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Reviews *Reenvisioned*: Supporting Enhanced Practice Improvement for Hospitalists

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As part of the *Journal of Hospital Medicine's*® commitment to our readership, we are excited to announce innovative new review formats, designed for busy hospitalists. The state of knowledge in our field is changing rapidly, and the 21st century poses a conundrum to clinicians in the form of increasingly complex studies and guidelines amidst ever-decreasing time to digest them. As a result, it can be challenging for hospitalists to access and interpret recently published research to inform their clinical practice. Because we are committed to practical innovation for hospitalists, starting in 2019, *JHM* will offer focused yet informative content that places important advances into relevant clinical or methodological context and provides our readers with information that is accessible, meaningful, and actionable—all in a more concise format.

Our new *Clinical Guideline Highlights for the Hospitalist* is a brief, targeted review of recently published clinical guidelines, distilling the major recommendations relevant to hospital medicine and placing them in context of the available evidence. This review format also offers a critique of gaps in the literature and notes areas ripe for future study. In this issue, we debut two articles using this new approach—one aimed at adult hospitalists and the other at pediatric hospitalists—regarding recently published studies and guidelines about maintenance intravenous fluids.[1-5]

In 2019, we will also introduce a second new format, called *Progress Notes*. These reviews will be shorter than JHM's traditional review format, and will accept two types of articles: clinical and methodological. The clinical *Progress Notes* will provide an update on the last several years of evidence related to diagnosis, treatment, risk stratification, and/or prevention of a clinical problem highly pertinent to hospitalists. The methodological *Progress Notes* will provide our readers with insight into the application of quantitative, qualitative, and quality improvement methods commonly used in work published in this journal. Our aim is to use *Progress Notes* as a way to enhance both clinical practice and scholarship efforts by our readers.

Finally, we will introduce "Hospital Medicine: The Year in Review," an annual feature that concisely compiles and critiques the top articles in both adult and pediatric hospital medicine over the past year. The "Year in Review" will serve as a written corollary to the popular "Updates in Hospital Medicine" presentation at the Society of Hospital Medicine annual meeting, and will highlight important research that advanced our field or provided us a fresh perspective on hospitalist practice.

As we introduce these new review formats, it is important to note that *JHM* will continue to accept traditional, long-form reviews on any topic relevant to hospitalists, with a preference for rigorous systematic reviews or meta-analyses. Equally important is that *JHM*'s overarching commitment remains unchanged: support clinicians, leaders, and scholars in our field in their pursuit of delivering evidence-based, high-value clinical care. We hope you enjoy these new article formats and we look forward to your feedback.

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Beyond Reporting Early Warning Score Sensitivity: The Temporal Relationship and Clinical Relevance of "True Positive" Alerts that Precede Critical Deterioration

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BACKGROUND: Clinical deterioration is difficult to detect in hospitalized children. The pediatric Rothman Index (pRI) is an early warning score that incorporates vital signs, laboratory studies, and nursing assessments to generate deterioration alerts.

OBJECTIVES: (1) Evaluate the timing of pRI alerts and clinicians recognizing deterioration or escalating care prior to critical deterioration events (CDEs) and (2) determine whether the parameters triggering alerts were clinically related to deterioration.

DESIGN: CDEs are unplanned transfers to the intensive care unit with noninvasive ventilation, tracheal intubation, and/or vasopressor infusion in the 12 hours after transfer. Using one year of data from a large freestanding children's hospital without the pRI, we analyzed CDEs that would have been preceded by pRI alerts. We (1) compared the timing of pRI alerts to time-stamped notes describing changes in patient status and orders reflecting escalations of care and (2) identified score component(s) that caused alerts to trigger and determined whether these were clinically related to CDE etiology.

RESULTS: Fifty CDEs would have triggered pRI alerts if the pRI had been in use (sensitivity 68%). In 90% of CDEs, the first clinician note reflecting change in patient status and/or the first order reflecting escalation of care preceded the first pRI alert. All of the vital sign and laboratory components of the pRI and 51% of the nursing components were clinically related to the etiology of the CDE.

CONCLUSIONS: Evidence that clinicians were aware of deterioration preceded pRI alerts in most CDEs that generated alerts in the preceding 24 hours. *Journal of Hospital Medicine* 2019:14:138-143. Published online first August 29, 2019. © 2018 Society of Hospital Medicine.

Patients at risk for clinical deterioration in the inpatient setting may not be identified efficiently or effectively by health care providers. Early warning systems that link clinical observations to rapid response mechanisms (such as medical emergency teams) have the potential to improve outcomes, but rigorous studies are lacking.[1] The pediatric Rothman Index (pRI) is an automated early warning system sold by the company PeraHealth that is integrated with the electronic health record. The system incorporates vital signs, labs, and nursing assessments from existing electronic health record data to provide a single numeric score that generates alerts based on low absolute scores and acute decreases in score (low scores indicate high mortality risk).[2] Automated alerts or rules based on the pRI score are meant to bring important changes in clinical status to the attention of clinicians.

Adverse outcomes (eg, unplanned intensive care unit [ICU] transfers and mortality) are associated with low pRI scores, and scores appear to decline prior to such events.[2] However, the limitation of this and other studies evaluating the sensitivity of early warning systems[3-6] is that the generated alerts are assigned "true positive" status if they precede clinical deterioration, regardless of whether or not they provide meaningful information to the clinicians caring for the patients. There are two potential critiques of this approach. First, the alert may have preceded a deterioration event but may not have been clinically relevant (eg, an alert triggered by a finding unrelated to the patient's acute health status, such as a scar that was newly documented as an abnormal skin finding and as a result led to a worsening in the pRI). Second, even if the preceding alert demonstrated clinical relevance to a deterioration event, the clinicians at the bedside may have been aware of the patient's deterioration for hours and have already escalated care. In this situation, the alert would simply confirm what the clinician already knew.

To better understand the relationship between early warning system acuity alerts and clinical practice, we examined a cohort

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of hospitalized patients who experienced a critical deterioration event (CDE)[7] and who would have triggered a preceding pRI alert. We evaluated the clinical relationship of the alert to the CDE (ie, whether the alert reflected physiologic changes related to a CDE or was instead an artifact of documentation) and identified whether the alert would have preceded evidence that clinicians recognized deterioration or escalated care.

METHODS

Patients and Setting

This retrospective cross-sectional study was performed at Children's Hospital of Philadelphia (CHOP), a freestanding children's hospital with 546 beds. Eligible patients were hospitalized on nonintensive care, noncardiology, surgical wards between January 1, 2013 and December 31, 2013. The CHOP Institutional Review Board (IRB) approved the study with waivers of consent and assent. A HIPAA Business Associate Agreement and an IRB Reliance Agreement were in place with PeraHealth to permit data transfer.

Definition of Critical Deterioration Events

Critical deterioration events (CDEs) were defined according to an existing, validated measure[7] as unplanned transfers to the ICU with continuous or bilevel positive airway pressure, tracheal intubation, and/or vasopressor infusion in the 12 hours after transfer. At CHOP, all unplanned ICU transfers are routed through the hospital's rapid response or code blue teams, so these patients were identified using an existing database managed by the CHOP Resuscitation Committee. In the database, the elements of CDEs are entered as part of ongoing quality improvement activities. The time of CDE was defined as the time of the rapid response call precipitating unplanned transfer to the ICU.

The Pediatric Rothman Index

The pRI is an automated acuity score that has been validated in hospitalized pediatric patients.[2] The pRI is calculated using existing variables from the electronic health record, including manually entered vital signs, laboratory values, cardiac rhythm, and nursing assessments of organ systems. The weights assigned to continuous variables are a function of deviation from the norm.[2,8] (See Supplement 1 for a complete list of variables.)

The pRI is integrated with the electronic health record and automatically generates a score each time a new data observation becomes available. Changes in score over time and low absolute scores generate a graduated series of alerts ranging from medium to very high acuity. This analysis used PeraHealth's standard pRI alerts. Medium acuity alerts occurred when the pRI score decreased by ≥30% in 24 hours. A high acuity alert occurred when the pRI score decreased by ≥40% in 6 hours. A very high acuity alert occurred when the pRI absolute score was ≤ 30.

Development of the Source Dataset

In 2014, CHOP shared one year of clinical data with PeraHealth as part of the process of deciding whether or not to implement the pRI. The pRI algorithm retrospectively generated scores and acuity alerts for all CHOP patients who experienced CDEs between January 1, 2013 and December 31, 2013. The pRI algorithm was not active in the hospital environment during this time period; the scores and acuity alerts were not visible to clinicians. This dataset was provided to the investigators at CHOP to conduct this project.

Data Collection

Pediatric intensive care nurses trained in clinical research data abstraction from the CHOP Critical Care Center for Evidence and Outcomes performed the chart review for this study. Chart abstraction comparisons were completed on the first 15 charts to ensure interrater reliability, and additional quality assurance checks were performed on intermittent charts to ensure consistency and definition adherence. We managed all data using Research Electronic Data Capture.[9]

To study the value of alerts labeled as "true positives," we restricted the dataset to CDEs in which acuity alert(s) within the prior 72 hours would have been triggered if the pRI had been in clinical use at the time.

To identify the clinical relationship between pRI and CDE, we reviewed each chart with the goal of determining whether the preceding acuity alerts were clinically associated with the etiology of the CDE. We determined the etiology of the CDE by reviewing the cause(s) identified in the note written by rapid response or code blue team responders or by the admitting clinical team after transfer to the ICU. We then used a tool provided by PeraHealth to identify the specific score components that led to worsening pRI. If the score components that worsened were (a) consistent with a clinical change as opposed to a documentation artifact and (b) an organ system change that was plausibly related to the CDE etiology, we concluded that the alert was clinically related to the etiology of the CDE.

We defined documentation artifacts as instances in nursing documentation in which a finding unrelated to the patient's acute health status, such as a scar, was newly documented as abnormal and led to worsening pRI. Any cases in which the clinical relevance was unclear underwent review by additional members of the team, and the determination was made by consensus.

To determine the temporal relationship among pRI, CDE, and clinician awareness or action, we then sought to systematically determine whether the preceding acuity alerts preceded documented evidence of clinicians recognizing deterioration or escalation of care. We made the *a priori* decision that acuity alerts that occurred more than 24 hours prior to a deterioration event had questionable clinical actionability. Therefore, we restricted this next analysis to CDEs with acuity alerts during the 24 hours prior to a CDE. We reviewed time-stamped progress notes written by clinicians in the 24 hours period prior to the time of the CDE and identified whether the notes reflected an adverse change in patient status or a clinical intervention. We then compared the times of these notes with the times of the alerts and CDEs. Given that documentation of change in clinical status often occurs after clinical intervention, we also reviewed new orders placed in the 24 hours prior to each CDE to determine escalation of care. We identified the following

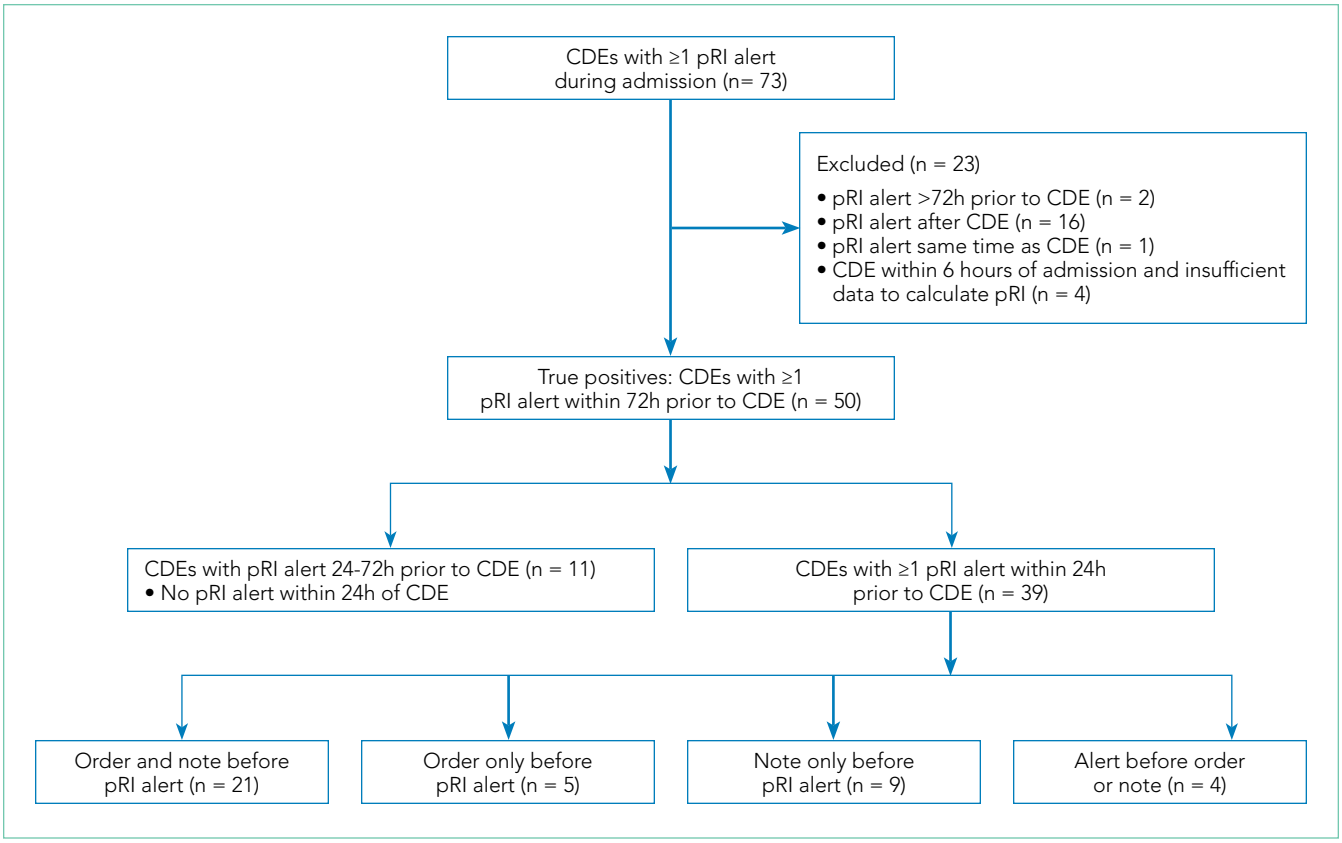

FIG. CDEs selected for inclusion and temporal relationships among escalation orders, clinician notes, and acuity alerts.

Abbreviation: CDEs, critical deterioration event; pRI, pediatric Rothman Index.

orders as reflective of escalation of care independent of specific disease process: administration of intravenous fluid bolus, blood product, steroid, or antibiotic, increased respiratory support, new imaging studies, and new laboratory studies. We then compared the time of each order with the time of the alert and CDE.

RESULTS

During the study period, 73 events met the CDE criteria and had a pRI alert during admission. Of the 73 events, 50 would have triggered at least one pRI alert in the 72-hour period leading up to the CDE (sensitivity 68%). Of the 50 events, 39 generated pRI alerts in the 24 hours leading up to the event, and 11 others generated pRI alerts between 24 and 72 hours prior to the event but did not generate any alerts during the 24 hours leading up to the event (Figure).

Patient Characteristics

The 50 CDEs labeled as true positives occurred in 46 unique patients. Table 1 displays the event characteristics.

Acuity Alerts

A total of 79 pRI alerts preceded the 50 CDEs. Of these acuity alerts, 44 (56%) were medium acuity alerts, 17 (22%) were high acuity alerts, and 18 (23%) were very high acuity alerts. Of the 50 CDEs that would have triggered pRI alerts, 33 (66%) would have triggered a single acuity alert and 17 (34%) would have triggered multiple acuity alerts.

Of the 50 CDEs, 39 (78%) had a preceding acuity alert within 24 hours prior to the CDE. In these cases, the alert preceded the CDE by a median of 3.1 hours (interquartile range of 0.7 to 10.3 hours).

We assessed the score components that caused each alert to trigger. All of the vital sign and laboratory components were assessed as clinically related to the CDE's etiology. By contrast, about half of nursing assessment components were assessed as clinically related to the etiology of the CDE (Table 2). Abnormal cardiac, respiratory, and neurologic assessments were most frequently assessed as clinically relevant.

Escalation Orders

To determine whether the pRI alert would have preceded the earliest documented treatment efforts, we restricted evaluation to the 39 CDEs that had at least one alert in the 24-hour window prior to the CDE. When we reviewed escalation orders placed by clinicians, we found that in 26 cases (67%), the first clinician order reflecting escalation of care would have preceded the first pRI alert within the 24-hour period prior to the CDE. In 13 cases (33%), the first pRI alert would have preceded the first escalation order placed by the clinician. The first pRI alert and the first escalation order would have occurred within the same 1-hour period in 6 of these cases.

Provider Notes

When we reviewed clinician notes for the 39 CDEs that had at least one alert in the 24-hour window prior to the CDE, we found that in 36 cases, there were preceding notes documenting adverse changes in patient status consistent with signs of deterioration or clinical intervention. In 30 cases (77%), the first clinician note preceded the first pRI alert within the 24-hour period prior to the CDE. In nine cases (23%), the first pRI alert would have preceded the first note. The first pRI alert and the first note would have occurred within the same 1-hour period in 4 of these cases.

Temporal Relationships

In Supplement 2, we present the proportion of CDEs in which the order or note preceded the pRI alert for each abnormal organ system.

The Figure shows the temporal relationships among escalation orders, clinician notes, and acuity alerts for the 39 CDEs with one or more alerts in the 24 hours leading up to the event. In 21 cases (54%), both an escalation order and a note preceded the first acuity alert. In 14 cases (36%), either an escalation order or a note preceded the first acuity alert. In four cases (10%), the alert preceded any documented evidence that clinicians had recognized deterioration or escalating care.

DISCUSSION

The main finding of this study is that 90% of CDE events that generated "true positive" pRI alerts had evidence suggesting that clinicians had already recognized deterioration and/or were already escalating care before most pRI alerts would have been triggered.

