersome nature of the actually connecting and getting it to work. That’s kind of the down side of it.</td>
<td>Referring physician</td>
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<td>The integration of [telemedicine and interpreter services], I think, will, at some point in time, hopefully happen. And where there will be a translator that can pop onto the robot itself and help provide those services. The way it works now is not as seamless, and at times, depending on what’s going on and how busy it is in the room, it can end up being fairly difficult, I think, and can impact the overall efficiency of the process.</td>
<td>Referring physician</td>
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<td>Workaround using smartphones</td>
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<td>The experienced nurses [who know how to use the telemedicine equipment] also tend to be our best nurses in pediatric situations . . . So, if there’s competing demands for skills, we’re obviously going to commit them to the physical care . . . we have a clerk that can always make phone calls, they’re just not well versed on how to get the machine setup.</td>
<td>Referring physician</td>
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<td>The ERs often have their cart laid out in a hallway or something, and then you’re supposed to be able to [remotely] drag the cart to the room. But, I don’t actually—I’ve never been able to do that well. So, then you have to wait for somebody to walk by and say, ‘Do you mind taking me to the patient’s room?’ . . . I wish that there was a way to just, like, say, ‘Let’s do telemedicine,’ and then you turn it on, and you’re there. But, it’s never like that.</td>
<td>Accepting physician</td>
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<td>Vulnerability and impression management</td>
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<td>They would take their phone and scroll through the CT and then send a video of that to Dr. X so they can get an idea of what they’re looking at. They’ve done it with X-rays and things like that . . . It’s just regular, the texting a message app on their phone, and they will actually go to the computer and scroll through it. Now, with videotape as they’re scrolling through, the doctor can get a picture of it.</td>
<td>Transfer center nurse</td>
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<td>In the helicopter, you can text. I text very often coming back in the helicopter with the physicians.</td>
<td>Transport nurse</td>
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<td>When you don’t do one for a little while, and you’re sort of fumbling. And you feel a little bit silly fumbling when someone is watching you do it . . . Sometimes when I’m on the phone talking to outside docs, I will look things up on the computer system because sometimes they call with things that are more rare. Or, I need to look up a dose or something like that. So, I’ll be multitasking. I’ll be talking to them, and I’ll quickly look something up. You can’t really do that when they’re watching you on a camera.</td>
<td>Accepting physician</td>
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allowed the family to virtually meet the accepting physician before the transport, which brought comfort and reassurance to the family. Nurses and physicians also described how telemedicine brought the referring hospital’s bedside nurse into the conversation with the accepting physician, something that did not occur with telephone communication. Telemedicine allowed the nurse to provide and receive additional information.

**Category 6: Strengthening the Involvement of the Consultant.** Telemedicine expanded the role of the accepting physician during the transfer consultation, resulting in increased involvement in clinical management and perceived better recommendations. Referring physicians and nurses explained how telemedicine enabled accepting physicians to provide them with deeper levels of support, including reassurance and emotional support. Telemedicine increased involvement of the accepting physician in communicating with the patient’s family. First, accepting physicians virtually saw and talked directly with the family; they were then more likely to engage further with the family, such as calling with updates until the family arrived at the receiving hospital. This improved family communication was reported by almost every participant to be one of the most beneficial aspects of

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### Table 3 (continued)

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<tr>
<td>Expanding roles and clarifying processes</td>
<td>Physicians as gatekeepers to using telemedicine</td>
<td>Sometimes, I feel like there have been cases where we felt, as nurses, that the transfer was unnecessary. And we may have voiced that to the intern or one of the residents to a certain extent, but it kind of seems to be a pretty hierarchical, top down thing to where once they’ve kind of decided that that’s what they’re going to do we just comply with the plan . . . perhaps we might be a little bit more assertive in suggesting telemedicine be utilized by the team of physicians.</td>
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<td>It’s not usually prompted by the nurses, generally. It’s prompted by the doctors. ‘I want, you know, telemed in this room.’ . . . Most of the time, it is the doctor that preempts it. But I’ve never been the one to initiate it, that I could think of off the top of my head. But I’m sure a nurse could.</td>
<td>Referring nurse</td>
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<td>Deciding when to use telemedicine</td>
<td>We’ll get a call like, oh, the baby’s seizing, hurry up and get there. And sometimes it takes us at least an hour to get there—and we get there and the baby’s been seizing the whole time. Whereas, if they’d done telemedicine and actually looked at the baby, I think we could have intervened, you know, an hour ahead of time instead of waiting for us to get there.</td>
<td>Transport nurse</td>
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<td>There’s not a direct relationship between how sick the kid and their likelihood to initiate the telemedicine call. I think it’s so much provider preference and probably the culture at their institution.</td>
<td>Accepting physician</td>
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<td>And each attending seems to kind of have their own way of doing things and also their own institutional knowledge, or lack thereof, about how things are done at Hospital X and the resources that are available . . . [telemedicine use is] generated by the attending and the residents and whatever that team decides that they want to do on that particular case, on that particular day.</td>
<td>Referring nurse</td>
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<td>I just feel like there’s a lot of resistance . . . I think if there was some sort of algorithm that made, or really encouraged the doctors to implement telemedicine, I think that would be helpful. Because they just don’t think about it on that side.</td>
<td>Transport nurse</td>
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<td>Who is present on the telemedicine consultation</td>
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<td>Sometimes, I’ve seen patients where they move the telemedicine unit into the patient’s room and the patient is kind of there by themselves. That’s a little less helpful. From a process point of view, it’s really nice to have somebody else in that room.</td>
<td>Accepting physician</td>
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<td>To be totally honest—I would say half the time the doctor is not there [on the telemedicine consultation].</td>
<td>Accepting physician</td>
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<td>Telemedicine process duplicating work</td>
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<td>The other issue with the telemedicine consult that’s different than our regular phone call or phone calls is a bridge call, which allows the transport team, [charge nurse, accepting physician, referring provider] . . . all those groups, to hear the same story. . . When we use telemedicine, we don’t have that . . . And that’s very frustrating . . . adds not only inefficiency, but potential errors in transmitting the story.</td>
<td>Accepting physician</td>
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<td>We’re calling and we’re saying, ‘Hey, we’ve got a critically ill kiddo. My doc needs to talk to the tele-intensivist, pediatric intensivist.’ Then I shouldn’t also have to have a long conversation with [the transfer center nurse] . . . I think any time that we have to have additional communication back and forth by phone in the emergency department, it draws us away from patient care and it’s extremely difficult for us.</td>
<td>Referring physician</td>
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Table 4
Theme 3: Effectiveness—Telemedicine Increases Collaboration Among Health Care Providers and Patients/Families in the Patient Care Process

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<td>Communicating with more collaboration</td>
<td>Integrating the family into the conversation</td>
<td>I do think that, no matter what, it benefits—I presume it benefits the families ... It’s helpful for them to be like, ‘Hi, I’m Dr. X. I’m helping with the transport. I’m gonna be here when you get here. If you any questions,’ etcetera, etcetera. Because they get that sort of bridge of contact.</td>
<td>Accepting physician</td>
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<td>I would want to fly with my kid. That would be hard, to let my kid go. So, it would be nice to see a face and go, ‘Okay, this is who’s going to be there.’ Or somebody telling you what’s to be expected. It gives them an opportunity to ask questions of that hospital, too.</td>
<td>Referring nurse</td>
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<td>Bringing the bedside nurse into the conversation</td>
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<td>It’s nice to get everybody’s view of what’s going on with that patient including very much the nursing view ... when we have these interfacility transports, it’s often a doctor-to-doctor conversation to get the consult going ... Telemedicine is nice because you can often get the nurse’s perspective of what’s going on with the patient as well as the doctor’s. And it can give you a fuller picture and then the nurses can talk to the receiving nurses. So, I think being able to talk to the referring, you see the referring doc and the referring nurse and sometimes, even the referring respiratory therapist is very helpful.</td>
<td>Accepting physician</td>
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<td>Strengthening the involvement of the consultant</td>
<td>Involvement in the clinical management</td>
<td>It helped us with the resuscitation and it helped us with the ventilator settings and management. They were able to see how the baby was doing and really provided good guidance.</td>
<td>Referring physician</td>
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<td>Our physician was on telemedicine prior to us departing, then went off telemedicine and came back on when we got there. Our physician and the physician there both worked together in making the right decision to inform mom what potential outcomes could be with the baby and also survival of transport. We withdrew support there with the physician on telemedicine here, and then with the physician up there both working together, and it ended up being very nice to have our physician there to help facilitate that.</td>
<td>Transport nurse</td>
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<td>[The tele-intensivist was] able to, like, pull a neurologist into the room, and we were having a conversation all together. And, like, you know, we’re all flipping through books and our resources to try and come up with, like, the best game plan for this patient and get as rapid a transfer as possible and get them stabilized, and it just, it ended up working out really, really well. And that’s the way that I think that should work, you know?</td>
<td>Referring physician</td>
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<td>Emotional support to the bedside providers</td>
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<td>Having the telemedicine person be there, physically there, the family could see that the specialist was involved and there was lots of discussion and anticipatory guidance about brain death and what might be coming down the line. And they were there, they kind of took control and said, ‘If this child stops having a beating heart again, then we’re not going to keep going because there’s, you know, evidence he’s got brain death, but we’ll still take care of him.’ ... Feeling like they’re saying, ‘You’re doing what you can. You haven’t missed a step. This is happening.’ That was the main thing.</td>
<td>Referring physician</td>
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<td>Communicating and building relationships with the patient’s family</td>
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<td>I think with telemedicine, the difference is feeling not that Lone Ranger. Yes, physically, you’re the only one there, and oftentimes, the deficit is not physically being able to do something. It’s having the knowledge or expertise to know what to do when something isn’t going as expected or there’s a deviation from, there’s a unique situation and you’re not quite sure how to handle it for a pediatric patient. And so, having the support, the knowledge support, makes it feel less intimidating.</td>
<td>Referring physician</td>
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<td>The mom was right there at the bedside and saw Dr. X on telemedicine up close and had a lengthy conversation of what our options were. We could take the baby back, but may not survive transport. The baby’s very sick. Or we can withdraw. So giving her all that information with the physician up front and personal was extremely beneficial.</td>
<td>Transport nurse</td>
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<td>It’s always good – is that the family, and I was able to introduce myself. And tell them what I was worried about, get some history, and kind of give them a heads up about what was to come. So, that they weren’t so surprised when they got here. And then I was able to call them on the phone while they were driving down ‘cause the kid flew, but they couldn’t fly. And they could attach my voice to my face.</td>
<td>Accepting physician</td>
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<td>All of a sudden, the mother started demanding a transfer, so that she could speak with a specialist. Yeah, it was ugly. It was really sad. So, I had the idea, why don’t we put her in touch with the neonatologist via telemedicine? We did that, and it was great. And she heard the very, very difficult and painful things she needed to hear which was ‘No, your baby is not going to survive,’ a difficult conversation for her, but we were able to get that done via telemedicine.</td>
<td>Referring physician</td>
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<td>And I think that’s been one of the biggest benefits is they have a connection to a physician and potentially to a nurse who will be caring for their child when they come to this facility.</td>
<td>Accepting physician</td>
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telemedicine. Participants shared that even if telemedicine did not always alter the clinical management of a patient, participants perceived that telemedicine almost always enhanced the family’s experience.

**DISCUSSION**

This study gathered perspectives from telemedicine users to understand facilitators and barriers to using telemedicine for pediatric emergency transfer consultations. All participants had experienced pediatric emergency telemedicine consultations at least five times, and 18% had experienced more than 30 telemedicine consultations. Informed by our respondents, we constructed a conceptual model that illustrates influencers of the acceptability, usability, and effectiveness of telemedicine for transfer consultations (Figure 1) pertaining to the three study themes. Acceptability influences usability, which influences effectiveness. Additionally, usability and effectiveness also feedback to influence acceptability. We theorize that 1) interventions are needed to address telemedicine biases, 2) telemedicine processes need to adapt to address technology-related needs, and 3) the end-users need to be informed of the broad effectiveness of telemedicine—particularly the increased collaboration between providers and patients/families. Our data support the belief that these strategies will collectively assist with gaining telemedicine buy-in for pediatric emergency transfer consultations, which will ultimately increase the effectiveness of telemedicine.

Many of the barriers to telemedicine acceptability identified in this study are consistent with previously reported findings. These barriers include technology challenges, poor workflow integration, and uncertainty of the benefits.13-18 To our knowledge, classifying certain barriers as negative biases toward telemedicine is unique to our study. We use the term “bias” because our stakeholders, especially physicians, had inclinations or prejudices against telemedicine that contradicted their own or others’ statements. We must address these biases to gain end-user buy-in. Although a prior mixed-methods pediatric telemedicine study highlighted the need to gain buy-in among community clinicians,14 another study emphasized the need to gain buy-in from both referring and accepting physicians.13 Our study identified the greatest resistance among accepting physicians; we thus propose efforts to address buy-in should target this group. As depicted by the arrows in the conceptual model (Figure 1), improving usability and effectiveness perceptions are strategies to improve acceptability.

Telemedicine technology challenges are commonly reported in the literature, but prior studies largely report technology learning barriers and technically challenged individuals.13,27,28 As such, existing strategies to address technology issues focus on educational programs, trainings, and frequent test calls.13,28 Our study identified that technology barriers extended beyond the equipment. To address these broader technology issues and improve telemedicine usability perceptions, we need to adapt our local telemedicine processes to better address end user concerns.

First, many telemedicine platforms permit multiple users to videoconference simultaneously. Adapting our processes to include other individuals (e.g., professional interpreters, transport nurses, transfer center nurses) on the consultation is one way to address the reported usability problems related to integrating nurses and interpreter services in the conversation. Second, telemedicine consultations can be performed on various types of equipment; our current processes use designated telemedicine carts and desktops. Adapting our processes to encourage providers to use the equipment type of their choice (e.g., smartphone, laptop) would likely improve usability, as well as efficiency. Leveraging new technology would allow for busy ED providers to participate in the consult “on the fly,” instead of waiting for a telemedicine cart to power on and connect. Finally, future research is needed to understand and address the negative impressions identified. Possibly, processes can be implemented to minimize the perceived pressures on accepting physicians to respond immediately to telemedicine consultation requests and to mitigate their concerns during telemedicine consultations. Tackling the broad technology challenges might improve workflow integration and time constraint issues reported in our study and in prior telemedicine literature.13,16

Regarding the effectiveness of telemedicine, recognized benefits include improving care quality, enhancing family and physician experience, reducing transfers, decreasing costs, and providing educational value to clinicians.4,7,10,11,29 Despite this body of literature, our study and prior studies suggest that uncertainty regarding telemedicine’s benefits continues to impede its adoption.13,30 Ray et al.14 proposed developing guidelines for which specific clinical conditions are appropriate for telemedicine use. However, our
CONCLUSIONS

Physicians and nurses in our study provided valuable insights on their experiences with and perceptions of telemedicine. Addressing negative biases to gain buy-in, adapting processes to meet technology-related needs, and informing end-users of the broad effectiveness of telemedicine are potential strategies that may be incorporated into future interventions to enhance telemedicine use for pediatric emergency transfer consultations.

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.13763/full

Data Supplement S1. Supplemental material.
Benefits of Rhythm Control and Rate Control in Recent-onset Atrial Fibrillation: The HERMES-AF Study

Alfonso Martín, MD, PhD, Blanca Coll-Vinent, MD, PhD, Coral Suero, MD, Amparo Fernández-Simón, MD, PhD, Juan Sánchez, MD, PhD, Mercedes Varona, MD, Manuel Cancio, MD, Susana Sánchez, MD, PhD, José Carbajosa, MD, PhD, Francisco Malagón, MD, Eugeni Montull, MD, and Carmen del Arco, MD, PhD, on behalf of the HERMES-AF investigators

ABSTRACT

Background: Although rhythm control has failed to demonstrate long-term benefits over rate control in longstanding episodes of atrial fibrillation (AF), there is little evidence concerning recent-onset ones. We analyzed the benefits of rhythm and rate control in terms of symptoms alleviation and need for hospital admission in patients with recent-onset AF.

Methods: This was a multicenter, observational, cross-sectional study with prospective standardized data collection carried out in 124 emergency departments (EDs). Clinical variables, treatment effectiveness, and outcomes (control of symptoms, final disposition) were analyzed in stable patients with recent-onset AF consulting for AF-related symptoms.

Results: Of 421 patients included, rhythm control was chosen in 352 patients (83.6%), a global effectiveness of 84%. Rate control was performed in 69 patients (16.4%) and was achieved in 67 (97%) of them. Control of symptoms was achieved in 396 (94.1%) patients and was associated with a heart rate after treatment ≤ 110 beats/min (odds ratio [OR] = 14.346, 95% confidence interval [CI] = 3.90 to 52.70, p = 0.001) and a rhythm control strategy (OR = 2.78, 95% CI = 1.02 to 7.61, p = 0.046). Sixty patients (14.2%) were admitted: discharge was associated with a rhythm control strategy (OR = 2.22, 95% CI = 1.20-4.60, p = 0.031) and admission was associated with a heart rate > 110 beats/min after treatment (OR = 29.71, 95% CI = 7.19 to 123.07, p < 0.001) and acute heart failure (OR = 9.45, 95% CI = 2.91 to 30.65, p < 0.001).

Conclusion: In our study, recent-onset AF patients in whom rhythm control was attempted in the ED had a high rate of symptoms’ alleviation and a reduced rate of hospital admissions.

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Received November 5, 2018; revision received January 21, 2019; accepted January 22, 2019.

The HERMES-AF Investigators and participating centers are shown in Data Supplement S1, Appendix S1. This work was supported by an unintentional grant from Sanofi Spain, which had no influence on the design of the study or the content of this article. EM is employed by Sanofi Spain, which manufactures a product related to the subject matter. AM, BCV, FM, CS, JS, MV, MC, SS, JC, and CdA supervised the acquisition of the data and undertook recruitment of participating centers and patients; BCV provided statistical advice; AM and BCV were responsible of analysis and interpretation of the data, including quality control; AM and BCV drafted the manuscript; and all authors contributed to manuscript revisions for important intellectual content. AM and BCV take responsibility for the paper as a whole. Supervising Editor: Brian C. Hiestand, MD.

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Atrial fibrillation (AF) is the most prevalent arrhythmia attended in the acute setting. In most Western countries, patients with AF, particularly those with recent-onset episodes, are usually referred to emergency departments (EDs) and the majority of them are highly symptomatic. The management of these episodes, whether the first detected or recurrent, is controversial. Although a rhythm control strategy does not increase long-term survival in the general population of patients with AF compared to rate control, previous studies suggest that reestablishment of sinus rhythm (SR) in the short-term in patients with recent-onset AF may alleviate symptoms, improve hemodynamic status, avoid or shorten hospitalization, improve quality of life, and reduce the incidence of recurrent AF. Moreover, and taking into account that the sooner the cardioversion is attempted the higher the possibilities of success in maintaining SR, opting for acute rhythm control could be decisive in patients eligible for long-term SR maintenance.

Despite this rationale, recent-onset episodes are scarcely represented in most clinical trials comparing rhythm control to rate control. Although ED cardioversion of recent-onset AF has demonstrated to be both safe and effective, there is little evidence concerning the benefits of both rate and rhythm control in the acute management of recent-onset AF, and no study to date has compared rhythm and rate control strategies in patients presenting with a recent-onset AF. In fact, a wait-and-see approach is also advocated by some authors for the management of these patients. Therefore, and excluding unstable patients, recommendations for treatment are almost empirical and in most cases are not categorical. Thus, the most widespread guidelines base their recommendation of management strategy on the presence of hemodynamic compromise, type of AF, duration of the episode, long-term prospects of SR maintenance, and patient or physician preferences, among others. However, due to the heterogeneity of AF management in daily practice and the special conditions of acute care, clear recommendations are needed to improve the quality of management. Finally, the outcome measures of acute management are not those of the long-term setting; since survival and major cardiac events are greatly influenced by the long-term management not only of AF itself but also mainly of structural heart disease, stroke risk, and cardiovascular risk factors among others, acute treatment objectives should chiefly focus on relieving of symptoms and reducing the need for hospital admission. Consequently, these should be considered currently as main outcomes of ED management of recent-onset AF.

The aim of the HERMES-AF (Hospital Emergence Management Strategies of Atrial Fibrillation) study was to analyze the benefits of rhythm control and rate control in terms of symptoms alleviation and need for hospital admission in ED patients with recent-onset AF.

METHODS

Study Design

The HERMES-AF study was developed with the aims of analyzing the outcome of AF management and stroke prophylaxis in hospital EDs. Stroke prophylaxis results are published elsewhere; this is a substudy with a post hoc analysis of the results of rhythm control and rate control performed in the ED for patients with recent-onset episodes. This multicenter, observational, cross-sectional study with prospective standardized data collection and evaluation was carried out in 124 Spanish EDs from May 23 to June 5, 2011. The study was coordinated by the Arrhythmia Division of the Spanish Society of Emergency Medicine. In accordance with European Union regulations, it was approved by the review board for ethics in scientific research of each participating hospital and patients’ informed consent was obtained in all cases. All data concerning patients and participating physicians remained confidential.

Study Setting and Population

The study centers (Data Supplement S1, Appendix S1, available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13703/full) were selected according to the national catalog of hospitals of the Spanish Ministry of Health and Social Policy to guarantee that the sample was representative of the Spanish health care system. The existing centers were ranked by size, type, affluence, and geographic location and a stratified list of the different types of hospitals was drawn up. Thus, 50% of the 249 hospitals in Spain participated in the study, representing 56% of total ED visits and 59% of the hospital beds in Spain, and were representative of the Spanish health system with regard to the proportion of centers at each level of...
complexity, their public or private ownership and the proportion of teaching, academic, or general hospitals.

We included consecutive patients older than 18 years attended in the medical area of the ED during the study period, in whom AF was demonstrated in an electrocardiogram obtained when the treating physician considered it necessary during clinical evaluation. Multiple visits were not included. Patients already enrolled in any clinical trial and patients with atrial flutter were excluded.

**Study Protocol**

The ED physicians provided treatment and prospectively filled out data forms for each patient. Information was collected by interviewing patients and their relatives and was later checked and/or completed by chart review. The lead investigator in each center reviewed the medical records of the patients included to avoid protocol violations and to confirm the data collected. No therapeutic recommendations or specific education about AF and its management were provided by the study’s scientific committee during the data collection; the treating physicians were free to decide the patients’ treatment and were also unaware of the study objectives.

The information included on the data collection sheet is available in Data Supplement S1, Methods Supplement S1. Age was both considered as a continuous variable and stratified in <65, 65 to 74, and ≥75 years, the threshold selected in most of risk of stroke scores for AF patients. Recent-onset AF was defined as any AF episode with a known duration < 48 hours. Rhythm control treatment was considered effective when SR was achieved and lasted up until disposition (discharge or admission). Rate control treatment was considered effective when heart rate recorded at discharge from the ED was ≤110 beats/min, according to contemporary European Society of Cardiology (ESC) guidelines recommendations. We considered structural heart disease as the presence of any cardiac disease except mild cardiac hypertrophy and valve prolapse without valve failure. Heart failure was defined according to the 2008 ESC guidelines of diagnosis and treatment of acute and chronic heart failure. Due to the absence of validated scales specific to acute AF to measure improvement in patients’ symptoms in the time of data collection, we used a clinical approach: relief of symptoms was considered achieved when patients asked specifically about symptoms at discharge from the ED by the treating physician and whether or not admitted to hospital or reported the absence of the symptoms that caused the consultation, irrespective of the achievement of rhythm or rate control.

**Outcome Measures**

As the main objective of the study was to determine the clinical benefits of AF management, the primary outcome measure was relief of symptoms. The secondary outcome measure was the number of hospital admissions.

**Data Analysis**

The primary and secondary outcome measures were considered the independent variables in separate analyses of the relationship between the strategy attempted (rhythm or rate control) and each of the outcomes. These analyses were only performed in stable patients with recent-onset episodes (whether first-detected AF or recurrent) who were attended in the ED because of symptoms related to AF (Figure 1). This group of patients could be assumed to be candidates to both strategies because the option would not be limited by previous anticoagulation or need for emergent cardioversion. On the other hand, the presence of symptoms was essential to establish the onset of the episode and to measure relief of symptoms. To avoid selection bias favoring the rhythm control strategy, patients who spontaneously converted to SR before any treatment, patients presenting with acute stroke to the ED, and completely disabled patients were also excluded from the study. Selection of patients was independently performed by two investigators.

Statistical analysis was carried out with the SPSS 18.0 statistical software. Continuous variables are presented as mean and standard deviation (SD), and discrete variables as absolute values and percentages. Normality of continuous data was assessed with the Kolmogrov-Smirnov test, and association between quantitative variables was evaluated using the ANOVA variance analysis test or the Kruskal-Wallis test when the distribution was not normal. The only quantitative variables included in the model (age and heart rate at discharge) were dichotomized. Even so, previously the presence of outliers and collinearity was ruled out. Univariate analysis was performed using logistic regression models. A direct multivariate analysis was performed including other items that could have an influence on the endpoints: demographic variables (age—stratified in <65, 65–74, and ≥75 years,
gender), relevant clinical variables (presence of ventricular dysfunction or heart failure at inclusion or stroke risk as measured with the CHA2DS2-VASc scale), and heart rate at discharge (dichotomized as >110 beats/min or ≤110 beats/min). The Hosmer-Lemeshow test was used to analyze the model’s goodness of fit. Differences were considered to be statistically significant with a p-value less than 0.05 or when the 95% confidence interval (CI) of the odds ratio (OR) excluded the value of 1.

RESULTS

Characteristics of Study Subjects
During the study period, 110,909 patients were attended in the general medical areas of the 124 participating EDs, of which 3,485 had a diagnosis of AF and 3,276 (94%) were included (Data Supplement S1, Table S1). Fifteen patients died during the ED stay, all of them diagnosed of permanent AF. There were 421 hemodynamically stable patients who consulted for AF-related symptoms and who were considered the target population (Figure 1), 13% of the AF patients included. Clinical and epidemiologic features of these patients are detailed in Table 1.

Management of Recent-onset AF
Rhythm control was the chosen strategy in 352 patients (83.6% of the target population) and was effective in 296 (84.1%) of them. Reasons argued by the treating physicians for selecting rate control and not performing rhythm control are listed in Table 2. Only two minor adverse effects were observed in these patients (transient malaise and dizziness). Regimes used for rhythm control and rate control are shown in Table 3. Among patients in whom rhythm control was chosen, the only factor associated (negatively) to SR achievement was acute heart failure (55.5% vs. 84.8%, OR = 4.477, 95% CI = 1.164 to 17.226, p = 0.029)

Rate control was the chosen strategy in the remaining 69 patients (16.4%, Table 3), in whom AF was accepted, although eight of them (11.6%) did not receive drug therapy because of spontaneous rate control (<110 beats/min at presentation). Rate control was finally achieved in 67 patients (97.1%), with only one severe side effect: One of the patients treated with diltiazem presented severe bradycardia requiring pacemaker implantation.