The impacts of early warning scores on patient safety outcomes are not well established. In a recent 21-hospital cluster-randomized trial of the BedsidePEWS, a pediatric early warning score system, investigators found that implementing the system does not significantly decrease all-cause mortality in hospitalized children, although hospitals using the BedsidePEWS have low rates of significant CDEs.[10] In other studies, early warning scores were often coimplemented with rapid response teams, and separating the incremental benefit of the scoring tool from the availability of a rapid response team is usually not possible.[11]

Therefore, the benefits of early warning scores are often inferred based on their test characteristics (eg, sensitivity and positive predictive value).[12] Sensitivity, which is the proportion of patients who deteriorated and also triggered the early warning score within a reasonable time window preceding the event, is an important consideration when deciding whether an early warning score is worth implementing. A challenging follow-up question that goes beyond sensitivity is how often an early warning score adds new knowledge by identifying patients on a path toward deterioration who were not yet recognized. This study is the first to address that follow-up question. Our results revealed that the score appeared to precede evidence of clinician recognition of deterioration in 10% of CDEs. In some patients, the alert could have contributed to

TABLE 1. **True Positive Critical Deterioration Event Characteristics**

Characteristic	n (%)
Total events	50
Patient age	
< 6 months	1 (2)
6 months to < 1 year	2 (4)
1 year to < 4 years	12 (24)
4 years to < 12 years	18 (36)
12 years to < 18 years	12 (24)
≥ 18 years	5 (10)
Length of stay	
< 7 days	3 (6)
7 days to < 14 days	10 (20)
14 days to < 30 days	10 (20)
≥ 30 days	27 (54)
Transferring service	
Oncology	14 (28)
Pulmonary	10 (20)
General Pediatrics	9 (18)
Surgical	5 (10)
Adolescent	4 (8)
Other	8 (16)
Etiology of Critical Deterioration Event*	
Respiratory insufficiency	40 (80)
Concern for sepsis	39 (78)
Hemodynamic instability	21 (42)
Electrolyte derangements	16 (32)
Altered mental status/Neurological changes	8 (16)
Cardiopulmonary arrest	1 (2)
Heart failure	1 (2)
Highest level of support after transfer to the ICU	
Invasive ventilation with vasopressor	6 (12)
Invasive ventilation without vasopressor	12 (24)
CPAP or BiPAP with vasopressor	3 (6)
CPAP or BiPAP without vasopressor	22 (44)
Vasopressor alone	7 (14)

*Total exceeds 100% because some CDEs were documented as having multiple etiologies

Abbreviations: BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; ICU, intensive care unit

TABLE 2. **Clinical Relevance of Nursing Assessment pRI Score Components**

Nursing Assessment Component	Total Number of Abnormal Assessments, n	Nursing Assessments Clinically Related to CDE, n (%)	Nursing Assessments Not Clinically Related to CDE, n (%)
Cardiac	10	10 (100)	0 (0)
Food	11	3 (27)	8 (72)
Gastrointestinal	8	1 (12)	7 (88)
Genitourinary	9	2 (22)	7 (78)
Musculoskeletal	4	1 (25)	3 (75)
Neurologic	11	10 (91)	1 (9)
Peripheral vascular system	4	2 (50)	2 (50)
Psychosocial	4	1 (25)	3 (75)
Respiratory	8	7 (88)	1 (12)
Safety	0	0 (0)	0 (0)
Skin	4	0 (0)	4 (100)
Total	73	37 (51)	36 (49)

Abbreviations: CDE, critical deterioration event; pRI, pediatric Rothman Index.

a detection of deterioration that was not previously evident. In the portion of CDEs in which the alert and escalation order or note occurred within the same one-hour window, the alert could have been used as confirmation of clinical suspicion. Notably, we did not evaluate the 16 cases in which a CDE preceded any pRI alert because we chose to focus on "true positive" cases in which pRI alerts preceded CDEs. These events could have had timely recognition by clinicians that we did not capture, so these results may provide an overestimation of CDEs in which the pRI preceded clinician recognition.

Prior work has described a range of mechanisms by which early warning scores can impact patient safety.[13] The results of this study suggest limited incremental benefit for the pRI to alert physicians and nurses to new concerning changes at this hospital, although the benefits to low-resourced community hospitals that care for children may be great. The pRI score may also serve as evidence that empowers nurses to overcome barriers to further escalate care, even if the process of escalation has already begun. In addition to empowering nurses, the score may support trainees and clinicians with varying levels of pediatric expertise in the decision to escalate care. Evaluating these potential benefits would require prospective study.

We used the pRI alerts as they were already defined by PeraHealth for CHOP, and different alert thresholds may change score performance. Our study did not identify additional variables to improve score performance, but they can be investigated in future research.

This study had several limitations. First, this work is a single-center study with highly skilled pediatric providers, a mature rapid response system, and low rates of cardiopulmonary arrest outside ICUs. Therefore, the results that we obtained were not immediately generalizable. In a community environment with nurses and physicians who are less experienced in caring for ill children, an early warning score with high sensitivity may be beneficial in ensuring patient safety.

Second, by using escalation orders and notes from the patient chart, we did not capture all the undocumented ways in which clinicians demonstrate awareness of deterioration. For example, a resident may alert the attending on service or a team may informally request consultation with a specialist. We also gave equal weight to escalation orders and clinician notes as evidence of recognition of deterioration. It could be that either orders or notes more closely correlated with clinician awareness.

Finally, the data were from 2013. Although the score components have not changed, efforts to standardize nursing assessments may have altered the performance of the score in the intervening years.

CONCLUSIONS

In most patients who had a CDE at a large freestanding children's hospital, escalation orders or documented changes in patient status would have occurred before a pRI alert. However, in a minority of patients, the alert could have contributed to the detection of deterioration that was not previously evident.

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retrospectively. This service was provided free of charge in 2014 during the time period when Children's Hospital of Philadelphia was considering purchasing and implementing PeraHealth software, which it subsequently did. We did not receive any funding for the study from PeraHealth. PeraHealth personnel did not influence the study design, the interpretation of data, the writing of the report, or the decision to submit the article for publication.

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Reducing Unnecessary Treatment of Asymptomatic Elevated Blood Pressure with Intravenous Medications on the General Internal Medicine Wards: A Quality Improvement Initiative

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BACKGROUND: Asymptomatic elevated blood pressure (BP) is common in the hospital. There is no evidence supporting the use of intravenous (IV) antihypertensives in this setting.

OBJECTIVE: To determine the prevalence and effects of treating asymptomatic elevated BP with IV antihypertensives and to investigate the efficacy of a quality improvement (QI) initiative aimed at reducing utilization of these medications.

DESIGN: Retrospective cohort study.

SETTING: Urban academic hospital.

PATIENTS: Patients admitted to the general medicine service, including the intensive care unit (ICU), with ≥1 episode of asymptomatic elevated BP (>160/90 mm Hg) during hospitalization.

INTERVENTION: A two-tiered, QI initiative.

MEASUREMENTS: The primary outcome was the monthly proportion of patients with asymptomatic elevated BP treated with IV labetalol or hydralazine. We also analyzed median BP and rates of balancing outcomes (ICU transfers, rapid responses, cardiopulmonary arrests).

RESULTS: We identified 2,306 patients with ≥1 episode of asymptomatic elevated BP during the 10-month preintervention period, of which 251 (11%) received IV antihypertensives. In the four-month postintervention period, 70 of 934 (7%) were treated. The odds of being treated were 38% lower in the postintervention period after adjustment for baseline characteristics, including length of stay and illness severity (OR = 0.62; 95% CI 0.47-0.83; *P* = .001). Median SBP was similar between pre- and postintervention (167 vs 168 mm Hg; *P* = .78), as were the adjusted proportions of balancing outcomes.

CONCLUSIONS: Hospitalized patients with asymptomatic elevated BP are commonly treated with IV antihypertensives, despite the lack of evidence. A QI initiative was successful at reducing utilization of these medications. *Journal of Hospital Medicine* 2019;14:144-150. © 2019 Society of Hospital Medicine

Elevated blood pressure (BP) is common among hospitalized adults, with prevalence estimates between 50% and 70%.[1] Many factors can cause or exacerbate BP elevations in the setting of acute illness, such as pain, anxiety, medication withdrawal, and volume status, among others.[2] While there are clear evidence-based recommendations for treating hypertension (HTN) in the ambulatory setting,[3] guidelines for the management of elevated BP in the hospital are lacking.[4,5]

Hypertensive crises are generally recognized as warranting rapid reduction in BP;[6-8] however, these represent the minority of cases.[9,10] Far more common in the hospital are patients with asymptomatic elevated BP, a population for which there is no high-quality evidence and no guidelines supporting the use of intravenous (IV) antihypertensives.[11,12] Treatment with such medications has been associated with highly variable clinical responses[13-15] and may result in adverse events, such as hypotension.[10]

To date, only a small number of studies have investigated the treatment of asymptomatic elevated BP among hospitalized adults.[10,13-15] These have suggested that IV antihypertensives are utilized frequently in this setting, often for only modestly elevated BPs; however, the studies have tended to be small, not racially diverse, and limited to noncritically ill patients. Furthermore, while it is generally accepted that reducing the use of IV antihypertensives among asymptomatic patients would have no adverse impact, to our knowledge there have been no published studies which have instituted such an initiative while measuring balancing outcomes.

The purpose of this study was to further the existing literature by defining the prevalence and effects of IV antihypertensive medication utilization among a medically complex, multiracial population of asymptomatic medical inpatients using a large electronic dataset and to evaluate the impact of a division-wide,

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two-tiered quality improvement (QI) initiative on the rates of IV antihypertensive utilization and patient outcomes.

METHODS

Setting

The study was conducted at the University of California, San Francisco (UCSF), an 800-bed tertiary care, academic medical center. It was approved by the UCSF Institutional Review Board. General medicine patients at UCSF are distributed between teaching and direct-care (hospitalist) services. The intensive care unit (ICU) is "open," meaning the medicine service acts as the primary team for all nonsurgical ICU patients. This study included all adult general medicine patients admitted to UCSF Medical Center between January 1, 2017 and March 1, 2018, including those in the ICU.

Study Population and Data Collection

The UCSF Medical Center uses the electronic health record (EHR) Epic (Epic 2017, Epic Systems Corporation, Verona, Wisconsin) for all clinical care. We obtained computerized EHR data from Clarity, the relational database that stores Epic's inpatient data in thousands of tables, including orders, medications, laboratory and radiology results, vital signs, patient demographics, and notes. We identified all adult patients hospitalized on the general medicine service with ≥1 episode of elevated BP (>160/90 mm Hg) at any point during their hospitalization who were not on a vasopressor medication at the time of the vital sign recording.

We further identified all instances in which either IV labetalol or hydralazine were administered to these patients. These two agents were chosen because they are the only IV antihypertensives used commonly at our institution for the treatment of asymptomatic elevated BP among internal medicine patients. Only those orders placed by a general medicine provider or reconciled by a general medicine provider upon transfer from another service were included. For each medication administration timestamp, we collected vital signs before and after the administration, along with the ordering provider and the clinical indication that was documented in the electronic order. To determine if a medication was administered with concern for end-organ injury, we also extracted orders that could serve as a proxy for the provider's clinical assessment—namely electrocardiograms, serum troponins, chest x-rays, and computerized tomography scans of the head—which were placed in the one hour preceding or 15 minutes following administration of an IV antihypertensive medication.

To assess for comorbid conditions, including a preexisting diagnosis of HTN, we collected International Classification of Diseases (ICD)-9/10 diagnosis codes. Further, we also extracted All Patient Refined Diagnosis-Related Group (APR-DRG) weights, which are a standardized measure of illness severity based on relative resource consumption during hospitalization.[16,17]

Patients were categorized as having either "symptomatic" or "asymptomatic" elevated BP. We defined symptomatic elevated BP as having received treatment with an IV medication with provider concern for end-organ injury, as defined above. We further identified all patients in which tight BP control may be clinically indicated on the basis of the presence of any of the following ICD-9/10 diagnosis codes at the time of hospital discharge: myocardial infarction, ischemic stroke, intracranial hemorrhage, subarachnoid hemorrhage, subdural hematoma, aortic dissection, hypertensive emergency, or hypertensive encephalopathy. All patients with symptomatic elevated BP or any of the above ICD-9/10 diagnoses were excluded from the analysis, since administration of IV antihypertensive medications would plausibly be warranted in these clinical scenarios.

The encounter numbers from the dataset were used to link to patient demographic data, which included age, sex, race, ethnicity, primary language, and insurance status. Finally, we identified all instances of rapid response calls, ICU transfers, and code blues (cardiopulmonary arrests) for each patient in the dataset.

Blood Pressure Measurements

BP data were collected from invasive BP (IBP) monitoring devices and noninvasive BP cuffs. For patients with BP measurements recorded concomitantly from both IBP (ie, arterial lines) in addition to noninvasive BP cuffs, the arterial line reading was favored. All systolic BP (SBP) readings >240 mm Hg from arterial lines were excluded, as this has previously been described as the upper physiologic limit for IBP readings.[18]

Primary Outcome

The primary outcome for the study was the proportion of patients treated with IV antihypertensive medications (labetalol or hydralazine). Using aggregate data, we calculated the number of patients who were treated at least once with an IV antihypertensive in a given month (numerator), divided by the number of patients with ≥1 episode of asymptomatic elevated BP that month (denominator). The denominator was considered to be the population of patients "at risk" of being treated with IV antihypertensive medications. For patients with multiple admissions during the study period, each admission was considered separately. These results are displayed in the upper portion of the run chart (Figure).

Secondary Outcomes

To investigate blood pressure trends over time, we analyzed BP in three ways. First, we analyzed the median SBP for the entire population. Second, to determine clinical responses to IV antihypertensive medications among patients receiving treatment, we calculated the population medians for the pretreatment SBP, the change in SBP from pretreatment baseline, and the posttreatment SBP. Third, we calculated the average median SBP on a monthly basis for the duration of the study. This was achieved by calculating the median value of all SBPs for an individual patient, then averaging across all patients in a given month. The average monthly median SBPs are displayed in the lower portion of the Figure.

To investigate whether the intervention was associated with negative patient outcomes, the proportions of several balancing outcomes were compared between pre- and postinterven-

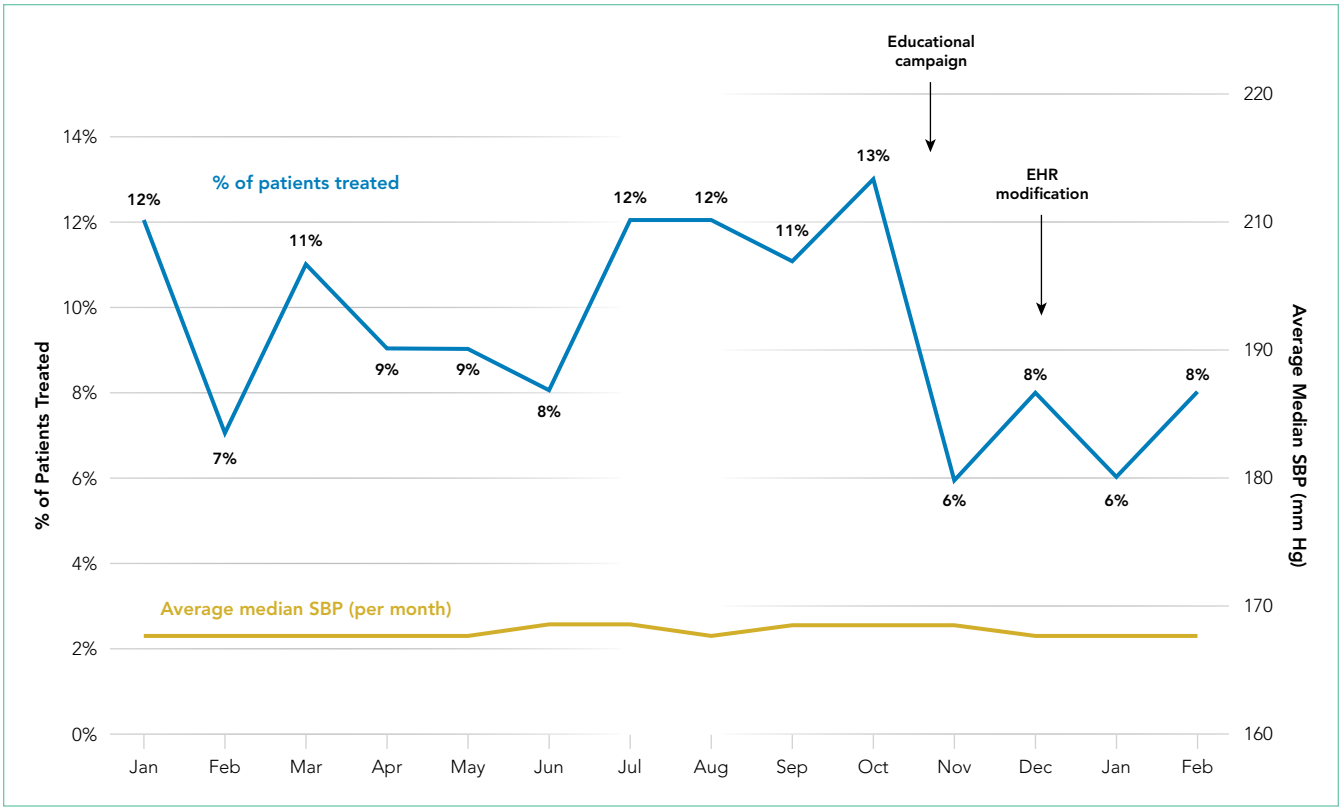

FIG. Percentage of patients with asymptomatic elevated blood pressure receiving intravenous antihypertensive medications, and average median SBP, per month.

Abbreviations: EHR, electronic health record; SBP, systolic blood pressure.

tion periods, including ICU transfers, rapid response calls, and code blues (cardiopulmonary arrests).

Development and Implementation of an Intervention to Reduce Excessive IV Antihypertensive Use

After establishing the baseline prevalence of IV antihypertensive medication use at our institution, we developed a QI initiative with the goal of reducing IV antihypertensive medication utilization by the general medicine service for the treatment of asymptomatic patients. We hypothesized that potential contributors to overutilization might include lack of education, provider/nursing discomfort, and a system designed to mandate provider notification for even modestly elevated BPs. The QI initiative, which took place between October 2017 and December 2017, was designed to address these potential contributors and was comprised of a division-wide, two-tiered, bundled intervention. Our choice of a two-tiered approach was based on the fact that successful culture change is challenging, along with the existing evidence that multifaceted QI interventions are more often successful than single-tiered approaches.[19]

The first tier of the initiative included an educational campaign referred to colloquially as "NoIVForHighBP," which targeted residents, hospitalists, and nursing staff. The campaign consisted of a series of presentations, best practice updates, handouts, and posters displayed prominently in shared workspaces. The educational content focused on alternative approaches to the management of asymptomatic elevated BP in the hospital, such as identification and treatment of pain, anxiety, volume overload, or other contributing factors (see supplemental materials). These educational outreaches occurred periodically between October 4, 2017 and November 20, 2017, with the bulk of the educational efforts taking place during November. Therefore, November 1, 2017 was designated the start date for the intervention period.

The second tier of the intervention included the liberalization of the EHR BP notification parameters on the standard inpatient admission order set from >160/90 mm Hg to >180/90 mm Hg. This change took effect on 12/6/2017. The decision to modify the BP notification parameters was based on the hypothesis that mandatory notifications for modestly elevated BPs may prompt providers to reflexively order IV antihypertensive medications, especially during times of cross-coverage or high clinical workload.

Statistical Analysis

All statistical analyses were performed using Stata software version 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, Texas: StataCorp LLC). Baseline patient characteristics were compared using nonparametric tests of significance. Population median SBPs were compared between pre- and postintervention periods using Mood's Median Test, which was selected because the data were distributed nonnormally, and variances between samples were unequal.

TABLE 1. **Comparison of Baseline Patient Characteristics between Pre- and Postintervention Periods**

	Preintervention, n = 2,306	Postintervention, n = 934	*P* Value
Age, median (IQR)	67 (55-80)	69 (57-83)	.01
Sex, n (%)			.09
Male	1,186 (51)	450 (48)	
Female	1,120 (49)	485 (52)	
Race, n (%)			.22
White	917 (40)	372 (40)	
Black	442 (19)	149 (16)	
Asian	523 (23)	237 (25)	
Hispanic	216 (9)	88 (9)	
Other	199 (9)	88 (9)	
Primary language, n (%)			
Non-English	475 (21)	222 (24)	.05
Insurance, n (%)			.09
Commercial	314 (14)	119 (12)	
Medicaid	532 (23)	184 (20)	
Medicare	1,439 (62)	625 (67)	
Other[a]	21 (0.9)	6 (0.6)	
Hypertension present on admission, n (%)	1,732 (75)	659 (71)	.01
APR-DRG Weight, median (IQR)	1.34 (0.99-1.77)	1.48 (1.00-1.82)	< .001
Inpatient length of stay, median (IQR)	4.6 (2.8-8.0)	5.1 (2.9-9.2)	.004

[a]Includes uninsured, workers' compensation, and other unspecified government insurance plans
Abbreviations: APR-DRG, all patient refined diagnosis-related groups; IQR, interquartile range.

Among patients treated with IV antihypertensive medications, we compared the proportion of pretreatment SBPs falling into each of three specified ranges (SBP <180 mm Hg, SBP 180-199 mm Hg, and SBP >200 mm Hg) between baseline and intervention periods using chi-squared tests.

Using aggregate data, we compared the unadjusted proportion of patients treated with IV antihypertensive medications between pre- and postintervention periods using a chi-squared test. Next, using patient-level data, a logistic regression analysis was performed to examine the association between receipt of IV antihypertensive medications and time (dichotomized between pre- and postintervention periods) while adjusting for age, sex, race, ethnicity, primary language, insurance status, preexisting HTN, length of stay, and APR-DRG weight.

Rates of balancing outcomes were compared using chi-squared tests. A logistic regression analysis using patient-level data was also performed to investigate the association between each of these outcomes and the intervention period (pre vs post) while adjusting for age, sex, race, ethnicity, primary language, insurance status, preexisting HTN, length of stay, and APR-DRG weight.

RESULTS

Baseline Period

We identified 2,306 patients with ≥1 episode of asymptomatic elevated BP during the 10-month preintervention period. Patients on average experienced 9 episodes of elevated BP per hospitalization, representing 21,207 potential opportunities for treatment. Baseline characteristics are summarized in Table 1. In general, this represents an older population that was medically complex and multiracial.

Of these patients, 251 (11%) received IV hydralazine and/or labetalol at least once during their hospitalization, with a total of 597 doses administered. Among those treated, a median of 2 doses were given per patient (IQR: 1-4), 64% of which were hydralazine. The majority (380 [64%]) were ordered on an "as needed" basis, while 217 (36%) were administered as a one-time dose. Three-quarters of all doses were ordered by the teaching service (456 [76%]), with the remaining 24% ordered by the direct-care (hospitalist) service.

During the baseline period among patients receiving IV antihypertensive medications, the median SBP of the population prior to treatment was 187 mm Hg (IQR 177-199; Table 2). Treatment was initiated in 30% of patients for an SBP <180 mm Hg and in 75% for an SBP <200 mm Hg. The median time to follow-up BP check was 34 minutes (IQR 15-58). The median decrement in SBP was 20 mm Hg (IQR 5-37); however, the response to treatment was highly variable, with 2% of patients experiencing no change and 14% experiencing an increase in SBP. Seventy-nine patients (14%) had a decrement in SBP >25% following treatment.

TABLE 2. **Patient-Level Logistic Regression Analysis of the Association between Receipt of Intravenous Antihypertensive Medication and Exposure to QI Intervention**[a]

Variable	Odds of Treatment (95% CI)	*P* Value
Postintervention period	0.62 (0.47-0.83)	.001
Race		
White	ref.	ref.
Asian	1.33 (0.92-1.93)	.13
Hispanic	1.49 (0.96-2.20)	.08
Black	1.81 (1.29-2.53)	.001
Other/unknown	1.38 (0.86-2.20)	.18
Age		
18-53	ref.	ref.
54-66	0.68 (0.48-0.97)	.03
67-77	0.55 (0.35-0.84)	.01
78-116	0.80 (0.51-1.24)	.32
Sex		
Male	ref.	ref.
Female	1.10 (0.86-1.40)	.46
Language		
English	ref.	ref.
Non-English	0.98 (0.68-1.40)	.90
Insurance		
Commercial	ref.	ref.
Medicaid	0.97 (0.63-1.51)	.89
Medicare	1.26 (0.81-1.95)	.31
Other	0.34 (0.04-2.82)	.32
Preexisting hypertension	4.25 (2.75-6.56)	<.001
APR-DRG weight	1.13 (1.07-1.20)	<.001
Inpatient length of stay	1.02 (1.01-1.03)	<.001

[a]Exposure dichotomized to pre- and postintervention time periods. Model adjusts for age, sex, race, ethnicity, primary language, insurance status, preexisting HTN, length of stay, and APR-DRG weight.

Abbreviation: APR-DRG, all patient refined diagnosis related-groups; HTN, hypertension.

Description of Quality Improvement Results

Following the QI initiative, a total of 934 patients experienced 9,743 episodes of asymptomatic elevated blood pressure over a 4-month period (November 1, 2017 to February 28, 2018). As shown in Table 1, patients in the postintervention period had a slightly higher median age (67 [IQR 55-80] vs 69 [IQR 57-83]; *P* = .01), a higher median APR-DRG weight (1.34 [IQR 0.99-1.77] vs 1.48 [1.00-1.82]; *P* < .001), and a longer median length of stay (4.6 [2.8-8.0] days vs 5.1 [2.9-9.2] days; *P* = .004). There was also a higher proportion of nonEnglish speakers, fewer Black patients, and a lower proportion of preexisting HTN, in the postintervention period.

Of the 934 patients with ≥1 episode of asymptomatic elevated BP, 70 (7%) were treated with IV antihypertensive medications, with a total of 196 doses administered. The proportion of patients treated per month during the postintervention period ranged from 6% to 8%, which was the lowest of the entire study period and below the baseline average of 10% (Figure).

In a patient-level logistic regression pre-post analysis adjusting for age, sex, race, ethnicity, primary language, insurance status, preexisting HTN, length of stay, and APR-DRG weight, patients admitted to the general medicine service during the postintervention period had 38% lower odds of receiving IV antihypertensive medications than those admitted during the baseline period (OR = 0.62; 95% CI 0.47-0.83; *P* = .001). In this adjusted model, the following factors were independently associated with increased odds of receiving treatment: APR-DRG weight (OR 1.13; 95% CI 1.07-1.20; *P* < .001), Black race (OR 1.81; 95% CI 1.29-2.53; *P* = .001), length of stay (OR 1.02; 95% CI 1.01-1.03; *P* < .001), and preexisting HTN (OR 4.25; 95% CI 2.75-6.56; *P* < .001). Older age was associated with lower odds of treatment (Table 2).

Among patients who received treatment, there were no differences between pre- and postintervention periods in the proportion of pretreatment SBP <180 mm Hg (29% vs 32%; *P* = .40), 180-199 mm Hg (47% vs 40%; *P* = .10), or >200 mm Hg (25% vs 28%; *P* = .31; Table 3).

Population-level median SBP was similar between pre- and postintervention periods (167 mm Hg vs 168 mm Hg, *P* = .78), as were unadjusted rates of rapid response calls, ICU transfers, and code blues (Table 3). After adjustment for baseline characteristics and illness severity at the patient level, the odds of rapid response calls (OR 0.84; 95% CI 0.65-1.10; *P* = .21) and ICU transfers (OR 1.01; 95% CI 0.75-1.38; *P* = .93) did not differ between pre- and postintervention periods. A regression model was not fit for cardiopulmonary arrests due to the low absolute number of events.

CONCLUSIONS

Our results suggest that treatment of asymptomatic elevated BP using IV antihypertensive medications is common practice at our institution. We found that treatment is often initiated for only modestly elevated BPs and that the clinical response to these medications is highly variable. In the baseline period, one in seven patients experienced a decrement in BP >25% following treatment, which could potentially cause harm.[11] There is no evidence, neither are there any consensus guidelines, to support the rapid reduction of BP among asymptomatic patients, making this a potential valuable opportunity for reducing unnecessary treatment, minimizing waste, and avoiding harm.

While there are a few previously published studies with similar results, we add to the existing literature by studying a larger population of more than 3,000 total patients, which was uniquely multiracial, including a high proportion of non-English speakers. Furthermore, our cohort included patients in the ICU, which is reflected in the higher-than-average APR-DRG weights. Despite being critically ill, these patients arguably still do not warrant aggressive treatment of elevated BP when asymptomatic. By excluding symptomatic BP elevations using surrogate markers for end-organ damage in addition to discharge diagnosis codes indicative of conditions in which

TABLE 3. **Treatment Characteristics, Response to Treatment, and Outcomes Compared between Pre- and Postintervention Periods**

	Baseline Period	Postintervention	
Treatment Characteristics	**n = 597 doses**	**n = 196 doses**	***P* Value**
Choice of medication, n (%)			
Hydralazine	380 (64%)	97 (50%)	<.001
Labetalol	217 (36%)	99 (50%)	
Hour of medication administration, n (%)			
Daytime (9AM – 5PM)	185 (31%)	72 (37%)	.14
Cross-cover (5PM – 9AM)	412 (69%)	124 (63%)	
Pre-treatment SBP, n (%)			
<180 mmHg	170 (29%)	62 (32%)	.40
180-199 mmHg	281 (47%)	79 (40%)	.10
>200 mmHg	146 (24%)	55 (28%)	.31
Medication Effects	n = 597 doses	n = 196 doses	
Median SBP, mmHg (IQR)			
Pre-treatment	187 (177-199)	186 (175-203)	.45
Post-treatment	165 (150-185)	171 (154-186)	.18
Magnitude of blood pressure decrease, n (%)			
SBP decreased <10%	186 (48%)	61 (41%)	.99
SBP decreased 10-25%	223 (38%)	67 (45%)	.42
SBP decreased >25%	79 (14%)	20 (14%)	.27
Outcomes	n = 2,306 patients	n = 934 patients	
Receipt of IV antihypertensive, n (%)	251 (11%)	70 (7%)	.003
Balancing outcomes, n (%)			
Rapid response calls	294 (12%)	114 (11%)	.72
ICU transfers	188 (8%)	81 (9%)	.65
Code blue	17 (0.74%)	9 (0.96%)	.51

Abbreviations: ICU, intensive care unit; IV, intravenous; SBP, systolic blood pressure.

tight BP control may be warranted, we were able to study a more critically ill patient population. We were also able to describe which baseline patient characteristics convey higher adjusted odds of receiving treatment, such as preexisting HTN, younger age, illness severity, and black race.

Perhaps most significantly, our study is the first to demonstrate an effective QI intervention aimed at reducing unnecessary utilization of IV antihypertensives. We found that this can feasibly be accomplished through a combination of educational efforts and systems changes, which could easily be replicated at other institutions. While the absolute reduction in the number of patients receiving treatment was modest, if these findings were to be widely accepted and resulted in a wide-spread change in culture, there would be a potential for greater impact.

Despite the reduction in the proportion of patients receiving IV antihypertensive medications, we found no change in the median SBP compared with the baseline period, which seems to support that the intervention was well tolerated. We also found no difference in the number of ICU transfers, rapid response calls, and cardiopulmonary arrests between groups. While these findings are both reassuring, it is impossible to draw definitive conclusions about safety given the small absolute number of patients having received treatment in each group. Fortunately, current guidelines and literature support the safety of such an intervention, as there is no existing evidence to suggest that failing to rapidly lower BP among asymptomatic patients is potentially harmful.[11]

There are several limitations to our study. First, by utilizing a large electronic dataset, the quality of our analyses was reliant on the accuracy of the recorded EHR data. Second, in the absence of a controlled trial or control group, we cannot say definitively that our QI initiative was the direct cause of the improved rates of IV antihypertensive utilization, though the effect did persist after adjusting for baseline characteristics in patient-level models. Third, our follow-up period was relatively short, with fewer than half as many patients as in the preintervention period. This is an important limitation, since the impact of QI interventions often diminishes over time. We plan to continually monitor IV antihypertensive use, feed those data back to our group, and revitalize educational efforts should rates begin to rise. Fourth, we were unable to directly measure

which patients had true end-organ injury and instead used orders placed around the time of medication administration as a surrogate marker. While this is an imperfect measure, we feel that in cases where a provider was concerned enough to even test for end-organ injury, the use of IV antihypertensives was likely justified and was therefore appropriately excluded from the analysis. Lastly, we were limited in our ability to describe associations with true clinical outcomes, such as stroke or myocardial infarction, which could theoretically be propagated by either the use *or* the avoidance of IV antihypertensive medications. Fortunately, based on clinical guidelines and existing evidence, there is no reason to believe that reducing IV antihypertensive use would result in increased rates of these outcomes.

Our study reaffirms the fact that overutilization of IV antihypertensive medications among asymptomatic hospitalized patients is pervasive across hospital systems. This represents a potential target for a concerted change in culture, which we have demonstrated can be feasibly accomplished through education and systems changes.

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Assess Before Rx: Reducing the Overtreatment of Asymptomatic Blood Pressure Elevation in the Inpatient Setting

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BACKGROUND: Asymptomatic blood pressure elevation is common in the inpatient setting. National guidelines recommend treating with oral agents to slowly decrease blood pressure; however, many clinicians use intravenous antihypertensive medications, which can lead to unpredictable changes in blood pressure.

OBJECTIVE: To decrease the number of inappropriate orders (without symptoms of hypertensive emergency or order for NPO) of intravenous antihypertensives and adverse events associated with intravenous orders.

DESIGN: Quasi-experimental study with multidisciplinary intervention.

PARTICIPANTS: Inpatients with a one-time order for an intravenous antihypertensive agent from January 2016 to February 2018.

MAIN MEASURES: The main outcomes were the total numbers of orders and inappropriate orders, adverse events, and alternate etiologies per 1,000 patient-days. As a balancing measure, patients were monitored for adverse events when blood pressure was elevated and not treated.

KEY RESULTS: There were a total of 260 one-time orders of intravenous antihypertensives on two medical units. Inappropriate orders decreased from 8.3 to 3.3 per 1,000 patient days (P = .0099). Adverse events associated with intravenous antihypertensives decreased from 3.7 to 0.8 per 1,000 patient days (P = .0072).

CONCLUSION: This initiative demonstrated a significant reduction in inappropriate use of IV antihypertensives and an associated reduction in adverse events. *Journal of Hospital Medicine* 2019;14:151-156. © 2019 Society of Hospital Medicine

With the presence of hypertension in 25% of patients admitted to the hospital,[1] its proper management is imperative. A hypertensive crisis is a severe elevation of blood pressure, defined as systolic ≥180 mm Hg and/or diastolic ≥120 mm Hg. It is further classified as either a hypertensive emergency which includes the presence of end-organ damage,[2] or hypertensive urgency, defined as asymptomatic blood pressure elevation.[3] Although hypertensive emergencies account for only 1%-2% of patients with hypertension,[4] they are associated with a high one-year mortality rate (>79%).[5] Hypertensive emergency requires immediate reduction of blood pressure with IV antihypertensive drugs to limit organ damage. In contrast, as per national guidelines, inpatient management of hypertensive urgency requires gradual reductions of blood pressure over hours to days using oral antihypertensives.[2] It is also recommended that alternative etiologies, such as anxiety or pain, be considered before treatment is initiated.[1]

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Clinicians often inappropriately treat asymptomatic hypertension in the inpatient setting,[6,7] using intravenous (IV) antihypertensive medications despite evidence showing potential harm.[5,8] This can lead to unpredictable reductions in blood pressure.[7,9] A recent retrospective analysis demonstrated that 32.6% of patients had a blood pressure reduction greater than 25% after the use of an IV antihypertensive.[7] Reductions greater than 25% lead to shifts in autoregulation, which may result in patient harm, such as hypotension, decreased renal perfusion, and stroke.[9] IV medications are also more expensive than oral agents, due to the additional cost of administration.

Although overtreatment of asymptomatic hypertension with IV antihypertensive medications is common,[7] initiatives to address this in inpatient settings are lacking in the literature. The aim of this quality improvement initiative was to reduce unnecessary IV antihypertensive treatment for hypertensive urgency in the inpatient setting.

METHODS

Setting

An interdisciplinary quality improvement intervention was initiated on two inpatient medicine units at an urban, 1,134-bed tertiary medical center affiliated with the Icahn School of Medicine at Mount Sinai. Members of the Mount Sinai High Value

Care Committee and the Student High Value Care Initiative[10] developed this project. The intervention was implemented in stages from March 2017 to February 2018. It targeted nurses, housestaff, nurse practitioners, and attendings on general medical teaching and nonteaching services. The components of the intervention included education, a treatment algorithm, audit and feedback, and electronic medical record (EMR) change. This project was submitted to the Quality Committee in the Department of Medicine and determined to be a quality improvement project rather than research and thus, an IRB submission was not required.

Treatment Algorithm and Education

A clinical algorithm was designed with nursing and cardiology representatives to provide guidance for nurses regarding the best practice for evaluation of inpatient hypertension, focusing on assessing patients before recommending treatment ("Assess Before Rx"; Figure 1). Educational sessions reinforcing the clinical algorithm were held monthly at nursing huddles. These involved an introduction session providing the background and purpose of the project, with follow-up sessions including interactive mock cases on the assessment of hypertensive urgency.

A second treatment algorithm was designed, with housestaff and cardiology input, to provide guidance for the internal medicine housestaff and nurse practitioners. It utilized a similar approach regarding identification, evaluation, and assessment of alternate etiologies but included more detailed treatment recommendations with a table outlining the oral medications used for hypertensive urgency (Figure 2). The flowchart and table were uploaded to an existing mobile application used by housestaff and nurse practitioners for quick access. The mobile application is frequently used by housestaff and contains many clinical resources. Additionally, e-mails including the purpose of the project and the treatment algorithm were sent to rotating housestaff at the start of each new medicine rotation.

Audit and Feedback

Monthly feedback was e-mailed to the nurses, which reinforced the goals and provided positive feedback on outcomes with an announcement of the "Nurse of the Month." The winners were selected based on the most accurate and appropriate documentation of their assessments determined through retrospective chart review.

Targeted e-mail feedback was also sent to providers who ordered IV antihypertensives without the appropriate indication. The e-mails included the medical record number, date and time of the order, any alternate etiologies that were documented, and any adverse events that occurred as a result of the medication.

Systems Change: Electronic Medical Record Orders

EMR advisory warnings were placed on IV antihypertensive orders of labetalol and hydralazine. The alerts served to nonintrusively remind providers to assess for symptoms before placing the order to ensure that the order was appropriate.

Data Collection and Assessment

Seven-month preintervention (January-July 2016) and 12-month postintervention (March 2017-February 2018) data were compared. The months prior to intervention were excluded to account for project development and educational lag. Data were obtained from EMR utilization reports of one-time orders of IV labetalol and hydralazine, and retrospective chart review. Patients who were pregnant, less than 18 years of age, or postoperative were excluded. Orders were designated as inappropriate if there was no evidence of hypertensive emergency through documentation in progress notes, or if the patient was able to take oral medication (not NPO). Adverse events were defined as a blood pressure drop of more than 25%, a change in the heart rate by more than 20 beats per minute, or the need for IV fluids, based on previous studies.[7] Although decreased blood pressure is not necessarily dangerous in and of itself, adverse events arising from blood pressure decreasing too rapidly from IV antihypertensives are well documented.[9,11] The presence of alternate etiologies of high blood pressure that were documented in progress notes, including pain, anxiety, agitation, and holding of home blood pressure medications, were recorded. The numbers of inappropriate orders pre- and postintervention were compared. Confounding factors of patient age and length of stay (LOS) were compared pre- and postintervention in order to rule out other factors to which the intervention's effect could be attributed. Additionally, as a balancing measure, a random sample of patients with elevated blood pressure were monitored on a biweekly basis for adverse events that occurred as a result of not receiving IV treatment, including stroke, myocardial infarction, and pulmonary edema.

For this study, orders were reported on the standardized form of orders per 1,000 patient days. This was calculated as the number of orders divided by the total number of patient days from the two medicine units. For the univariate analysis, pre- and postintervention orders were compared for the different order categories using a t-test. Results were considered statistically significant at $P < .05$. Data analysis was conducted using SAS v. 9.4 (SAS Institute, Cary, North Carolina).

Additionally, a cost analysis was performed to estimate the hospital-wide annual cost of inappropriate orders. The analysis used the cost per dose[12] and included nurse-time derived from the median salary of those on our units. The hospital-wide cost was extrapolated to estimate the potential annual savings for the institution.