Control of Symptoms
Control of symptoms was achieved in 396 patients (94.1%), including 335 of 352 (95.2%) patients in the rhythm control group and 61 of 69 (88.4%) patients in the rate control group. The rhythm control strategy and a heart rate of ≤110 beats/min after treatment were associated with control of symptoms, whereas chronic and acute heart failure were negatively
associated with it. In a multivariate analysis, the association with rhythm control and heart rate at discharge remained significant (Table 4).

### Admissions

None of the patients included in the target population died in the ED. Sixty patients (14.2%) were admitted to hospital, and 361 patients (85.7%) were discharged. Discharge was independently associated with a rhythm control strategy (OR = 2.22, 95% CI = 1.20–4.60, p = 0.031), and admission was independently associated with a heart rate of >110 beats/min after treatment (OR = 29.71, 95% CI = 7.19 to 123.07, p < 0.001) and acute heart failure (OR = 9.45, 95% CI = 2.91 to 30.65, p < 0.001; Table 5).

### DISCUSSION

HERMES-AF is a large study representative of the acute setting daily practice, as the population base covers the centers attending half of the emergencies in all of Spain. It is the first to prospectively analyze the relationship of the rhythm control strategy with symptoms’ relief and with the rate of hospital admissions. As in previous studies, the heterogeneity of treatments implemented in daily practice was evident, reflecting the multiple types of AF patients attended but also the variety of treatment options for any given patient. This variety implies that at present there is no specific recommendation about the best way to treat recent-onset episodes in the acute phase. International guidelines make recommendations about global rhythm or rate control strategy (OR = 2.22, 95% CI = 1.20–4.60, p = 0.031), and admission was independently associated with a heart rate of >110 beats/min after treatment (OR = 29.71, 95% CI = 7.19 to 123.07, p < 0.001) and acute heart failure (OR = 9.45, 95% CI = 2.91 to 30.65, p < 0.001; Table 5).

### Table 1

Demographic and Clinical Characteristics of the Target Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (N = 421)</th>
<th>Rhythm Control (n = 352)</th>
<th>Rate Control (n = 69)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>63.6 ± 14</td>
<td>62.7 ± 13.9</td>
<td>68.1 ± 13.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td>0.026</td>
</tr>
<tr>
<td>&lt;65</td>
<td>102 (24.2)</td>
<td>77 (21.9)</td>
<td>25 (36.2)</td>
<td></td>
</tr>
<tr>
<td>65–75</td>
<td>124 (29.5)</td>
<td>104 (29.5)</td>
<td>20 (29.0)</td>
<td></td>
</tr>
<tr>
<td>≥75</td>
<td>195 (46.3)</td>
<td>171 (48.5)</td>
<td>24 (34.8)</td>
<td></td>
</tr>
<tr>
<td>Gender (women)</td>
<td>222 (52.7)</td>
<td>187 (53.1)</td>
<td>35 (50.7)</td>
<td>0.715</td>
</tr>
<tr>
<td>Hypertension</td>
<td>253 (60.1)</td>
<td>204 (57.9)</td>
<td>49 (71.0)</td>
<td>0.043</td>
</tr>
<tr>
<td>Diabetes</td>
<td>75 (17.8)</td>
<td>65 (18.5)</td>
<td>10 (14.5)</td>
<td>0.430</td>
</tr>
<tr>
<td>Chronic heart failure and/or left ventricular dysfunction</td>
<td>43 (10.2)</td>
<td>32 (9.0)</td>
<td>11 (15.9)</td>
<td>0.086</td>
</tr>
<tr>
<td>CHA2DS2-VASc</td>
<td></td>
<td></td>
<td></td>
<td>0.106</td>
</tr>
<tr>
<td>0</td>
<td>58 (13.8)</td>
<td>54 (15.3)</td>
<td>4 (5.8)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>94 (22.3)</td>
<td>78 (22.2)</td>
<td>16 (23.2)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>269 (63.9)</td>
<td>220 (62.5)</td>
<td>49 (71.0)</td>
<td></td>
</tr>
<tr>
<td>Previous AF</td>
<td>235 (55.8)</td>
<td>188 (53.4)</td>
<td>47 (68.1)</td>
<td>0.024</td>
</tr>
<tr>
<td>Symptoms*</td>
<td></td>
<td></td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>Palpitations</td>
<td>351 (83.4)</td>
<td>301 (85.5)</td>
<td>50 (72.5)</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>117 (27.8)</td>
<td>93 (26.4)</td>
<td>24 (34.8)</td>
<td>0.156</td>
</tr>
<tr>
<td>Syncope</td>
<td>13 (3.1)</td>
<td>9 (2.5)</td>
<td>4 (5.8)</td>
<td>0.155</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>67 (15.9)</td>
<td>53 (15.0)</td>
<td>14 (20.3)</td>
<td>0.277</td>
</tr>
<tr>
<td>Dizziness</td>
<td>54 (12.8)</td>
<td>42 (11.9)</td>
<td>12 (17.4)</td>
<td>0.215</td>
</tr>
<tr>
<td>Acute heart failure</td>
<td>16 (3.8)</td>
<td>9 (2.5)</td>
<td>7 (10.1)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

*Some patients presented with more than one symptom.

### Table 2

Reasons for Not Performing Rhythm Control in the Target Population, Reported by the Attending Physicians (n = 69)

<table>
<thead>
<tr>
<th>Reason</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician’s rejection*</td>
<td>19 (19.8)</td>
</tr>
<tr>
<td>Doubts about the real duration of the episode</td>
<td>18 (18.7)</td>
</tr>
<tr>
<td>High likelihood of recurrence</td>
<td>18 (18.7)</td>
</tr>
<tr>
<td>Decision of cardioversion transferred to other health care setting</td>
<td>10 (10.4)</td>
</tr>
<tr>
<td>Partial disability</td>
<td>5 (5.2)</td>
</tr>
<tr>
<td>Nonanticoagulated</td>
<td>4 (4.1)</td>
</tr>
<tr>
<td>Unspecified</td>
<td>22 (23)</td>
</tr>
</tbody>
</table>

*Rhythm control considered not indicated or unsafe.
control strategies in AF, but none of them specifically addresses categorical recommendations in the acute setting, including EDs, reflecting the absence of conclusive evidence. In addition, long-term prognosis in newly diagnosed AF has been shown to be worse than for longstanding episodes, making even more important to establish the best strategy in the ED, where up to 25% of patients with recent-onset AF present with first-detected episodes (13% of all ED AF patients in our series). Important multicenter studies have compared rhythm and rate control strategies, but without taking into account the acute phase. Recent-onset episodes are scarcely represented in these studies; the vast majority of patients included had persistent AF, and their comorbidities differ greatly from those with recent-onset episodes.

On the other hand, cardioversion of recent-onset AF in the ED has been demonstrated to be both safe and effective in other studies carried out in the ED setting, and when SR was restored early it was also associated with a shorter length of hospital stay and a lower rate of readmissions. Our data point out in the same direction: cardioversion was feasible in the ED, irrespective of the type and size of hospital, and rhythm control was achieved in the vast majority of patients with no relevant side effects. Complementary to these findings, this large multicenter, population-based study has shown that in patients with recent-onset episodes reporting to the ED and who are eligible for rhythm control, this strategy both associates a high success in the alleviation of AF-related symptoms and also allows a high rate of subsequent ED discharge. Taking all this into account, rhythm control in the ED seems to be not only safe and effective but also beneficial for patients with recent-onset AF and therefore could be part of the standard management of these patients in the acute setting.

Table 3
Treatment for Rhythm Control and Rate Control in the Target Population

<table>
<thead>
<tr>
<th>Rhythm control</th>
<th>Number (%) of Patients (n = 352)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrical cardioversion†</td>
<td>39 (11.1)</td>
</tr>
<tr>
<td>Pharmacologic cardioversion*‡</td>
<td>271 (77.0)</td>
</tr>
<tr>
<td>Flecaïnide</td>
<td>97 (27.6)</td>
</tr>
<tr>
<td>Propafenone</td>
<td>9 (2.6)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>171 (48.6)</td>
</tr>
<tr>
<td>Other</td>
<td>13 (3.9)</td>
</tr>
<tr>
<td>Rate control (n = 69)</td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td>15 (21.7)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>27 (39.1)</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>16 (23.2)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (8.7)</td>
</tr>
</tbody>
</table>

*Some patients received more than one drug
†Eighteen patients underwent electrical cardioversion after pharmacologic cardioversion failed.
‡Vernakalant was not available in Spain at the time of data collection.

Table 4
Factors Related to Relief of Symptoms in the Target Population (N = 421)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control of Symptoms Achieved (n = 396)*</th>
<th>Control of Symptoms Not Achieved (n = 25)*</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>p-value</td>
<td>OR</td>
</tr>
<tr>
<td>Rhythm control attempted</td>
<td>2.584</td>
<td>1.068–6.251</td>
<td>0.035</td>
<td>2.786</td>
</tr>
<tr>
<td>Age 65–74 years</td>
<td>1.169</td>
<td>0.648–2.048</td>
<td>0.302</td>
<td>1.522</td>
</tr>
<tr>
<td>Age ≥ 75 years</td>
<td>0.703</td>
<td>0.238–2.074</td>
<td>0.523</td>
<td>0.929</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>0.869</td>
<td>0.385–1.962</td>
<td>0.736</td>
<td>0.734</td>
</tr>
<tr>
<td>Previous AF</td>
<td>0.992</td>
<td>0.440–2.240</td>
<td>0.985</td>
<td>0.902</td>
</tr>
<tr>
<td>Chronic heart failure and/or ventricular dysfunction</td>
<td>0.326</td>
<td>0.123–0.868</td>
<td>0.025</td>
<td>0.405</td>
</tr>
<tr>
<td>Acute heart failure</td>
<td>0.249</td>
<td>0.066–0.938</td>
<td>0.040</td>
<td>0.471</td>
</tr>
<tr>
<td>CHA2DS2-VASc = 1</td>
<td>1.227</td>
<td>0.265–5.691</td>
<td>0.670</td>
<td>1.174</td>
</tr>
<tr>
<td>CHA2DS2-VASc ≥ 2</td>
<td>0.761</td>
<td>0.216–2.672</td>
<td>0.398</td>
<td>0.692</td>
</tr>
<tr>
<td>Heart rate after treatment ≤ 110 beats/min</td>
<td>13.821</td>
<td>4.030–47.405</td>
<td>&lt;0.001</td>
<td>14.346</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation.
*Data are reported as n (%).
Since this is a single-country study, the external validity of our results must be addressed. Thus, differences in the ED management of recent-onset AF among countries has been described, not only concerning the selection of rate or rhythm control but also in the procedure (DC-cardioversion or antiarrhythmic drugs);\textsuperscript{2,21} these could also reflect differences among different health care systems, chiefly concerning the rates of hospital admission.\textsuperscript{9} Nevertheless, the characteristics and clinical presentation of the population included are an accurate reflection of those of AF patients attended in European Union EDs\textsuperscript{1,10,12,22,23} and nearly similar to those described in studies and registries from Canada\textsuperscript{9,10,21} and also to some from the United States;\textsuperscript{21,24} therefore, and at least as a first approach, our results are widely applicable to other countries, principally those with similar health care systems.

Symptoms alleviation is of the upmost importance in acute AF, and patients with AF exhibit a wide variety of clinical symptoms. Various hemodynamic derangements, including rapid ventricular rates, loss of organized atrial contraction, irregularity of cardiac rhythm, and bradycardia, may explain some of the AF-related symptoms that increasingly cause consultation and require treatment.\textsuperscript{25} Moreover, the available data suggest that quality of life is considerably impaired in patients with AF, compared to that of age-matched controls,\textsuperscript{26} and some studies show that restoration of SR is associated with improved quality of life and better exercise performance,\textsuperscript{26–28} but to date available evidence to compare the benefit of different treatments is insufficient.\textsuperscript{12–14} In that respect, this study found that SR restoration in the acute phase is also associated with high success in alleviation of symptoms that caused ED consultation, irrespective of heart rate at discharge or associated clinical conditions. Although the finding of the persistence of symptoms in some 20\% of patients in whom a rate control objective ($\leq 110$ beats/min at rest) was achieved could be striking, it probably reflects the fact that not only heart rate itself but also the loss of atrial contraction (that may markedly decrease cardiac output, particularly when diastolic ventricular filling is impaired), the irregularity of ventricular response, and atrial and atrioventricular dysynchrony are playing an important role in the development of AF-related symptoms.\textsuperscript{25,29} Thus, effective rhythm control provides not only control of the heart rate, but also restores atrial and atrioventricular synchrony and reduces heart rate irregularity to physiological limits, and this would result in better hemodynamic characteristics\textsuperscript{4,6,13,26–28} and therefore fewer AF-related symptoms.

Finally, the reduction in the rate of admissions found in rhythm control patients might help to improve quality of life and is also a very important issue in terms of costs. The high economic burden of AF has long been established, with inpatient costs been one of the factors that contribute to this economic burden the most.\textsuperscript{30} Rhythm control might be taken into account as an issue to reduce admissions and subsequently reduce costs.

### Table 5
Factors Related to Hospital Admissions in the Target Population ($N = 421$)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients Admitted ($n = 60^*$)</th>
<th>Patients Discharged ($n = 361^*$)</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Rhythm control attempted</td>
<td></td>
<td></td>
<td>0.426</td>
<td>0.226-0.327</td>
</tr>
<tr>
<td>Age 65–74 years</td>
<td>20 (33.3)</td>
<td>104 (28.8)</td>
<td>1.593</td>
<td>0.825-3.079</td>
</tr>
<tr>
<td>Age $\geq$ 75 years</td>
<td>21 (35.0)</td>
<td>174 (48.2)</td>
<td>1.897</td>
<td>0.967-3.719</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>29 (48.3)</td>
<td>193 (53.5)</td>
<td>0.814</td>
<td>0.471-1.407</td>
</tr>
<tr>
<td>Previous AF</td>
<td>33 (55.0)</td>
<td>202 (55.9)</td>
<td>0.962</td>
<td>0.555-1.667</td>
</tr>
<tr>
<td>Chronic heart failure and/or ventricular dysfunction</td>
<td>10 (16.7)</td>
<td>33 (9.1)</td>
<td>1.988</td>
<td>0.923-4.283</td>
</tr>
<tr>
<td>Acute heart failure</td>
<td>10 (16.7)</td>
<td>6 (1.7)</td>
<td>11.833</td>
<td>4.122-33.969</td>
</tr>
<tr>
<td>CHA$2$DS$_2$-VASc = 1</td>
<td>9 (15.0)</td>
<td>85 (23.5)</td>
<td>0.662</td>
<td>0.240-1.825</td>
</tr>
<tr>
<td>CHA$2$DS$_2$-VASc $\geq$ 2</td>
<td>43 (71.7)</td>
<td>226 (62.6)</td>
<td>1.189</td>
<td>0.527-2.685</td>
</tr>
<tr>
<td>Heart rate after treatment $\leq 110$ beats/min</td>
<td>9 (15.0)</td>
<td>3 (0.8)</td>
<td>0.048</td>
<td>0.013-0.182</td>
</tr>
</tbody>
</table>

*Data are reported as $n$ (%).
LIMITATIONS

A main limitation of our study is the strategy used to describe relief from AF-related symptomatology. To our knowledge, no tool for measuring symptoms relief in acute AF was available and validated at the time of the study period,\textsuperscript{14,16,19} so we used a clinical approach that could be easily reproduced in other studies as well as in daily practice and thus could be useful in setting a decision-making process. Nevertheless, a simple and validated tool to measure patient improvement after treatment in acute AF is desirable.\textsuperscript{14,16,27} In this sense, the evaluation of the symptom relieving was done unblinded, that is, with knowledge of strategy choice and also knowing the result of the intervention and could influence the investigators’ perception of the effectiveness of each therapy. To minimize this, the investigators were free to decide patients’ management and were also unaware to the study objectives.

The HERMES-AF was an observational nonrandomized study, focused in acute management with no follow-up, so causation from the associations found in our data should not be inferred and warrant further investigation (prospective randomized studies) to evaluate these associations and the midterm safety of acute rhythm control. In this sense, our study was not designed to compare rate and rhythm control strategies, so conclusions in this matter cannot be made; our aim was to highlight the good results of rhythm control in ED patients with recent-onset AF in terms of symptoms’ alleviation and ED discharge and the potential benefits of its application in daily practice.

In addition participation in an investigative study may have had an impact on the clinicians, despite the absence of training and lack of patient management recommendations. It is possible that their involvement in the study may have led to prescribing a different treatment than they would have in other circumstances. The clinical characteristics of the patients in whom rhythm control was attempted differed from the rest of the sample, particularly the prevalence of acute heart failure chest pain, dizziness, and structural heart disease; this could have an impact on treatment decision because these patients could be considered less eligible for rhythm control or the decision deferred to the impatient setting after admission. Moreover, in the diagnosis of acute heart failure, although based on the ESC guidelines recommendations and scrutinized by the lead investigator of each center, a certain variability could not completely be ruled out and this could constitute a source of bias. Therefore, we performed a multivariate analysis trying to discard any possible bias and found that even controlling for these factors rhythm control was a major determinant of symptom alleviation, mostly in patients with heart failure (Table 4). Additionally, the reasons argued by the treating physicians for not attempt rhythm control captured by our study are limited and should be considered as an exploratory view of an intricate phenomenon, particularly in complex patients. Finally, our data show only short-term results, so effectiveness and outcomes beyond the acute phase should not be inferred.

CONCLUSIONS

In this large study concerning acute atrial fibrillation management, rhythm control in recent-onset atrial fibrillation is a safe, effective, and feasible strategy to be performed in the ED daily clinical practice. Additionally, patients in whom rhythm control was attempted had a high rate of alleviation of atrial fibrillation-related symptoms and a low rate of subsequent admission to hospital. These results suggest that acute rhythm control could play a substantial role in the standard management of recent-onset atrial fibrillation in the ED and warrant further randomized studies to establish its role in the acute setting.

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.13703/full

Data Supplement S1. Supplemental material.
Subdissociative-dose Ketamine Is Effective for Treating Acute Exacerbations of Chronic Pain

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ABSTRACT

Background: Subdissociative-dose ketamine (SDDK) is used to treat acute pain. We sought to determine if SDDK is effective in relieving acute exacerbations of chronic pain.

Methods: This study was a randomized double-blind placebo-controlled trial conducted May 2017 to June 2018 at a public teaching hospital (ClinicalTrials.gov #NCT02920528). The primary endpoint was a 20-mm decrease on a 100-mm visual analog scale (VAS) at 60 minutes. Power analysis using three groups (0.5 mg/kg ketamine, 0.25 mg/kg ketamine, or placebo infused over 20 minutes) estimated that 96 subjects were needed for 90% power. Inclusion criteria included age > 18 years, chronic pain > 3 months, and acute exacerbation (VAS ≥ 70 mm). Pain, agitation, and sedation were assessed by VAS at baseline and 20, 40, and 60 minutes after initiation of study drug. Telephone follow-up at 24 to 48 hours used a 10-point numeric rating scale for pain.

Results: A total of 106 subjects were recruited, with three excluded for baseline pain < 70 mm. After randomization, 35 received 0.5 mg/kg ketamine, 36 received 0.25 mg/kg ketamine, and 35 received placebo. Three subjects receiving 0.5 mg/kg withdrew during the infusion due to adverse effects, and one subject in each group had incomplete data, leaving 97 for analysis. Initial pain scores (91.9 ± 8.9 mm), age (46.5 ± 12.6 years), sex distribution, and types of pain reported were similar. Primary endpoint analysis found that 25 of 30 (83%) improved with 0.5 mg/kg ketamine, 28 of 35 (80%) with 0.25 mg/kg ketamine, and 13 of 32 (41%) with placebo (p = 0.001). More adverse effects occurred in the ketamine groups with one subject in the 0.25 mg/kg group requiring a restraint code for agitation. A total of 89% of subjects were contacted at 24 to 48 hours, and no difference in pain level was detected between groups.

Conclusion: Ketamine infusions at both 0.5 and 0.25 mg/kg over 20 minutes were effective in treating acute exacerbations of chronic pain but resulted in more adverse effects compared to placebo. Ketamine did not demonstrate longer-term pain control over the next 24 to 48 hours.

Pain management is a primary objective for most patients presenting to the emergency department (ED), and patients with chronic pain may account for 10% to 16% of total ED visits.1-3 Both the Department of Health and Human Services and the Institute of Medicine have identified the management of pain as a significant public health problem in the United States.4 Currently the vast majority of painful conditions within the ED are treated with either opioid or nonsteroidal anti-inflammatory drugs (NSAIDs). Treatment of
chronic pain syndromes in the ED can be particularly challenging, since many subjects with these conditions have become tolerant to the effects of opioids and NSAIDs; therefore, alternative strategies are needed.

Ketamine \([\text{2-(o-chlorophenyl)-2-methylamino cyclohexanone}]\) is a phencyclidine derivative with unique analgesic, amnestic, and dissociative properties.\(^5,6\) It acts primarily as a competitive antagonist at the N-methyl-L-aspartate (NMDA) receptor within the limbic system to modulate autonomic responses to stimuli.\(^5,7\) As a treatment option for pain, ketamine has numerous advantages over opioids including a stable hemodynamic profile and lack of respiratory depression.\(^7\) Recent studies have demonstrated ketamine’s effectiveness for pain control in patients who present to the ED with acute pain syndromes when infused in a subdissociative dose by itself or in conjunction with NSAIDs.\(^8,9\) There has also been a recent consensus statements on the use of intravenous (IV) ketamine infusions for the treatment of chronic pain.\(^10\)

The objective of this study was to determine whether subdissociative-dose ketamine (SDDK) can improve pain control in subjects with chronic pain presenting to the ED with an acute exacerbation. If found effective, SDDK may offer an alternative medication to treat patients with acute on chronic pain.

**METHODS**

**Study Design**

This was a prospective, randomized double-blind placebo-controlled trial to evaluate the efficacy of SDDK for the treatment of acute on chronic pain in the ED. The study was conducted under FDA IND #134,272, listed under Clinicaltrials.gov #NCT02920528, and approval through the Los Angeles Biomedical Research Institute’s Institutional Review Board was obtained.

**Study Setting**

The study was conducted in the ED of an academic safety-net, urban hospital in Los Angeles County with approximately 75,000 ED visits per year. Inclusion criteria consisted of subjects over the age of 18 with a history of chronic pain presenting to the ED with exacerbation of their chronic pain as their primary complaint. Chronic pain was defined as pain that lasted greater than 3 months. Subjects were evaluated by research associates who were physically in the department for 80 hours per week and available on call to enroll patients at all other times if the treating providers identified their patients as potential research subjects. To be included in this study, the pain exacerbation had to have been self-reported as at least 70 mm on a 100-mm visual analog pain scale. Subjects were excluded from the study if found to have history of overt psychosis, severe hypertension defined by systolic blood pressure > 180 or diastolic blood pressure > 110, unstable angina, coronary artery disease, congestive heart failure, porphyria, thyroid disease, or seizure disorder or if they were unable to provide informed consent in either English or Spanish.

**Study Protocol**

Subjects were given a pain questionnaire to fill out describing the cause of their pain (if known), its duration, and characterizing features. The subject then rated their pain and level of self-reported agitation and sedation on three separate 100-mm nonhatched visual analog scales (VASs).

A computer-generated randomization scheme was used prospectively to randomize each subject to one of the three study groups. An IV line was then placed in the upper extremity for infusion of either 0.5 mg/kg ketamine or 0.25 mg/kg ketamine or an equal amount of saline placebo over 20 minutes via an automated pump. The study medications were prepared by a pharmacist while all study investigators, nurses, treating clinicians, and the subject remained blinded to the study group in which they were enrolled. Each subject was asked to wear a pair of sunglasses throughout their study participation so that the study investigators, clinicians, and nurses would remain blinded to the presence or degree of possible involuntary eye movements caused by study medication.

At time 20 minutes, subjects were asked to rate their pain, agitation, and sedation on new 100-mm nonhatched VAS without access to the baseline VAS. If the subject’s pain was not sufficiently relieved by the study medications at pain reassessment intervals at time 20, 40, or 60 minutes, rescue therapy consisting of any additional analgesic medication was offered to the subject at the discretion of the treating physician, with the exception of the use of ketamine. Whether rescue medications were given or not, VAS was also recorded at time 40 and 60 minutes in a similar manner. In addition to continuous monitoring of vital signs, subjects were monitored for side effects including self-reported or observed hallucinations, disorientation, agitation/anxiety, dysphoria, nausea, or vomiting, which were recorded.
We contacted subjects by telephone at 24 to 48 hours following discharge from the ED to assess for persistence or recurrence of pain using a 10-point numeric rating scale for pain with subjects rating their pain from 1 to 10, where 10 represented the worst pain.

**Data Analysis**

The primary endpoint was clinically significant pain relief defined a priori as a decrease in the pain VAS of at least 20 mm from baseline, which was arbitrarily chosen as the minimal amount that may be important to this group of patients and was extrapolated from studies of acute pain management in the ED. Using an effect size of 20-mm change in VAS as the marker for a successful outcome and the proportion of successes by group as the analysis point, we performed a power analysis using three groups: 0.5 mg/kg ketamine, 0.25 mg/kg ketamine, and placebo and found that a sample size of 96 subjects would be required to detect a statistically significant difference among groups with a power of 90% ($\alpha = 0.05$). Expecting a loss of 10% of subjects due to patient withdrawal or incomplete data, 106 subjects were recruited. Only subjects who completed the 60-minute study and had data recorded for each of the time points were included in the analysis.

Mean pain, agitation, and sedation were recorded using the VAS from time 0 (baseline) to time 60 minutes (conclusion of the study) for each of the three groups. Comparisons between groups for the primary outcome of pain reduction of at least 20 mm in the VAS was done by repeated-measures analysis of variance. A Kaplan-Meier analysis for persistence of pain over time was completed and comparisons were made using the Haybittle-Peto method. A Fisher’s exact test of contingency was used to compare numbers of subjects requiring rescue medications between the groups. Scores from the 10-point numeric rating scale for pain obtained at 24- to 48-hour follow-up were compared between groups using the Mann-Whitney U-test.

**RESULTS**

A convenience sample of 106 patients was enrolled in the study from May 2017 to June 2018. Three consented subjects were excluded from randomization because they did not meet the baseline pain VAS of at least 70 mm. Randomization resulted in 35 subjects in the 0.5 mg/kg ketamine group, 36 in the 0.25 mg/kg ketamine group, and 35 in the placebo group.