RESULTS

A total of 260 one-time orders of IV antihypertensives were analyzed in this study, 127 in the seven-month preintervention period and 133 in the 12-month postintervention period. The majority, 67.3% (n = 175), were labetalol orders. Inappropriate orders (ie, neither NPO nor hypertensive emergency) decreased from 8.3 to 3.3 orders per 1,000 patient days ($P = .0099$; Figure 3).

In total, there were 86 adverse events (33.1%), the majority of which (94.2%, n = 81) were a >25% decrease in blood pressure

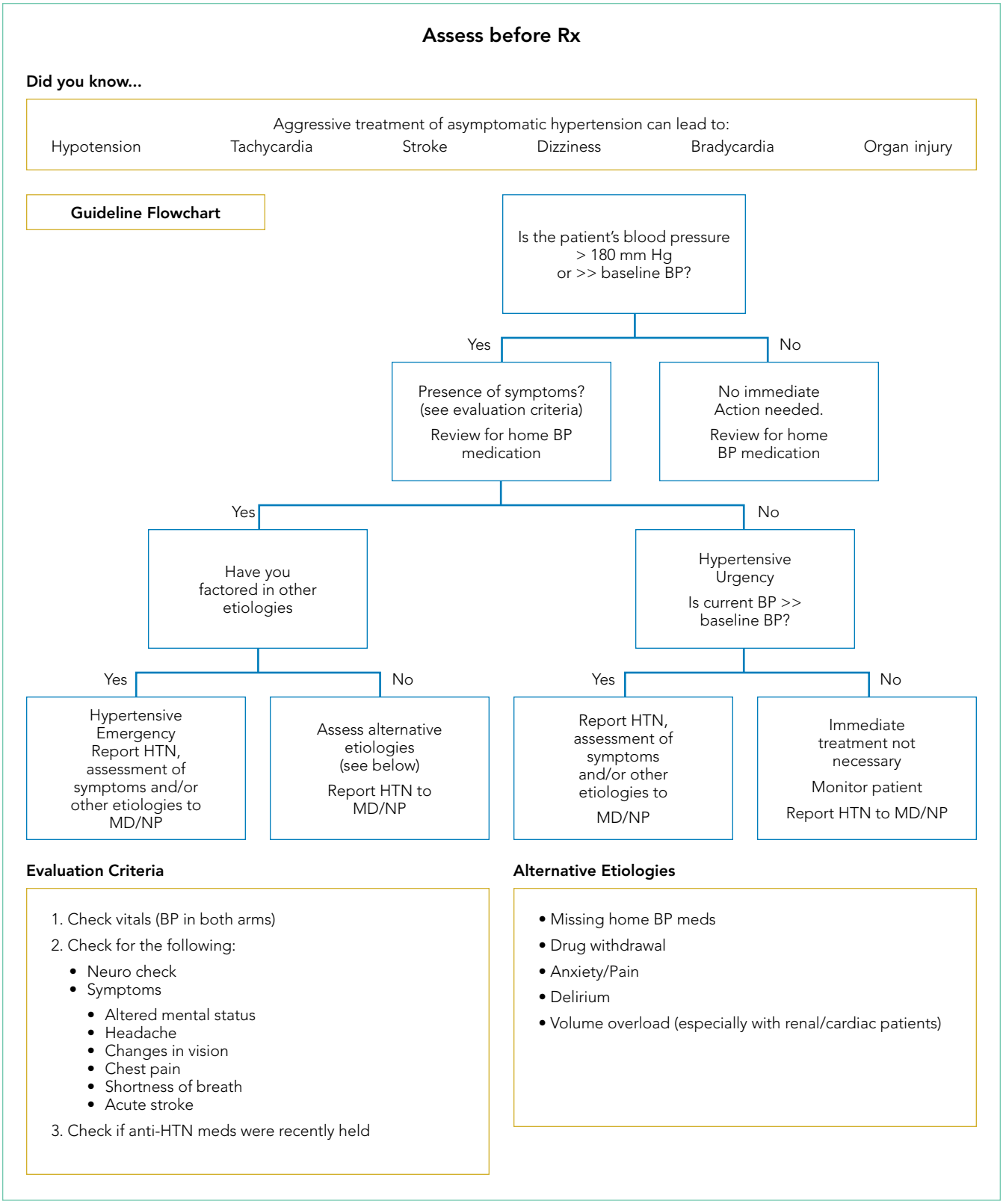
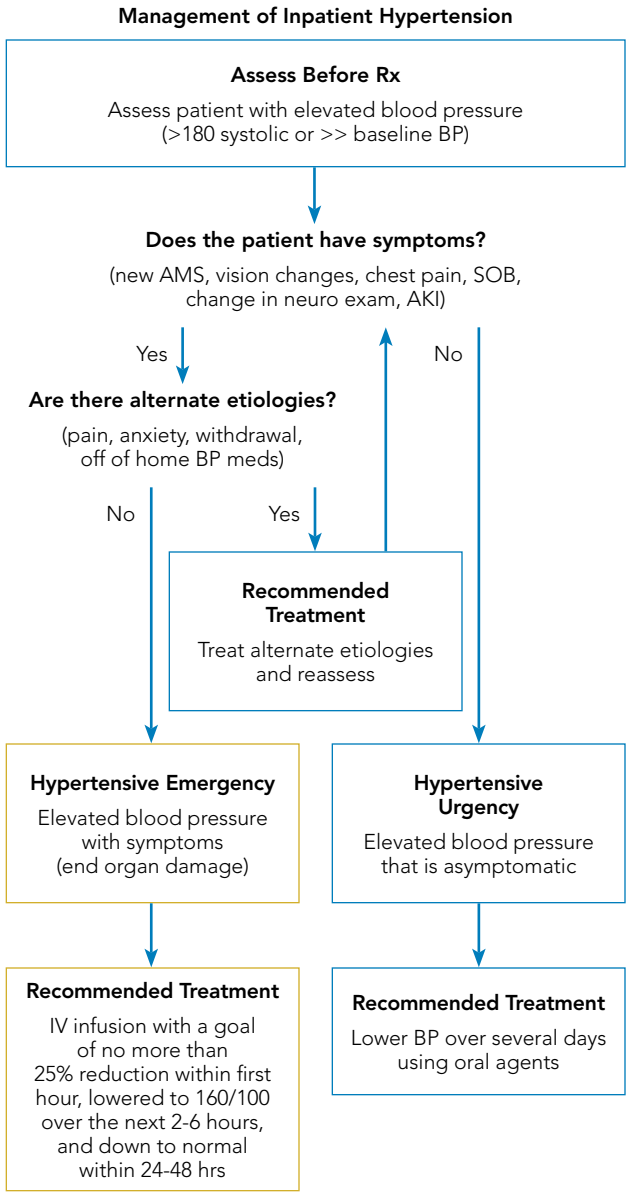


FIG 1. Nurse Inpatient Hypertension Guideline

Abbreviations: BP, blood pressure; HTN, hypertension; MD/NP, doctor of medicine/nurse practitioner.

(Table 1). The number of adverse events per 1,000 patient days decreased from 4.4 in the preintervention period to 1.9 postintervention, $P = .0112$. Of the inappropriate orders, adverse events decreased from 3.7 to 0.8 per 1,000 patient days, $P =$



Hypertensive Urgency

Medication	Onset of Action	Duration of Action	Initial Dosing	Additional Comments/ Adverse Reactions
Labetalol PO	20 min to 2 hrs	8 to 12 hrs	100 mg	Beta- and alpha-blocker, avoid in bradycardia <60
Hydralazine PO	~45 min	2 to 6 hrs	10 mg	May cause unpredictable and prolonged antihypertensive effects, reflex tachycardia
Amlodipine PO	6 to 12 hrs	>24 hrs	5 mg	Slow onset of action
Nifedipine PO	30 min	24 hrs	30 mg	Avoid immediate release as may cause hypotension, use sustained release (Procardia XL)
Lisinopril PO	1 hr	24 hrs	2.5 to 20 mg	Avoid in hyperkalemia AKI

IV agents should be reserved for Hypertensive Emergancy only, or if patient is NPO as it leads to unpredictable and rapid drops in BP, among other adverse events

FIG 2. Housestaff Inpatient Hypertension Management Guidelines

Abbreviations: AKI, acute kidney injury; AMS, acute mountain syndrome; BP, blood pressure; IV, intravenous; NPO, nothing by mouth; PO, by mouth; SOB, shortness of breath.

.0072. Overall, there were 76 orders (29.2%) with documented alternate etiologies. The number of orders per 1,000 patient days with an alternate etiology decreased from 4.7 in the preintervention period to 1.2 postintervention, $P = .0044$ (Table 2). Descriptive analysis of patient characteristics pre- and postintervention were not statistically significant; for age 68.4 vs 70.7, $P = .0823$ and for LOS 14.8 vs 15.4, $P = .0769$. As a balancing measure, 111 patients with elevated blood pressure were monitored for adverse events during the postintervention period. Among patients who did not receive IV medication based on our algorithm, there were no adverse events.

Cost analysis estimated a $17,890 annual hospital-wide cost for unnecessary IV antihypertensive medications before the intervention. The estimate was calculated using the number of orders on the two medical units observed during the seven-month preintervention period, extrapolated to a 12-month period and to the total number of 15 medical units in the hospital. The intervention on the two studied medical units themselves led to an estimated $1,421 cost reduction (59.6%). Had the intervention been implemented hospital-wide with similar results, the resulting cost reduction would have amounted to $10,662.

DISCUSSION

Our initiative successfully demonstrated a significant reduction of 60% in inappropriate one-time orders of IV antihyperten-

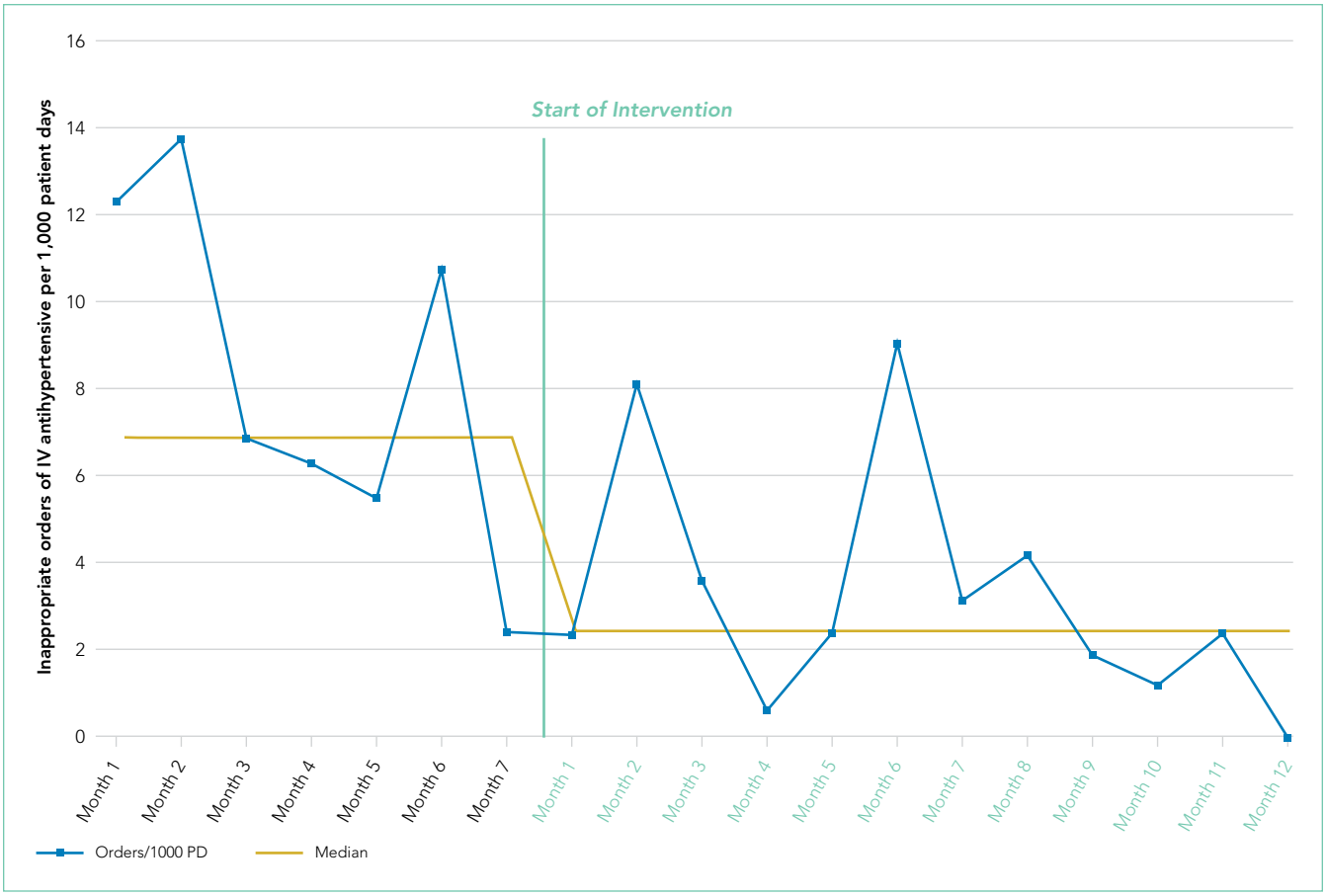


FIG 3. U-Control Chart, Pre- and Postintervention Inappropriate Orders per 1,000 Patient Days

sives per 1,000 patient days. Accordingly, the number of adverse events per 1,000 patient days decreased by 57%. There was also a decrease in the number and percentage of IV orders with documented alternate etiologies. We hypothesize that this was due to nurses and physicians assessing and treating these conditions prior to treating hypertension in the intervention period, consequently avoiding an IV order.

The goal of the intervention was to have nurses assess for end-organ damage and alternate etiologies and include this information on their assessment provided to the physician, which would result in appropriate treatment of elevated blood pressure. By performing an interdisciplinary intervention, we addressed the knowledge deficit of both nurses and physicians, improved the triage of elevated blood pressure, and likely decreased the number of pages to providers.

To our knowledge, this is the first intervention addressing the inpatient overuse of IV antihypertensive medications for the treatment of asymptomatic hypertension. Additionally, this study bolsters prior evidence that the use of IV antihypertensives in asymptomatic patients leads to a large number of adverse events.[7] A third of patients in the preintervention period had documented alternate etiologies of their blood pressure elevation, highlighting the need to assess and potentially treat these causes prior to treating blood pressure itself.

Reducing unnecessary treatment of asymptomatic blood

TABLE 1. **Adverse Events and Alternative Etiology of IV Antihypertensive Medications**

Adverse Events	**n (%)**
Blood Pressure Drop >25%	81 (94.2)
Bradycardia	6 (7.0)
Tachycardia	2 (2.3)
Symptomatic Dizziness	2 (2.3)
Need for IV Fluids	0 (0.0)
Alternative Etiology[a]	**n (%)**
Anxiety	22 (28.9)
Pain	38 (50.0)
Steroids	5 (6.6)
Withdrawal	1 (1.3)
Off Home Antihypertensives	10 (13.2)

[a]Not mutually exclusive
Abbreviation: IV, intravenous.

TABLE 2. **Analyses of One-Time Orders of IV Antihypertensive Medications**

	Pre Intervention (7 months)	Post Intervention (12 months)	*P* Value
Overall Orders / 1,000 patient days	11.4	6.8	**.0345**
Inappropriate Orders / 1,000 patient days	8.3	3.3	**.0099**
Adverse Events / 1,000 patient days			
From All Orders	4.4	1.9	**.0112**
From Inappropriate Orders	3.7	0.8	**.0072**
Alternate Etiology Orders / 1,000 patient days	4.7	1.2	**.0044**

pressure elevation is challenging. Evidence shows that both clinicians and patients overestimate the benefits and underestimate the harms of medical interventions.[13,14] This unfortunately leads to unjustified enthusiasm for medical treatments, which can worsen outcomes.[15] Additionally, there may be a lack of knowledge of the guidelines, as well as the amount of time required in the full assessment of hypertensive urgency, that creates a culture of "treating the number."

Changing physician behavior is difficult.[16] However, active forms of continuing education and multifaceted interventions, such as ours, are most effective.[17] Our message focused on patient safety and harm reduction, addressed clinicians' safety concerns, and included stories of real cases where this overuse led to adverse events—all of which are encouraged in order to facilitate clinician engagement.[18]

There were limitations to this study. Only blood pressure elevations associated with an IV antihypertensive order and not all blood pressure elevations meeting the criteria for hypertensive urgency in general were examined. Additionally, our documentation of symptoms of hypertensive emergency and alternate etiologies was based only on documentation in the medical record. Ideally, we would have liked to conduct an interrupted time series analysis to assess the effect of the intervention over time; however, there were not enough orders of IV antihypertensives to perform such an analysis.

CONCLUSION

Treatment of asymptomatic blood pressure with IV antihypertensive medications can lead to patient harm. To reduce inappropriate treatment, our Student High Value Care team set out to challenge this common practice. Our interdisciplinary intervention successfully reduced unnecessary IV antihypertensive treatment. This may serve as a model for other institutions.

Disclosures: There are no relevant conflicts of interest to disclose for any authors.

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Adherence to Recommended Inpatient Hepatic Encephalopathy Workup

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Hepatic encephalopathy (HE) is characterized by altered sensorium and is the most common indication for hospitalization among patients with cirrhosis. Liver societal guidelines for inpatient HE revolve around identification of potential precipitants. In this retrospective study, we aimed to determine adherence to societal guidelines for evaluation of HE in 78 inpatients. The adherence rate to societal recommended guidelines for workup of HE was low, with only 17 (22%) patients having complete diagnostic workup within 24 hours of admission. Notably, 23 (30%) patients were not subjected to blood culture analysis, 16 (21%) were missing urinalysis, and 15 (20%) were missing chest radiograph. In patients with ascites (N = 34), 26 (77%) did not have a diagnostic paracentesis to exclude spontaneous bacterial peritonitis. In contrast, serum ammonia determination, a laboratory test not endorsed by societal guidelines for workup of HE, was ordered in 74 (95%) patients. These findings underscore the limited adherence to societal guidelines in hospitalized patients with HE. *Journal of Hospital Medicine* 2019;14:157-160. © 2019 Society of Hospital Medicine

Clinical guidelines are periodically released by medical societies with the overarching goal of improving deliverable medical care by standardizing disease management according to best available published literature and by reducing healthcare expenditure associated with unnecessary and superfluous testing.[1] Unfortunately, nonadherence to guidelines is common in clinical practice[2] and contributes to the rising cost of healthcare.[3] Health resource utilization is particularly relevant in management of cirrhosis, a condition with an annual healthcare expenditure of $13 billion.[4] Hepatic encephalopathy (HE), the most common complication of cirrhosis, is characterized by altered sensorium and is the leading indication for hospitalization among cirrhotics. The joint guidelines of the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) for diagnostic workup for HE recommend identification and treatment of potential precipitants.[5] The guidelines also recommend against checking serum ammonia levels, which have not been shown to correlate with diagnosis or severity of HE.[6-8] Currently, limited data are available on practice patterns regarding guideline adherence and unnecessary serum ammonia testing for initial evaluation of HE in hospitals. To overcome this gap in knowledge, we conducted the present study to provide granular details regarding the diagnostic workup for hospitalized patients with HE.

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METHODS

This study adopted a retrospective design and recruited patients admitted to the Virginia Commonwealth University Medical Center between July 1, 2016 and July 1, 2017. The institutional review board approved the study, and the manuscript was reviewed and approved by all authors prior to submission. All chart reviews were performed by hepatologists with access to patients' electronic medical record (EMR).