Three subjects in the 0.5 mg/kg ketamine group requested to have their ketamine infusions halted before the completion of the 20-minute infusion: one subject because of feelings of agitation (stopped at 17 minutes), the second at 10 minutes because of nausea and vomiting, and the third at 10 minutes because of dysphoria and hallucinations. The data for the three subjects were excluded from the final analysis of pain reduction and from other comparisons. In addition, one subject in each group had incomplete data and was excluded, leaving a total of 97 subjects for analysis (Figure 1).

Initial pain scores in mm (91.4 ± 8.5, 93.2 ± 8.9, 91.2 ± 9.3), age in years (47.8 ± 11.5, 44.3 ± 11.2, 47.6 ± 15), male sex (12/18, 14/21, 14/18), and types of pain reported were similar between the 0.5 mg/kg ketamine, 0.25 mg/kg ketamine, and placebo groups. Demographics are listed in Table 1, including

![Figure 1](image-url). Consort diagram of patients enrolled and analyzed in the study. VAS = visual analog scale.
Table 1
Patient Demographic Characteristics and Initial VAS Scores for Each Study Group

<table>
<thead>
<tr>
<th></th>
<th>Total Analyzed (N = 97)</th>
<th>Group 1 (n = 30), 0.5 mg/kg Ketamine</th>
<th>Group 2 (n = 35), 0.25 mg/kg Ketamine</th>
<th>Group 3 (n = 32), Placebo</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46.5 ± 12.6</td>
<td>47.8 ± 11.5</td>
<td>44.3 ± 11.2</td>
<td>47.6 ± 15</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Female</td>
<td>57</td>
<td>18</td>
<td>21</td>
<td>18</td>
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<tr>
<td>Male</td>
<td>40</td>
<td>12</td>
<td>14</td>
<td>14</td>
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<tr>
<td>Baseline VAS (mm)</td>
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<td></td>
<td></td>
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<tr>
<td>Pain</td>
<td>91.9 ± 8.9</td>
<td>91.4 ± 8.5</td>
<td>93.2 ± 8.9</td>
<td>91.2 ± 9.4</td>
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<td>Agitation</td>
<td>31.6 ± 38</td>
<td>25.5 ± 36.5</td>
<td>34.2 ± 41.4</td>
<td>34.4 ± 35.9</td>
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<tr>
<td>Sedation</td>
<td>15.2 ± 29.3</td>
<td>19.6 ± 32</td>
<td>13.3 ± 29.2</td>
<td>12.8 ± 26.6</td>
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<tr>
<td>Pain characteristics</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Types of pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Musculoskeletal</td>
<td>68</td>
<td>21</td>
<td>24</td>
<td>23</td>
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<td>Radicular pain</td>
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<td>5</td>
<td>5</td>
<td>4</td>
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<td>Fibromyalgia</td>
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<td>2</td>
<td>1</td>
<td>1</td>
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<td>Chronic headache</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Chronic abdominal pain</td>
<td>3</td>
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<td>2</td>
<td></td>
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<tr>
<td>Cancer</td>
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<td>1</td>
<td>3</td>
<td>2</td>
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<tr>
<td>Rheumatoid arthritis</td>
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<tr>
<td>Duration</td>
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<td></td>
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<tr>
<td>3–6 months</td>
<td>16</td>
<td>7</td>
<td>7</td>
<td>2</td>
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<tr>
<td>6–12 months</td>
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<td>1–5 years</td>
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<td>&gt;5 years</td>
<td>21</td>
<td>3</td>
<td>11</td>
<td>7</td>
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<tr>
<td>Pain medications at home</td>
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<td></td>
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<tr>
<td>One drug</td>
<td>54</td>
<td>17</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Multi</td>
<td>43</td>
<td>13</td>
<td>15</td>
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<tr>
<td>NSAIDs</td>
<td>61</td>
<td>22</td>
<td>20</td>
<td>19</td>
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<tr>
<td>Opioids</td>
<td>55</td>
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<td>21</td>
<td>20</td>
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<tr>
<td>Gabapentin</td>
<td>16</td>
<td>6</td>
<td>4</td>
<td>6</td>
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<tr>
<td>Cyclobenzaprine</td>
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<tr>
<td>Oral corticosteroids</td>
<td>2</td>
<td></td>
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<td></td>
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<tr>
<td>Marijuana</td>
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<td></td>
<td>1</td>
<td></td>
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<tr>
<td>Pain specialist evaluation</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>28</td>
<td>9</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>No</td>
<td>69</td>
<td>21</td>
<td>26</td>
<td>22</td>
</tr>
<tr>
<td>ED visits</td>
<td></td>
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<td>First time</td>
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<td>6</td>
<td>7</td>
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<tr>
<td>Once a week</td>
<td>11</td>
<td>4</td>
<td>3</td>
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<tr>
<td>Once or twice a month</td>
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<td>5</td>
<td>8</td>
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<td>Once in 3 months</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Once in 6 months</td>
<td>13</td>
<td>5</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Once in a year or two</td>
<td>21</td>
<td>5</td>
<td>10</td>
<td>6</td>
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<tr>
<td>Visit expectations</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Pain to be at least halved</td>
<td>12</td>
<td>4</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Pain to be tolerable</td>
<td>48</td>
<td>15</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>Pain to be barely noticeable</td>
<td>14</td>
<td>6</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>To become pain free</td>
<td>23</td>
<td>9</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

NSAIDs = nonsteroidal anti-inflammatory drugs; VAS = visual analog scale.
description of the type, quality, and duration of chronic pain; number of times presenting to an ED with pain; whether they had seen a pain specialist; and medications that had been tried to control the pain.

Overall, 66 subjects experienced a successful improvement of their pain as defined by a decrease in VAS of 20 mm over course of the study. Both ketamine groups were superior to placebo: 0.5 mg/kg ketamine, 25 of 30 (83.3%), and 0.25 mg/kg ketamine, 28 of 35 (80%), versus placebo, 13 of 32 (40.6%; p = 0.001). Survival analysis was performed to measure the persistence of pain among groups longitudinally during the ED stay (event = decrease in pain by 20 mm; censored = received rescue medication; Haybittle-Peto p = 0.002). There was no statistically significant difference in pain relief between ketamine doses.

Kaplan-Meier survival analysis for persistence of pain is illustrated in Figure 2A and the pain VAS time curves are shown in Figure 2B.

There were significantly more adverse events documented in the ketamine groups versus placebo. Twelve subjects in the 0.5 mg/kg ketamine (40%) and 14 subjects (40%) in the 0.25 mg/kg ketamine group reported or were observed to have a side effect but tolerated the infusion and completed the study. One subject in the placebo group reported an adverse effect (Table 2). Three subjects in the 0.5 mg/kg ketamine group also disenrolled from the study during the infusion because of adverse effects and were not included in the above analysis. One subject in the 0.25 mg/kg ketamine group required activation of a patient restraint code secondary to agitation.

![Figure 2](image)

**Figure 2.** (A) Kaplan-Meier survival analysis. The persistence (survival) of pain over time, by group. Time intervals are 0, 20, 40, and 60 minutes. Product-limit survival estimate boundaries set at time 0 and time 60 minutes. This figure represents the probability that an individual will not have sufficient pain control response by group over time. Censored cases (hash marks) include those who withdrew from the study at the corresponding interval. (B) Pain time-curve. *Seven subjects received rescue medications after 20 minutes and were excluded from the 40- and 60-minute time points. **Five more subjects received rescue medications after 40 minutes and were excluded from the 60-minute time point. VAS = visual analog scale.
Subjects in the placebo group required more rescue medications than the ketamine groups and requested the rescue medication at an earlier time. Rescue medications were administered to seven subjects (23.3%) in the 0.5 mg/kg ketamine group, 12 subjects (34.3%) in the 0.25 mg/kg ketamine group, and 17 subjects (53.1%) in the placebo group ($p = 0.03$). Rescue medications utilized alone or in combination consisted of IV or oral opiates ($n = 29$), IV or oral NSAIDs ($n = 18$), oral acetaminophen ($n = 2$), IV benzodiazepines ($n = 1$), and one trigger-point injection. Some patients required multiple doses.

Follow-up at 24 to 48 hours was achieved in 89 (91.8%) of cases, with an equal distribution among groups. On the 10-point numeric rating scale for pain with 10 being the worst, there was no difference between groups with the median and interquartile ranges: 6 (3–8) for the 0.5 mg/kg group, 5 (4–7) for the 0.25 mg/kg group, and 5 (4–8) for the placebo arm. Of the 21 subjects who reported a pain score of at least 8 out of 10, there was also no difference in distribution between groups.

**DISCUSSION**

Ketamine is an analgesic that has been shown to help to decrease acute pain in the ED.\textsuperscript{11–13} With the morbidity and mortality associated with the ongoing opioid epidemic, there is an urgent need to find nonopioid alternatives to treat pain that are safe and effective.\textsuperscript{14–17} Our study demonstrated efficacy for SDDK at 0.5 and 0.25 mg/kg infused over 20 minutes to reduce pain in our population of chronic pain patients during their ED stay. This is not surprising since ketamine is an NMDA antagonist with a long history of use for pain relief in the ED when used during procedural sedation.\textsuperscript{18} Our study is the first to analyze the effects of a single infusion of SDDK initiated in the ED on patients with acute exacerbations of chronic pain.

Chronic pain sufferers may differ from those with acute pain because of a process known as central sensitization where patients may have an exaggerated response to nociceptive stimuli resulting in hyperalgesia.\textsuperscript{19} The mechanism is mediated through the nociception-induced release of neuropeptides and glutamate, which act at the spinal NMDA receptors. Since ketamine is an NMDA antagonist, it may help to reset (down-regulate) the receptor cells and help to create a lasting change in the perception of the pain.\textsuperscript{5,19} However, while the ketamine worked acutely during their ED visit, our study did not demonstrate a lasting effect at the 24- to 48-hour follow-up, which may limit its usefulness in treating this group of patients. This is similar to the outcome found in other ketamine infusion studies where the effect did not persist past the acute pain reduction.\textsuperscript{20,21}

Our subjects suffered from more adverse effects when they were treated with ketamine compared to placebo. These effects included well-known side effects of dysphoria, anxiety, and hallucination and were seen in 17% of the patients receiving ketamine.\textsuperscript{20,22} In addition, two of the three subjects who were not included in the analysis because they stopped the 0.5 mg/kg ketamine infusion reported unpleasant out-of-body experience, similar to what is usually seen in emergence reaction.\textsuperscript{23} Most subjects recovered from these symptoms over time without additional reversal agents except for one in ketamine 0.25 mg/kg group who required the administration of a benzodiazepine and the activation of a patient restraint code in the ED.

Interestingly, in our study the placebo arm had significant improvement in their pain. In this study, the reason was probably twofold. First, in the design of the study, we used a minimum of 20-mm improvement on the VAS to be significant. Although this was based on previous work on pain scores where a change of at least 13 mm on the pain VAS is considered significant,\textsuperscript{24} our subjects had a mean VAS of over 90 mm on arrival and a greater change may be needed for clinical improvement in a group that starts with a very high VAS score.\textsuperscript{25} Second, the placebo effect on a chronic condition may be very effective especially in a design where the patients received a sham IV infusion over 20 minutes. Similar to previous studies, 40% of our subjects who were randomized to the placebo arm reported clinically significant pain reduction and did not ask for rescue medication.\textsuperscript{26}

### Table 2

<table>
<thead>
<tr>
<th>Side Effects Associated With Each Study Group</th>
<th>0.5 mg/kg Ketamine ($n = 30$)</th>
<th>0.25 mg/kg Ketamine ($n = 35$)</th>
<th>Placebo ($n = 32$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>3</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Hallucination</td>
<td>2</td>
<td></td>
<td></td>
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<tr>
<td>Anxiety</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety and dizziness</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Anxiety and palpitation</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Dysphoria</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Symptoms started 6 to 10 hours after the study.*
LIMITATIONS

There are a number of limitations to this study. First, the diagnosis of chronic pain can be difficult along with what would constitute a meaningful reduction in pain for this patient population. We included all types of persistent pain with the understanding that changes in the pain pathways might be similarly affected by ketamine. Ketamine has a long history of acting as an analgesic but whether it can affect neuronal pathways that have been subject to chronic pain is unknown. As our demographics show, many of our patients presented with similar pain syndromes but the variability in types of pain reported may have limited the ability to detect differences between groups. Randomization should have decreased the likelihood that one of the treatment group arms received a disproportionate share of types of pain syndromes; however, we cannot affirm that a larger trial would not identify a subgroup of patients with chronic pain who would benefit more from one therapy over the other. In addition, our patients’ visit expectations as detailed in Table 1 were unknown prior to the design of this study, and a decrease of 20 mm on the pain VAS may have underestimated the pain reduction expected for a clinically meaningful improvement and should help guide further studies in this population.

The duration of the study in the ED was also relatively short and was designed to study whether just one 20-minute infusion of SDDK could lead to improvement in the patient’s report of chronic pain. Recognition of adverse effects could have been better defined and in future studies we recommend utilizing a validated tool. We used VASs for agitation and sedation. In addition, our research associates were at the bedside asking and observing the subjects whether they were experiencing nausea, dizziness, or anxiety; reported dysphoria, or exhibited hallucinations. Except for one patient who required a restraint code, all adverse effects were mild. Finally, although we failed to find any meaningful reduction in pain within the 24- to 48-hour follow-up period, a prolonged infusion or multiple infusions over a period of days to weeks may be needed for a longer-term benefit in these patients becomes evident.

CONCLUSION

Ketamine infusions at both 0.5 mg/kg and 0.25 mg/kg over 20 minutes were effective in acutely controlling pain in a group of patients with chronic pain when compared with placebo. There was no evidence that ketamine resulted in longer-term pain control over the next 24 to 48 hours. Ketamine was associated with more side effects than placebo.

References

The Emergency Department Response to Women Experiencing Intimate Partner Violence: Insights From Interviews With Clinicians in Australia

Angela J. Dawson, PhD, MA,1 Chris Rossiter,2 Anna Doab, MPH, RN,1 Bernadine Romero, RN,3 Lesley Fitzpatrick, MNurs, RN,4 and Margaret Fry, PhD, RN5

ABSTRACT

Background and Objectives: Emergency departments (EDs) are essential providers of compassionate, immediate treatment and referral for women experiencing intimate partner violence (IPV). IPV, largely perpetrated by men against women, exerts a substantial burden on the health systems and economies of all nations. There is little known about how staff in Australian EDs respond to the challenges such violence generates. We therefore examined the clinical team response to women experiencing IPV in two large Australian metropolitan hospital EDs.

Methods: We undertook qualitative semistructured interviews and focus group discussions with 35 social workers, nurses, and doctors. Transcripts were recorded and transcribed verbatim. We analyzed the data thematically. We first undertook line-by-line coding and organized content into descriptive categories. Latent and manifest patterns were identified across the data and mapped to key themes in negotiation with all authors.

Results: Respondents emphasized challenges identifying IPV resulting from professional uncertainty or discomfort and women’s fear of the ramifications of disclosure. Emergency clinicians routinely referred women to social workers after medical treatment and described effective collaboration across professions. Social workers outlined difficulties coordinating care with health and community agencies. Staff highlighted challenges maintaining nonjudgmental attitudes and managing their own feelings—especially clinicians who had personally experienced violence.

Conclusions: Emergency departments can provide caring environments for women experiencing IPV. Effective interprofessional teamwork across nursing, medical, and social work professionals may mitigate the need for formal screening tools. Supportive workforce environments can improve staff understanding, reduce stigma, enhance appropriate treatment, and counsel health professionals experiencing violence. However, staff training and advocacy and referral relationships with local programs require strengthening. A connected multisystems-level response is required to coordinate and resource services for all affected by violence.

Intimate partner violence (IPV) is a significant public health issue in high income countries with an overall 12-month period prevalence of 4%.1 IPV is largely perpetrated by men against women and is therefore a key determinant of women’s and children’s health that exerts a substantial burden on the health systems and economies of all nations. There is little known about how staff in Australian EDs respond to the challenges such violence generates. We therefore examined the clinical team response to women experiencing IPV in two large Australian metropolitan hospital EDs.

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Received November 9, 2018; revision received February 15, 2019; accepted February 24, 2019.
Funded by University of Technology Sydney: Health Futures grant and the Northern Sydney Local Health District Primary and Community Care Women’s Health Fund.
The authors have no potential conflicts to disclose.
Supervising Editor: Ula Hwang, MD, MPH.
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 doi: 10.1111/acem.13721
economies of all nations. IPV is defined as the preventable physical, sexual, or psychological abuse of a past or current intimate partner. This form of violence causes more illness, disability, and deaths than any other risk factor for Australian women aged 25 to 44. In the United States IPV represents the second leading cause of death and injury among women of childbearing age. There are significant associations between lifetime experiences of partner violence and self-reported poor health. In 2016, approximately one in four Australian women (2.2 million) had experienced IPV, with an estimated annual cost to the national economy of $12.6 billion, including $617.2 million specifically on health costs.

Intimate partner violence causes acute and chronic injuries, pain syndromes, depression, posttraumatic stress, substance-use disorders, and gynecologic and maternal health concerns. Women experiencing IPV seek care from hospital emergency departments (EDs) three times more often than nonabused women. Women experiencing IPV who present at EDs require immediate evidence-based care to ensure their safety and well-being. Australian research has highlighted gaps in emergency health providers’ responses to IPV, particularly the underreporting of IPV in regional hospitals. For example, evidence for underreporting was found in one study where 4% of women who did not report IPV indicated experiences of abuse on nine measures of types of violence, including six taken from the Conflict Tactics Scale.

The ED is usually the first—and sometimes the only—place where women experiencing IPV interact with the health system. Women experiencing IPV are more likely to seek health care than to contact criminal justice or social services agencies. This offers emergency clinicians a unique opportunity to identify, treat, and enact a coordinated response, supporting women and managing their immediate and ongoing care. While there are many reasons why IPV may be undetected in EDs, two prominent reasons are the reluctance of women to disclose such experiences and inadequate training of health care clinicians in the recognition of signs and symptoms of IPV.

There are relatively few studies in Australasian hospital EDs focusing on the experience of health professionals caring for women with IPV. Some research has evaluated education and institutional protocols to assist clinicians to identify and respond to IPV and has demonstrated improved clinician knowledge, assessment, and referral practices up to 6 months postimplementation. Another study surveyed ED staff about screening practices, finding that medical officers and nurses lack knowledge and capacity to identify and respond to IPV. Qualitative research with ED health professionals remains limited. One New Zealand study interviewed 11 emergency nurses about screening for partner abuse finding that nurses who felt comfortable asking women about IPV were more likely to do so. Two Australian studies investigated the attitudes, perspectives, and practices of emergency nurses reporting that nurses distanced themselves from women and felt that they were lacking in skills and institutional support to adequately respond. There is therefore a lack of studies examining the characteristics that shape team work, decision making, practice, and approaches to IPV by emergency clinicians.

This study aimed to examine the knowledge, opinions, and motivations that shape the decisions and practice of teams of clinicians in busy metropolitan EDs when caring for women who experience IPV. We undertook a qualitative study to understand how nurses, doctors, and social workers recognize and respond to IPV.

METHODS
This study was informed by the concept of teamwork, specifically interprofessional collaboration (IPC). Petri describes IPC as the process of working together in a team with more than one person from a different professional group, working toward a common goal through mutual trust and respect, with effective communication skills, and recognition of different roles and responsibilities that contribute to outcomes. The literature has described the benefits of IPC in improving teamwork, patient-centered care, and clinical outcomes.

Study Design
Qualitative research has the potential to generate valuable new insights about how to best prepare, manage, and support emergency clinical teams to improve women-centered care. We adopted a descriptive qualitative design to examine participants’ experiences regarding events and actions specifically related to IPV in their workplace. As in naturalist inquiry, we sought to examine everyday responses to IPV and the associated knowledge and attitudes of ED professionals working in large metropolitan hospitals through semistructured individual and focus group discussions.
The local health authority and university human research ethics committees approved the study.

**Participants**

We interviewed 35 health professionals across two hospitals (Table 1). This included 14 face-to-face interviews and five focus groups, ranging from three to five nurse participants. Three social workers worked exclusively in the participating EDs; two worked occasional shifts in the ED in addition to other roles. Twenty-eight participants were female. The seven men were doctors or nurses.

**Setting**

The study took place at two tertiary teaching hospitals in metropolitan locations. Both are public hospitals with about 600 beds; their EDs received approximately 80,000 presentations in 2016. Both are comparable with respect to attendance patterns, clinical leadership positions, under/postgraduate training, staff education programs, information systems, resources, and staffing. They were selected for their diverse catchment areas: hospital 1 is located within 10 km of the city center in a relatively affluent area of the city and hospital 2 lies within 20 km of the city center and serves an area that is younger in age profile and more mixed ethnically and socioeconomically.

**Recruitment**

The lead author met the senior staff in each hospital to seek interest and support for the study. This was facilitated by one author [MF] who is an academic emergency nurse.

The study was open to all clinical staff working in the two EDs. They were invited to participate via a flyer and information sessions provided by clinical nurse consultants in both hospitals, who arranged convenient interview times with interested individuals. We used purposive heterogeneity sampling to recruit clinicians in the two EDs to identify common patterns across the three groups of health professionals. Clinicians were therefore recruited purposively by clinical nurse consultants who gave targeted information sessions to doctors, nurses, and social workers and gained consent for the researchers to contact them. Table 1 indicates response rates.

All respondents gave informed consent to participate in the study. Interviews and focus groups were held until the concurrent analysis process revealed saturation of themes and no new insights. At this point, all researchers agreed that saturation had been reached and recruitment and interviewing ceased. No participants dropped out of the study.

**Table 1**

<table>
<thead>
<tr>
<th>Hospital Characteristics and Study Participants</th>
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<tr>
<td><strong>Hospital 1</strong></td>
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<tr>
<td><strong>Type of hospital</strong></td>
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<td><strong>Setting</strong></td>
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<td><strong>ED presentations 2016-2017</strong></td>
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<td><strong>No. of FTE positions of physicians in ED staff (%)</strong></td>
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<td><strong>No. (%) of those that participated in the study</strong></td>
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<td><strong>No. of nurses in ED staff (%)</strong></td>
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<td><strong>No. (%) of those that participated in the study</strong></td>
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<tr>
<td><strong>No of social workers in ED staff (%)</strong></td>
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<td><strong>No. (%) of those that participated in the study</strong></td>
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<td><strong>Information systems</strong></td>
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<td><strong>FTE</strong> = full-time equivalent.</td>
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Three female researchers, comprising two nurses and one public health social scientist, conducted the interviews and focus groups in hospital training rooms. One author worked in the hospital where she conducted interviews, but not in the ED. The discussions took place between July and December 2016 and lasted between 13 and 49 minutes. Twenty-one nurses participated in seven focus group discussions held...
during continuing professional development sessions; more senior nurses (nurse unit managers), clinical nurse educators (CNE), doctors, and social workers were interviewed individually after their shifts. This approach was tailored to participants’ workload and time availability. While the environment of the interviews may have been more conducive to sharing personal details about their experiences, focus groups rendered a collegial setting where nurses were able to build upon and confirm each other’s experiences, perceptions, and needs.

The interviews and focus group discussions were audio-recorded with participants’ consent, professionally transcribed, and then imported to NVivo 11 for management and analysis. The transcripts contained no identifying information.

A semistructured schedule (see Table 2) was systematically used for all focus group discussions and interviews and consisted of eleven questions. These addressed participant experience with women experiencing IPV (Qs 1, 2, 4, and 6), the ED’s policies and procedures for working with affected women (Qs 3, 4, 7, 8, and 9), challenges in providing effective care (Qs 2, 5, 8, and 10), and suggestions for new policies, services, or processes for caring for women who have experienced IPV (Qs 5, 6, 9, and 11).

**Data Analysis**

We analyzed the data thematically following the approach outlined by Terry et al. We initially grouped responses according to interview questions to gain a sense of the data. The data were then coded iteratively, line by line led by one researcher in discussion with the other researchers who undertook the data collection. Categories were then determined based on emergent patterns. These were discussed with all authors and categories combined and renamed as themes.

**RESULTS**

The analysis resulted in seven themes related to identifying women experiencing IPV, meeting their needs appropriately, and responding to the challenges of IPV personally and professionally. Themes are outlined in Table 3 and illustrated by quotes from participants from all professions and both hospitals.

### IPV: Identifying a Hidden Problem

Most respondents recognized the pervasiveness of IPV. However, many affected women were reluctant to disclose IPV, hampering identification by emergency health professionals. Some clinicians were unsure about recognizing signs and symptoms of IPV. Despite these challenges, some respondents reported improved capacity to identify women presenting with IPV, following education programs and greater public awareness. Several respondents felt better able to identify women with IPV over time as they became more experienced and exposed to the range of emergency conditions. Respondents reported that some women were more inclined to reveal IPV to female doctors or to nurses; the sex of clinicians may influence a woman to disclose her injury and situation.