Patient Population

Patients were identified from the EMR system by using ICD-9 and ICD-10 codes for cirrhosis, hepatic encephalopathy, and altered mental status. All consecutive admissions with these diagnosis codes were considered for inclusion. Adult patients with cirrhosis resulting from any etiology of chronic liver diseases with primary reason for admission of HE were included. If patients were readmitted for HE during the study period, then only the data from index HE admission was included in the analysis and data from subsequent admissions were excluded. The other exclusion criteria included non-HE causes of confusion, acute liver failure, and those admitted with a preformulated plan (eg, direct hepatology clinic admission or outside hospital transfer). Patients who developed HE during their hospitalization where HE was not the indication for admission were also excluded. Finally, all patients admitted under the direct care of hepatology were excluded.

Diagnostic Workup

The recommendations of the AASLD and the EASL for workup for HE include obtaining detailed history and physical examination supplemented by diagnostic evaluation for potential HE precipitants including infections, electrolyte disturbances, dehydration, renal failure, glycemic disturbances, and toxin

TABLE. **Baseline Clinical Characteristics of Patients (N = 78) Admitted with Hepatic Encephalopathy**

Characteristic	Entire Cohort (N = 78)	Complete Workup (n = 17)	Incomplete Workup (n = 61)	*P* Value
Age (years)	59.3 ± 9	60.1 ± 11	59.1 ± 8	.36
Male gender (%)	53 (68)	13 (77)	40 (66)	.56
Ethnicity (%)				.53
Caucasian	54 (69)	10 (59)	44 (72)	
Black	22 (28)	7 (41)	15 (25)	
Other	2 (23)	0 (0)	2 (3)	
BMI (kg/m2)	28.8 ± 7	29.8 ± 10	28.5 ± 6	.49
Etiology of Cirrhosis (%)				.52
Hepatitis C	41 (53)	9 (53)	32 (53)	
Alcohol	14 (18)	4 (24)	10 (16.4)	
Nonalcoholic steatohepatitis	13 (17)	2 (12)	11 (18)	
Other	10 (13)	2 (12)	8 (19)	
Complications of Cirrhosis (%)				
History of HE	53 (68)	13 (77)	40 (66)	.56
Ascites	34 (44)	0 (0)	34 (56)	<.001
Esophageal Varices	42 (54)	10 (59)	32 (53)	.79
TIPS	14 (18)	3 (18)	11 (18)	1.00
Hepatocellular carcinoma	4 (5)	2 (12)	2 (3)	.21
Pertinent Laboratory Values				
AST (IU/L)	79.1 ± 52	111.7 ± 75	71 ± 39	<.01
ALT (IU/L)	41.2 ± 33	57.4 ± 55	36.8 ± 22	.02
Bilirubin (mg/dL)	3.3 ± 5	5.4 ± 10	2.8 ± 2	.05
Albumin (g/mL)	2.9 ± 1	2.9 ± 1	2.9 ± 1	.64
Creatinine (mg/dL)	1.5 ± 1	1.3 ± 1	1.6 ± 2	.52
Sodium (mg/dL)	136.8 ± 6	136.8 ± 4	136.8 ± 7	.99
Platelet Count (x1012)	110.3 ± 79	101.1 ± 80	112.9 ± 80	.59
INR	1.7 ± 1	1.6 ± 1	1.7 ± 0.6	.69
MELD Score	17 ± 8	16.1 ± 10	17.0 ± 8	.71

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HE, hepatic encephalopathy; INR, international normalized ratio; MELD, model for end stage liver disease; TIPS, intrahepatic portosystemic shunt

ingestion (eg, alcohol, illicit drugs).[5] Based on the guideline recommendation, this study defined a "complete workup" as including all of the following elements: infection evaluation (blood culture, urinalysis/urine culture, chest radiograph, diagnostic paracentesis in the presence of ascites), electrolyte/renal evaluation (serum sodium, potassium, creatinine, and glucose), and toxin evaluation (urine drug screening). Any HE admission that was missing elements from the aforementioned battery of tests was defined as "incomplete workup." In patients admitted with decompensated cirrhosis, serum ammonia testing was considered inappropriate unless there was a nuanced explanation supporting its use documented within the EMR. The frequency and specialty of the physician ordering serum ammonia level tests were determined. The financial burden of unnecessary ammonia testing was estimated by assigning a laboratory charge ($258) for each patient.

Statistical Analysis

Continuous and categorical variables are reported as means (± standard deviation), median (interquartile range or IQR), or proportion (%) as appropriate. Across-group differences were compared using Student t-test for normally distributed continuous variables and Mann-Whitney U test for skewed data. Fisher's exact test was used to compare proportion. HE evalua-

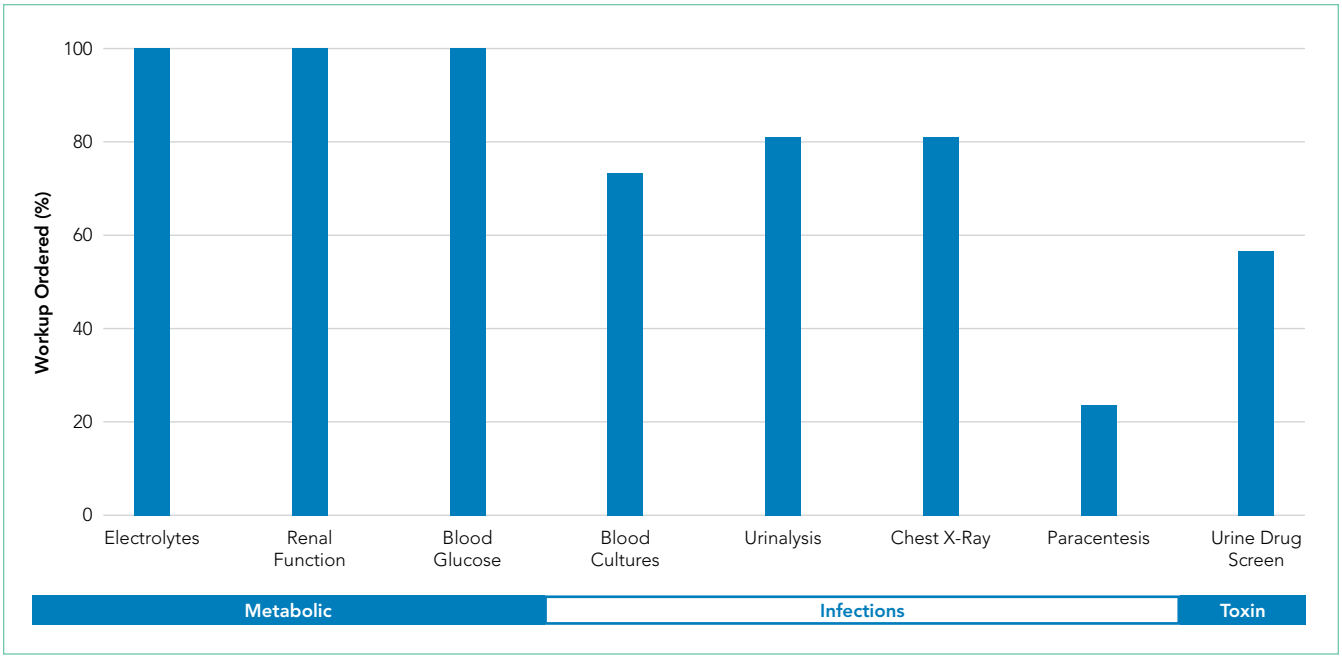

FIG. Adherence to the Recommended Diagnostic Evaluation of HE Precipitants
Abbreviation: HE, hepatic encephalopathy

tions were quantified by the number of patients with complete workup and by the number of patients with missing components of the workup. A nominal *P* value of less than .05 was considered statistically significant. All statistical analyses were performed using SPSS Statistics version 24.0 (IBM Corporation, Armonk, New York).

RESULTS

Cohort Characteristics

The baseline cohort demographics are listed in the Table. Of the 145 patients identified using diagnostic codes for cirrhosis, 78 subjects met the study criteria. The most common exclusion criteria included non-HE etiology of altered mental status (n = 37) and patients with readmissions for HE during the study period (n = 30). The mean age of the study cohort was 59.3 years, and the most common etiology of cirrhosis was hepatitis C (n = 41), alcohol induced (n = 14), and nonalcoholic steatohepatitis (n = 13).

Initial Diagnostic Evaluation

The major precipitants of HE in the study cohort were ineffective lactulose dosing (n = 43), infections (n = 25), and electrolyte disturbances/renal injury (n = 6). At the time of admission, 53 patients were on therapy for HE. Only 17 (22%) patients had complete diagnostic workup within 24 hours of hospital admission. The individual components of the complete workup are shown in the Figure. Notably, 23 (30%) patients were missing blood cultures, 16 (21%) were missing urinalysis, 15 (20%) were missing chest radiograph, and 34 (44%) were missing urine drug screening. Of the 34 patients with ascites on admission, only eight (23%) had diagnostic paracentesis performed on admission to rule out spontaneous bacterial peritonitis.

Serum Ammonia Testing

Serum ammonia testing was performed on 74 patients (94.9%), and no patient met the criteria for appropriate testing. Forty patients already had a known diagnosis of HE prior to index admission. Furthermore, 10 (14%) patients had serum ammonia testing repeated after admission without documentation in the EMR to justify repeat testing. Emergency Department (ED) physicians ordered ammonia testing in 57 cases (77%), internists ordered the testing in 11 cases (15%), and intensivists ordered the testing in two cases (3%). The patient's charges for serum ammonia testing at the time of admission and for repeat testing were $19,092 and $2,580, respectively.

DISCUSSION

This study utilized HE in patients with decompensated cirrhosis as a framework to analyze adherence to societal guidelines. The adherence rate to AALSD/EASL recommended inpatient evaluation of HE is surprisingly low, and most patients are missing key essential elements of the diagnostic work up. While the diagnostic tests that are ordered as part of a panel are completed universally (renal function, electrolytes, and glucose testing), individual testing is less inclined to be ordered (blood cultures, urine culture/urinalysis, CXR, UDS) and procedural testing, such as diagnostic paracentesis, is often missed. This last finding is in line with published literature showing that 40% of patients admitted with ascites or HE did not have diagnostic paracentesis during hospital admission despite 24% reduction of inhospital mortality among patients undergoing the procedure.[9]

Although serum ammonia testing is not endorsed by the AASLD/EASL guidelines for HE,[5] it is ordered nearly universally. The cost of an individual test is relatively low, but the cumulative cost of serum ammonia testing can be substantial because

HE is the most common indication for hospitalization among patients with cirrhosis.[4] Initiatives, such as the Choosing Wisely® campaign, encourage high-value and evidence-based care by limiting excessive and unnecessary diagnostic testing.[10] The Canadian Choosing Wisely campaign specifically includes avoidance of serum ammonia testing for diagnosis of HE to provide high-value care in hepatology.[11]

Although the exact reasons for nonadherence to recommended HE evaluations are unclear, a potential method to mitigate excessive testing is to utilize the EMR and ordering system.[3] EMR-based strategies can curb unnecessary testing in inpatient settings.[12] The use of HE order sets, the inclusion of clinical decision support systems, and the restriction of access to specialized testing can be readily incorporated into the EMR to encourage adherence to guideline-based care while limiting unnecessary testing.

This study should be interpreted in the context of study limitations. Given the retrospective design of the study, salient factors in decisions behind diagnostic testing cannot be assessed. Future studies should utilize mixed-model methodology to elucidate reasons behind these decisions. The present study used a strict definition of complete workup including all the mentioned elements of the diagnostic workup for HE; however, in clinical practice, providers could be justified in not ordering certain tests if the specific clinical scenario does not lead to its use (eg, chest X-ray deferred in a patient with clear lung exam, no symptoms, or hypoxia). Similarly, UDS was included as a required element for a complete workup. While it may be ordered in a case-by-case basis to screen for illicit drug abuse, UDS is also a critical element of the workup to screen for opioid use as a precipitant of HE. Finally, considering the strict study entry criteria, we excluded repeated admissions for HE during the study period and therefore likely underestimate the cost burden of serum ammonia testing.

In conclusion, valuable guideline-based diagnostic testing is often missing in patients admitted for HE while serum ammonia testing is nearly universally ordered. These findings underscore the importance of implementing educational strategies, such as the Choosing Wisely® campaign, and EMR-based clinical decision support systems to improve health resource utilization in patients with cirrhosis and HE.

Disclosures: The authors have nothing to disclose.

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Statistical Modeling and Aggregate-Weighted Scoring Systems in Prediction of Mortality and ICU Transfer: A Systematic Review

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BACKGROUND: The clinical deterioration of patients in general hospital wards is an important safety issue. Aggregate-weighted early warning systems (EWSs) may not detect risk until patients present with acute decline.

PURPOSE: We aimed to compare the prognostic test accuracy and clinical workloads generated by EWSs using statistical modeling (multivariable regression or machine learning) versus aggregate-weighted tools.

DATA SOURCES: We searched PubMed and CINAHL using terms that described clinical deterioration and use of an advanced EWS.

STUDY SELECTION: The outcome was clinical deterioration (intensive care unit transfer or death) of adult patients on general hospital wards. We included studies published from January 1, 2012 to September 15, 2018.

DATA EXTRACTION: Following 2015 PRIMSA systematic review protocol guidelines; 2015 TRIPOD criteria for predictive model evaluation; and the Cochrane Collaboration guidelines, we reported model performance, adjusted positive predictive value (PPV), and conducted simulations of workup-to-detection ratios.

DATA SYNTHESIS: Of 285 articles, six studies reported the model performance of advanced EWSs, and five were of high quality. All EWSs using statistical modeling identified at-risk patients with greater precision than aggregate-weighted EWSs (mean AUC 0.80 vs 0.73). EWSs using statistical modeling generated 4.9 alerts to find one true positive case versus 7.1 alerts in aggregate-weighted EWSs; a nearly 50% relative workload increase for aggregate-weighted EWSs.

CONCLUSIONS: Compared with aggregate-weighted tools, EWSs using statistical modeling consistently demonstrated superior prognostic performance and generated less workload to identify and treat one true positive case. A standardized approach to reporting EWS model performance is needed, including outcome definitions, pretest probability, observed and adjusted PPV, and workup-to-detection ratio. *Journal of Hospital Medicine* 2019;14:161-169. © 2019 Society of Hospital Medicine

Ensuring the delivery of safe and cost-effective care is the core mission of hospitals,[1] but nearly 90% of unplanned patient transfers to critical care may be the result of a new or worsening condition.[2] The cost of treatment of sepsis, respiratory failure, and arrest, which are among the deadliest conditions for hospitalized patients,[3,4] are estimated to be $30.7 billion annually (8.1% of national hospital costs).[5] As many as 44% of adverse events may be avoidable,[6] and concerns about patient safety have motivated hospitals and health systems to find solutions to identify and treat deteriorating patients expeditiously. Evidence suggests that many hospitalized patients presenting with rapid decline showed warning signs 24-48 hours before the event.[7] Therefore, ample time may be available for early identification and intervention in many patients.

As early as 1997, hospitals have used early warning systems (EWSs) to identify at-risk patients and proactively inform clinicians.[8] EWSs can predict a proportion of patients who are at risk for clinical deterioration (this benefit is measured with sensitivity) with the tradeoff that some alerts are false (as measured with positive predictive value [PPV] or its inverse, workup-to-detection ratio [WDR][9-11]). Historically, EWS tools were paper-based instruments designed for fast manual calculation by hospital staff. Many aggregate-weighted EWS instruments continue to be used for research and practice, including the Modified Early Warning Systems (MEWS)[12] and National Early Warning System (NEWS).[13,14] Aggregate-weighted EWSs lack predictive precision because they use simple addition of a few clinical parameter scores, including vital signs and level of consciousness.[15]

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Recently, a new category has emerged, which use multivariable regression or machine learning; we refer to this category as "EWSs using statistical modeling". This type of EWS uses more computationally intensive risk stratification methods to predict risk[16] by adjusting for a larger set of clinical covariates, thereby reducing the degree of unexplained variance. Although these EWSs are thought to be more precise and to generate fewer false positive alarms compared with others,[14,17-19] no review to date has systematically synthesized and compared their performance against aggregate-weighted EWSs.

Purpose

The purpose of this systematic review was to evaluate the recent literature regarding prognostic test accuracy and clinical workloads generated by EWSs using statistical modeling versus aggregate-weighted systems.

METHODS

Search Strategy

Adhering to PRISMA protocol guidelines for systematic reviews, we searched the peer-reviewed literature in PubMed and CINAHL Plus, as well as conference proceedings and online repositories of patient safety organizations published between January 1, 2012 and September 15, 2018. We selected this timeframe because EWSs using statistical modeling are relatively new approaches compared with the body of evidence concerning aggregate-weighted EWSs. An expert PhD researcher confirmed the search results in a blinded independent query.

Inclusion and Exclusion Criteria

We included peer-reviewed articles reporting the area under the receiver operator curve (AUC),[20] or the equivalent c-statistic, of models predicting clinical deterioration (measured as the composite of transfer to intensive care unit (ICU) and/or mortality) among adult patients in general hospital wards. We excluded studies if they did not compare an EWS using statistical modeling with an aggregate-weighted EWS, did not report AUC, or only reported on an aggregate-weighted EWS. Excluded settings were pediatrics, obstetrics, emergency departments, ICUs, transitional care units, and oncology. We also excluded studies with samples limited to physiological monitoring, sepsis, or postsurgical subpopulations.

Data Abstraction

Following the TRIPOD guidelines for the reporting of predictive models,[21] and the PRISMA and Cochrane Collaboration guidelines for systematic reviews,[22-24] we extracted study characteristics (Table 1), sample demographics (Appendix Table 4), model characteristics and performance (Appendix Table 5), and level of scientific evidence and risk of bias (Appendix Table 6). To address the potential for overfitting, we selected model performance results of the validation dataset rather than the derivation dataset, if reported. If studies reported multiple models in either EWS category, we selected the best-performing model for comparison.

Measures of Model Performance

Because predictive models can achieve good case identification at the expense of high clinical workloads, an assessment of model performance would be incomplete without measures of clinical utility. For clinicians, this aspect can be measured as the model's PPV (the percentage of true positive alerts among all alerts), or more intelligibly, as the WDR, which equals 1/PPV. WDR indicates the number of patients requiring evaluation to identify and treat one true positive case.[9-11] It is known that differences in event rates (prevalence or pretest probability) influence a model's PPV[25] and its reciprocal WDR. However, for systematic comparison, PPV and WDR can be standardized using a fixed representative event rate across studies.[24,26] We abstracted the reported PPV and WDR, and computed standardized PPV and WDR for an event rate of 4%.

Other measures included the area under the receiver operator curve (AUC),[20] sensitivity, and specificity. AUC plots a model's false positive rate (x-axis) against its true positive rate (y-axis), with an ideal scenario of very high y-values and very low x-values.[27] Sensitivity (the model's ability to detect a true positive case among all cases) and specificity (the model's ability to detect a true noncase among all noncases[28]) are influenced by chosen alert thresholds. It is incorrect to assume that a given model produces only one sensitivity/specificity result; for systematic comparison, we therefore selected results in the 50% sensitivity range, and separately, in the 92% specificity range for EWSs using statistical modeling. Then, we simulated a fixed sensitivity of 0.51 and assumed specificity of 0.87 in aggregate-weighted EWSs.

RESULTS

Search Results

The PubMed search for "early warning score OR early warning system AND deterioration OR predict transfer ICU" returned 285 peer-reviewed articles. A search on CINAHL Plus using the same filters and query terms returned 219 articles with no additional matches (Figure 1). Of the 285 articles, we excluded 269 during the abstract screen and 10 additional articles during full-text review (Figure 1). A final review of the reference lists of the six selected studies did not yield additional articles.

Study Characteristics

There were several similarities across the selected studies (Table 1). All occurred in the United States; all compared their model's performance against at least one aggregate-weighted EWS model;[14,17-19,29] and all used retrospective cohort designs. Of the six studies, one took place in a single hospital;[29] three pooled data from five hospitals;[17,18,30] and two occurred in a large integrated healthcare delivery system using data from 14 and, subsequently, 21 hospitals.[14,19] The largest study[14] included nearly 650,000 admissions, while the smallest study[29] reported slightly less than 7,500 admissions. Of the six studies, four used multivariable regression,[14,17,19,29] and two used machine learning techniques for outcome prediction.[18,30]

TABLE 1. **Characteristics of Six Early Warning System Studies Using Statistical Modeling for the Detection of Deterioration Risk**

Study	Setting; Location	No. of Hospitals; Time Period; Hospitalizations; Event Rate	Study Purpose; Outcome	Research Design; Model; Missing Data
Escobar et al., 2012[19]	Health system Northern California, United States	14 hospitals with EHRs deployed November 2006-December 2009 39,782 shift units 4,036 events Event rate: 0.102	Evaluation of EDIP multivariable regression model using EHR data and comparing results against MEWS (an aggregate-weighted tool) Composite outcome: transfer to ICU, death on ward when patient was full code	Retrospective case-control study Multivariable logistic regression
Alvarez et al., 2013[29]	Academic medical center Dallas, Texas, United States	One hospital May 2009-March 2010 7,466 hospitalizations 585 events Event rate: 0.078	Comparison of multivariable regression model vs MEWS Composite outcome: cardiopulmonary arrest, acute respiratory compromise, unexpected death, transfer to ICU	Retrospective cohort study Multivariable logistic regression Management/adjustment of missing data not discussed
Churpek et al., 2014[17]	University health system Illinois, United States	Five medical centers (One tertiary academic, four from a university health system) November 2008-January 2013 269,999 hospitalizations 16,452 events Event rate: 0.061	Development and validation of a deterioration risk score using EHR data, comparison of model performance against VitalPAC EWS Composite outcome: cardiac arrest, ICU transfer, death on ward	Retrospective cohort study Multivariable survival analysis Management/adjustment of missing data: carried previous value forward or imputed median value if no previous value was available
Churpek et al., 2016[18]	University health system Illinois, United States	Five medical centers (one tertiary academic, four from a university health system) November 2008-January 2013 269,999 hospitalizations 16,452 events Event rate: 0.061	Comparison of different machine learning algorithms, multivariable regression model, and MEWS Composite outcome: cardiac arrest, ICU transfer, death on ward without attempted resuscitation	Retrospective cohort study Machine learning (random forest was the best-performing model) Management/adjustment of missing data: carried previous value forward or imputed median value if no previous value was available
Kipnis et al., 2016[14]	Health system Northern California, United States	21 hospitals January 2010-December 2013 649,418 hospitalizations 19,153 events Event rate: 0.030	Comparison of AAM an automated electronic early warning system using EHR data, eCART (Churpek et al., 2014) and NEWS (Kovacs et al. 2016) Composite outcome: transfer to ICU, death on ward when patient was full code	Retrospective cohort study, predictive risk for death, unanticipated ICU transfer followed/not followed by a surgical intervention Multivariable logistic regression Missing data were imputed
Green et al., 2018[30]	University health system Illinois, United States	Five medical centers (one tertiary academic, four from a university health system) November 2008-August 2013 107,868 hospitalizations 6,142 events Event rate: 0.057	Comparison of eCART machine learning model (random forest), "Between the Flags" calling criteria, MEWS, and NEWS Composite outcome: cardiac arrest, ICU transfer, death on ward within 24 hours	Retrospective cohort study Machine learning (random forest) (excluded patients used for model derivation in previous work by Churpek et al.)

Abbreviations: AAM, advance monitor alarm; EDIP, early detection of impending physiologic deterioriation; EHR, electronic health record; EWS, early warning system; ICU, intensive care unit; MEWS, modified early warning system; NEWS, national early warning system.

Outcome Variables

The primary outcome for inclusion in this review was clinical deterioration measured by the composite of transfer to ICU and some measure of mortality. Churpek et al.[10,11] and Green et al.[30] also included cardiac arrest, and Alvarez et al.[22] included respiratory compromise in their outcome composite.

Researchers used varying definitions of mortality, including "death outside the ICU in a patient whose care directive was full code;"[14,19] "death on the wards without attempted resuscitation;"[17,18] "an in-hospital death in patients without a DNR order at admission that occurred on the medical ward or in ICU within 24 hours after transfer;"[29] or "death within 24 hours."[30]

Predictor Variables

We observed a broad assortment of predictor variables. All models included vital signs (heart rate, respiratory rate, blood pressure, and venous oxygen saturation); mental state; laboratory data; age; and sex. Additional variables included comorbidity, shock index,[31] severity of illness score, length of stay, event time of day, season, admission category, and length of stay,[14,19] among others.

Model Performance

Reported PPV ranged from 0.16 to 0.42 (mean = 0.27) in EWSs using statistical modeling and 0.15 to 0.28 (mean = 0.19) in

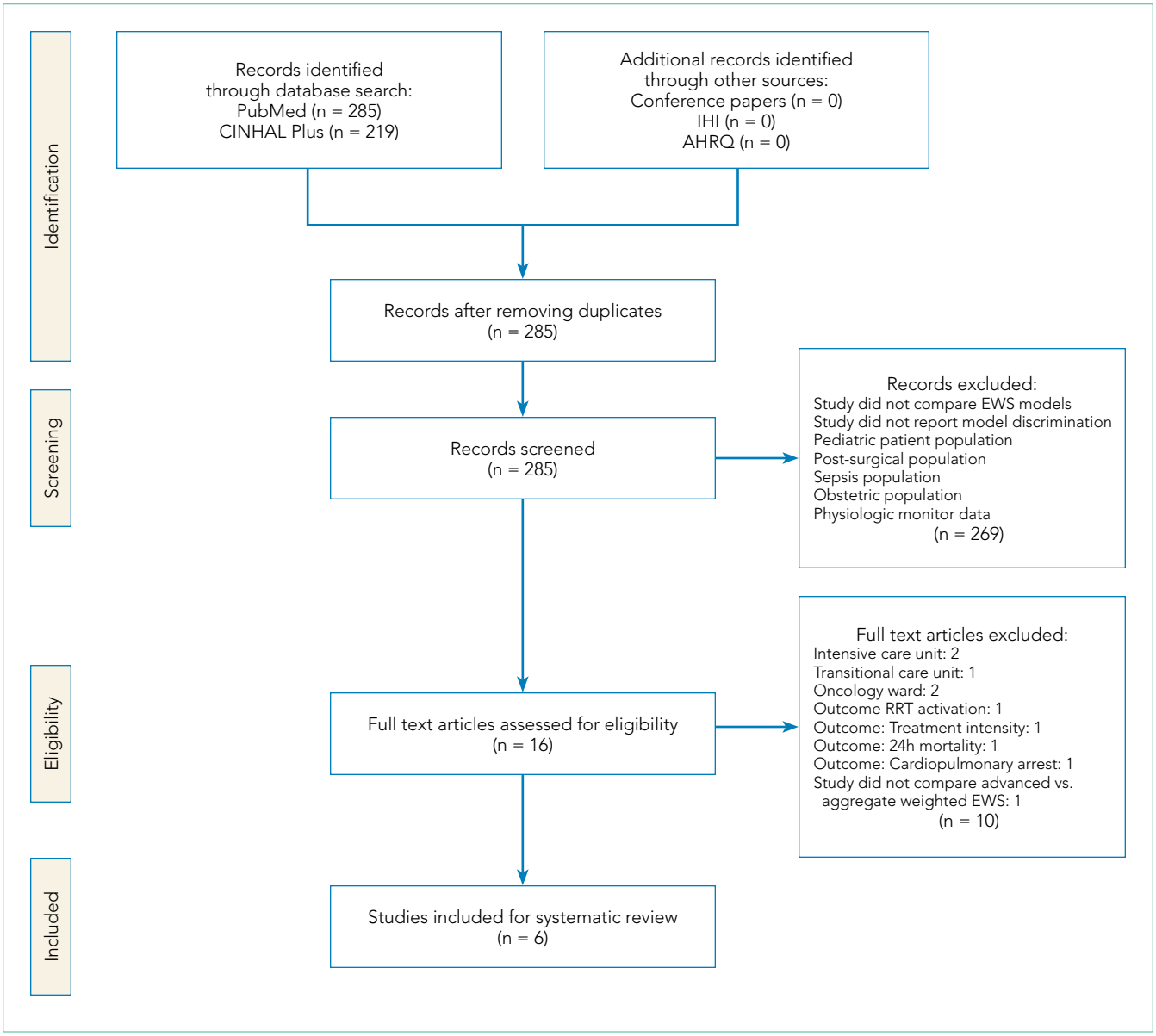

FIG 1. PRISMA Flow Diagram of Study Selection. Adapted from Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1. doi: 10.1186/2046-4053-4-1.

Abbreviations: AHRQ, Agency for Healthcare Research and Quality; EWS, early warning system; IHI, Institute for Healthcare Improvement.

aggregate-weighted EWS models. The weighted mean standardized PPV, adjusted for an event rate of 4% across studies (Table 2), was 0.21 in EWSs using statistical modeling versus 0.14 in aggregate-weighted EWS models (simulated at 0.51 sensitivity and 0.87 specificity).

Only two studies[14,19] reported the WDR metric (alerts generated to identify one true positive case) explicitly. Based on the above PPV results, EWSs using statistical modeling generated a standardized WDR of 4.9 in models using statistical modeling versus 7.1 in aggregate-weighted models (Figure 2). The delta of 2.2 evaluations to find and treat one true positive case equals a 45% relative increase in RRT evaluation workloads using aggregate-weighted EWSs.

AUC values ranged from 0.77 to 0.85 (weighted mean = 0.80) in EWSs using statistical modeling, indicating good model discrimination. AUCs of aggregate-weighted EWSs ranged from 0.70 to 0.76 (weighted mean = 0.73), indicating fair model discrimination (Figure 2). The overall AUC delta was 0.07. However, our estimates may possibly be favoring EWSs that use statistical modeling by virtue of their derivation in an original research population compared with aggregate-weighted EWSs that were derived externally. For example, sensitivity analysis of eCART,[18] an EWS using machine learning, showed an AUC drop of 1% in a large external patient population,[14] while NEWS AUCs[13] dropped between 11% and 15% in two large external populations (Appendix Table 7).[14,30] For hospitals adopting an externally developed EWS using statistical modeling, these results suggest that an AUC delta of approximately 5% can be ex-

pected and 7% for an internally developed EWS.

The models' sensitivity ranged from 0.49 to 0.54 (mean = 0.51) for EWSs using statistical modeling and 0.39 to 0.50 (mean = 0.43). These results were based on chosen alert volume cutoffs. Specificity ranged from 0.90 to 0.94 (mean = 0.92) in EWSs using statistical modeling compared with 0.83 to 0.93 (mean = 0.89) in aggregate-weighted EWS models. At the 0.51 sensitivity level (mean sensitivity of reported EWSs using statistical modeling), aggregate-weighted EWSs would have an estimated specificity of approximately 0.87. Conversely, to reach a specificity of 0.92 (mean specificity of reported EWSs using statistical modeling, aggregate-weighted EWSs would have a sensitivity of approximately 0.42 compared with 0.50 in EWSs using statistical modeling (based on three studies reporting both sensitivity and specificity or an AUC graph).

Risk of Bias Assessment

We scored the studies by adapting the Cochrane Collaboration tool for assessing risk of bias [32] (Appendix Table 5). Of the six studies, five received total scores between 1.0 and 2.0 (indicating relatively low bias risk), and one study had a score of 3.5 (indicating higher bias risk). Low bias studies[14,17-19,30] used large samples across multiple hospitals, discussed the choice of predictor variables and outcomes more precisely, and reported their measurement approaches and analytic methods in more detail, including imputation of missing data and model calibration.

DISCUSSION

In this systematic review, we assessed the predictive ability of EWSs using statistical modeling versus aggregate-weighted EWS models to detect clinical deterioration risk in hospitalized adults in general wards. From 2007 to 2018, at least five systematic reviews examined aggregate-weighted EWSs in adult inpatient settings.[33-37] No systematic review, however, has synthesized the evidence of EWSs using statistical modeling.

The recent evidence is limited to six studies, of which five had favorable risk of bias scores. All studies included in this review demonstrated superior model performance of the EWSs using statistical modeling compared with an aggregate-weighted EWS, and at least five of the six studies employed rigor in design, measurement, and analytic method. The AUC absolute difference between EWSs using statistical modeling and aggregate-weighted EWSs was 7% overall, moving model performance from fair to good (Table 2; Figure 2). Although this increase in discriminative power may appear modest, it translates into avoiding a 45% increase in WDR workload generated by an aggregate-weighted EWS, approximately two patient evaluations for each true positive case.

Results of our review suggest that EWSs using statistical modeling predict clinical deterioration risk with better precision. This is an important finding for the following reasons: (1) Better risk prediction can support the activation of rescue; (2) Given federal mandates to curb spending, the elimination of some resource-intensive false positive evaluations supports high-value care;[38] and (3) The Quadruple Aim[39] accounts for clinician wellbeing. EWSs using statistical modeling may offer benefits in terms of clinician satisfaction with the human–system interface because better discrimination reduces the daily evaluation workload/cognitive burden and because the reduction of false positive alerts may reduce alert fatigue.[40,41]

Still, an important issue with risk detection is that it is unknown which percentage of patients are uniquely identified by an EWS and not already under evaluation by the clinical team. For example, a recent study by Bedoya et al.[42] found that using NEWS did not improve clinical outcomes and nurses frequently disregarded the alert. Another study[43] found that the combined clinical judgment of physicians and nurses had an AUC of 0.90 in predicting mortality. These results suggest that at certain times, an EWS alert may not add new useful information for clinicians even when it correctly identifies deterioration risk. It remains difficult to define exactly how many patients an EWS would have to uniquely identify to have clinical utility.

Even EWSs that use statistical modeling cannot detect all true deterioration cases perfectly, and they may at times trigger an alert only when the clinical team is already aware of a patient's clinical decline. Consequently, EWSs using statistical modeling can at best augment and support—but not replace—RRT rounding, physician workup, and vigilant frontline staff. However, clinicians, too, are not perfect, and the failure-to-rescue literature suggests that certain human factors are antecedents to patient crises (eg, stress and distraction,[44-46] judging by precedent/experience,[44,47] and innate limitations of human cognition[47]). Because neither clinicians nor EWSs can predict deterioration perfectly, the best possible rescue response combines clinical vigilance, RRT rounding, and EWSs using statistical modeling as complementary solutions.

Our findings suggest that predictive models cannot be judged purely on AUC (in fact, it would be ill-advised) but also by their clinical utility (expressed in WDR and PPV): How many patients does a clinician need to evaluate?[9-11] Precision is not meaningful if it comes at the expense of unmanageable evaluation workloads, and our findings suggest that clinicians should evaluate models based on their clinical utility. Hospitals considering adoption of an EWS using statistical modeling should consider that externally developed EWSs appear to experience a performance drop when applied to a new patient population; a slightly higher WDR and slightly lower AUC can be expected. EWSs using statistical modeling appear to perform best when tailored to the targeted patient population (or are derived in-house). Model depreciation over time will likely require recalibration. In addition, adoption of a machine learning algorithm may mean that original model results are obscured by the black box output of the algorithm.[48-50]

Findings from this systematic review are subject to several limitations. First, we applied strict inclusion criteria, which led us to exclude studies that offered findings in specialty units and specific patient subpopulations, among others. In the interest of systematic comparison, our findings are limited to general wards. We also restricted our search to recent studies that reported on models predicting clinical deterioration,

TABLE 2. **Early Warning System Model Performance in Five Studies Using Statistical Modeling versus Aggregate-Weighted Scores from January 1, 2012 to September 15, 2018**

	Alvarez et al. (2013)	Churpek et al. (2014)	Churpek et al. (2016)	Kipnis et al. (2016)	Green et al. (2018)	Total	Simulated estimate
Early Warning Systems Using Statistical Modeling							
AUC (95% CI)	0.85 (0.82-0.87)	0.77 (0.76-0.77)	0.8 (0.80-0.80)	0.82 (0.81-0.83)	0.8 (0.80-0.80)	0.80[a]	*0.80*[a]
Sensitivity	0.52	0.54	0.50	0.49	0.50	0.51[b]	0.51[b]
Specificity	0.94	0.90	0.93	0.92	0.90	0.92[b]	0.92[b]
PPV	0.42	0.20	0.32	0.16	0.23	0.27[b]	0.21[b]
Standardized PPV	0.27	0.18	0.23	0.20	0.17	0.21[b]	0.21[b]
WDR	2.4	4.9	3.2	6.3	4.3	4.2[b]	4.9[b]
Standardized WDR	3.8	5.4	4.4	4.9	5.8	4.9[b]	4.9[b]
Aggregate-Weighted Early Warning Systems							
AUC (95% CI)	0.75 (0.71-0.78)	0.73 (0.72-0.73)	0.7 (0.70-0.70)	0.76 (0.75-0.78)	0.72 (0.72-0.72)	0.73[a]	0.73[a]
Sensitivity	0.42	0.39	0.50	0.40	0.42	0.43[b]	0.51
Specificity	0.91	0.90	0.83	0.93	0.90	0.89[b]	0.87
PPV	0.28	0.16	0.16	0.15	0.20	0.19[b]	0.14
Standardized PPV	0.16	0.14	0.11	0.19	0.15	0.15[b]	0.14
WDR	3.5	6.4	6.2	6.7	4.9	5.6[b]	7.1
Standardized WDR	6.1	7.2	9.2	5.2	6.7	6.9[b]	7.1
Deltas							
AUC delta	0.10	0.04	0.10	0.06	0.08	0.07	0.07
Standardized WDR delta	2.4	1.7	4.8	0.3	0.9	2.0	2.2

Note: We removed Escobar et al. (2012) from analysis because Kipnis et al. (2016) used the same model.
[a] Weighted
[b] Mean
Abbreviations: AUC, area under the curve; PPV, positive predictor value; WDR, workup to detection ratio.

which we defined as the composite of ICU transfer and/or death. Clinically, deteriorating patients in general wards either die or are transferred to ICU. This criterion resulted in exclusion of the Rothman Index,[51] which predicts "death within 24 hours" but not ICU transfer. The AUC in this study was higher than those selected in this review (0.93 compared to 0.82 for MEWS; AUC delta: 0.09). The higher AUC may be a function of the outcome definition (30-day mortality would be more challenging to predict). Therefore, hospitals or health systems interested in purchasing an EWS using statistical modeling should carefully consider the outcome selection and definition.

Second, as is true for systematic reviews in general,[52] the degree of clinical and methodological heterogeneity across the selected studies may limit our findings. Studies occurred in various settings (university hospital, teaching hospitals, and community hospitals), which may serve diverging patient populations. We observed that studies in university-based settings had a higher event rate ranging from 5.6% to 7.8%, which may result in higher PPV results in these settings. However, this increase would apply to both EWS types equally. To arrive at a "true" reflection of model performance, the simulations for PPV and WDR have used a more conservative event rate of 4%. We observed heterogenous mortality definitions, which did not always account for the reality that a patient's death may be an appropriate outcome (ie, it was concordant with treatment wishes in the context of severe illness or an end-of-life trajectory). Studies also used different sampling procedures; some allowed multiple observations although most did not. The variation in sampling may change PPV and limit our systematic comparison. However, regardless of methodological differences, our review suggests that EWSs using statistical modeling perform better than aggregate-weighted EWSs in each of the selected studies.