### Asking the Right Questions

Some respondents referred to asking the “right questions,” which might encourage women to disclose IPV.
### Themes and Representative Quotes

<table>
<thead>
<tr>
<th>Themes</th>
<th>Representative Quotes</th>
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<tr>
<td><strong>IPV: identifying a hidden problem</strong></td>
<td>[There’s] probably a whole lot more than we realize, I suspect. Obviously, there’s situations where it’s clear … that’s easy. It’s the ones where you have to look for it, where it’s a bit more subtle. The atypical presentation of something or other where you have to look a bit harder, and I suspect we miss a lot of those. (D2 H2)</td>
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<td>The nursing [and] medical staff are much more attuned to picking up the type of presentations that might fit in that category. There’s a lot more training now … so it’s certainly to the front of their minds. So, I reckon they’re picking up more. (SW3 H2)</td>
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<td>[Identifying] traits or kind of injuries or putting it together if the story doesn’t really sound right or being able to identify whether or not someone is at risk … comes with experience as well. A junior triage nurse compared to a senior one might not pick that up … [when] you’ve been there for a long time you think: something about this story is not right. (CNE1 H2)</td>
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<td>My female doctors—often they’re getting information that I wouldn’t have got … They’re good at getting information from the patient what I wouldn’t get as a male. (D3 H1)</td>
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<td><strong>Asking the right questions</strong></td>
<td>I’m so comfortable when someone’s suicidal just asking all these questions that you would think that you wouldn’t usually ask. But with … ‘so did your boyfriend slap you today or did he punch you?’ No, we’re not [comfortable]. (NG1 H1)</td>
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<td>That’s all we ask them to do [ask questions]. We don’t want them to assess the women and get into the legalities or the trauma and stuff like that. We just want them to refer to us … I’ve had that a few times where the nurse has kind of probed a little bit too much … They just need to stick to the medical … are they in pain? What are their injuries? … not get into the counseling. (SW1 H2)</td>
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<td>[I] wouldn’t go into too many probing questions. I would leave that to the social worker and the medical officer to do … that person doesn’t want to have to tell it over and over again to whole a lot of people … we come along and we tend to their physical needs and obviously being emotionally sensitive and compassionate to the circumstance as well. (NG5 H2)</td>
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<td>We do a lot of training with the nursing staff and with the junior medical officers just to be able to identify, ask a few screening questions and then refer … [to] just ask the screening questions that they do in antenatal and mental health, just about whether they have fear of their partner, fear of going home, has anyone hit, slapped and intimidated you? (SW1 H2)</td>
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<td>So, one triage nurse is down the other end, which is in full view, and that’s like you might as well have a megaphone. (NG3 H2)</td>
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<td>Even if they start disclosing, you want to give them a solid 20 minutes … from a triage and fast-tracking perspective you’re with the patient for a short time and you’ve got that limited interaction and you’ve got to identify things quickly. There’s not that much time to get a great rapport. (NG2 H1)</td>
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<td>Sneakily we try and maneuver so that the woman is on her own … for a short period of time, where we’ll task the partner to do something and we’ll come in and ask the questions. (N7 H1)</td>
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<td><strong>Keeping women safe</strong></td>
<td>They’ll stay here and the social workers will refer on the next day. We’re very good at keeping people in hospital and safe. We’ve got a very good ED department. The doctors and the nurses are very respectful of social work. If we say we can’t do X, Y and Z, they’ll be like, ‘okay we’ll keep them in emergency until we come on during the day.’ (SW5 H2)</td>
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<td>If there were security issues—because we’ve had people who’ve come in and they’re concerned that their husband will come back—we get security. We also contact the administration manager, so clerical staff who work at triage are aware that no visitors are allowed for the certain person … (CNE2 H1)</td>
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<td>At least they know they can get help in the emergency department. They can come back at any time. I always tell them ‘there’s a social worker here 24 hours a day, seven days a week, if you ever need help, you just come back’. They know this is a place of safety … and that ‘we’re going to believe you and that you’re not responsible’ … [to reinforce] that they’re believed and that their safety is paramount … (SW1 H2)</td>
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<td>Once spouses and kids go to work and school they tend to come in to be seen on Mondays … They wouldn’t come in in an emergency crisis, they’d come in a couple of days later … I’m assuming to get medical attention, and a lot of people would know that there’s a social worker in the emergency department. (SW5 H2)</td>
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<td><strong>“Call social work”</strong></td>
<td>So, anyone suspected of domestic violence, we page the social worker. So, regardless of what time it is … [it’s] ED procedure … we don’t ask them do they want a social worker, it’s basically, whoever we suspect of being involved in domestic violence. They automatically get a social worker referral. (NG5 H2)</td>
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<td>They should now well know that it’s an automatic—a blanket referral to social work irrespective of whether the woman wants it or doesn’t want it and we’ll deal with them not wanting it. (SW3 H2)</td>
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<td><strong>Working as a team</strong></td>
<td>There’s good communication between the social work and us. So they will always negotiate where they’re at and where they’re up to with their discharge process. (NG3 H2)</td>
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<td>I think often we rely on the nurses who’re spending more time at the bedside, who sometimes have a more informal relationship to pick up and flag. So sometimes the nurses will come to me and say, ‘look, I’m concerned,’ or … if I sense that something’s odd, I might ask the nurse to spend a little bit more time trying to just see what they think … I think if the nursing staff pick it up, they also flag directly to social work, or to the nurse in charge who will contact social work … I think the doctor’s role is more managing the injuries, documenting the injuries; it’s a much more medicized approach. (D1 H2)</td>
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### Table 3 (continued)

<table>
<thead>
<tr>
<th>Themes</th>
<th>Representative Quotes</th>
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<tr>
<td><strong>Providing continuous care</strong></td>
<td>So, at the same time that their medical needs ... or mental health [are] being addressed, then we can also start looking at doing an assessment of their circumstances. That will involve normally a safety assessment, safety risk assessment ... a psychosocial assessment of where are her strengths or her resources, what’s she already doing, what information might she want. Are there any services we need to refer? (SW/H1)</td>
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<td>We do as much as we can in emergency in terms of safety planning, informing them of all their rights and their options in terms of apprehended violence order, in terms of making a police statement ... informing the helpline if there’s children who have been a witness ... if a woman is willing to be followed up by our domestic violence service, we make a referral to them ... They need to have a plan in place and do it with all—have all their options explained to them ... at the very least we talk about safety for tonight, safety for tomorrow, safety for the next week ... It’s a lot of informing them, educating women as they’re ready because they’re very highly traumatized a lot of them. (SW/H2)</td>
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<td>There’s very little we can do being in an emergency department. Our job is to quickly assess and treat the initial problems ... once we’ve got the patients stable we ship them off. So, I don’t think emergency is a place to—unfortunately it can’t be the place to change [attitudes] ... we are a place where domestic violence will be identified for the first time but then [once we] identify it we can’t have much more to do with it. (NG/H1)</td>
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<td>You can’t offer ongoing counseling ... it’s explaining you’re the ED social worker so you’re not really the best equipped to help someone through recovering from DV and you can’t offer anything ongoing. (SW/H2)</td>
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<td></td>
<td>It always starts with what does the woman actually want to do. If she’s undecided, then we might advocate keeping her in hospital as a safe place to do some thinking. That’s happened before. Our ED’s really good with that ... Then, if the woman wants to go home, fine. We just look at what resources are safe for her to take with her and what services can we safely lead her into. That’s enough [for some women] ... if we’re looking at alternative arrangements then we look at crisis accommodation or refuge accommodation. (SW/H4)</td>
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<td></td>
<td>It would be nice to offer—if I was giving women options—that they were actual options, like not saying to them ‘would you like me to organize a refuge?’ and then going to ring up the DV hotline to find there are none, and they have to go and stay in a hotel that’s actually quite dangerous because that’s where they put everyone who can’t get accommodation that night, so they’re at risk ... (SW/H2)</td>
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<td>I think the acute sector needs to do some work to network [with the ED] in that—all of those support services that are out there. There needs to be somebody coordinating that, and there isn’t a sort of dedicated position anywhere around domestic violence. (SW/H4)</td>
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<tr>
<td><strong>The intersection of the personal and professional</strong></td>
<td>I think it did affect me, because she had injuries. He fractured three ribs, and she had a fractured cheekbone ... I thought: how can you bash someone? I felt angry, because I couldn’t imagine hurting my partner or hurting my mother, or my sister, or my colleagues. (NG/H2)</td>
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<td>I think we layer down some of that trauma as well. Sometimes you feel that hopelessness and that helplessness ... we see women re-presenting within days, having been reassaulted by their partner. That can be quite demoralizing and very difficult to then continue to maintain that nonjudgment that’s so important. (SW/H4)</td>
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<td>Being the victim of both sides of it, it affects me quite a lot, to be bluntly honest. There’s ways of dealing with it, there’s support out there, there’s counselling. What doesn’t break you makes you stronger really. I’m fine, I’m over it. I’m just saying it affects us all differently. (NG/H1)</td>
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CNE = clinical nurse educator; D = doctor; H = hospital; NG = nurses group; SW = social worker.

and stay at the ED. One social worker suggested “more direct” questioning (social worker 1 hospital 2) as the best approach, while others highlighted different ways to gain rapport: “you need to be nonjudgmental; you have to be kind and soft” (doctor 4 hospital 1). Other clinicians reported feeling uncomfortable asking about IPV and that they lacked skills in eliciting disclosure.

One nurse noted that she hesitated when questioning women “because there’s been situations in the past where a nurse asked all the questions and the social workers thought that that impacted on her ability to open up later on down the track” (nurse 6 hospital 2, emphasis added). Although respondents agreed that nurses should pursue and potentially confirm their suspicions, social workers maintain responsibility for investigating potential and confirmed IPV and for counseling women.

Some nurse and medical participants indicated that standardized questioning for IPV was not common practice within their EDs; some were unaware of any formal screening tools. Others felt that screening for IPV in addition to other risk factors in ED would be burdensome. Clinicians were also largely unaware of IPV-related polices, directives, and protocols, although one manager described “a pathway, the domestic violence pathway ... and every month or so I scan it and send this out to staff ... It’s on our website” (nurse manager 1 hospital 1). One doctor reflected that knowing about such documents was not enough, “Nearly always our issue is three-fold: identifying, knowing there’s a policy and knowing how to use
it, and the fact that it’s actually there” (doctor 4 hospital 1).

Clinicians routinely reported referring to social workers after asking brief questions. Social work participants were clear about hospital protocols for responding to IPV; they reported using some questions to elicit a woman’s situation rather than specific screening tools. Social workers were actively involved in educating ED staff, offering in-service and mandatory training about recognizing and communicating with women about their experiences of IPV. Despite the ED’s potential for identifying and caring for women experiencing IPV, many respondents recognized practical limitations, given the physical environment and hectic pace in most EDs.

Women may attend EDs for IPV-related conditions accompanied by the perpetrator, adding to the complexity of communicating with women about violence. Nurses and doctors described strategies they used to give women the opportunity to disclose.

Keeping Women Safe
Emergency department clinicians highlighted their role in establishing women’s immediate safety as well as treating medical conditions and potentially planning longer-term options. Participants referred to various strategies employed to separate women from suspected perpetrators who accompany them to hospital and to support women remaining in the ED overnight and seeing the social worker. Staff also recognized security concerns particularly when the suspected perpetrator wished to accompany or visit the woman.

Social workers reported emphasizing to women that they were welcome to return to the ED if they felt unsafe. Two participants specifically mentioned how some women re-presented given the opportunity, such as during office or school hours.

“Call Social Work”
Nurses and doctors described the accepted practice of referring on to social workers any women with disclosed or suspected IPV once they had provided the necessary medical care. One doctor encapsulated ED procedure: “So I think our system is: call social work” (doctor 1 hospital 2). Women were referred to social workers regardless of their requests or wishes.

Working as a Team
There was a strong sense of collaboration between staff in the ED in both hospitals when describing the response to IPV: “the team part, that communication between us all is really important” (nurse in group interview 5 hospital 2). This collaboration extended across nursing, medical, and social work professions.

Clinicians clearly appreciated the role social workers played: “I think social work is our biggest fallback and our biggest support” (doctor 1 hospital 2). Many respondents described the trust and collaboration between professions; two social workers specifically reported feeling “very respected” (social worker 2 hospital 2).

All professionals acknowledged their specific role within the team, collaborating to ensure women receive necessary medical care and support. Social workers were also clear about their role focus that was to address women’s safety and psychosocial needs while supporting clinicians to deliver medical care.

Providing Continuous Care
Social workers are critical to supporting women presenting to ED. However, both the resources constraints in most EDs and their primary purpose of providing immediate medical care limit their capacity to provide longer-term support or advocacy. Social workers also recognized their limitations in providing continuous care from their position in ED.

Participants described multiple services and facilities to help women experiencing IPV. They listed crisis housing, albeit as “last scenario” given the disruption it causes to young children, and liaison with police, Centrelink (government income support), and child protection authorities if appropriate. Yet, several participants reported the limited support options available to women attending ED in crisis. Many IPV agencies are over-loaded, unable to support women discharged from the ED. Community services are often unavailable after-hours, further limiting options. Respondents highlighted the need for better coordination and integration of services across acute health and community sectors at all levels.

The Intersection of the Personal and Professional
Participants discussed their personal experience of IPV and how their interaction with women with IPV had affected them. Some participants noted that it was sometimes difficult to control their values and feelings about the women involved and the perpetrators. Clinicians encountered IPV not only professionally; some also spoke of their direct personal experience.
DISCUSSION

This qualitative study provides important insights into the knowledge, attitudes, and practices of professionals in large metropolitan EDs about IPV. The findings indicate consistent teamwork and commitment to keeping women safe. Many nurses and doctors were not aware of screening tools or IPV-related polices and protocols within their hospitals. Social workers were cognizant of hospital directives but did not use screening tools. Nearly all emergency nurses and doctors were clear about the need to refer to social workers if they suspected IPV or if a woman had disclosed it.

There is insufficient evidence to support universal IPV screening in health care settings, with a recent Cochrane review concluding that targeted strategies may be more effective. The authors propose training “health professionals to ask women who show signs of abuse or those in high-risk groups, and provide them with a supportive response and information, and plan with them for their safety.” In our study, emergency clinicians reported that training, increased experience, and public advocacy had helped them to consider IPV when assessing women in the ED and to refer to social workers. Despite this, some nurses felt uncomfortable asking women potentially sensitive questions and cited the challenge of engaging in meaningful rapport with women in the fast-paced ED environment where maintaining privacy can be difficult. This highlights the need for role clarification of different providers, to ensure that providers do not ask women the same questions, thereby reducing unnecessary additional trauma and improving efficiency.

While the World Health Organization recommends women-centered care as key to health service responses to IPV, the ED’s focus on medical emergencies means that appropriate referral is required to facilitate appropriate in-depth primary and social care. This highlights the importance of female clinical staff reiterated by participants in our study. Other research has noted that female health care staff score significantly higher than their male counterparts in understanding abusive relationships and that women show a preference for female staff, significantly staff who are empathetic and compassionate. Staff with lived experience of IPV may also be beneficial in supporting women. While female staff, or those with lived experience, may be unavailable to attend to women presenting with IPV, appropriate attitudes and knowledge remain key to effective detection and communication with women. This requires targeted professional training and supportive supervision.

Our study also draws attention to the central role of social workers to deliver women-centered care within the ED. This highlights the importance of adequate workforce planning, resourcing, and support particularly for social workers to counsel and refer women. Emergency clinicians were consistent in alerting social workers when encountering women with IPV. While they did not always consult the women specifically, their intention appeared to be to provide them with the opportunity for individualized and confidential consultation. Recent research has investigated trauma-informed organizational models of care, noting women’s voices and the need for private one-on-one consultations in the ED with social workers.

Counseling and referral for ED patients has been found to increase women’s willingness to complete safety plans and access local IPV resources. Ongoing training for social workers is essential to increase referrals to advocacy services and improve the identification of women affected by IPV. Training programs have been found to be more effective if conducted in conjunction with changes at system and organization level, including standardized documentation and protocols for improved assessment, management, and referral. Training must also aim to improve clinicians’ knowledge of national and local hospital policy on IPV and to raise awareness of screening tools.

The health care partnership between the ED social worker and the broader health system is critical to linking women experiencing IPV to community, social, and primary health care services. However, due to the complex nature of IPV and the numerous sectors involved, continuous and coordinated care is challenging. In our study, participants described repeat ED attendance for nonurgent issues, demonstrating that women are not always able to access the care they need in the community. Formalizing links between the ED social worker and community, social, and primary health care agencies may assist to strengthen relationships and build a broader safety net for those at risk or experiencing IPV.

Clinical contact with IPV raised strong emotions among the health professionals in the sample, although they did not indicate that they felt it affected the care they provided to women. Feelings about perpetrators did appear to reinforce their resolve to keep women safe within the ED. Professional development
about IPV issues should address clinicians’ own responses, mindful of the fact that some may have personal as well as professional experience of IPV.

Improved referral relationships for IPV could help support professionals across sectors to better coordinate their actions to respond and support women. For example, follow-up outreach through home visiting has been effective in minimizing IPV and improving outcomes.\textsuperscript{47} In the case of women with young children, child and family health nurses or social workers within child protection agencies in collaboration with the ED social worker could facilitate this. This requires more than a comprehensive health system approach to IPV\textsuperscript{48} and demands a coordinated multisector process that acknowledges the complex social determinants of violence. This approach is recognized by the United Kingdom’s safeguarding measures that coordinate responses to abuse and neglect for children and adults at risk, including women affected by IPV,\textsuperscript{49,50} through integrating care and support across local authorities and health services.

While our research indicates that health professionals take responsibility for their emotional well-being, the study has also highlighted the importance of workplace-based confidential counseling and leave for staff who are experiencing IPV. The prevalence of IPV among health professionals been found to be higher than that in the general population, calling for health workplace policies and protocols to acknowledge this common trauma.\textsuperscript{51} The Royal Women’s Hospital in Victoria, Australia, has, for example, established a new program “Strengthening Hospital Responses to Family Violence”\textsuperscript{51} that provides training for health care workers to support both staff and patients. In addition, the Victorian Government has introduced several policies to help staff who have experienced IPV, including access to 20 days of family violence leave.\textsuperscript{52}

**LIMITATIONS**

The study was potentially limited by its focus on women rather than on all individuals experiencing IPV. Sample bias may be present given participants self-selected and comprised clinicians who expressed interest in discussing IPV. Notably, even within this sample, some respondents indicated limited awareness of women experiencing IPV. Moreover, findings rely on self-report, rather than observation or documentation of actual practice. The focus on large metropolitan hospitals may differ from other settings—facilities and resources may be more limited in smaller hospitals, and women seeking health care in smaller communities may face additional issues of privacy or limited ongoing support options.

**CONCLUSIONS**

Emergency departments can provide compassionate, immediate treatment and referral for women experiencing interpersonal violence. This study demonstrates effective interprofessional collaboration between all professionals in two busy metropolitan EDs with the aim of optimizing the health and safety of women experiencing interpersonal violence. It further illustrates that social workers play a key role an anchoring the professional team together and optimizing the transition of care back to the community for women experiencing interpersonal violence. The research identifies the need for role clarification around detecting interpersonal violence to improve the quality of care. Staff training and advocacy and referral relationships with local community programs also requires strengthening.

An integrated multisystems-level response is required to better coordinate and resource services for all affected by violence. Supportive workforce environments can improve staff understanding, reduce stigma, and counsel health professionals experiencing violence.

The authors thank all the clinicians that participated in this study and Dr. Kim Fields, Director Primary and Community Health Northern Sydney Local Health District.

**References**


2018 Academic Emergency Medicine Consensus Conference: A Workforce Development Research Agenda for Pediatric Care in the Emergency Department

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ABSTRACT
Each year, more than 30 million children visit U.S. emergency departments (EDs). Although the number of pediatric emergency medicine specialists continues to rise, the vast majority of children are cared for in general EDs outside of children’s hospitals. The diverse workforce of care providers for children must possess the knowledge, experience, skills, and systemic support necessary to deliver excellent pediatric emergency care. There is a crucial need to understand the factors that drive the professional development and support systems of this diverse workforce. Through the iterative process culminating with the 2018 Academic Emergency Medicine consensus conference, we have identified five key research themes and prioritized a specific research agenda. These themes represent critical gaps in our understanding of the development and maintenance of the pediatric emergency care workforce and allow for a prioritization of future research efforts. Only by more fully understanding the gaps in workforce needs, and the necessary steps to address these gaps, can outcomes be optimized for children in need of emergency care.

BACKGROUND
Over four decades, emergency medicine (EM) has evolved from a fledgling specialty to a pillar for acute care for patients of all ages. The evolution of pediatric emergency medicine (PEM) has mirrored the evolution of EM itself, with subspecialization possible following either pediatrics or EM residency training. However, with just over 2,000 board-
certified PEM physicians, PEM subspecialists are not available to staff every emergency department (ED). While the overall number of PEM subspecialists continues to steadily increase, they continue to be clustered in urban centers and children’s hospitals. As a result, the vast majority of children are cared for in general EDs, outside of children’s hospitals, managed by a broad coalition of physician and nonphysician providers with varied training in the care of acutely ill and injured children. This diversification of the workforce results in an uneven distribution of skills and experience.

A decade ago, the Institute of Medicine expressed a “continued concerns about the ability of the emergency care workforce to care properly for pediatric patients.” Among these concerns included uneven training, variable continuing education, lack of structured competency assessment for pediatric emergency care providers, inadequate practice guidelines and care standards, and the lack of local and regional pediatric emergency readiness and care coordination. While the decade since publication of this report has undoubtedly yielded many improvements, the diverse providers of emergency care for children continue to face increasing demand with uneven capacity.

The diverse workforce of care providers for children must possess the knowledge, experience, skills, and systemic support necessary to deliver high-quality pediatric emergency care. Advances in pediatric care require ongoing education and coordination across a diversity of providers. There is a crucial need to understand the factors that drive the professional development and support systems of this diverse workforce. High-quality, coordinated research investigating the dynamic components of the workforce will help to identify areas of concern and points of strength. A robust research agenda must inform the ongoing and evolving understanding of the factors driving the development and maintenance of the pediatric emergency care workforce. Through the iterative process at the 2018 Academic Emergency Medicine consensus conference (Figure 1), we have identified five key research themes and prioritized specific research questions within each theme. These themes represent critical gaps in our understanding of the development and maintenance of the pediatric emergency care workforce and allow for a prioritization of future research efforts.

**METHODS**

The Pediatric Workforce Development Working Group, using the iterative consensus process described elsewhere in this report, sought to develop consensus on a prioritized research agenda for the pediatric emergency care workforce. The working group consisted of emergency physicians, PEM subspecialists, advanced practice providers (APPs), and patient advocates, chosen based on a range of expertise, interest, and experience by the

![Figure 1. Schematic of the consensus process to identify research priorities in workforce development in pediatric emergency care. The planning committee for the consensus conference identified five broad themes, areas of need for PEM research. A designated working group then identified research themes within the broader theme of “workforce development.” Using preconference stakeholder polling and in-person discussion on the day of the conference, these themes were ordered. Finally, specific research questions were prioritized to inform a final workforce-related research agenda. PEM = pediatric emergency medicine.](image-url)
The consensus process culminated on May 15, 2018, in Indianapolis, Indiana, where a multidisciplinary cohort of attendees, representing key stakeholders including patients and patient advocates, general emergency physicians, PEM subspecialists, APPs, and funding agencies, gathered to discuss and prioritize a pediatric emergency workforce development research agenda.

During a 90-minute breakout session focused specifically on workforce development for pediatric emergency care, individual participants used audience response software (slido.com) to identify the highest priority themes in the workforce development research agenda. Next, through group discussion for consensus building, specific research questions were identified as being of highest priority. Participants used audience response software to again vote for the highest-priority research questions. Group discussions were recorded and reviewed to ensure that outcomes reflected consensus-building conversations. The consensus results in this article have been informed by this process.

**Workforce-related Outcome Gaps in Pediatric Emergency Care**

In every instance in which children encounter the emergency care system, the workforce must be prepared to provide excellent, high-quality pediatric emergency care. At each step of the care process demands are placed on the workforce to provide pediatric-specific emergency care. However, the training, skills, and competency requirements and optimal distribution of the workforce and other resources are not fully understood. Only by more fully understanding the gaps in workforce needs and the necessary steps to address these gaps can outcomes be optimized for children in need of emergency care.

**Creation of a Research Agenda**

The workforce responsible for care of children in emergencies is a broad coalition of health care professionals. The general EM workforce must be prepared to manage the acute health needs of ill and injured children and in fact are responsible for the large majority of children’s emergency care. The PEM subspecialty workforce, on the other hand, tends to be clustered in children’s hospitals and urban centers. While PEM subspecialists tend to the minority of pediatric emergency visits, they provide expertise and guidance through communication and outreach, are a referral resource for children needing escalating levels of care, and are a conduit by which children in general emergency centers may access pediatric specialty care. In addition, PEM subspecialists in academic centers are responsible for a large proportion of pediatric knowledge generation and research. The workforce development needs of both of these segments of the pediatric emergency workforce—the larger sector outside of specialty centers and the smaller PEM-trained sector—must be understood and optimized to ensure excellence in pediatric care no matter where or when it is needed. It is within this framework of understanding that this consensus process has been undertaken.

The Pediatric Workforce Development Working Group’s membership—including emergency physicians, APPs, and patient advocates—identified broad themes under which prioritized research questions could be categorized. Working group members reviewed the existing literature within these themes and identified knowledge gaps. These themes were reviewed through a broad-reaching online survey of stakeholders (qualtrics.com) and felt to represent the best general targets for a research agenda. Armed with this background, the working group coordinated the workforce development breakout session around these themes (Table 1).

**Pediatric Readiness.** Table 2 delineates a number of potential research questions related to pediatric emergency workforce readiness. Almost 90% of acutely ill and injured children are cared for in facilities that do not have a primary focus on pediatric care. Comfort and expertise in the care of ill and injured
Regionalization of care—where tertiary pediatric centers function in a hub and spoke fashion to extend pediatric expertise and facilitate the care of children—is an example of developing such readiness. In some settings, this involves providing workforce resources to outlying nonchildren’s hospitals, with pediatric specialists staffing community EDs, inpatient floors, or intensive care units. In other instances, specialists from tertiary centers have rotating schedules in outpatient clinics or other settings.

Increasingly, community hospitals are staffing pediatric-specific emergency centers either within general EDs or as free-standing enterprises. Sacchetti et al. modeled the potential impact of placing PEM subspecialists in a community hospital environment, examining the impact on ED care of children after the introduction of 10 pediatric emergency specialists into a simulated medical community. In a restrictive model, the addition of 10 PEM providers to the community would impact 27% of the pediatric ED care in the community. In the highest-impact distributive models, adding PEM providers would impact up to 69% of pediatric care. If self-diversion were to occur this high-impact model, then 46% of patients would need to bypass the closest ED and travel to a pediatric ED to have this same effect on patient care.

Several organizations have interventions in place to facilitate closing the gap for pediatric emergency readiness. The Emergency Medical Services for Children (EMSC) program, the American Academy of Pediatrics (AAP), the American College of Emergency Physicians (ACEP), and the Emergency Nurses Association, have partnered to disseminate information, participate in the development of quality improvement resources to help EDs provide effective emergency care to children, and identify “champions” to work with EMSC State Partnership managers to facilitate pediatric ED readiness in all hospital EDs. A goal of the National Pediatric Readiness Project is the sharing of expertise with all facilities and through assessment and facility recognition as ready to care for pediatric care. More data are needed to establish high-quality regional pediatric emergency care, with specific research into methods to establish and maintain high standards for care across individual providers and institutions.

**Epidemiology.** Table 3 outlines potential research questions related to the epidemiology of the pediatric emergency care workforce. The field of PEM began as

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**Table 1**

Research Themes in Workforce Development for Pediatric Emergency Care (PEC)

- Pediatric workforce readiness
- Epidemiology of the PEC workforce
- Roles of APPs in the PEC workforce
- Career pathways in the PEC workforce
- Stressors on the PEC workforce and workforce burnout

Themes were proposed by the Workforce Development Working Group and refined through survey data of a broad swath of stakeholders in pediatric emergency care. APPs = advanced practice providers.

**Table 2**

Potential Research Questions Related to Pediatric Readiness in the Emergency Care Workforce

- What is the best way to establish a minimum pediatric workforce standard at every facility that cares for children?
- Can standardized triage guidelines and order pathways facilitate excellence in pediatric care? How does the workforce in low- and medium-volume EDs maintain their pediatric skills?
- How do pediatric centers network with low- and medium-pediatric-volume EDs to disseminate best practices and maintain a high quality of care across providers and institutions? What is the best model for distributing pediatric emergency workforce among these departments? How do low-, medium-, and high-volume pediatric EDs address challenges with surge volumes and coordinate care regionally?
- Telemedicine has been shown to be an adjunct in providing resources to low- and medium-volume pediatric emergency care. Can telemedicine be utilized as a tool to facilitate high-quality regional pediatric care?
- Studies have shown pediatric simulation to be a valuable tool to enhance the quality of pediatric care in community EDs. Can simulation be expanded regionally or nationally to enhance pediatric care in lower-volume EDs?
- Pediatric leadership (“pediatric champions”), from both nursing and physician perspectives, has been shown to enhance pediatric care. Can this model be optimized to improve pediatric emergency care?

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children is variable in these settings. All hospital EDs must have both the appropriate resources (equipment, care plans, pathways for consultation) and workforce to provide effective emergency care for children. Gausche-Hill et al. reported that 69.4% of surveyed EDs had low or medium pediatric volume and treated fewer than 14 children per day. The reported mean of a weighted pediatric readiness score (WPRS) increased with pediatric patient volume, from 61.4 for low-pediatric-volume EDs compared with 89.8 for high-pediatric-volume EDs.

Access to the pediatric-ready EDs varies according to geography. Ray et al. found that although 93.7% of children could travel to any ED within 30 minutes, only 33.7% of children could travel to an ED with a WPRS of 100, 55.3% could travel to an ED with a WPRS at or above the 90th percentile, and 70.2% could travel to an ED with a WPRS at or above the 75th percentile.
an organized subspecialty in the 1980s with focused discussions on the specific needs of children who are acutely ill or injured.\textsuperscript{14,15} Pediatrics-based fellowships were implemented in the mid-1980s, with programs designed for graduates of EM training developed shortly thereafter.\textsuperscript{16} The PEM workforce has been growing steadily, from 236 PEM fellows in 2002 to 517 in 2017. Today there are more than 2500 PEM physicians certified, with 80\% between 30 and 60 years of age and 18\% greater than 60 years of age.\textsuperscript{1,17} However, as the early wave of subspecialists approaches retirement and there is increasing turnover and new leadership, the impacts of a changing demographic are not well understood. Research will need to develop prediction models to anticipate these future needs.

Over the past few years, more institutions have dedicated space to pediatric emergency care, and pediatric urgent care centers have continued to proliferate. Both ACEP and the AAP have specific recommendation on who should staff a pediatric ED, advocating for training for emergencies (ACEP) and training in the care of children (AAP).\textsuperscript{18} To compensate for uneven PEM expertise, institutions must determine requirements and competencies required to care for children in their EDs. These include procedure competency, sedation competency, and trauma competencies, as well as ongoing competency demonstration through assessment. Some institutions employ alternative experts in pediatrics, such as pediatric nurse practitioners (NPs) and physician assistants (PAs), to add additional expertise. As the scope of practice of EM and PEM providers continues to change based on needs and increasing ED volumes and acuity, a reevaluation of this data may be needed.

Given the relative dearth of PEM subspecialists relative to the distribution of pediatric emergency visits, regionalization of care is a logical approach to dispersing PEM expertise throughout the system to reduce health disparities. The use of telemedicine, regional medical direction for trauma and emergency medical services, pediatric base stations, “adoption” of smaller rural and community centers by larger tertiary care hospitals, and patients empaneled to seek subspecialty care through prearranged agreements are some strategies that might ensure that all children, regardless of geography, have a designated center to receive high-quality care.

**Career Pathways in PEM.** Table 4 outlines potential research questions related to career pathways in pediatric emergency care. Subspecialization in PEM is a career path that allows a physician to attain additional expertise and skills to care for acutely ill or injured children, along with expertise in education, research, or administration and policy. Graduates of PEM programs typically fall into one or more of four main areas of expertise: clinicians and clinician scientists, research scientists, educators, or administrative leaders. A survey of PEM physicians in 2016 found that the majority (62.9\%) practiced in the ED of a

### Table 3
Potential Research Questions Related to the Epidemiology of the Emergency Care Workforce

- Is PEM subboard certification a requirement for working in the pediatric ED?
- What are PEM resources in rural and suburban EDs? Can technological tools such as GIS mapping better identify the distribution of PEM provider location relative to pediatric emergency occurrences?
- What portion of PEM-trained providers exclusively work in urgent care or low-acuity EDs? What factors might lead to this distribution of expertise?
- Can we define what knowledge and skills are required at different levels of pediatric care (urgent care vs. community ED vs. tertiary ED)?
- Can we describe experiences to date with regionalization of pediatric care? What are the lessons learned and barriers overcome to provision of regional care?
- Can participation in broader research networks such as PECARN provide a route to conduct collaborative PEM research and improve access and distribution of pediatric workforce resources?
- Is there an alternate certification process for becoming a PEM clinical expert for community/rural hospitals? Could this bolster distribution of pediatric expertise to a broader workforce?

PEM = pediatric emergency medicine.
free-standing children's hospital. The distribution of professional activities showed the majority of time (60%) was spent in direct patient care, 50% had involvement in research, and about 50% had dedicated time for other activities, including emergency medical services (7.3%), disaster (6.9%), child abuse (5.0%), transport (3.6%), toxicology (2.3% of respondents), and other (13.6%). Additionally, 21.3% had dedicated time for quality/safety.

For physicians residency-trained in EM, additional subspecialization in PEM provides an opportunity to provide education specific to children, to be part of national pediatric research networks, to develop and direct pediatric EDs within nonchildren's hospitals, and act as a clinical resource for pediatric bedside and clinical teaching. They may also be advocates for children and represent the field in national organizations as committee and section members. Additionally, an EM-trained PEM physician will have the flexibility to provide care for both children and adults. This combination may allow for greater job opportunities and recruitment by institutions that prefer this cross-coverage ability. In general hospitals, many EM/PEM-trained physicians practice clinically, seeing a subset of adult patients or spending a subset of their clinical shifts in an adult ED. Maintaining expertise in either population may remain a challenge, depending on the mix of clinical need. EM/PEM providers may be challenged to maintain adult expertise if their primary practice is with children. Likewise, if the volume of critically ill children is low, they may also be challenged to maintain expertise with acutely ill/injured children.

One of the current objectives of national organizations, including the Pediatric Emergency Medicine Committee of ACEP, is to encourage EM-trained physicians to enter the PEM workforce. While the benefits discussed above are clearly attractive, other barriers exist, which prevent many EM-trained physicians from specializing into pediatrics. These barriers include the following:

- **Investment in PEM fellowship may not be perceived as being of sufficient value to offset the opportunity cost of 2 to 3 years of trainee pay and workload.**
- **There is little salary benefit to EM graduates from training in PEM; they may even face a salary cut if working on a pediatric pay scale.**
- **High expectations to see and maintain expertise in care of both adults and children.**
- **Lack of sufficient protected time from clinical work to provide meaningful contributions in other areas (research, education, advocacy, administration).**

Another emerging career path for PEM physicians is in pediatric urgent care. Although not a traditional pathway, as urgent care centers are becoming more prevalent, some PEM-trained physicians are choosing to be involved in this growing sector. Recommendations for preparedness, workforce staffing, and supervision have been published. Nontraditional fellowship training has begun to be developed to prepare pediatricians for work in this clinical setting, which may require a narrower set of expertise than that achieved through traditional PEM fellowships.

**Role of APPs in Pediatric Emergency Care.** Table 5 outlines potential research questions related to the roles of APPs in pediatric emergency care. PAs and NPs, collectively referred to as APPs, are a growing part of the emergency care workforce. APPs provide urgent and emergency care to children across the spectrum, from primary care to urgent care centers, to general EDs and pediatric EDs in community and academic children’s hospitals alike. Between 1993 and 2005, APPs saw nearly 7% of the approximately 1.3 billion ED visits, increasing across the study period from 2.9% in 1993 to 13% in 2005. A more recent study by Wiler et al. showed that from 2006 to 2009, two-thirds of all EDs used APPs and that APPs were involved with just over 13% of all ED visits, nearly half of which were visits by pediatric

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<th>Table 5</th>
<th>Potential Research Questions Related to the Role of APPs in the Pediatric Emergency Care Workforce</th>
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<td>• What PEM training do APPs receive in school, on the job, and for continuing medical education? Are there identifiable differences in the nature and degree of this training between classes of APPs?</td>
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<td>• What is the role of APP postgraduate training (e.g., residency/fellowship)?</td>
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<td>• What is/should be the scope of practice of APPs and how does it relate to the setting, patient populations, or acuity level they are responsible for seeing?</td>
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<td>• What PEM procedures are being performed by APPs relative to other providers?</td>
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<td>• Are APPs efficient in pediatric care when examining metrics such as productivity, left without being seen rates, and ED length of stay?</td>
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<td>• What are the outcomes, by acuity level, for children seen by APPs?</td>
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<td>• What is parent/caregiver understanding of the nature and role of APPs in emergency care of children? Are parents satisfied when their child is cared for by an APP versus a physician?</td>
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APP = advanced practice provider.
patients. Their roles have also evolved from caring for only or primarily low-acuity patients to caring for more complex patients and performing procedures. Despite the widespread use of APPs, there are still gaps in our understanding of their utilization in the EM and PEM literature.

There are qualitative differences in the degree and nature of training to achieve the two professional APP roles (PA and NP) and differences even within these routes of training in terms of specific clinical exposure and paths toward specialization in pediatric and/or emergency care. Recognizing that broad training as an NP or PA does not necessarily confer the type of specific expertise required for pediatric emergency care, a number of apprenticeship or residency-style models have evolved to provide APPs with the skills and experience specific to the emergency care of children. While many of these training programs are in their infancy, they have the potential to provide a path toward specialization and to raise the quality of care provided children.

In an era of increasing restriction on physician resident duty hours, as well as increasing financial pressures facing hospital systems, APPs are likely to provide an ever-increasing proportion of clinical care in academic and community centers alike. More data are needed on the role and performance of these providers.

**Burnout in the PEM Workforce.** Specific research questions related to the impacts of burnout in the pediatric/EM workforce are listed in Table 6. Identification and prevention of physician burnout during medical training and practice may have significant direct and indirect implications to the workforce. The term “burnout” first appeared in the literature in the early 1970s to describe a feeling of emotional exhaustion, cynical or negative attitude toward others, and a tendency to devalue oneself or low personal accomplishment. The “burnout syndrome” is highly correlated with the chronic stress of careers associated with “people work” and appears to be more common in physicians than other professionals. The 2016 Survey of America’s Physicians Practice Patterns and Perspectives found that regulatory/documentation burden, little influence in the direction of the health care system, and loss of clinical autonomy are pivotal. Burnout can lead to patient safety concerns including issues with professionalism, increased risk of medical error and patient/family rapport, and provider safety and wellness.

There are limited data on the impact of specific stressors on burnout in the PEM workforce. Data are mixed as to the effects of intrinsic factors (e.g., physician age, sex, social support) and external factors (e.g., seasonal volume, hospital resources) on burnout. In the EM literature, inpatient boarding in the ED is frequently cited as a workforce stressor, one that the Institute of Medicine sought to end, stating that such practices negatively impacted the patient’s experience and added to “an already stressful work environment, enhancing the potential for errors, delays in treatment, and diminished quality of care.” One study of boarding patients found that “impediments posed by structure/organization (i.e., physical environments, provider skill sets/practice, distractions, and handoffs inherent in providing care to boarded patients) may compromise processes (such as patient observation, comfort, diagnosis, and therapy).” These structural weaknesses and compromised processes may in result in poor productivity and decreased work satisfaction. As emergency physicians are asked to be increasingly clinically efficient in the face of fixed resources, resource supply issues have significant impact on physician satisfaction. Even after controlling for “workflow and patient characteristics and for various institutional and physician characteristics, institutional resource constraints are found to be major contributors to emergency physician job dissatisfaction.”

Pediatric EM subspecialty providers are thought to be at high risk for burnout and compassion fatigue. Whereas the practice of pediatrics seems to be protective against burnout, EM continues to top the list of medical specialties at risk. Given that
most care provided to ill and injured children currently occurs by general emergency physicians, how these factors relate is unknown. Rates of reported burnout in PEM practitioners range from 25% to 80%. Interestingly, Leigh et al. noted that of 42 subspecialties compared to family medicine, PEM was found to have the highest physician career satisfaction, even though EM ranked only 31st.

Current evidence does not support one best approach to address the issue of physician burnout. Accrediting bodies have begun to identify risks factors for burnout among resident and fellow physicians. Unfortunately, the indirect effects of actions meant to limit trainee burnout appear to have only worsened the burden placed on practicing physicians in academic centers. It would seem an ideal time for health care organizations, policy makers, and academic programs to intervene, working together to understand and promote effective generalizable interventions that improve physician well-being and ultimately patient satisfaction and outcomes. To successfully train, recruit, and retain providers who can continue to provide excellent pediatric emergency care, a broader look at burnout and wellness factors will be required.

Building Consensus

During the workforce development breakout session at the 2018 AEM Consensus Conference, each participant was asked to identify two areas of highest priority under the workforce development umbrella. With audience response software (slido.com), the themes of workforce stressors/burnout and career pathways into the pediatric emergency care workforce were identified as high priority by the majority of attendees (Figure 2).

After breakout discussions, facilitated by members of the workforce development working group, participants were then asked to prioritize more specific research questions related to the pediatric emergency care workforce, identifying high-priority research agenda items by electronic polling. Results of the poll were kept confidential until voting was complete, and no individual participant’s vote was revealed. Through this iterative process, a prioritized set of both broad research themes under the umbrella of workforce development and specific research agenda questions within these themes were developed. Specific research questions related to the impact of regionalization of care, as well as burnout and strains on the pediatric emergency care workforce, were identified as having highest priority by this engaged group of stakeholders (Figure 3).

Challenges

The pediatric emergency workforce is, as emphasized elsewhere, decidedly not a uniform entity, and the needs in one setting or locale may differ widely from those in another. The workforce is not defined solely by the relatively small cadre of PEM-specialized physicians any more than it is defined by pediatric care in general EDs outside of children’s hospital. The workforce must necessarily be viewed as a collaborative
coalition, but as such its needs are not uniform or even entirely understood. Subsets of the pediatric workforce may require specific efforts to further define and elucidate; providers in rural EDs, PEM subspecialty training programs in both pediatrics and EM, and a research workforce may all have very specific needs. In particular with relation to the pediatric workforce, prediction of future needs is difficult. Because the future needs of children are difficult to predict, a research agenda with an eye toward the future must necessarily be fluid and flexible. This research agenda is a best estimate of the greatest research needs in pediatric emergency care workforce development at one point in time.

CONCLUSION

Through an iterative process engaging key stakeholders in pediatrics and emergency medicine across the spectrum of care, we have identified several key areas of research interest that should inform the next decade of pediatric emergency care workforce research. Highlighting the importance of understanding stressors and factors that lead to burnout within this workforce, participants in this consensus process have reinforced the notion that systems and processes that may identify and alleviate these stressors will be of high priority in the coming years. In addition, participants recognize that the ongoing regionalization of pediatric specialty care will have a tremendous impact on the pediatric emergency care workforce. By delineating best practices in terms of workforce development and support, future research will be critical in narrowing outcome gaps and ensuring excellence in the care of ill and injured children anytime and anywhere.

The authors thank the participants in the Workforce Development breakout group at the AEM Consensus Conference: Jennifer Mitzman, Ron Ruffing, Susan Fuchs, Elizabeth Weinstein, Robert Johnson, Riffani Johnson, Maegan Reynolds, Sandy Herr, Michelle Stevenson, Michelle Macy, Jen. Reed, Joelle Simpson, Richard Ruddy, Matt Hansen, Fran Balamuth, Kabur Yadav, and Nathan Kupperman. In addition, the authors thank Melissa McMillian (SAEM), Isabelle Chea, Chris Amato, MD, and the following patient advocates: Paula Denslow, Troy Denslow, Kim Mears, and Parris Shelley.

Author Contributions: CM chaired the Pediatric Workforce Development Working Group, contributed to the planning and design of the AEM Consensus Conference and the Workforce Development breakout group, acquired and interpreted the data presented, and drafted and revised the manuscript; AD was a contributing member of the Pediatric Workforce Development Working Group, contributed to the planning and design of the AEM Consensus Conference and the Workforce Development breakout group, contributed to the acquisition and interpretation of the data presented, and contributed to the drafting and revision of the manuscript. AB was a contributing member of the Pediatric Workforce Development Working Group, contributed to the planning and design of the AEM Consensus Conference and the Workforce Development breakout group, contributed to the
the acquisition and interpretation of the data presented, and contributed to the drafting and revision of the manuscript. FW was a contributing member of the Pediatric Workforce Development Working Group, contributed to the planning and design of the AEM Consensus Conference and the Workforce Development breakout group, and contributed to the drafting and revision of the manuscript. KK was a contributing member of the Pediatric Workforce Development Working Group, contributed to the planning and design of the AEM Consensus Conference and the Workforce Development breakout group, contributed to the acquisition and interpretation of the data presented, and contributed to the drafting and revision of the manuscript. MKB was a contributing member of the Pediatric Workforce Development Working Group, contributed to the planning and design of the AEM Consensus Conference and the Workforce Development breakout group, contributed to the acquisition and interpretation of the data presented, and contributed to the drafting and revision of the manuscript. PTI co-chaired the conference planning committee and was a contributing member of the Pediatric Workforce Development Working Group, contributed to the planning and design of the AEM Consensus Conference and the Workforce Development breakout group, contributed to the acquisition and interpretation of the data presented, and contributed to the drafting and revision of the manuscript. PDI co-chaired the conference planning committee and was a contributing member of the Pediatric Workforce Development Working Group, contributed to the planning and design of the AEM Consensus Conference and the Workforce Development breakout group, contributed to the acquisition and interpretation of the data presented, and contributed to the drafting and revision of the manuscript. MS was a contributing member of the Pediatric Workforce Development Working Group, contributed to the planning and design of the AEM Consensus Conference and the Workforce Development breakout group, contributed to the acquisition and interpretation of the data presented, and contributed to the drafting and revision of the manuscript.

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Diagnostic Accuracy of Lung Ultrasound Performed by Novice Versus Advanced Sonographers for Pneumonia in Children: A Systematic Review and Meta-analysis

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ABSTRACT

Background: Childhood pneumonia is a leading cause of mortality worldwide. Growing evidence suggests that lung ultrasound (LUS) may be a reliable diagnostic alternative to chest x-ray for childhood pneumonia. However, it is unclear whether sonographer experience affects the diagnostic accuracy of LUS. We summarize the diagnostic accuracy of LUS for pneumonia and compare the performance between novice and advanced sonographers with a systematic review and meta-analysis.

Methods: We searched PubMed and EMBASE from inception to February 2018 for eligible studies that evaluated the utility of LUS in children suspected of having pneumonia against the reference standard of either imaging results alone or a combination of clinical, laboratory, and imaging results. We reported the study using the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies. We used QUADAS-2 to appraise the included studies’ methodologic quality. We employed a random-effect bivariate model and a hierarchical summary receiver operating characteristic curve to evaluate LUS’s performance characteristics. We conducted subgroup analyses and meta-regression based on level of sonographer training to summarize and compare LUS’s diagnostic accuracy for pneumonia between novice (training ≤ 7 days) and advanced sonographers.

Results: Twenty-five studies (n = 3,353) were included in the meta-analysis. For diagnosing pneumonia, LUS demonstrated an overall sensitivity of 0.94 (95% confidence interval [CI] = 0.89 to 0.97), specificity of 0.92 (95% CI = 0.78 to 0.98), positive likelihood ratio of 12.40 (95% CI = 4.00 to 38.10), and negative likelihood ratio of 0.07 (95% CI = 0.04 to 0.12), with an area under ROC curve of 0.97 (95% CI = 0.95 to 0.98). Meta-regression revealed a significant difference in the diagnostic accuracy for pneumonia for LUS between novice and advanced sonographers (p < 0.01).
Conclusion: LUS can accurately diagnose pneumonia in children. However, this test demonstrates operator-dependent variability, with more experienced sonographers having higher diagnostic accuracy. Further work on evidence-based educational methods to train novice sonographers in LUS is required.

Childhood pneumonia is a leading cause of death in both developed and developing countries. In developed countries, the annual incidence is 33 per 10,000 in children 0 to 5 years of age with a mortality rate of less than one per 1,000 children per year. In developing countries, however, the estimated annual incidence is 2,900 per 10,000 in children 0 to 5 years of age with a mortality rate of approximately 26 per 1,000 live births per year.

The diagnosis of pneumonia remains challenging for several reasons. Pediatric patients may be unable to provide a clear history depending on their age. Signs and symptoms also vary considerably due to different etiologies of infection. Traditionally, the diagnosis of pneumonia in children is made based on the combined use of chest x-ray (CXR) and clinical presentation. However, CXR exposes patients to radiation and also has limited sensitivity and specificity for diagnosing pneumonia when used in isolation. Chest computed tomography (CT) has outstanding diagnostic accuracy for pneumonia, but its excessive radiation exposure, high cost, and possible need for sedation limits its routine use in diagnosing uncomplicated pneumonia. Moreover, in resource-poor settings, there is limited access to CXR and CT.

Lung ultrasound (LUS) is increasingly studied as an alternative imaging modality for the diagnosis of childhood pneumonia. Ultrasound is noninvasive, does not have ionizing radiation, and provides real-time assessment, making it an attractive option for certain diagnostic applications in children. Studies measuring the diagnostic accuracy of LUS for childhood pneumonia generally report excellent sensitivity and specificity. Two meta-analyses further support the diagnostic accuracy of LUS for pneumonia. However, ultrasound’s accuracy varies by user skill and training, as evidenced in studies of pediatric appendicitis, while other applications such as skin and soft tissue infections have been demonstrated to only require minimal training. To date, the limited numbers of studies included in meta-analyses did not allow for subgroup analyses comparing the diagnostic accuracy of LUS for childhood pneumonia performed by novice versus advanced sonographers. It is currently unknown whether LUS’s accuracy is significantly dependent on sonographer experience. Therefore, this study’s objective was to quantitatively and qualitatively evaluate the diagnostic accuracy of LUS for pneumonia in children and to determine if sonographer experience affects diagnostic accuracy.

METHODS

Data Sources and Searches
This meta-analysis was performed in accordance with the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (The PRISMA-DTA). General bibliographic databases (PubMed and EMBASE) were searched from inception to February 2018. MeSH terms from PubMed and Emtree terms from Embase were combined with free text words. The “OR” connector was used for similar concepts; the “AND” connector was used to combine concepts. The following search terms for ultrasonography were combined using the OR connector: “ultrasound” OR “medical sonography” OR “sonography” OR “ultrasonography” OR “echography” OR “echo-gram.” Similarly, the search terms for pneumonia was defined using the following syntax: “aspiration pneumonia” OR “atypical pneumonia” OR “bacterial pneumonia” OR “bronchial pneumonia” OR “ventilator-associated pneumonia” OR “pneumonia” OR “acute respiratory distress syndrome” OR “pneumonitis.” The search results of ultrasonography and pneumonia were combined using the AND connector. The search was limited to human studies and children with age less than 21 years. There was no restriction on publication date, language, or country. In addition to the electronic search, reference lists in all known reviews and primary studies were checked manually.

Two authors (KPC and PYT) independently conducted the study selection and data extraction. A uniform search strategy was developed through a consensus meeting. Discrepancies between the reviewers were resolved by a consensus meeting initially and arbitration by a third reviewer if consensus could not be reached. The initial evaluation was based on screening of titles and abstracts. At the full-text screening stage, two authors reviewed each article and group consensus was used to resolve conflicts.
Selection Criteria
Types of Studies. We considered eligible studies investigating the diagnostic accuracy of ultrasonography for pneumonia except for case reports, case series with a sample size of less than 10 cases, animal studies, and studies without original data (e.g., reviews, editorials, commentaries).

Types of Participants. We considered eligible studies enrolling pediatric patients presenting with symptoms suggestive of pneumonia in the emergency department (ED) and inpatient settings. Symptoms utilized in the eligible studies include but not limit to tachypnea, dyspnea, cough, decreased breath sounds, or fever.

Index Tests. We defined the index test as LUS use in a patient presented with symptoms suggestive of pneumonia. A test was considered positive if signs of pneumonia were positive, including the presence of hepatization, pleural effusions, or alveolar-interstitial syndrome. Alveolar-interstitial syndrome was defined as the presence of comet-tail artifacts (B-lines) perpendicular to the pleural line.

Reference Tests. We defined reference tests as the sole or use in combination of the following: CXR, chest CT scan, and clinical diagnoses.

Data Abstraction and Quality Assessment
We extracted data on overall study characteristics, study design, settings, patient characteristics, sonographer experience, ultrasound transducer type, patient inclusion criteria, sonographic diagnostic criteria for pneumonia, reference test(s), and quantitative data required for construction of a standard diagnostic test 2 x 2 table. In studies that reported multiple pairs of sensitivity and specificity data, we used the data with the highest reported Youden index (sensitivity + specificity – 1). We used the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool to assess the methodologic quality of the select studies prior to conducting the meta-analyses. That instrument evaluates the risk of bias and the applicability in four domains of the included studies: flow and timing, the objectivity of reference test and index test, and patient selection.

Quantitative Data Synthesis
From the final included studies, we calculated pooled sensitivity and specificity and positive and negative likelihood ratios (LR+ and LR–, respectively) with the 95% confidence intervals (CIs) of LUS for diagnosing pneumonia in children. To understand differences in LUS’s diagnostic accuracy between advanced and novice ultrasonographers, a priori we stratified studies into two groups based on training in ultrasound reported in the included studies and further compared the diagnostic accuracies between two groups. Advanced ultrasonographers included radiologists, sonography technicians with imaging interpreted by radiologists, and clinicians with more than 7-day training in ultrasonography. Novice sonographers were defined as physicians with no prior experiences in ultrasound received no or minimal training (≤7 days) in LUS. The cutoff of 7 days’ training was made as a group consensus amongst the authors based on the length training specified in the included studies. Sensitivity analysis was conducted excluding studies that did not specify the training level of sonographer. We used a bivariate model to derive summary effect estimates. When 2 x 2 tables contained zero cells, we performed continuity correction by adding 0.5 to each cell. We constructed a hierarchical summary receiver operating characteristic (HSROC) curve and calculated the area under the curve (AUROC). Fagan plot analyses were conducted using the presumed pretest probabilities of pneumonia of 25, 50, and 75%, and the corresponding positive and negative posttest probabilities of pneumonia were further calculated. The degree of between-study heterogeneity was calculated using the I^2 test. For I^2 above 50%, in addition to stratifying by sonographer training, we performed subgroup analyses and meta-regression to explore potential sources of heterogeneity, including study setting (i.e., ED, inpatient or intensive care unit [ICU] setting), point-of-care lung ultrasound (POCUS) by clinicians versus radiology-performed lung ultrasound (RADLUS), and the types of references test. The presence and effect of publication bias were examined using Deek’s tests. If publication bias was present, the trim-and-fill method proposed by Duval and Tweedie was used to reach an asymmetric funnel plot and imputed summary estimate. Galbraith test was used to explore heterogeneity across studies. Statistical analysis was conducted using STATA (Version 12.0, StataCorp), with user-written “midas” programs. Meta-regression and the HSROC plot were constructed using R statistical software (Foundation for Statistical Computing). All statistical tests were two-sided with the Type I error rate set as 0.05. Thus, a p-value less than 0.05 was interpreted as reaching statistical significance.
RESULTS

Literature Search
This study’s selection of final included studies is summarized in Figure 1. Based on predefined search criteria, we identified 242 studies from PubMed and 2,420 studies from EMBASE database. After 47 duplicated studies and excluding 2,501 studies based on predefined criteria were removed, a total of 114 articles were retrieved for detailed review. Additionally, four articles were manually added from the reference lists of the known reviews and the included primary studies, and 25 studies were excluded due to various reasons detailed in Figure 1, leaving a total of 25 studies for final analysis.