Third, systematic reviews may be subject to the issue of publication bias because they can only compare published results

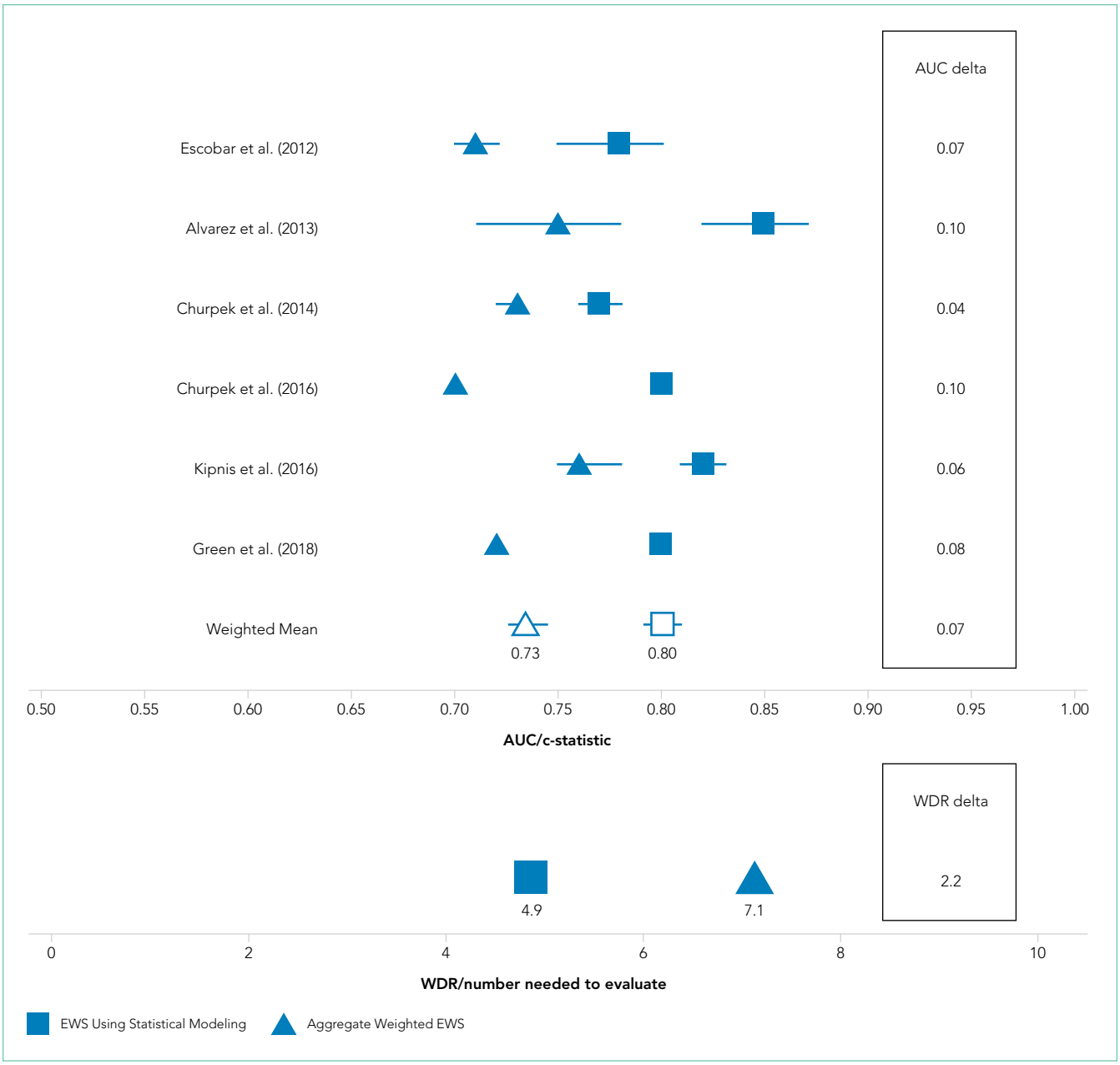

FIG 2. Early Warning System Model Discrimination and Standardized Workup to Detection Ratios in 6 Studies Using Statistical Modeling vs Aggregate-Weighted Scores from January 1, 2012 to September 18, 2018

Note: AUC describes the models' ability to predict an outcome accurately, with 0.50 indicating no ability to predict an outcome. For AUC higher is better. Standardized WDR: Number needed to find one true deterioration case. For WDR, lower is better.

Abbreviations: AUC, area under the curve; EWS, early warning system; WDR, workup to detection ratio.

and could possibly omit an unknown number of unpublished studies. However, the selected studies uniformly demonstrated similar model improvements, which are plausibly related to the larger number of covariates, statistical methods, and shrinkage of random error.

Finally, this review was limited to the comparison of observational studies, which aimed to answer how the two EWS classes compared. These studies did not address whether an alert had an impact on clinical care and patient outcomes. Results from at least one randomized nonblinded controlled trial suggest that alert-driven RRT activation may reduce the length of stay by 24 hours and use of oximetry, but has no impact on mortality, ICU transfer, and ICU length of stay.[53]

CONCLUSION

Our findings point to three areas of need for the field of predictive EWS research: (1) a standardized set of clinical deterioration outcome measures, (2) a standardized set of measures capturing clinical evaluation workload and alert frequency, and (3) cost estimates of clinical workloads with and without deploy-

ment of an EWS using statistical modeling. Given the present divergence of outcome definitions, EWS research may benefit from a common "clinical deterioration" outcome standard, including transfer to ICU, inpatient/30-day/90-day mortality, and death with DNR, comfort care, or hospice. The field is lacking a standardized clinical workload measure and an understanding of the net percentage of patients uniquely identified by an EWS.

By using predictive analytics, health systems may be better able to achieve the goals of high-value care and patient safety and support the Quadruple Aim. Still, gaps in knowledge exist regarding the measurement of the clinical processes triggered by EWSs, evaluation workloads, alert fatigue, clinician burnout associated with the human-alert interface, and costs versus benefits. Future research should evaluate the degree to which EWSs can identify risk among patients who are not already under evaluation by the clinical team, assess the balanced treatment effects of RRT interventions between decedents and survivors, and investigate clinical process times relative to the time of an EWS alert using statistical modeling.

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Clinical Guideline Highlights for the Hospitalist: Maintenance Intravenous Fluids in Infants and Children

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GUIDELINE TITLE: 2018 American Academy of Pediatrics (AAP) Clinical Practice Guideline: Maintenance Intravenous Fluids in Children

RELEASE DATE: November 26, 2018

PRIOR VERSION: Not Applicable

DEVELOPER: Multidisciplinary subcommittee of experts assembled by the AAP

FUNDING SOURCE: AAP

TARGET POPULATION: Patients 28 days to 18 years of age requiring maintenance intravenous fluids (IVFs).

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Hospitalized children with inadequate fluid intake are often administered maintenance intravenous fluids (IVFs) to support metabolic needs and sensible losses. Historically, hypotonic IVFs have been the standard, based on theoretical water and electrolyte requirements for estimated energy expenditure.[1] However, when combined with increased levels of arginine vasopressin (AVP) seen in acutely ill children which impairs free-water excretion,[2] hypotonic IVF can result in hyponatremia. The recently published guideline by the American Academy of Pediatrics (AAP)[3] is the first to provide an evidence-based recommendation on the use of maintenance IVF therapy in children.

KEY RECOMMENDATION FOR HOSPITALISTS

Patients between the ages of 28 days and 18 years should receive isotonic solutions with appropriate potassium chloride and dextrose for maintenance IVFs (evidence quality: high; recommendation strength: strong)

Isotonic fluids, such as 0.9% NaCl (normal saline), Hartmann solution and PlasmaLyte, contain a sodium concentration similar to that of plasma (135-144 mEq/L). Lactated Ringer solution (LR) is near-isotonic (sodium 130 mEq/L), but was not used in any of the reviewed studies and therefore not included in the recommendation. Excluded are patients with neurosurgical disorders, congenital or acquired cardiac disease, hepatic disease, cancer, renal dysfunction, diabetes insipidus, voluminous watery diarrhea, severe burns, or patients in the neonatal intensive care unit.

The primary benefit of the AAP recommendation is the reduced risk of iatrogenic hyponatremia and its associated sequelae, including complications or impact on cost of care. The number needed to treat with isotonic fluids was 7.5 to prevent any hyponatremia and 27.8 to prevent moderate hyponatremia (<130 mEq/L). Increases in readmission rates, length of stay, and cost of hospitalization have been reported in a recent meta-analysis reviewing the economic burden of hyponatremia in both adults and children.[4]

Potential harms from the use of isotonic fluids include hypernatremia, hyperchloremic metabolic acidosis, and fluid overload, although available data have not demonstrated an increased risk of these complications. In light of a recent normal saline (NS) shortage in the United States, limited availability is also a consideration. Plasmalyte is more costly than NS and is currently incompatible with the addition of dextrose.

CRITIQUE

Methods in Preparing Guideline

The guideline development committee included broad representation by pediatric experts in primary care, hospital medicine, emergency medicine, critical care medicine, nephrology, anesthesiology, surgery and quality improvement, as well as a guideline methodologist/informatician and epidemiologist.

Search strategies from recently published systematic reviews of clinical trials comparing isotonic with hypotonic maintenance IVFs were used to identify studies eligible for inclusion. A total of 17 studies with 2,455 total patients were initially identified and included. One additional study meeting inclusion criteria was found after the committee convened and excluded from the guideline.[5] Three reviewers from the subcommittee performed a structured critical appraisal of each article. The methods of each trial were assessed for risk-of-bias in multiple domains, including randomization, allocation concealment, performance, detection, attrition and reporting. Forest plots were generated using random-effects models and Mantel-Haenzel statistics with the outcome of hyponatremia.

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The guideline underwent review by various stakeholders including AAP councils, committees, and sections, and individuals considered experts in the field.

A strength of the guideline is the high quality of the evidence and the consistent findings. All of the included studies were randomized clinical trials and the number of included patients was large. Of the 17 included studies, 16 reported a risk ratio favoring isotonic fluids over hypotonic fluids in the prevention of developing hyponatremia; the results of the study that favored hypotonic fluids were not statistically significant on their own. A sensitivity analysis was performed to exclude one study with a 20% weight, determined by multiple factors such as sample size, confidence interval, and an unusually high rate of hyponatremia in the isotonic and hypotonic fluids groups (33.3 % and 70%, respectively).[6] After exclusion, there was no change in the overall estimated risk in hypotonic fluids leading to hyponatremia. Only one trial had two sources of high risk of bias (allocation concealment, attrition) and the remaining had only low or unclear risk of biases in the various domains.

The study that was excluded due to its late identification similarly shows increased risk of hyponatremia in groups administered hypotonic fluids (risk ratio 6.5-8.5), and would likely not affect the estimated risk.[5]

Despite differences in types of patients enrolled, rate of administered fluids, type of IVF, frequency of lab testing, and study duration, the I^2 (degree of heterogeneity) of the forest plot of all included studies remained low at 14% and the increased risk of hyponatremia from hypotonic fluids remained consistent.

Due to study design differences, a limitation of the guideline is that no recommendation is made regarding the type of isotonic fluids and the rate of IVF administration. Additionally, due to the low frequency of clinically significant sequelae of hyponatremia, such as hyponatremic encephalopathy, it remains uncertain how many patients would need to be treated with isotonic fluids to prevent a rare but potentially devastating event.

Sources of Potential Conflict of Interest or Bias

The guideline was developed and funded by the AAP. A formal conflict of interest management policy was followed, and subcommittee members had no conflicts of interests or financial relationships relevant to the guideline to disclose.

Generalizability

Given the large number of patients included in the studies and heterogeneity of the population included, the recommendation applies to most patients cared for by pediatric hospitalists. Several patient exclusions relevant to the pediatric hospitalist deserve mention: neonates, kidney disease, and voluminous diarrhea. Neonates under the age of 28 days, including febrile neonates, are excluded from the guideline because of the immature concentrating abilities of neonatal kidneys. Patients with renal impairment were excluded from the guideline recommendation because several studies excluded patients with kidney disease. Hospitalists often care for children who sustain prerenal acute kidney injury from severe dehydration. In this condition, the kidney conserves water through the release of AVP. While an excluded population, these patients would be even more susceptible to develop hyponatremia if administered hypotonic fluids. Patients with "voluminous diarrhea" are excluded from the guideline because those with gastroenteritis with ongoing losses may require IVFs at rates higher than maintenance, and are particularly vulnerable to electrolyte derangements. The guideline, however, does not define voluminous diarrhea, leaving it to the discretion of the treating clinician.

Finally, it is critical to mention that IVF should be considered a therapy to be judiciously used, and discontinued when possible. While the guideline addresses the choice of fluid composition, alternatives to orally or enterally hydrate a patient are always preferred.

AREAS IN NEED OF FUTURE STUDY

While the guideline strongly recommends isotonic fluids for maintenance therapy, the choice of isotonic fluid remains with the clinician. Most included studies used NS for their isotonic groups, but Hartmann's solution and Plasmalyte were represented in a few studies. LR, one of the more widely used balanced solutions, though slightly hypotonic (130 mEq/L), was not studied. The exclusion of LR from the included studies is unfortunate, as the benefit of balanced solutions compared to NS after significant fluid resuscitation has been shown in the setting of severe sepsis and shock.[7] Hyperchloremic metabolic acidosis after fluid resuscitation with NS has raised concern about continuing NS as maintenance fluid and possibly worsening acidosis or hyperchloremia and its adverse effects.[8] Further studies on the potential benefit of LR as maintenance fluid, or the potential harms of unbalanced solutions as maintenance fluids in the setting of significant resuscitation are needed.

Disclosures: The authors have nothing to disclose.

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Clinical Guideline Highlights for the Hospitalist: The Use of Intravenous Fluids in the Hospitalized Adult

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GUIDELINE TITLE: Intravenous Fluid Therapy in Adults in Hospital

RELEASE DATE: December, 2013

PRIOR VERSION: Not Applicable

DEVELOPER: Multidisciplinary Guideline Development Group within the United Kingdom's National Clinical Guideline Centre

FUNDING SOURCE: National Institute for Health and Care Excellence

TARGET POPULATION: Hospitalized adult patients

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Hospitalized patients often receive intravenous fluids (IVF) when they cannot meet physiologic needs through oral intake in the setting of medical or surgical illness. Prescribing the optimal IVF solution to the appropriate patient is a complex decision and often occurs without the same degree of institutionalized restrictions or guidance developed for other inpatient pharmacologic agents. There is wide variation in clinical utilization of IVF due to the lack of data to guide decision making.[1] When data do exist, they typically focus on a limited number of clinical situations.[2] Thus, even though IVF are often considered low-risk, the frequency and lack of consistency with which they are used can result in errors, complications, and over-use of medical resources.[3]

KEY RECOMMENDATIONS FOR THE HOSPITALIST

(Evidence quality: not described in the guideline, recommendation strength: not described in the guideline)

Recommendation 1

To aid in fluid management and avoid complications, the guidelines recommend that patients on IVF require careful assessment of volume status, including a detailed history, physical exam, clinical monitoring, and daily labs.[2]

Clinical history should focus on understanding fluid losses and intake; physical exam should include vital signs, evidence of orthostatic hypotension, capillary refill, jugular venous pulsation, and assessment for pulmonary edema. Subsequent clinical monitoring should include fluid balance (Ins and Outs) and daily weights. All patients starting or continuing IVF should have a basic metabolic panel at least daily according to the guidelines, though the authors note this frequency may be too high for some patients and needs further study.[2]

Recommendation 2

The guidelines describe four types of IV fluids that can be administered: crystalloids, balanced crystalloids, glucose solutions, and non blood-product colloids.[2]

Crystalloids include isotonic saline with 154 millimoles (mmol) of sodium and chloride. Balanced crystalloids, such as lactated Ringer's solution, are more physiologic, with less sodium and chloride, and the addition of magnesium, potassium, and calcium. Glucose solutions are quickly metabolized and, thus, are an effective way to deliver free water. Non blood-product colloids include particles that are retained within the circulation, including proteins such as human albumin.

Recommendation 3

For each indication to administer IVF, the guidelines recommend the following formulations and considerations:[2]

For general resuscitation, use crystalloids with sodium content of 130-154 mmol, delivered in a bolus of at least 500 milliliters (mL) over 15 minutes or less. For sepsis, infuse at least 30 mL/kg.[4] For routine maintenance, restrict the volume to 25-30 mL/kg/day of water, and include 1 mmol/kg/day of potassium, sodium, and chloride along with 50-100 g/day of glucose to prevent starvation ketosis, though glucose should be avoided in most diabetic patients. With obesity, adjust the IVF to ideal body weight, and for patients who are older, frail, or admitted with renal or cardiac impairment, consider prescribing a lower range of fluid (20-25 mL/kg/day). For redistribution or replacement, use sodium chloride or balanced crystalloids or consider colloids, which have a theoretical advantage in expanding intravascular volume while

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limiting interstitial edema. Note that colloids are more expensive, and definitive evidence supporting increased efficacy is lacking. Clinicians should monitor closely for hypovolemia, hypervolemia, and electrolyte abnormalities, particularly hypo- and hypernatremia that carry associated mental status implications and risk of central pontine myelinolysis. The inadvertent overuse of IVF is common in hospital settings, particularly when maintenance fluids are not discontinued upon patient improvement or when patients move between care areas. Thus, regular clinical reassessment of volume status is important.

Recommendation 4

In both noncritically ill and critically ill hospitalized patients, there is a benefit to using balanced crystalloids compared to isotonic saline in preventing major adverse kidney events and death.[5,6]

Two important studies in 2018 added new information to the existing NICE guidelines, addressing the previously unanswered question of the benefits of balanced crystalloids versus isotonic saline, one among non-critically ill patients and the other among critically ill patients.[5,6] Prior data suggested that the use of isotonic saline is associated with multiple complications, including hyperchloremic metabolic acidosis, acute kidney injury, and death. In the non-critically ill population, the use of balanced crystalloids resulted in lower incidence of major adverse kidney events (absolute difference of 0.9%), but did not change the number of hospital days (the primary outcome).[5] In the critically ill population the use of balanced crystalloids resulted in lower rates of death, new renal replacement therapy, or persistent renal dysfunction,[6] and the authors found preferential use of balanced crystalloids could prevent one out of every 94 patients admitted to the ICU from experiencing these adverse outcomes. Given the similar cost associated with isotonic saline and balanced crystalloids, these new findings suggest hospitalists should select balanced crystalloids if there is no compelling clinical reason to use isotonic saline.

CRITIQUE

While conflicts of interest are often a concern in clinical guidelines due to influence by pharmaceutical, device, and specialty interests, the United Kingdom's National Clinical Guideline Centre (NGC), which developed the NICE guidelines, is hosted by the Royal College of Physicians and has governance partnerships with the Royal College of Surgeons of England, Royal College of General Practitioners, and Royal College of Nursing. Each guideline produced by the NGC is overseen by an independent guideline committee comprised of healthcare professionals and patient representatives, and as a result, concern for conflicts of interest is low.