Study Characteristics
Among the included 25 studies, there were a total of 3,389 patients presenting with symptoms suggestive of pneumonia. Detailed characteristics of the 25 studies could be found in Table 1. Eighteen prospective cohort studies, five retrospective cohort studies, one randomized controlled trial, and one case-control study were included. Three studies were conducted in North America, one in South America, one in Europe, five in Asia, and one in both South American and Asia. Study subjects were mostly infants, children, and adolescents except for two studies that included neonates. Sixteen studies used advanced sonographers, seven studies used novice sonographers, and two studies used sonographers of unknown training level in LUS (Table 2). The LUS training novice sonographers received varied greatly, ranging from 1 hour to the a priori-defined cutoff of 7 days of training. Ten studies were carried out in the ED, and 13 in an inpatient setting with four in the ICU and nine in the ward. High-frequency linear transducers (5–10 MHz) were most frequently utilized. The presence of hepatization, alveolar-interstitial syndrome (i.e., increased B-lines surrounding the hepatization) and pleural effusions were most commonly used to define pneumonia (Table 3). As a reference test for pneumonia, six studies used a combination of clinical

Figure 1 PRISMA flowchart of systemic literature search process. LUS = lung ultrasound.
Techniques, Equipment, and Diagnostic Criteria of LUS for Pneumonia

Commonly used probes in the included studies were the high-frequency small linear and microconvex transducers. Many studies directly adopted or modified the structured protocol proposed by Copetti and Cattarossi\textsuperscript{33} that systematically scans bilateral lung fields using LUS. That protocol divides lung fields into anterior, lateral, and posterior zones that are further subdivided into upper and lower halves. In each zone, it is recommended to scan along the anatomical lines, including parasternal, midclavicular, anterior axillary, midaxillary, posterior axillary, midscapular, and paravertebral. Sonographic characteristics for pneumonia include 1) consolidation (i.e., hepatization), 2) air-bronchograms, 3) alveolar-interstitial syndrome with increased B-lines seen from the deep edge of the consolidation, and 4) pleural effusion (Data Supplement S1, Figure S1 and Video S1, available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13818/full). Sonographic characteristics for pneumonia and other differential diagnoses are summarized and compared in Table 4. Median time to LUS completion ranged from 6.42 minutes to 15 minutes.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Country</th>
<th>Study design</th>
<th>Age (Years)</th>
<th>N</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>TN</th>
<th>Prevalence</th>
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<td>Copetti and Cattarossi\textsuperscript{33}</td>
<td>2008</td>
<td>Italy</td>
<td>Prospective</td>
<td>5.1 ± 5.0</td>
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<td>4</td>
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<td>Egypt</td>
<td>Prospective</td>
<td>0.03 ± 0.02</td>
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<td>64</td>
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<td>7</td>
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<td>0</td>
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<td>5.6 ± 4.6</td>
<td>103</td>
<td>52</td>
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<td>Prospective</td>
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<td>Retrospective</td>
<td>5 ± 3</td>
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<td>Urbanowska et al.\textsuperscript{37}</td>
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<td>Poland</td>
<td>Prospective</td>
<td>4.3 (2.2–7.2)</td>
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<td>Peru and Nepal</td>
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<td>Taiwan</td>
<td>Retrospective</td>
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<td>Samson et al.\textsuperscript{32}</td>
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<td>Spain</td>
<td>Prospective</td>
<td>2.5 (1.5–4.4)</td>
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<td>Denmark</td>
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<td>RCT</td>
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<td>Belgium</td>
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<td>81</td>
<td>72</td>
<td>2</td>
<td>3</td>
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<td>0.93</td>
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</table>

FN = false negative; FP = false positive; IQR = interquartile range; N = sample size; RCT = randomized control trial; TN = true negative; TP = true positive.

\textsuperscript{a}Data are reported as mean ± SD or median (IQR) unless otherwise specified.

\textsuperscript{b}Data are reported as mean (range).

\textsuperscript{c}Data are reported as median (range).
<table>
<thead>
<tr>
<th>Authors</th>
<th>Sonographer</th>
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<th>US Machine Brand</th>
<th>Array Type (High, Medium, Low)</th>
<th>Area</th>
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<td>Copetti and Cattarossi³³</td>
<td>Trained emergency physicians</td>
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<td>Esaote Megas CVX (Esaote)</td>
<td>7.5- to 10-MHz linear probe and 3.5- to 5-MHz convex probe</td>
<td>Anterior, lateral, and posterior chest wall; perpendicular, oblique, and parallel scans</td>
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<tr>
<td>Iuri et al.³⁴</td>
<td>Radiologist</td>
<td>Unclear</td>
<td>ATL HDI 5000 unit (Philips)</td>
<td>2- to 5-MHz convex probe and 5- to 12-MHz linear probe</td>
<td>Anterior and posterior chest wall; longitudinal and transverse scans</td>
</tr>
<tr>
<td>Seif El Dien et al.⁴⁵</td>
<td>Radiologist</td>
<td>Unclear</td>
<td>Nemio XG SSA-580A (Toshiba)</td>
<td>7-MHz linear probe</td>
<td>Anterior, lateral, and posterior chest wall; transverse, longitudinal, and inclined transverse or inclined longitudinal scans</td>
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<tr>
<td>Shah et al.²⁸</td>
<td>EM residents with mixed experience</td>
<td>1 hour</td>
<td>MicroMaxx (Sonosite) and GS60 (Siemens)</td>
<td>7.5- to 10-MHz linear probe</td>
<td>6-zone LUS imaging protocol similar to Copetti and Cattarossi</td>
</tr>
<tr>
<td>Liu et al.⁴⁶</td>
<td>Physicians with experience</td>
<td>Neonatologist</td>
<td>GE Voluson E8/E6 (GE)</td>
<td>9- to 12-MHz linear probe</td>
<td>Chest divided in three areas by anterior and posterior axillary lines; oblique scans</td>
</tr>
<tr>
<td>Esposito et al.¹¹</td>
<td>Residents with limited experience</td>
<td>7 hours</td>
<td>MyLab 25 Gold (Esaote)</td>
<td>2.5- to 6.6-MHz convex probe and 7.5- to 12-MHz linear probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal and oblique scans</td>
</tr>
<tr>
<td>Reali et al.³⁵</td>
<td>Physicians with experience</td>
<td>&gt;100 examinations</td>
<td>MyLab 25 Gold (Esaote)</td>
<td>7.5- to 10-MHz linear probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, oblique, and parallel scans</td>
</tr>
<tr>
<td>Caiulo et al.³⁶</td>
<td>Sonographer</td>
<td>Unclear</td>
<td>Sono57500 (Philips)</td>
<td>5-MHz convex probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, oblique, and parallel scans</td>
</tr>
<tr>
<td>Urbankowska et al.³⁷</td>
<td>Sonographer</td>
<td>Unclear</td>
<td>ProSound a6 (Aloka)</td>
<td>3- to 7- and 5- to 9-MHz linear probes</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal and transverse scans</td>
</tr>
<tr>
<td>Iorio et al.³⁸</td>
<td>Expert sonographer</td>
<td>Unclear</td>
<td>ProSound a6 (Aloka)</td>
<td>3- to 7- and 5- to 9-MHz linear probes</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, oblique, and parallel scans</td>
</tr>
<tr>
<td>Ianniello et al.²⁹</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Siemens Acuson Sequoia 512 system (Siemens)</td>
<td>4-MHz convex probe and 7.5- to 10-MHz linear probe</td>
<td>Anterior and posterior chest wall; longitudinal and transversal scans</td>
</tr>
<tr>
<td>Zol’Ak et al.⁴⁰</td>
<td>Unclear</td>
<td>Unclear</td>
<td>SonoSite M-Turbo (Fujiﬁlm)</td>
<td>5- to 10-MHz linear probe, 2- to 5-MHz convex abdominal probe, and 3.5- to 5-MHz microconvex probe</td>
<td>Anterior and posterior (if feasible) chest wall</td>
</tr>
<tr>
<td>Chavez et al.⁴⁹</td>
<td>Physicians with limited experience</td>
<td>7 days</td>
<td>SonoSite MicroMaxx and M-Turbo (Fujiﬁlm)</td>
<td>6- to 13-MHz linear probe</td>
<td>Anterior, lateral, and posterior chest wall; parasagittal and coronal scans</td>
</tr>
<tr>
<td>Ho et al.⁴⁷</td>
<td>Physicians with experience</td>
<td>Expert pulmonologist</td>
<td>Sono57500 (Philips)</td>
<td>5-MHz convex probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, oblique, and parallel scans</td>
</tr>
<tr>
<td>Samson et al.³²</td>
<td>Physicians with limited experience</td>
<td>2-hour lecture + 1 hour of hands-on practice</td>
<td>S-Nerve Sonosite (Fujiﬁlm)</td>
<td>6- to 15-MHz linear probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, oblique, and parallel scans</td>
</tr>
<tr>
<td>Zhan et al.⁴¹</td>
<td>Residents with limited experience</td>
<td>3 days</td>
<td>Sonosite Titan (Fujiﬁlm) and GE LOGIQe (GE)</td>
<td>5- to 10-MHz and 5- to 13-MHz linear probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, oblique, and parallel scans</td>
</tr>
<tr>
<td>Ambroggio et al.²⁹</td>
<td>Radiologist</td>
<td>1 hour</td>
<td>Aplio XG (Toshiba)</td>
<td>2- to 6-MHz convex and 5- to 12-MHz linear probes; 4- to 10-MHz curved and 5- to 12-MHz linear probes for smaller children</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal and transverse scans</td>
</tr>
</tbody>
</table>
Quality Assessment
The quality of included studies was assessed using QUADAS-2, as summarized in Figure 2 and Data Supplement S1, Tables S1 and S2. In general, included studies were of good quality with minimal bias and applicability concerns in the following domains: included a clear definition of targeted patient population, clear illustration of how index and reference tests were performed to diagnose pneumonia, and study flow. However, few studies focused on ICU patients or were conducted prospectively, which we considered at risk of patient selection bias that could represent the general population.44,45,47 Further, some studies did not clarify whether LUS was performed before or after the reference test.10,39,40,44,49

Overall Meta-analysis of the Diagnostic Accuracy of Ultrasound for Pneumonia
Twenty-five studies evaluated the diagnostic accuracy of LUS for pneumonia in children (Table 5 and Data Supplement S1, Figure S2). The pooled sensitivity and specificity were 0.94 (95% CI = 0.89 to 0.97) and 0.92 (95% CI = 0.78 to 0.98), respectively. The pooled LR+ and LR− were 12.4 (95% CI = 4.0 to 38.1) and 0.07 (95% CI = 0.04 to 0.12), respectively. The AUROC curve was 0.97 (95% CI = 0.95 to 1.00; Table 5). High heterogeneity (I2 = 100%, 95% CI = 99% to 100%) was present across the included studies. This supports the subgroup analyses based on sonographer training level as well as different conditions to explore sources of heterogeneity.

Subgroup Analyses
Sonographer Experience. It was determined a priori to stratify included studies into an advanced sonographer group (n = 16) and a novice sonographer group (n = 7). The subgroup analyses of the advanced sonographers showed a sensitivity of 0.96 (95% CI = 0.93 to 0.97), a specificity of 0.90 (95% CI = 0.54 to 0.99), a LR+ of 9.7 (95% CI = 1.5 to 61.9), a LR− of 0.05 (95% CI = 0.03 to 0.08), and an AUROC of 0.97 (95% CI = 0.95 to 0.98). The subgroup analyses of the novice sonographers showed a sensitivity of 0.80 (95% CI = 0.54 to 0.93), a specificity of 0.96 (95% CI = 0.91 to 0.98), a LR+ of 19.8 (95% CI = 7.6 to 51.5), a LR− of 0.21 (95% CI = 0.08 to 0.56), and an AUROC of 0.97 (95% CI = 0.95 to 0.98). Meta-regression was further conducted and suggested a significant difference in the diagnostic accuracy

<table>
<thead>
<tr>
<th>Authors</th>
<th>Sonographer</th>
<th>LUS Training</th>
<th>US Machine Brand</th>
<th>Array Type (High, Medium, Low)</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones et al.30</td>
<td>Physicians with mixed experience</td>
<td>1 hour</td>
<td>SonoSite M-Turbo (Fujifilm)</td>
<td>5- to 10-MHz linear probe</td>
<td>Six-zone LUS imaging protocol similar to Copetti and Cattarossi</td>
</tr>
<tr>
<td>Guerra et al.42</td>
<td>Physicians with experience</td>
<td>Unclear</td>
<td>MyLab 25 Gold (Esaote)</td>
<td>5- to 10-MHz linear and 3.5- to 5-MHz convex probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, oblique, and parallel scans</td>
</tr>
<tr>
<td>Claes et al.43</td>
<td>Radiologist</td>
<td>Unclear</td>
<td>iU-22 (Philips)</td>
<td>L 12- to 5-MHz linear probe and C 9- to 4-MHz convex probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, transverse, up-down, and mediolateral scans</td>
</tr>
<tr>
<td>Yadav et al.48</td>
<td>Radiologist</td>
<td>10 days</td>
<td>LOGIQ P5 (GE)</td>
<td>High-resolution microconvex probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, oblique, and parallel scans</td>
</tr>
<tr>
<td>Yilmaz et al.</td>
<td>Physicians with experience</td>
<td>&gt;100 examinations</td>
<td>SonoSite Edge (Fujifilm)</td>
<td>6- to 13-MHz linear probe</td>
<td>Anterior, lateral, and posterior chest wall; longitudinal, oblique, and parallel scans</td>
</tr>
<tr>
<td>Ellington et al.10</td>
<td>Physicians with experience</td>
<td>7 days</td>
<td>MicroMaxx (Fujifilm)</td>
<td>HFL38/13- to 6-MHz linear probe</td>
<td>Unclear</td>
</tr>
<tr>
<td>Boursiani et al.31</td>
<td>Radiologist</td>
<td>25 years</td>
<td>Unclear</td>
<td>5- to 8-MHz microconvex probe, 5- to 12-MHz linear probe, and 3- to 5-MHz convex probe</td>
<td>Anterior and posterior chest wall; longitudinal and transverse scans</td>
</tr>
<tr>
<td>Man et al.44</td>
<td>Radiologist</td>
<td>Unclear</td>
<td>Accuvix V20 Medison; Toshiba Xario 200</td>
<td>3.5- to 5-MHz linear probe and 7- to 11-MHz convex probe</td>
<td>Anterior and posterior chest wall; longitudinal and transverse scans</td>
</tr>
</tbody>
</table>

LUS = lung ultrasound; US = ultrasound.
<table>
<thead>
<tr>
<th>Authors</th>
<th>LUS Setting</th>
<th>Inclusion Criteria</th>
<th>Sonographic Diagnostic Criteria (Index Test)</th>
<th>Criterion Standard (Reference Test)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copetti and Cattarossi&lt;sup&gt;33&lt;/sup&gt;</td>
<td>ED</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation</td>
<td>Clinical diagnosis based on patients’ presentation and imaging results</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Iuri et al.&lt;sup&gt;34&lt;/sup&gt;</td>
<td>ED</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation or alveolar-interstitial syndrome</td>
<td>CXR</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Seif El Dien et al.&lt;sup&gt;45&lt;/sup&gt;</td>
<td>ICU</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation</td>
<td>CXR</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Shah et al.&lt;sup&gt;28&lt;/sup&gt;</td>
<td>ED</td>
<td>Clinically suspected pneumonia requiring CXR</td>
<td>Consolidation or alveolar-interstitial syndrome</td>
<td>CXR</td>
<td>Community-acquired pneumonia</td>
</tr>
<tr>
<td>Liu et al.&lt;sup&gt;46&lt;/sup&gt;</td>
<td>ICU</td>
<td>Pneumonia signs and symptoms + lab findings</td>
<td>Consolidation or alveolar-interstitial syndrome</td>
<td>clinical diagnosis based on patients’ presentation and imaging results</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Esposito et al.&lt;sup&gt;11&lt;/sup&gt;</td>
<td>ICU</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation or alveolar-interstitial syndrome</td>
<td>CXR</td>
<td>Community-acquired pneumonia</td>
</tr>
<tr>
<td>Reali et al.&lt;sup&gt;35&lt;/sup&gt;</td>
<td>Hospitalized</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation or alveolar-interstitial syndrome</td>
<td>Clinical diagnosis based on patients’ presentation and imaging results</td>
<td>Community-acquired pneumonia</td>
</tr>
<tr>
<td>Caiulo et al.&lt;sup&gt;36&lt;/sup&gt;</td>
<td>Hospitalized</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation or alveolar-interstitial syndrome</td>
<td>CXR</td>
<td>Community-acquired pneumonia</td>
</tr>
<tr>
<td>Urbankowska et al.&lt;sup&gt;57&lt;/sup&gt;</td>
<td>Hospitalized</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation, alveolar-interstitial syndrome or pleural effusion</td>
<td>CXR</td>
<td>Community-acquired pneumonia</td>
</tr>
<tr>
<td>Iorio et al.&lt;sup&gt;38&lt;/sup&gt;</td>
<td>Hospitalized</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation, alveolar-interstitial syndrome or pleural effusion</td>
<td>Clinical diagnosis based on patients’ presentation and imaging results</td>
<td>Community-acquired pneumonia</td>
</tr>
<tr>
<td>Ianniello et al.&lt;sup&gt;39&lt;/sup&gt;</td>
<td>ED</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation or alveolar-interstitial syndrome</td>
<td>CXR</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Zol’ák et al.&lt;sup&gt;40&lt;/sup&gt;</td>
<td>ICU</td>
<td>Critically ill children with or without respiratory insufficiency and healthy children as control</td>
<td>Unclear</td>
<td>Clinical diagnosis based on patients’ presentation and imaging results</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Chavez et al.&lt;sup&gt;49&lt;/sup&gt;</td>
<td>Outpatient, inpatient, ED</td>
<td>Children with or without respiratory symptoms</td>
<td>Consolidation</td>
<td>WHO Case Management Algorithm for Pneumonia</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Ho et al.&lt;sup&gt;47&lt;/sup&gt;</td>
<td>Hospitalized</td>
<td>Clinically diagnosed pneumonia</td>
<td>Consolidation, alveolar-interstitial syndrome or pleural effusion</td>
<td>CXR</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Samson et al.&lt;sup&gt;32&lt;/sup&gt;</td>
<td>ED</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation, alveolar-interstitial syndrome or pleural effusion</td>
<td>CXR</td>
<td>Community-acquired pneumonia</td>
</tr>
<tr>
<td>Zhan et al.&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Hospitalized</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation or alveolar-interstitial syndrome</td>
<td>CXR</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Ambroggio et al.&lt;sup&gt;33&lt;/sup&gt;</td>
<td>Hospitalized</td>
<td>Hospitalized with a respiratory diagnosis</td>
<td>Consolidation</td>
<td>CT Scan</td>
<td>Consolidation</td>
</tr>
<tr>
<td>Jones et al.&lt;sup&gt;30&lt;/sup&gt;</td>
<td>ED</td>
<td>Clinically suspected pneumonia requiring CXR</td>
<td>Consolidation</td>
<td>CXR</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Guerra et al.&lt;sup&gt;42&lt;/sup&gt;</td>
<td>ED</td>
<td>Pneumonia signs and symptoms</td>
<td>Consolidation</td>
<td>CXR</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Ciaes et al.&lt;sup&gt;43&lt;/sup&gt;</td>
<td>ED</td>
<td>Clinically suspected pneumonia requiring CXR</td>
<td>Consolidation</td>
<td>CXR</td>
<td>Pneumonia</td>
</tr>
</tbody>
</table>
Table 4
Sonographic Characteristics of Common Pediatric Pulmonary Diseases

<table>
<thead>
<tr>
<th>LUS findings</th>
<th>Pneumonia</th>
<th>Atelectasis</th>
<th>Pneumothorax</th>
</tr>
</thead>
<tbody>
<tr>
<td>No A-lines(^a) within the consolidated area</td>
<td>Hepatization</td>
<td>Static air bronchograms(^d)</td>
<td>Absence of lung sliding (pleural line); “bar code sign” in M-mode</td>
</tr>
<tr>
<td>Alveolar-interstitial syndrome: increased B-lines(^b) surrounding consolidated area</td>
<td>Static air bronchograms(^d)</td>
<td>Lung point detected</td>
<td>No B-lines</td>
</tr>
<tr>
<td>Consolidation (hepatization)(^c)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of blood flow on color Doppler sonography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dynamic air bronchograms(^d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleural effusion(^e)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)A-lines: hyperechoic lines running parallel to the pleural line that are, in fact, reverberation artefacts of the pleural line.
\(^b\)B-lines: B-lines (alternatively referred to as lung comets or comet-tail artifacts) are hyperechoic lines arising from and running perpendicular to the pleura up to the deep edge of the image, without fading, and obliterating the A-lines where they cross.
\(^c\)Consolidation (i.e., hepatization): sonographic air bronchograms seen as multiple hyperechoic punctate or lenticular specs within the area of consolidation or branching tree-like structures.
\(^d\)Dynamic air bronchograms: inspiratory centrifugal movement of the air bronchograms greater than 1 mm. A sign helps differentiate pneumonia from atelectasis which is static on inspiration.
\(^e\)Pleural effusion: collection of anechoic or hypoechoic fluid in the pleural space ± internal structures and debris.

Figure 2 Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2). Each Domain is represented in a bar with the proportion of studies considered high risk, low risk, or unclear.
<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>LR⁺ (95% CI)</th>
<th>LR⁻ (95% CI)</th>
<th>DOR (95% CI)</th>
<th>AUROC (95% CI)</th>
<th>I² (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAP</td>
<td>25</td>
<td>0.94 (0.89–0.97)</td>
<td>0.92 (0.78–0.98)</td>
<td>12.40 (4.00–38.10)</td>
<td>0.07 (0.04–0.12)</td>
<td>180 (45–717)</td>
<td>0.97 (0.95–0.98)</td>
<td>100 (99–100)</td>
</tr>
<tr>
<td>Sonographers’ US training level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Advanced</td>
<td>16</td>
<td>0.96 (0.93–0.97)</td>
<td>0.90 (0.54–0.99)</td>
<td>9.70 (1.50–61.90)</td>
<td>0.05 (0.03–0.08)</td>
<td>204 (24–1768)</td>
<td>0.97 (0.95–0.98)</td>
<td>98 (97–99)</td>
</tr>
<tr>
<td>Novice</td>
<td>7</td>
<td>0.80 (0.54–0.93)</td>
<td>0.96 (0.91–0.98)</td>
<td>19.80 (7.60–51.50)</td>
<td>0.21 (0.08–0.56)</td>
<td>94 (17–523)</td>
<td>0.97 (0.95–0.98)</td>
<td>95 (91–99)</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>ED</td>
<td>10</td>
<td>0.93 (0.90–0.96)</td>
<td>0.88 (0.63–0.97)</td>
<td>7.70 (2.20–26.60)</td>
<td>0.07 (0.05–0.12)</td>
<td>103 (27–400)</td>
<td>0.96 (0.93–0.97)</td>
<td>98 (96–99)</td>
</tr>
<tr>
<td>Inpatient/ICU</td>
<td>13</td>
<td>0.95 (0.89–0.98)</td>
<td>0.91 (0.62–0.98)</td>
<td>10.40 (2.00–55.30)</td>
<td>0.05 (0.02–0.13)</td>
<td>195 (23–1657)</td>
<td>0.98 (0.96–0.99)</td>
<td>98 (98–99)</td>
</tr>
<tr>
<td>Performers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POCLUS</td>
<td>14</td>
<td>0.94 (0.84–0.98)</td>
<td>0.94 (0.71–0.99)</td>
<td>16.60 (7.20–100.00)</td>
<td>0.07 (0.02–0.18)</td>
<td>253 (26–2427)</td>
<td>0.98 (0.96–0.99)</td>
<td>99 (99–100)</td>
</tr>
<tr>
<td>RADLUS</td>
<td>8</td>
<td>0.91 (0.85–0.95)</td>
<td>0.86 (0.45–0.98)</td>
<td>6.40 (1.20–35.50)</td>
<td>0.11 (0.06–0.20)</td>
<td>59 (7–518)</td>
<td>0.93 (0.91–0.95)</td>
<td>90 (79–100)</td>
</tr>
<tr>
<td>Reference test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination*</td>
<td>9</td>
<td>0.95 (0.90–0.98)</td>
<td>0.98 (0.90–1.00)</td>
<td>60.10 (9.36–389.70)</td>
<td>0.05 (0.02–0.10)</td>
<td>1224 (130–11498)</td>
<td>0.99 (0.97–0.99)</td>
<td>83 (64–100)</td>
</tr>
<tr>
<td>CXR</td>
<td>20</td>
<td>0.94 (0.90–0.96)</td>
<td>0.78 (0.57–0.91)</td>
<td>4.30 (2.00–9.40)</td>
<td>0.08 (0.04–0.14)</td>
<td>56 (19–165)</td>
<td>0.95 (0.93–0.97)</td>
<td>99 (99–100)</td>
</tr>
</tbody>
</table>

AUROC = area under receiver operating characteristic curve; CAP = community-acquired pneumonia; DOR = diagnostic odds ratio; I² = heterogeneity; LR⁺ = positive likelihood ratio; LR⁻ = negative likelihood ratio; N = numbers of studies; POCLUS = point-of-care lung ultrasound; RADLUS = radiology-performed lung ultrasound.

*Combination included CXR with the sole or combinational use of the following sources of information: clinical symptoms/signs, chest CT scans, or laboratory findings.
between LUS performed by advanced versus novice sonographers \((p = 0.002; \text{Table 5, Figures 3 and 4})\).

**Setting.** Lung ultrasound was performed in the ED in 10 studies. Subgroup analyses showed sensitivity of 0.93 \((95\% \text{ CI} = 0.90 \text{ to } 0.96)\), a specificity of 0.88 \((95\% \text{ CI} = 0.63 \text{ to } 0.97)\), a LR+ of 7.7 \((95\% \text{ CI} = 2.2 \text{ to } 26.6)\), a LR− of 0.07 \((95\% \text{ CI} = 0.05 \text{ to } 0.12)\), and an AUROC of 0.96 \((95\% \text{ CI} = 0.93 \text{ to } 0.97)\).

LUS was performed in an inpatient setting, including ward and ICU, in 13 studies. Subgroup analyses showed a sensitivity of 0.95 \((95\% \text{ CI} = 0.89 \text{ to } 0.98)\), a specificity of 0.91 \((95\% \text{ CI} = 0.62 \text{ to } 0.98)\), a LR+ of 10.4 \((95\% \text{ CI} = 2.0 \text{ to } 55.3)\), a LR− of 0.05 \((95\% \text{ CI} = 0.02 \text{ to } 0.13)\), and an AUROC of 0.98 \((95\% \text{ CI} = 0.96 \text{ to } 0.99; \text{Table 5})\).

**POCLUS Versus RADLUS.** The subgroup analyses of 14 POCLUS studies showed a sensitivity of 0.94 \((95\% \text{ CI} = 0.84 \text{ to } 0.98)\), a specificity of 0.94 \((95\% \text{ CI} = 0.71 \text{ to } 0.99)\), a LR+ of 16.6 \((95\% \text{ CI} = 2.7 \text{ to } 100.0)\), a LR− of 0.07 \((95\% \text{ CI} = 0.02 \text{ to } 0.18)\), and an AUROC of 0.98 \((95\% \text{ CI} = 0.96 \text{ to } 0.99)\). The eight studies where LUS was performed by a trained sonographer or radiologist (RADLUS) showed a sensitivity of 0.91 \((95\% \text{ CI} = 0.85 \text{ to } 0.95)\), a specificity of 0.86 \((95\% \text{ CI} = 0.45 \text{ to } 0.98)\), a LR+ of 6.4 \((95\% \text{ CI} = 1.2 \text{ to } 35.5)\), a LR− of 0.11 \((95\% \text{ CI} = 0.06 \text{ to } 0.20)\), and an AUROC of 0.93 \((95\% \text{ CI} = 0.91 \text{ to } 0.95; \text{Table 5})\).

**Reference Test.** Among the studies using CXR alone \((n = 20)\) as the reference test, subgroup analyses showed a sensitivity of 0.94 \((95\% \text{ CI} = 0.90 \text{ to } 0.96)\), a specificity of 0.78 \((95\% \text{ CI} = 0.57 \text{ to } 0.91)\), a LR+ of 4.3 \((95\% \text{ CI} = 2.0 \text{ to } 9.4)\), a LR− of 0.08 \((95\% \text{ CI} = 0.04 \text{ to } 0.14)\), and an AUROC of 0.95 \((95\% \text{ CI} = 0.93 \text{ to } 0.97)\). By contrast, those studies using a combination of clinical, laboratory, and imaging results as the reference test \((n = 9)\) showed a sensitivity of 0.95 \((95\% \text{ CI} = 0.90 \text{ to } 0.98)\), a specificity of 0.98 \((95\% \text{ CI} = 0.98 \text{ to } 1.00)\), a LR+ of 60.1 \((95\% \text{ CI} = 9.36 \text{ to } 389.7)\), a LR− of 0.05 \((95\% \text{ CI} = 0.02 \text{ to } 0.10)\), and an AUROC of 0.99 \((95\% \text{ CI} = 0.97 \text{ to } 0.99; \text{Table 5 and Data Supplement S1, Figures S3 and S4})\).

Given the high heterogeneity in the overall analysis, meta-regression analysis was conducted to evaluate LUS setting, POCLUS versus RADLUS, and reference test as potential sources of heterogeneity. Results suggested that studies using CXR alone as the reference test showed a significantly lower diagnostic accuracy of LUS for diagnosing pneumonia in children \((p = 0.05)\). By contrast, the setting where LUS was performed and whether LUS was performed by a POCLUS or RADLUS did not impact the diagnostic accuracy of LUS.

**Publication Bias**

Deek’s funnel plot asymmetry test explored potential publication bias and suggested no significant
Publication bias (p = 0.77) among the included studies. Therefore, we did not perform the trim and fill (Figure S5).

**Fagan Plot Analysis**

The Fagan plot analysis suggested that the pretest probabilities (i.e., prevalence) of 25, 50, and 75% for pneumonia correspond to positive posttest probabilities of 80, 93, and 97% and negative posttest probabilities of 2, 6, and 17%, respectively (Data Supplement S1, Figure S6).

**DISCUSSION**

This study summarizes LUS’s excellent diagnostic accuracy for pneumonia in children. To our knowledge, this is the first article demonstrating significant differences in LUS’s diagnostic accuracy for pneumonia between novice and advanced sonographers. Those findings suggest that the sonographer’s experience level should be considered when using LUS to diagnose pneumonia in children. The implementation of a structured curriculum in LUS for diagnosing pneumonia is therefore needed to standardize the performance of sonographers in adopting this radiation-free diagnostic test for a common pediatric disease.

Lung ultrasound demonstrated excellent diagnostic accuracy in this meta-analysis and is comparable with findings of prior meta-analyses. Our comprehensive search strategy allowed for the inclusion of several studies not included in previous meta-analyses. Recently published quality prospective studies were also able to be included in this meta-analysis. The number of included studies allowed for subgroup analysis, which revealed several notable findings. First, the sonographer’s ultrasound training level significantly affects LUS’s diagnostic accuracy for pneumonia (p = 0.002). The difference in performance between advanced sonographers and novice sonographers is expected as the former received more training and are thus more seasoned and skilled in LUS. The amount of LUS training novice sonographers received ranged from a few hours of didactics to hands-on practice and nearly a full week of training. Given this finding, brief curricula are likely insufficient for novice sonographers to gain sufficient diagnostic competency in LUS and should be reconsidered. Second, the choice of criteria standard for the diagnosis of pneumonia significantly impacts the diagnostic accuracy of LUS. Studies that adopted CXR as the criterion standard had a significantly lower diagnostic accuracy compared with those that used a combination of tests as the criterion standard. The significant difference between reference tests utilized by included studies may be a result of several factors. CXR may not detect small consolidations that could be visualized on LUS. Also, many studies adopted CXR PA or AP view only without a lateral view that might reveal retrocardiac or subdiaphragmatic consolidations. As such, using CXR alone as the reference test may miss patients with pneumonia, resulting in an underestimated diagnostic accuracy of LUS for pneumonia. This finding is compatible with the findings of Balk et al., suggesting that CXR alone may not be the ideal diagnostic test for pneumonia.

It is noteworthy that several included studies showed LUS has particularly low diagnostic accuracy for pneumonia. The study conducted by Chavez et al. found a sensitivity of only 23% for pneumonia. That study used the WHO algorithm as the reference test, which is a list of clinical criteria without the inclusion of laboratory or imaging data. Since children with pneumonia may have variable presentations, using clinical judgment alone is likely insufficient. Zhan et al. and Ambroggio et al. also demonstrated low sensitivity of LUS in diagnosing pneumonia in children. Both of these studies used novice sonographers, suggesting confounding by insufficient training. Four studies with particularly low specificity shared some characteristics of note. Those include the use of CXR PA or AP views alone without lateral views as the reference test, which has limited use in detecting both small lesions (<1 cm) and retrocardiac lesions. Also, using CXR alone as the reference test without accounting for the patient’s clinical presentation may potentially miss pneumonia, potentially partially explaining the suboptimal diagnostic accuracy of CXR in those studies. Those findings indicate that CXR alone may not be an adequate standard to diagnose pneumonia and suggest that LUS may be a viable alternative, if not a superior test.

There are several benefits to LUS besides its diagnostic accuracy for pneumonia. LUS can monitor disease progression without added radiation exposure. The ability to monitor disease progression, without additional radiation exposure, and to adjust management accordingly is particularly important for patients who are unstable or critically ill. Furthermore, POCLUS has been shown to decrease length of stay in the ED in children with concern for pneumonia.
It is also noted that the use of POCLUS is associated with lower financial costs by reducing the use of more invasive and expensive diagnostic tests,\textsuperscript{54,55} shortened ED stay,\textsuperscript{30} and less complications associated with invasive procedures (e.g., thoracentesis).\textsuperscript{56}

This study also importantly reveals the training of LUS impacts its diagnostic accuracy for pneumonia. Those results indicate the need for a standardized curriculum, ideally consisting of a certain number of supervised scans and a posttest administered by ultrasound experts. However, there is no such curriculum as of yet.\textsuperscript{57} Future studies are needed to standardize the curriculum for LUS training and determine the amount of scans and duration of training required for a novice to achieve adequate proficiency in LUS.

**LIMITATIONS**

The results of this study should be interpreted in the context of its strength and limitations. Our work reconfirms the excellent diagnostic accuracy of LUS for pneumonia and also reveals that sonographer training significantly impacts LUS's diagnostic accuracy. However, this study bears several limitations that merit consideration. First, LUS does not reliably differentiate pneumonia from other conditions that also present with lung hepatization, such as atelectasis or pulmonary edema.\textsuperscript{58} That may lead to a higher false-positive rate and therefore a lower specificity. However, a detailed history and physical examination would also help clinicians narrow down the differential and exclude those conditions, rather than relying solely on LUS results. Second, a major limitation of LUS is its inability to provide additional information, such as the position of the airway, hypo- or hyperinflation of lung, and the cardiac silhouette, which are seen on CXR. That information is helpful to clinicians in differentiating dyspnea caused by pneumonia from other etiologies, such as pulmonary edema secondary to cardiac failure. POCUS of other organ systems (e.g., heart, trachea) in addition to the lung could help fill in the knowledge gap of POCLUS and aid in clinical decision making. Third, using ultrasound training duration to distinguish between novice and advanced sonographers may not accurately reflect competence as well as the numbers of scans required during training. We used training duration because only two included studies reported the numbers of scans during training, a more standardized metric for the measurement of US training. Regardless, duration of training is a sufficient surrogate in this study as most of the novice sonographers in the included studies had a very limited amount of training (e.g., 1 hour, 2 hours), and the training was not uniformly supervised or reviewed by expert sonographers. Such short and unstandardized training across studies very likely does not allow the novice to develop adequate competency in POCLUS. Thus, it may still be a functional way to classify those providers with short LUS training duration as novice sonographers. Furthermore, as shown in this study, the diagnostic accuracy of LUS is user-dependent, and individual study results may not be generalizable depending on the adequacy of the training methodology described. However, based on the results of several studies investigating structured training in ultrasound,\textsuperscript{11,32} the diagnostic accuracy of LUS by novice sonographers can likely be improved. Another limitation of this study is patient selection bias. Patients enrolled in the included studies may have more clinically serious pneumonia leading to ED presentation and possible admission, and thus the derived diagnostic accuracy of LUS for pneumonia may be overestimated. Finally, the use of CXR alone as the criterion standard test across multiple studies may confound our findings that ultrasound training affects LUS diagnostic accuracies for pneumonia. Ideally, a criterion standard test should be a combination of clinical, laboratory, and imaging results given that CXR alone may not be accurate enough and could thus affect the diagnostic accuracies of the index test. However, inadequate numbers of included studies using combinational testing as criterion standard (\(n = 9\)) prevented us from using combination tests as a criterion standard. Therefore, our findings should be interpreted taking that into account.

**CONCLUSION**

This systematic review and meta-analysis supports lung ultrasound as an accurate diagnostic test for pneumonia in children. However, lung ultrasound’s diagnostic accuracy is significantly affected by sonographer experience, revealing the need for a validated standardized training curriculum.

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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.13818/full

Data Supplement S1. Supplemental material.

Video S1. Sonograph.
Patient Versus Physician Perceptions of Frailty: A Comparison of Clinical Frailty Scale Scores of Older Adults in the Emergency Department

Scott M. Dresden, MD, MS, Timothy F. Platts-Mills, MD, MSc, Deepika Kandasamy, Lauren Walden, and Marian E. Betz, MD, MPH

Frailty is a state of vulnerability to impairments in mobility, balance, muscle strength, motor processing, physical function, disability, cognition, nutrition, endurance, and physical activity. Prevalence estimates vary widely from 4.0% to 59.1% (weighted estimate = 10.9%), with prevalence increasing with age. The risk of adverse outcomes for frail older adults including falls, delirium, disability, and death is increased compared to similarly aged individuals without frailty and may be a more important predictor of death than age for older adults.

Older adults account for nearly 20 million emergency department (ED) visits in the United States annually with volumes increasing as the population ages. Frailty is important for emergency physicians (EPs) to identify and understand because of its with implications on treatment decisions. For patients, being labeled as frail may contribute to the development of a frailty identity and lead to a loss of interest in participating in social and physical activities, increased stigmatization, and poor self-reported physical health.

It is unknown if EPs and patients identify and interpret frailty the same way. Additionally, it is unknown if there is an association between patient or EP perception of frailty and hospitalization which carries risks of complications like infection, delirium, and functional decline. The objectives of this study were to determine 1) if emergency physicians and older adults differ in their perceptions of frailty and 2) if those perceptions of frailty were related to disposition from the ED.

As a planned secondary analysis of a larger study, we performed a cross-sectional survey of community dwelling older adults 65 years old and older at two large U.S. EDs from July 2016 to April 2017. Patients were eligible if they understood English and were medically and cognitively able to participate and had not previously participated in this study. Research assistants (RAs) identified patients using the ED’s electronic tracking board and confirmed eligibility with...
treatment clinicians. RAs discussed the survey with patients and assessed patients’ ability to participate. The survey was self-administered or RA-administered based on patient choice. Patients received pamphlets connecting them with local resources. Completed surveys were recorded in Research Electronic Data Capture. The Colorado Multiple Institutional Review Board and the University of North Carolina–Chapel Hill Institutional Review Board approved this project.

The survey included questions regarding demographic, social, and health characteristics including age, sex, living arrangement, social connections, health services use, ED arrival method, ability to perform activities of daily living, and the Clinical Frailty Scale (CFS). The CFS is a global clinical measure of fitness and frailty that uses pictographs and clinical descriptions to help clinicians stratify older adults on a nine-point scale, one being very fit and nine being terminally ill. Self-reported CFS and EP-assigned CFS scores were recorded. Additional variables included anticipated disposition according to the treating clinician and method of arrival to the ED.

The primary outcome was agreement between patient-reported and EP-assigned CFS score. Secondary outcomes included differences in CFS scores by demographic, clinical, and social variables and differences in anticipated disposition by CFS score. Median CFS score was calculated. Wilcoxon rank-sum test was used to test for differences in patient-reported CFS score categories and EP-assigned CFS score categories across categories of demographic, clinical, and social variables. Agreement was determined using weighted Cohen’s kappa. Histograms were created for each CFS score.

Surveys were completed by 266 patients, 194 at site 1 and 72 at site 2. Patients reported significantly more CFS scores of 1–2 (very fit or well), while EPs reported significantly more CFS scores of 3 (managing well) or 6 to 8 (moderate to very severe frailty; Figure 1). There was moderate agreement (weighted $\kappa = 0.43$) of frailty between EPs and patients, site 1 had fair agreement (weighted $\kappa = 0.36$), and site 2 had moderate agreement (weighted $\kappa = 0.56$).

There were no significant differences in results of any variables, including CFS scores by site. Median patient-reported CFS scores were higher for patients who were older ($65–74 = 3$, $75–84 = 3$, $85–92 = 4$; $p = 0.007$), did not work or volunteer ($yes = 3$, $no = 4$; $p < 0.001$), did not drive ($yes = 3$, $no = 4$; $p < 0.001$), ate alone ($yes = 4$, $no = 3$; $p = 0.006$), had difficulty paying bills ($yes = 4$, $no = 3$; $p = 0.042$), were hospitalized in the past month ($yes = 4$, $no = 3$; $p = 0.007$), needed help with routine care ($yes = 4$, $no = 3$; $p < 0.001$), needed help with personal care ($yes = 6$, $no = 3$; $p < 0.001$), needed special equipment ($yes = 4$, $no = 3$; $p < 0.001$), or did not live in private housing ($private = 3$, $other = 4$; $p = 0.006$). There were no significant differences in patient-reported CFS score with regards to sex, difficulty affording food, having a primary care physician, ED arrival method, and patient disposition. Median EP-assigned CFS scores were higher for patients who were older ($65–74 = 3$, $75–84 = 4$, $85–92 = 4.5$; $p = 0.001$), did not live in private housing ($private = 3$, $other = 5$; $p = 0.009$), did not work or volunteer ($yes = 3$, $no = 4$; $p < 0.001$), did not go into the community regularly ($yes = 3$, $no = 4$; $p = 0.001$), did not drive ($yes = 3$, $no = 5$; $p < 0.001$), were hospitalized in the past month ($yes = 4$, $no = 3$; $p = 0.001$), needed help with routine care ($yes = 4.5$, $no = 3$; $p < 0.001$), needed help with personal care ($yes = 5$, $no = 3$; $p < 0.001$), or needed special equipment ($yes = 4$, $no = 3$; $p < 0.001$). There were no significant differences in physician-assigned CFS score with regard to sex, living situation, seeing family or friends regularly, eating alone regularly, difficulty affording food, difficulty paying bills, having a primary care physician, and ED arrival method.

There was no significant association between planned disposition and self-reported frailty ($p = 0.08$). However, higher EP-assigned CFS was associated with planned hospitalization or transfer to a nursing or rehabilitation facility (admission = 4, nursing/rehabilitation facility = 5.5, home = 3, uncertain = 3; $p = 0.014$).

We identified moderate agreement in assessment of frailty between EPs and ED patients age 65 and older as measured by the CFS. We found that EPs were less likely to rate older adults as very fit or well and more likely to report patients as moderately to very severely frail compared to patient self-report. Living alone, eating alone regularly, or having difficulty paying bills was associated with increased self-reported frailty, but not EP-reported frailty. Conversely, self-reported CFS was not associated with disposition, while higher EP-assigned CFS was associated with hospitalization or nursing home or rehabilitation facility transfer.

Measures of frailty like the CFS may help to identify older adults in the ED at risk of poor outcomes and who may benefit from additional services. It is unclear, however, who is the most appropriate rater of
frailty. A study of older adults in the ED with blunt trauma found poor agreement between the patient-reported and EP-assigned CFS. Patient-reported CFS had better agreement with the patient-reported Fatigue, Resistance, Ambulation, Illnesses, & Loss of Weight (FRAIL) scale, which is also patient-reported. However, it is not clear whether patient-reported CFS is more accurate at predicting important short-term outcomes like functional decline than EP-assigned CFS.

As EDs face additional pressure from an aging population and continued ED crowding, quick assessments of frailty like the CFS may help identify patients who would benefit from a more thorough assessment by a multidisciplinary team and may be useful in providing insight into patients’ environment (including potential challenges) and sense of well-being. It is currently unclear which of the many frailty scores is best for use in the ED. Since there are many different constructs of frailty, identifying the best measure to use and the optimal assessor depends on the outcome of interest. The Study of Osteoporotic Fracture (SOF) frailty index has been shown to have at least fair prediction of functional decline. Additionally the CFS; Fried Frailty Index; and the Stable, Unstable, Help, Bedridden (SUHB) scale all had good predictive properties for poor outcomes after an ED visit; however, the CFS was easier to administer in the ED. Additional study is needed to determine if patient or clinician reported frailty scores are more accurate at predicting poor outcomes.

The major limitation of this study is that it is unknown whether EP-assigned CSF scores or patient-reported CSF scores are more accurate at predicting short-term outcomes after an ED visit, and researchers did not separately administer a “criterion standard” objective assessment of frailty. Additionally, there are questions as to the reliability and validity of the CFS. Other limitations include convenience sampling; although RAs made every effort to identify all eligible patients, it is possible that bias was present in the selection process. Disposition may have changed after anticipated disposition was recorded. Finally, the secondary outcome of hospitalization is ultimately determined by the emergency physician, who also performed the CFS. Future studies should use clinical outcomes that are independent of the rater’s decision making such as functional decline, return to the ED, rehospitalization, and nursing home placement over a predetermined follow-up time.

Agreement between patient-reported and EP-assigned CFS is moderate for older adults in the ED; discordance was particularly notable at the less-frail end of the spectrum. Hospital admission or transfer to a nursing home or rehabilitation facility appeared associated with increased EP-assigned CFS but more detailed and controlled analyses would be useful to determine whether patients underestimate frailty or EPs overestimate it.

References

Hot Off the Press: Low-dose Magnesium Sulfate Versus High Dose in the Early Management of Rapid Atrial Fibrillation: Randomized Controlled Double-blind Study

Corey Heitz, MD,1 Justin Morgenstern, MD,2 Christopher Bond, MD,3 and William K. Milne, MD4

BACKGROUND

Atrial fibrillation (AF) is the most common cardiac dysrhythmia, increasing in prevalence with age.1 Options for emergency department (ED) management include rate control with various medications or rhythm control using either electrical cardioversion or chemical means.2 Magnesium sulfate (MgS) has been studied as an adjunctive therapy for AF, with varying results.3–6 The aim of the study was to determine if different doses of MgS would have differing synergistic effects on rate control agents being provided for control of AF.

ARTICLE SUMMARY

This study compares two doses of magnesium given concurrently with rate-controlling agents (left to the treating provider’s discretion). Patients over 18 years of age with rapid AF (>120 beats/min), without complicating features such as hypotension, impaired consciousness, renal insufficiency, wide complex tachycardias, acute myocardial infarction, or congestive heart failure, were randomized to receive placebo or 4.5 or 9 g of MgS along with initial rate control agent. MgS was given over 30 minutes. The primary outcomes were a ventricular rate within 4 hours of 90 beats/min or less or a reduction in ventricular rate by 20%. Secondary outcomes included time to therapeutic response, sinus rhythm conversion rate, and adverse events (defined as discontinuation of treatment or death).

QUALITY ASSESSMENT

This was a well-done, randomized controlled trial. The patients were recruited consecutively, and multiple centers were used. Treating providers and patients were blinded to therapy. Choice of treating agent was left up to the provider, which reduces standardization of patient care. As seen in the results, a large number of patients were treated with digoxin, which differs from most North American practice, reducing external validity of the study. In addition, the outcomes were not patient-oriented such as short-term stroke or cardiac outcomes, but instead were surrogate, objective numeric outcomes such as heart rate and sinus rhythm conversion.

KEY RESULTS

They enrolled 450 patients into the trial with one-third in each group. The mean age was 67 years and 60%
were women. Rate control agents used were digoxin (47%), diltiazem (31%), and beta-blockers (22%).

**Primary Outcomes**
- Low-dose (4.5 g MgS) placebo: absolute difference = 20.5%, risk ratio = 2.31, 95% confidence interval [CI] = 1.45 to 3.69;
- High-dose (9 g MgS) placebo: absolute difference = 15.8%, risk ratio = 1.89, 95% CI = 1.20 to 2.99;
- 5 g versus 9 g MgS: absolute difference = 4.7%, risk ratio = 0.81, 95% CI = 0.51–1.30.

**Secondary Outcomes**
Magnesium groups had faster time to resolution, and low dose had a higher sinus rhythm conversion rate and rhythm control at 24 hours. However, adverse events (flushing) were higher in patients treated with magnesium.
- Mean resolution time: 8.4 + 5 hours placebo, 6.1 + 1.9 hours low dose, 5.2 + 2 hours high dose;
- Sinus rhythm conversion at 4 hours: 6.7% placebo, 12.1% low dose, 7.8% high dose;
- Rhythm control at 24 hours: 10.7% placebo, 22.9% low dose, 13.0% high dose;
- Adverse events higher with MgS (flushing in 24 patients, transient hypotension in four patients [two high dose, one low dose, one placebo], bradycardia in one patient/group).

**AUTHORS’ COMMENTS**
Magnesium, in a dose of either 4.5 or 9 g, appears to be an effective adjunct for rate control, with an increase in minor side effects. However, a large proportion of patients in this study received digoxin, which differs from practice by many North American providers, and the outcomes are not patient-oriented, both of which limit the clinical application of the data.

**TOP SOCIAL MEDIA COMMENTARY**

**Comments from theSGEM.com**

Lauren Westafer

Hi Ken,

Thanks for doing this podcast. This article has received a significant amount of attention in the United States and I have some concerns about the rush to use these results to support giving magnesium in the acute rate control treatment of AF with RVR.

1. The primary outcome has little relevance to my practice, and I think that of many in the United States. The authors chose rate control at 4 hours. By 4 hours, I have usually either admitted or discharged these patients. In my practice, we typically control the rate within an hour, often much more quickly (of course, there are rare exceptions with patients with difficult to control rates).

2. The providers in this study largely used digoxin for rate control, which is likely why the aforementioned time point was used—it takes hours to kick in. We use diltiazem 0.25 mg/kg most commonly, although sometimes beta-blockers as well. The authors report that they looked at this subgroup and the results remained. However, looking at the figures, it appears that most patients did not achieve rate control for hours which makes me believe that there is a fundamental difference in dosing or practice even in those who used beta-blockers or calcium channel blockers.

3. I could not reproduce the RR mentioned in the article. I reached out to the authors but have not received a response. For the primary outcome of low mag vs placebo, I got a RR of 1.47. While the CI I calculated did not cross 1, maintaining statistical significance, I cannot help but be skeptical of the results.

Thanks for doing this podcast!

**Comments from Twitter**

Joshua (@reverendofdoubt)

why did [almost half] of pts get digoxin for afib rvr given its narrow therapeutic index/side effects? was that specifically in the pts with HF/LV dysfunction? or did they have hypotension as the reason?

Rick Pescatore DO (@Rick_Pescatore)

I think the lesson that mag is potentially helpful in atrial tachydysrhythmias holds true . . . as was borne out in LOMAGHI
Justin Stowens (@jstowens)

... and I’ve seen some pretty uncomfortable people in AF with RVR. Being in that uncomfortable state for 20% less time (4hrs average by LOMAGHI, I think?) might be considered patient oriented. But, of course, low cost shouldn’t be a reason to do it.

Twitter Poll

Do you use digoxin to treat rapid atrial fibrillation? #SGEMHOP thesgem.com/2019/02/sgem24... onlinelibrary.wiley.com/doi/full/ 10.11...

| Often >50% of the time | 2% |
| Sometime 25-50% | 8% |
| Rarely <25% | 54% |
| Never | 36% |

95 votes - Final results

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

**TAKE-TO-WORK POINTS**

Rate control for AF consists of a variety of medication options. MgS may be considered as an adjunct in cases of resistant rapid AF. Many of the patients in this study received digoxin, so application of the therapy to differing practices is limited.

**References**

Diagnostic Accuracy of Ultrasound for Confirmation of Endotracheal Tube Placement

Brit Long, MD\textsuperscript{1}, Alex Koyfman, MD\textsuperscript{2}, and Michael Gottlieb, MD, RDMS\textsuperscript{3}

Summary heading Transtracheal ultrasound can accurately guide and verify endotracheal tube placement

Positive LR findings LR+: 34 for transtracheal ultrasound confirmation of endotracheal tube placement

Negative LR findings LR–: 0.01 for transtracheal ultrasound confirmation of endotracheal tube placement

Who was in the studies 17 studies comprising 1,595 patients, with 12 studies conducted in the ED

NARRATIVE

Endotracheal intubation is a common intervention in the emergency department (ED) and prehospital setting. Direct visualization of endotracheal tube (ETT) placement through the vocal cords is limited at times, and esophageal intubation can be dangerous if not recognized.\textsuperscript{1} Therefore, additional methods (e.g., lung auscultation, esophageal detector devices, capnography) are necessary for confirmation of tube placement. However, these methods are not always reliable.\textsuperscript{2–4} Point-of-care ultrasonography (POCUS) has increasingly been used as a potential confirmatory tool for ETT confirmation. The 2015 Advanced Cardiac Life Support guidelines state that POCUS may be a useful adjunct for ETT confirmation.\textsuperscript{5}

The meta-analysis discussed here included prospective observational or randomized controlled trials evaluating transtracheal POCUS for ETT placement confirmation in patients older than 18 years.\textsuperscript{6} All studies included a confirmatory test for comparison (e.g., end-tidal capnography, colorimetric capnography, direct visualization). The primary outcome was diagnostic accuracy of transtracheal POCUS for ETT confirmation, with subgroup analyses including location, provider specialty, provider experience, transducer type, and POCUS technique. The authors also assessed time to confirmation as a secondary outcome.

The authors of the meta-analysis identified 17 studies (n = 1,595 patients) that met their inclusion criteria. Twelve studies were performed in the ED, and five studies were conducted in the operating room. Overall, POCUS was 98.7% sensitive (95% confidence interval [CI] = 97.8% to 99.2%) and 97.1% specific (95% CI = 92.4% to 99.0%), with a positive likelihood ratio (LR+) of 34.4 (95% CI = 12.7 to 93.1) and a negative likelihood ratio (LR–) of 0.01 (95% CI = 0.01 to 0.02). Area under the receiver operating characteristic curve demonstrated a high degree of accuracy (area under the curve = 0.994; 95% CI = 0.982 to 0.998). The mean time to confirmation was 13.0 seconds (95% CI = 12.0 to 14.0...

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Received April 1, 2019; revision received April 22, 2019; accepted April 25, 2019.

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

MG, BL, and AK conceived the idea for this manuscript and contributed substantially to the writing and editing of the review. The authors obtained approval from Dr. Zehtabchi for this submission, who also reviewed a draft of the manuscript before submission. This review does not reflect the views or opinions of the U.S. government, Department of Defense, U.S. Army, U.S. Air Force, Brooke Army Medical Center, or SAUSHEC EM Residency Program.

Supervising Editor: Shahriar Zehtabchi, MD.

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ACADEMIC EMERGENCY MEDICINE 2019;26:1096–1098.

ISSN 1553-2712 © 2019 by the Society for Academic Emergency Medicine doi: 10.1111/acem.13773
CAVEATS

Although POCUS is a valuable tool for confirmation of ETT placement, it is dependent on the individual provider’s ability to obtain and interpret appropriate images. Thus, it is important that providers receive adequate training before this technique is utilized routinely. Included studies demonstrated significant variation in POCUS training protocols. However, there was no significant difference in accuracy with respect to the training protocol. Of note, a prior study has demonstrated no statistically significant difference in accuracy but noted that providers preferred the linear versus curvilinear transducer, and the selected POCUS finding impact diagnostic accuracy of POCUS for ETT confirmation.

Further studies are needed to directly evaluate whether static versus dynamic technique, linear versus curvilinear transducer, and the selected POCUS finding impact diagnostic accuracy of POCUS for ETT confirmation.

Based on the existing evidence, POCUS appears to be highly sensitive and specific for guiding and verifying ETT placement. POCUS is easily available, rapid, noninvasive, and does not depend on ventilation for confirmation. Therefore, we have assigned a color recommendation of green (benefit > harm) to this technique.

Editor’s Note: Brass Tacks are concise reviews of published evidence. This series is a result of collaboration between Academic Emergency Medicine and the evidence-based medicine website, www.TheNNT.com. For inquiries please contact the section editor, Shahriar Zehtabchi, MD (Shahriar.zehtabchi@downstate.edu).

References


Procainamide Versus Amiodarone for Stable Ventricular Tachycardia

Kyle Kelson, MD1, and Ian deSouza, MD1

Color Yellow

Summary heading Procainamide for termination of stable VT is associated with fewer adverse cardiac events and may be more effective for cardioversion compared to amiodarone.

Benefits in NNT NNT of four in favor of procainamide to convert one more patient with stable VT to baseline rhythm.

Benefit in percentage 29% higher chance of conversion to baseline rhythm with procainamide as compared to amiodarone.

Harms in NNH NNH of three against amiodarone for one more patient to experience major adverse cardiac event.

Harms in percentage 32% higher chance of a major cardiac event with amiodarone compared to procainamide.

Efficacy endpoint(s) Pharmacologic conversion to baseline rhythm within 40 minutes without need for electrical cardioversion.

Harm endpoint(s) Major cardiac adverse events within 40 minutes of administration: clinical hypoperfusion, acute heart failure, hypotension, increased tachycardia, polymorphic ventricular tachycardia.

Who was in the studies? 74 adults with hemodynamically stable, wide-QRS tachycardia.

NARRATIVE

Electrical cardioversion is an effective treatment for termination of ventricular tachycardia (VT)1,2 but is typically performed with procedural sedation and thus involves associated risk. In hemodynamically stable VT, pharmacologic cardioversion is an option. Historically, lidocaine, amiodarone, procainamide, and sotalol have been used for pharmacologic cardioversion, based mostly on expert opinion. Lidocaine has fallen out of favor because it was shown to be inferior to both procainamide and sotalol.1,3–5 The use of amiodarone, initially suggested based on extrapolation from cardiac arrest treatment,6 has been challenged by two retrospective analyses, albeit limited in design.7,8 The American Heart Association (AHA) recommends procainamide (IIa) over amiodarone (IIb) for pharmacologic conversion of VT,1,4 whereas the European Resuscitation Council (ERC) favors amiodarone.5

A prior retrospective study9 failed to demonstrate a difference in efficacy between amiodarone and procainamide for cardioversion of stable VT. The trial discussed here10 is the only known randomized controlled trial (RCT) that compares the two drugs for this purpose. This multicenter study randomized 74 patients to receive procainamide (10 mg/kg over 20 minutes) or amiodarone (5 mg/kg over 20 minutes) for stable wide-QRS complex tachycardia presumed to be VT. The researchers found that subjects in the procainamide group were significantly less likely to experience harm as the primary outcome, a major adverse cardiac event (odds ratio [OR] = 0.1, 95% confidence interval [CI] = 0.04 to 0.6, absolute risk difference [ARD] = 32%, NNH = 3). They also report an advantage in a secondary outcome, conversion to baseline rhythm (OR = 3.3, 95% CI = 1.2 to 9.3, ARD = 29%, NNT = 4).

CAVEATS

Stable VT is uncommon in most settings and therefore difficult to investigate prospectively. This study was small with 74 subjects (out of a calculated sample

From the 1Department of Emergency Medicine, SUNY Downstate Medical Center, Brooklyn, NY. Received February 1, 2019; revision received April 11, 2019; accepted April 12, 2019. The authors have no relevant financial information or potential conflicts to disclose. Supervising Editor: Shahriar Zehtabchi, MD. Address for correspondence and reprints: Kyle Kelson, MD; e-mail: krkelson@gmail.com. ACADEMIC EMERGENCY MEDICINE 2019;26:1099–1101.
size of 302) enrolled over 6 years. It was stopped early due to difficulty in enrollment.

In addition to a small sample size, early stoppage, a lack of blinding, and unclear concealment of allocation, there are other potential confounding factors. Two electrophysiologists judged 90% of rhythms to be “probable/definite VT” implying that up to 10% of enrolled patients may have had supraventricular tachycardia (SVT). The prevalence of underlying cardiomyopathy and risk of hypotension may have differed in the proportions with SVT and VT. SVT can be terminated by amiodarone, and procainamide has been previously recommended for treatment of refractory SVT. Without knowing the comparative effectiveness of amiodarone and procainamide for SVT, potential contamination of 10% of patients having SVT has an unknown effect on the results.

The trial also excluded patients whose wide-QRS tachycardia was terminated with adenosine prior to randomization. These patients were considered to have SVT; however, a proportion of idiopathic VTs will respond to adenosine therapeutically. The exclusion of ischemia-related and adenosine-responsive VTs would potentially narrow applicability.

The trial used drug doses that deviated from those recommended by current guidelines. The amiodarone dose in the study (5 mg/kg over 20 minutes) is similar to the ERC recommendation but higher than the AHA’s 150 mg (2 mg/kg for a 75-kg patient) over 10 minutes, but a repeat dose would be comparable over a 20-minute period. This may have resulted in more adverse events due to a larger dose of amiodarone being administered rapidly than if practicing according to AHA guidelines assuming that the patient would respond to the first 150-mg bolus. On the other hand, the procainamide dose (10 mg/kg over 20 minutes) is about in the middle of the 20 to 50 mg/min range recommended by AHA, although practicing according to AHA guidelines would have continued the infusion past 20 minutes to a maximum dose of 17 mg/kg either until rhythm conversion or until an adverse effect (hypotension, QRS prolongation > 50%) occurred. This procainamide dosing in the trial may have resulted in both lower major adverse cardiac event rate and lower efficacy as compared to AHA dosing.

Finally, the study focused on major cardiac adverse events (defined as clinical hypoperfusion, hypotension, signs of heart failure, increase in tachycardia, or development of polymorphic VT) as a primary outcome, which we have reported as NNH. The benefit endpoint (conversion to the baseline rhythm) was only a secondary outcome, and the study was not powered to measure this outcome. This leaves the authors only able to conclude that procainamide resulted in fewer adverse events, while evidence of superior cardioversion efficacy is hypothesis-generating only.

In summary, the evidence from this RCT is weak. It may also be the best available data well into the future, as evidenced by the researchers’ laudable, ultimately Herculean, 6-year effort to generate even these data. While the results nominally favor the use of procainamide for pharmacologic conversion of stable VT and align with a recent review of the existing literature, a true answer will remain elusive until high-quality RCTs are performed. Electrical cardioversion likely remains the most effective therapy for VT. Whenever possible, the risks and benefits should be discussed with the patient and the choice of electrical versus pharmacologic cardioversion be made on a case-by-case basis. For this reason, we have assigned a color recommendation of “yellow” (unclear if benefits) to this summary.

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References


Resolution of Acute Priapism in Two Children With Sickle Cell Disease Who Received Nitrous Oxide

Michael H. Greenwald, MD¹,², Colleen K. Gutman, MD¹,², and Claudia R. Morris, MD¹,²

ABSTRACT

Background: Nitrous oxide (N₂O) is an inhalational medication that has anxiolytic, amnestic, potent venodilatory and mild-to-moderate analgesic properties commonly used in the emergency department (ED) setting. N₂O has a rapid onset of action (<5 minutes) and recovery (<5 minutes) and can be quickly titrated to effect without the need for IV access. It has few side effects, does not require renal or hepatic metabolism for excretion and has no reports of allergic reaction. Priapism is a serious complication of sickle cell disease (SCD) affecting approximately 35% of males, with an adverse impact on quality of life. Treatment options are limited and not evidence based, including hydration, alkalization, analgesia, oxygenation to prevent further sickling, and exchange transfusion. Patients who do not respond within 4 hours often require a painful invasive procedure that includes aspiration of blood from the corpus cavernosum and phenylephrine injections. Case reports have described a therapeutic benefit from oral pseudoephedrine, sildenafil, and intravenous (IV) arginine, however controlled clinical trials are lacking. Although a 50:50 nitrous oxide/oxygen mix is commonly used in France to enhance analgesia in patients with SCD and vasoocclusive pain events (VOE) not sufficiently responding to IV morphine, there are no reports of its use to treat priapism. We describe the effects of N₂O for the treatment of acute priapism associated with SCD in a pediatric ED.

Methods: This is a case series of two adolescent boys with Hb-SS who on 3 separate occasions presented to the ED with acute priapism that failed oral therapy (pseudoephedrine and opioids). N₂O gas was utilized to help facilitate IV catheter placement.

Results: In each presentation (at ages 8 and 10 years for patient 1; age 15 years for patient 2), the patient experienced complete resolution of the priapism within 4-15 min of receiving N₂O (max 60%). The patients were discharged from the ED following each presentation and had no recurrence during the subsequent week.

Conclusions: Priapism is a challenging complication of SCD associated with long-term morbidity and a paucity of treatment options. Opioids are commonly used. Given the risks and inconsistent results of current recommended therapy, N₂O may represent a potential opioid-sparing treatment option for priapism presenting to the ED that warrants further investigation. Although anecdotal, N₂O inhalation is an intervention to consider during a time when a treating ED physician may have few alternatives.
NOTE FROM THE EDITOR-IN-CHIEF

This special contribution presents a case series of a novel treatment. By policy, AEM does not typically review case reports or small case series. However, the editors considered the burden of disease caused by priapism in patients with sickle cell disease to be serious enough to warrant publication of this article. We hope this case series helps to motivate the organization and funding of a formal trial of nitrous oxide for this common condition.

Jeffrey A. Kline MD
Editor-in-Chief, AEM

OVERVIEW OF PRIAPISM IN PATIENTS WITH SICKLE CELL DISEASE

Priapism, an unwanted, persistent, painful penile erection unrelated to sexual stimulation, is a serious complication of sickle cell disease (SCD). The prevalence of priapism among males with SCD is high, with estimates ranging from 27.5% to 42% and the majority of individuals thought to have at least one episode by age 20. Priapism in SCD is primarily ischemic and is a urologic emergency. Males with SCD may also experience recurrent intermittent priapism (RIP), with recurrent self-limited episodes of prolonged erections that are associated with, and can progress to, major ischemic priapism. Ischemic priapism and RIP have an adverse impact on quality of life, are associated with high rates of erectile dysfunction and higher inpatient SCD costs, and are more likely to lead to hospital admission in males than vasoocclusive pain events (VOE). The mechanism is likely multifactorial but includes hemolysis-mediated dysregulation of the arginine–nitric oxide signaling pathway, downregulated phosphodiesterase-5 protein expression, and dysregulation of adenosine-mediated vasodilation in the penis. Testosterone deficiency and oxidative stress have also been implicated.

OVERVIEW OF TREATMENT OPTIONS FOR PRIAPISM IN SCD

Treatment options for priapism in SCD are limited and not evidence-based, including hydration, alkalization, analgesia, oxygenation to prevent further sickling, and exchange transfusion. A 2017 Cochrane Database analysis found a lack of evidence for the benefits or risks of treatment options that included stilboesterol, sildenafil, and ephedrine compared to placebo. Patients who do not respond to treatments within 4 hours often require a painful invasive procedure that includes aspiration of blood from the corpus cavernosum and phenylephrine injections. Despite the time-dependent nature of treatment, these procedures are performed less often and with longer times to intervention in patients presenting with priapism and SCD than those patients with priapism alone. Case reports have described a therapeutic benefit from oral pseudoephedrine, sildenafil, intravenous (IV) arginine, and IV ketamine, however, controlled clinical trials are lacking. Boys with SCD who receive care at the Aflac Cancer and Blood Disorder Center of Children’s Healthcare of Atlanta (CHOA) are educated to trial oral pseudoephedrine at home for episodes of priapism and to present to the ED in the case of treatment failure with sustained priapism of greater than 2 to 4 hours, depending on the severity. Once in the ED, these individuals are initially placed on our institutional nurse-initiated SCD pain protocol, which includes oral and/or parenteral opioids, IV ketorolac, and hypotonic maintenance IV fluids. In addition, a urology consultation is obtained for potential surgical interventions.

OVERVIEW OF NITROUS OXIDE GAS

Nitrous oxide (N₂O) is an inhalational medication that has anxiolytic, amnestic, potent venodilatory, and mild-to-moderate analgesic properties commonly used in the emergency department (ED) setting. N₂O has a rapid onset of action (<5 minutes) and recovery (<5 minutes) and can be quickly titrated to effect without the need for IV access. It has few side effects, does not require renal or hepatic metabolism for excretion, and has no reports of allergic reaction. N₂O can be used in ED settings for analgesia during painful procedures, such as IV placement, venipuncture, laceration repair, foreign body removal, and incision and drainage of abscesses, but it is not typically used in the treatment of pain in SCD in the United States. Of interest, a 50:50 N₂O:oxygen mix is commonly used in France to enhance analgesia in patients with SCD and VOE not sufficiently responding to IV morphine, although there are no reports of its use to treat...
priapism. We describe a case series of two patients with three instances of SCD-related priapism that had failed treatment with oral pseudoephedrine at home and that resolved completely after administration of N₂O. This work received an institutional review board determination of not human subjects research.

**CASE SERIES**

Over the past 4 years (January 2015–December 2018), a total of 71 episodes of priapism were evaluated in the ED in 26 unique patients at CHOA. Prior to this case series, a sentinel patient with SCD presented with priapism that resolved with N₂O administration. The details of this patient have been lost to memory, but the treating physician (MHG) made note of the association. In our case series, patient 1 was an 8-year-old male with HbSS SCD at the time of his first of two ED presentations reported here (Table 1). He had a history of recurrent priapism that had required surgical intervention in the past. Oral pseudoephedrine, ibuprofen, and hydrocodone were taken at home, and he received intranasal fentanyl in the ED prior to IV placement. His second presentation occurred 13 months later, when he was 10 years old. He had failed oral pseudoephedrine at home. No additional medications were given in the ED prior to IV placement. Patient 2 was a 15-year-old male with HbSS SCD and recurrent priapism. He had failed oral pseudoephedrine at home and was given opiates and nonsteroidal anti-inflammatory drugs on arrival to the ED. At all three presentations, N₂O (maximum 60%) was used to facilitate IV placement; patient 1 experienced detumescence after 15 minutes of N₂O on his first presentation and after 5 minutes on his second presentation. At the second presentation, IV placement with N₂O was trialed early in the visit prior to initiation of the SCD pain guidelines as the ED physician recognized him as the same patient whose previous priapism had rapidly resolved with N₂O administration. Patient 2 experienced detumescence after 4 minutes. In all three instances, there was no recurrence of priapism requiring intervention in the subsequent week. Although the sample size of this case series is small and causality cannot be assumed, our observations suggest that N₂O may be a novel treatment modality for SCD-related priapism. The mechanism for this finding is not clear and warrants further investigation.

**DISCUSSION**

Nitrous oxide has few side effects and rare serious adverse effects when used infrequently; however, recurrent N₂O use or abuse can cause neurologic complications through impact on vitamin B₁₂ (cobalamin) metabolism. Ogundipe et al. reported three cases of peripheral neuropathy in young adults with SCD who had frequent, prolonged N₂O exposure. In all three patients, the neuropathy resolved after administration of intramuscular vitamin B₁₂. Another case report of combined spinal cord degeneration was reported in a 20-year-old man with SCD due to abnormal cobalamin metabolism induced by repeated use of nitrous gas as treatment for recurrent VOEs. Patients with SCD may be at higher risk of B₁₂ deficiency due to increased erythrocyte turnover resulting from hemolysis or coexisting folate deficiency. Indeed, several studies have demonstrated lower plasma cobalamin levels in patients with SCD compared to African Americans without SCD. Kamineni and colleagues found B₁₂ deficiency (defined as a serum cobalamin level of <200 pg/mL) in 18.1% (19/105) of patients with SCD compared to 9.8% (11/112) in non-SCD patients. None of the SCD patients with low B₁₂ levels had neurologic symptoms that would help to identify them clinically. However, N₂O use for anxiolysis in the pediatric ED is typically brief, and in our case series all episodes of priapism resolved within 15 minutes with N₂O. One-time brief use of N₂O should be safe; however, repeated or prolonged exposure may pose neurologic risks in the B₁₂-deficient patient. Given the low cost of intramuscular B₁₂ injection, coadministration of cobalamin during N₂O therapy could mitigate risk of neurologic sequelae and warrants further consideration.

Priapism is a challenging complication of SCD associated with long-term morbidity and a paucity of treatment options. Given the risks and inconsistent results of current recommended therapy, N₂O may represent a novel treatment option for priapism presenting to the ED after treatment failure with oral vasodilators that warrants further investigation.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (Years)</th>
<th>Genotype</th>
<th>Time to Detumescence With N₂Oᵃ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>HbSS</td>
<td>15 min</td>
</tr>
<tr>
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<td>10</td>
<td>HbSS</td>
<td>5 min</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>HbSS</td>
<td>4 min</td>
</tr>
</tbody>
</table>

SCD = sickle cell disease
ᵃMax 60% N₂O in all instances.
References

To the Editor:

Dr. Driver and colleagues conducted a well-designed study to determine the effect of the administration of a neuromuscular-blocking agent before the administration of a sedative agent for rapid sequence intubation/induction (RSI) in the emergency department (ED) setting. This study suggests there is a reduction in the time to intubation by approximately 6 seconds by administering a neuromuscular blocking agent first, which defies conventional teaching that a sedative agent should be administered first. This brief reduction in time to intubation is only likely to be significant in the most critically ill patients requiring RSI in the ED, such as those with severe metabolic acidosis. I agree that patients who are most susceptible to a reduction in pH during ED RSI and during the safe apneic period are those who may benefit the most from future studies regarding the timing of RSI induction and neuromuscular-blocking agents.

Although the authors’ accurately state that there is no way to reliably measure the actual apnea times, I would like to propose the following amendment to their statement: end-tidal CO₂ capnography during ED RSI may be the most reliable method to determine the timing of the onset of apnea.

The use of end-tidal CO₂ capnography should not be a foreign concept to ED providers. In the American College of Emergency Physicians “Clinical Policy: Procedural Sedation and Analgesia in the Emergency Department,” end-tidal CO₂ capnography is a Level B recommendation to detect apnea earlier than pulse oximetry and/or clinical assessment alone. Furthermore, the Difficult Airway Society recommends that a continuous capnography waveform with appropriate inspired and end-tidal values of CO₂ is the criterion standard for confirming ventilation of the lungs. This guideline also suggests that end-tidal CO₂ should be available in every location where a patient may require anesthesia.

Our ED has addressed the issue of human factors in determining the time of intubation and the use of end-tidal CO₂, which suggests an advantage of 20 seconds versus clinical gestalt to determine the onset of apnea during ED RSI. Finally, I understand that adding an additional quantitative tool to help measure the onset of apnea may increase the complexity of tracheal intubation in the ED, but considering that seconds matter for our most critically ill patients undergoing RSI in the ED, I recommend that future ED airway studies intending to measure intubation times also include the use of end-tidal CO₂ measurements to best measure the onset of apnea.

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Supervising Editor: John H. Burton, MD

References


In Reply:

Thank you for your comments in response to our secondary analysis examining drug order in rapid sequence intubation. In research investigations where apnea is a key outcome, it seems reasonable to use waveform capnography, when feasible, to better quantify the onset of apnea. Its role in routine clinical care is less clear. Assuming that apnea detected by nasal waveform capnography correlates with onset of adequate or optimal intubating conditions (i.e., full muscle relaxation) and that capnography outperforms physician gestalt of muscle relaxation, routine use of waveform capnography could improve time to intubation. Your preliminary evidence supports this, and we look forward to future work in this area. In our experience, however, the effects of the sedative agent (either etomidate or ketamine) sometimes cause apnea prior to full neuromuscular blockade, misaligning the timing of apnea and muscle relaxation. Attempting intubation before full muscle relaxation can lead to vomiting or first attempt failure. Additionally, the use of flush rate preoxygenation occasionally washes out the capnography waveform, making apnea detection with this method difficult.

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REFERENCES

Jon B. Cole, MD
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Supervising Editor: John H. Burton, MD
It was another steamy summer night in the city. I was paying my dues as a brand new attending covering the holiday weekend. I was on my third of four night shifts in a row with the worst acid reflux of my life. We were busier than usual, seeing a variety of firework injuries on top of the bread-and-butter cases of a typical Saturday night. The night shift holiday potluck would go untouched that night till well after sunrise. The traumas rolled in one after the next keeping us on alert and our trauma surgeons cloaked in sweat in the OR. In a rare moment of refuge, I looked around at my amazing team and remarked on how they were handling the deluge of human suffering while foregoing their basic human necessities. The reprieve was short-lived when the next alert sounded.

"Philly PD Incoming—young female, stab wound to the neck."

Resources were mobilized with an all-too-familiar ease as we prepared for the worst, yet hoped for the best. I headed out to the ambulance bay to wait. I fought off an anticipatory shiver as the sirens approached. The police cruiser rounded the hospital and screeched to a halt. I threw open the back door. I heard someone whisper “Oh, God.” Lying across the laps of two others, there was a girl wearing a white sundress soaked in red. Frantic screams echoed in the ambulance bay. “Save my sister! Save my sister!” She was swept into the trauma bay, access obtained and her airway secured. But, there were no spontaneous respirations and there was no pulse. Barely a moment passed between the decision and the cut. The sound of ribs breaking filled the bay. Red covered the floor while a young healthy heart was delivered from its pericardium. Her tank was empty. Between the burning in my throat and pure adrenaline, I tried not to vomit as I helped my resident place a chest tube. Across the table, the trauma attending found the damage—a slash to the back of the heart. The heart filled as he held it closed and fibrillated back to life. But the recovery was improbable and the repair impossible. Despite the seamlessly run resuscitation, we were not in control. Time of death was called. Someone called for a moment of silence, but it was already quiet. Then, the hustle and bustle of a busy department called everyone back to order.

We had to clean up, decon, document, and move on to other patients and their emergencies. Before that, someone had to inform the family. I had already given the dreaded speech three times during that shift and at least eight times that week. I just could not do it again. I could not bring myself to tell yet another family that their young person had died tragically and unnecessarily. I halfheartedly listened to the residents running the list, as I popped what seemed like the 30th antacid of the shift before excusing myself abruptly. I walked out into the night air past the police tape and sat on the sidewalk. A single tear fell before I could prevent it. I stood up, took a deep breath and walked back into the chaos to finish the shift. The emotions had to wait until later.

Driving home, the tears came with more ease as Norah Jones “Humble Me” played on repeat. I arrived home, kissed my 3-year-old, and headed to bed. Sleep did not come. I walked like a zombie to the bathroom and vomited. My suspicions were confirmed. I was a new attending and I was also pregnant. After this revelation, I was able to finally close my eyes and find rest.
Re: SAEM Annual Meeting Abstracts