The NICE guidelines were created by a multidisciplinary team from multiple clinical specialties, and reviewed evidence addressing both clinical and health economic outcomes. Importantly, data from randomized controlled studies was relatively limited. The data excluded patients under 16 years of age, pregnant women, and those with severe liver or renal disease, diabetes or burns, as well as those in intensive care settings. Unfortunately, many medical patients cared for by hospitalists fall into one or more of these categories, limiting applicability of the guidelines.

Two important studies in 2018 added new information to the existing NICE guidelines, as outlined in Recommendation 4.[5,6] Both of these studies occurred at a single institution, limiting their generalizability, though each study included a diverse patient population. In the ICU study, treating clinicians were aware of the composition of the assigned crystalloid so the decision to initiate renal-replacement therapy may have been susceptible to treatment bias. In addition, censoring of data collection at hospital discharge may have underestimated the true incidence of death at 30 days and overestimated persistent renal dysfunction at 30 days. Importantly, the trial design did not allow comparison of lactated Ringer's solution versus Plasma-Lyte. The non-ICU study evaluated patients who began treatment in the emergency department and were subsequently admitted to non-ICU inpatient units—a population that mirrors much of hospitalist practice, however the un-blinded design makes bias a concern. Finally, lactated Ringer's solution represented more than 95% of the balanced crystalloids used in the trial, so additional study is required to compare Plasma-Lyte with both saline and lactated Ringer's solution.

AREAS IN NEED OF FUTURE STUDY

More evidence is needed to better understand the appropriate use of IVF in specific clinical scenarios, including to determine if balanced solutions, as compared with isotonic saline, are superior across a spectrum of clinical conditions. For patients with an indication for maintenance fluid administration, determining if a higher sodium content reduces the risk of hyponatremia without increasing the risk of volume overload will help guide practice. Finally, more comprehensive study of the incidence of overuse and complications as a consequence of IVF, as well as the optimal frequency of lab monitoring, is needed to guide understanding of how practicing hospitalists and health systems can help reduce harm and waste

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Postacute Care Transitions: Developing a Skilled Nursing Facility Collaborative within an Academic Health System

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Hospitals are under financial pressure to shorten hospitalizations and reduce readmissions. Current evidence suggests that postacute care-associated rehospitalizations could be reduced by focusing on a concentrated referral network of preferred high-quality skilled nursing facilities (SNFs). Hospitals, health systems, and health plans have taken several approaches to creating preferred provider networks to streamline and improve the quality of SNF discharges. We propose a collaborative framework for the establishment of a preferred postacute care network based on the experience of the Johns Hopkins Medicine Skilled Nursing Facility Collaborative and review early implementation challenges. *Journal of Hospital Medicine* 2019;14:174-177. © 2019 Society of Hospital Medicine

Hospitals and health systems are under mounting financial pressure to shorten hospitalizations and reduce readmissions. These priorities have led to an ever-increasing focus on postacute care (PAC), and more specifically on improving transitions from the hospital.[1,2] According to a 2013 Institute of Medicine report, PAC is the source of 73% of the variation in Medicare spending[3] and readmissions during the postacute episode nearly double the average Medicare payment.[4] Within the PAC landscape, discharges to skilled nursing facilities (SNFs) have received particular focus due to the high rates of readmission and associated care costs.[5]

Hospitals, hospital physicians, PAC providers, and payers need to improve SNF transitions in care. Hospitals are increasingly responsible for patient care beyond their walls through several mechanisms including rehospitalization penalties, value-based reimbursement strategies (eg, bundled payments), and risk-based contracting on the total cost of care through relationships with accountable care organizations (ACOs) and Medicare Advantage plans. Similarly, hospital-employed physicians and PAC providers are more engaged in achieving value-based goals through increased alignment of provider compensation models[6,7] with risk-based contracting.

Current evidence suggests that rehospitalizations could be reduced by focusing on a concentrated referral network of preferred high-quality SNFs;[8,9] however, less is known about how to develop and operate such linkages at the administrative or clinical levels.[8] In this article, we propose a collaborative framework for the establishment of a preferred PAC network.

SKILLED NURSING FACILITY PREFERRED PROVIDER NETWORK

One mechanism employed to improve transitions to SNFs and reduce associated readmissions is to create a preferred provider network. Increasing the concentration of hospital discharges to higher performing facilities is associated with lower rehospitalization rates, particularly during the critical days following discharge.[10]

While the criteria applied for preferred provider networks vary, there are several emerging themes.[10] Quality metrics are often applied, generally starting with Centers for Medicare and Medicaid Services (CMS) quality star ratings and Long-Term Care Minimum Data Set (MDS) metrics with additional criteria frequently layered upon those. Some examples include the extent of physician coverage,[11] the extent of nursing coverage (eg, nursing ratios or 24/7 nursing care), geographic access, and flexible admission times (including weekends and nights).[12] In addition, several outcome measures may be used such as 30-day readmission rates, patient/family satisfaction ratings, ED visits, primary care follow-up within seven days of PAC discharge, or impact on the total cost of care.

Beyond the specified criteria, some hospitals choose to build upon existing relationships when developing their preferred network. By selecting historically high-volume facilities, they are able to leverage the existing name recognition amongst patients and providers.[13] This minimizes retraining of discharge planners, maintains institutional relationships, and aligns with the patients' geographic preferences.[2,13] While the high volume SNFs may not have the highest quality ratings, some hospitals find they can leverage the value of preferred partner status to push behavior change and improve performance.[13]

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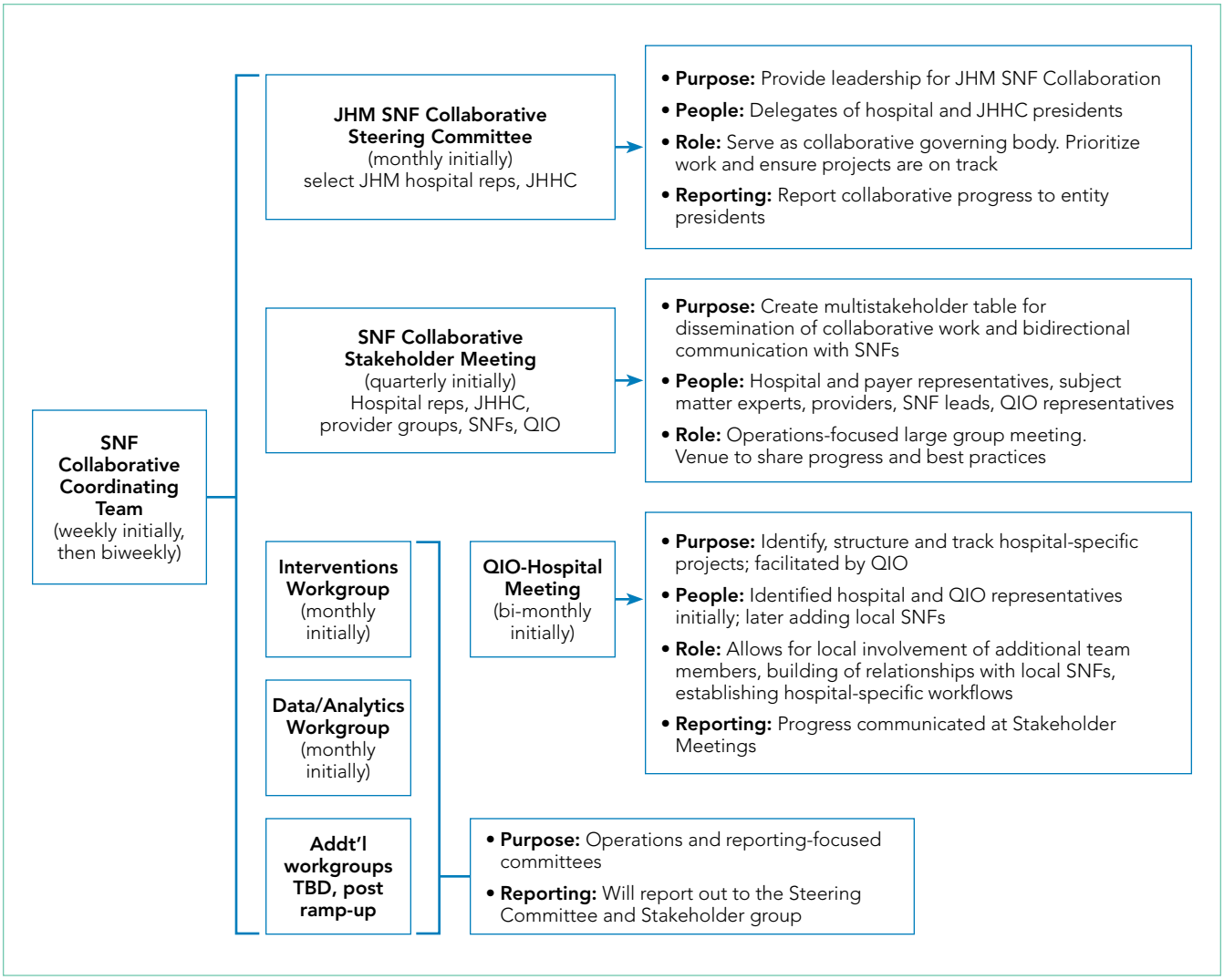

FIG. Skilled Nursing Facility Collaborative Governance Structure.
Abbreviations: JHM, John Hopkins Medicine; JHHC, Johns Hopkins HealthCare; QIO, quality improvement organization; SNF, skilled nursing facility.

PROPOSED HEALTH SYSTEM FRAMEWORK FOR CREATING A SKILLED NURSING FACILITY COLLABORATIVE

Here we propose a framework for the establishment of a preferred provider network for a hospital or health system based on the early experience of establishing an SNF Collaborative within Johns Hopkins Medicine (JHM). JHM is a large integrated health care system, which includes five hospitals within the region, including two large academic hospitals and three community hospitals serving patients in Maryland and the District of Columbia.[14]

JHM identified a need for improved coordination with PAC providers and saw opportunities to build upon successful individual hospital efforts to create a system-level approach with a PAC partnership sharing the goals of improving care and reducing costs. Additional opportunities exist given the unique Maryland all-payer Global Budget Revenue system managed by the Health Services Cost Review Commission. This system imposes hospital-level penalties for readmissions or poor quality measure performance and is moving to a new phase that will place hospitals directly at risk for the total Part A and Part B Medicare expenditures for a cohort of attributed Medicare patients, inclusive of their PAC expenses. This state-wide program is one example of a shift in payment structures from volume to value that is occurring throughout the healthcare sector.

Developing a formal collaboration inclusive of the five local hospitals, Johns Hopkins HealthCare (JHHC)—the managed care division of JHM—and the JHM ACO (Johns Hopkins Medicine Alliance for Patients, JMAP), we established a JHM SNF Collaborative. This group was tasked with improving the continuum of care for our patients discharged to PAC facilities. Given the number and diversity of entities involved, we sought to draw on efforts already managed and piloted locally, while disseminating best practices and providing added services at the collaborative level. We propose a collaborative multistakeholder model (Figure) that we anticipate will be adaptable to other health systems.

At the outset, we established a Steering Committee and a broad Stakeholder Group (Figure). The Steering Committee is

TABLE. **Initial Intervention Workgroup Priorities**

Priority	Example
Upgrading shared EMR transitions documentation	Recommend changes to the universal discharge summary template. Changes include more logical order such as prioritizing medications, adding advanced care planning and capacity documentation, incorporating functional status and standardized assessments, and added recommendations for the next phase of care
Standardizing metrics for physical, cognitive, and functional status	Broadly incorporating AM-PAC™ score into rehabilitation therapy assessments and discharge materials for objective measurement of functional status
Identifying prediction tools for optimal postdischarge locations	Reviewing landscape of risk-prediction tools for specific patient populations
Developing uniform patient/caregiver education materials	Draft patient education booklet on SNF basics and 'what to expect' to be integrated into the EMR patient education platform. Planning patient education video on postacute care options
Outlining strategies to increase provider communication and improve discharge handoffs	In addition to improving discharge documentation, review strategies to improve the accessibility of hospital providers after discharge

Abbreviations: AM-PAC, activity measure for postacute care; EMR, electronic medical record..

comprised of representatives from all participating JHM entities and serves as the collaborative governing body. This group initially identified 36 local SNF partners including a mixture of larger corporate chains and freestanding entities. In an effort to respect patient choice and acknowledge geographic preferences and capacity limitations, partner selection was based on a combination of publically available quality metrics, historic referral volumes, and recommendations of each JHM hospital. While we sought to align with high-performing SNFs, we also saw an opportunity to leverage collaboration to drive improvement in lower-performing facilities that continue to receive a high volume of referrals. The Stakeholder Group includes a broader representation from JHM, including subject matter experts from related medical specialties (eg, Physical Medicine and Rehabilitation, Internal Medicine, Emergency Medicine, and various surgical subspecialties); partner SNFs, and the local CMS-funded Quality Improvement Organization (QIO). Physician leadership was essential at all levels of the collaborative governing structure including the core Coordinating Team (Figure). Providers representing different hospitals were able to speak about variations in practice patterns and to assess the feasibility of suggested solutions on existing workflows.

After establishing the governance framework for the collaborative, it was determined that dedicated workgroups were needed to drive protocol-based initiatives, data, and analytics. For the former, we selected transitions of care as our initial focus area. All affiliated hospitals were working to address care transitions, but there were opportunities to develop a harmonized approach leveraging individual hospital input. The workgroup included representation from medical and administrative hospital leadership, JHHC, JMAP, our home care group, and SNF medical leadership. Initial priorities identified are reviewed in the Table. We anticipate new priorities for the collaborative over time and intend for the workgroup to evolve in line with shifting priorities.

We similarly established a multidisciplinary data and analytics workgroup to identify resources to develop the SNF, and a system-level dashboard to track our ongoing work. While incorporating data from five hospitals with varied patient populations, we felt that the risk-adjusted PAC data were critical to the collaborative establishment and goal setting. After exploring internal and external resources, we initially elected to engage an outside vendor offering risk-adjusted performance metrics. We have subsequently worked with the state health information exchange, CRISP,[15] to develop a robust dashboard for Medicare fee-for-service beneficiaries that could provide similar data.

IMPLEMENTATION

In the process of establishing the SNF Collaborative at JHM, there were a number of early challenges faced and lessons learned:

- In a large integrated delivery system, there is a need to balance the benefits of central coordination with the support for ongoing local efforts to promote partner engagement at the hospital and SNF level. The forums created within the collaborative governance structure can facilitate sharing of the prior health system, hospital or SNF initiatives to grow upon successes and avoid prior pitfalls.
- Early identification of risk-adjusted PAC data sources is central to the collaborative establishment and goal setting. This requires assessment of internal analytic resources, budget, and desired timeline for implementation to determine the optimal arrangement. Similarly, identification of available data sources to drive the analytic efforts is essential and should include a health information exchange, claims, and MDS among others.
- Partnering with local QIOs provides support for facility-level quality improvement efforts. They have the staff and onsite expertise to facilitate process implementation within individual SNFs.
- Larger preferred provider networks require considerable administrative support to facilitate communication with the entities, coordinate completion of network agreements, and manage the dissemination of SNF- and hospital-specific performance data.
- Legal and contractual support related to data sharing and HIPAA compliance is needed due to the complexity of the health system and SNF legal structure. Multiple JHM legal

entities were involved in this collaborative as were a mixture of freestanding SNFs and corporate chains. There was a significant effort required to execute both data-sharing agreements as well as charters to enable QIO participation.

- Physician leadership and insight are key to implementing meaningful and broad change. When devising system-wide solutions, incorporation and respect for local processes and needs are paramount for provider engagement and behavior change. This process will likely identify gaps in understanding the PAC patient's experience and needs. It may also reveal practice variability and foster opportunities for provider education on the needs of PAC teams and how to best facilitate quality transitions.

CONCLUSION

We proposed a framework for establishing a collaborative partnership with a preferred network of SNF providers. Depending on organizational readiness, significant upfront investment of time and resources could be needed to establish a coordinated network of SNF providers. However, once established, such networks can be leveraged to support ongoing process improvement efforts within a hospital or delivery system and can be used strategically by such health systems as they implement value-based health strategies. Furthermore, the lessons learned from transitions to SNFs can be applied more broadly in the PAC landscape including transitions to home from both the hospital and SNF.

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Things We Do For No Reason: Contact Precautions for MRSA and VRE

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Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason" (TWDFNR) series reviews practices that have become common parts of hospital care but may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent "black and white" conclusions or clinical practice standards but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CASE

A 67-year-old man is admitted to a telemetry ward for an acute myocardial infarction and treated with percutaneous coronary intervention. He is currently on day three of antibiotics for a methicillin-resistant *Staphylococcus aureus* (MRSA) lower extremity soft tissue infection that is healing without a draining wound. He is placed on contact precautions based on institutional infection control guidelines. The hospitalist overhears members of the team commenting on having to don gowns to see this patient each day and wonders aloud whether care is impacted by the use of contact precautions.

BACKGROUND

Contact precautions (CP) for patients with methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) infections are common in several hospitals. CP pose a significant burden to health systems, with an estimated 20%-25% of hospitalized patients on CP for MRSA or VRE alone.[1] CP are becoming increasingly more prevalent with state laws and the Veterans Affairs (VA) hospital system requiring active surveillance cultures (ASC) and subsequent CP when ASC are positive.[2]

WHY YOU MIGHT THINK CONTACT PRECAUTIONS ARE HELPFUL FOR MRSA AND VRE?

Supporters highlight the utility of CP in preventing the spread of infection, controlling outbreaks, and protecting healthcare workers from certain transmissible diseases. The Centers for Disease Control and Prevention (CDC) recommended CP after prior studies demonstrated their effectiveness during outbreaks of transmissible infections.[3] CP were included in bundles alongside interventions such as improving hand hygiene, chlorhexidine gluconate (CHG) bathing, and ASC with targeted or universal decolonization.[2] The VA MRSA bundle, for example, demonstrated a reduction of healthcare-associated MRSA in the ICU by 62% after implementation. The Society for Healthcare Epidemiology of America Research Network (SHEA) and the Infectious Diseases Society of America (IDSA) recommend CP for MRSA-infected and colonized patients in acute care settings to control outbreaks.[4,5] The CDC also has broad recommendations supporting CP for all patients infected and previously identified as being colonized with target multidrug-resistant organisms (MDROs) without identifying which are considered to be "targets."[6]

WHY CONTACT PRECAUTIONS MAY NOT BE HELPFUL FOR MRSA AND VRE

Despite current guidelines, cluster-randomized trials have not shown a benefit of initiating CP over usual care for the prevention of acquiring MRSA or VRE in the hospital. One study demonstrated no change in MRSA and VRE acquisition with broad screening and subsequent CP.[7] Another study evaluated a universal gown and glove policy in an ICU setting and found a reduction in MRSA acquisition, but no reduction in VRE acquisition.[8] A third study investigated hand hygiene and daily CHG bathing and noted a reduction in MRSA transmission rates, where CP for screened colonized patients had no effect on transmission of MRSA or VRE.[9]

In addition, a prospective trial at a large academic center over two six-month intervals utilized universal gloving with emollient-impregnated gloves compared with CP and found no difference in MRDO acquisition. Universal gloving was associated with higher hand hygiene rates than CP.[10] Another more recent retrospective observational study compared universal contact precautions (UCP) in ICUs to a historical nine-year baseline and concurrently to other nonuniversal CP ICUs. There was no significant decrease in MRDOs during the UCP period compared with baseline or with non-UCP units.[11]

Further interest in and scrutiny of CP prompted a recently published meta-analysis of 14 studies in which CP were eliminated. The rates of transmission of MRSA, VRE, or other MDROs studied were not impacted by discontinuation.[12] One of the studies included two large academic medical centers and assessed the impact of discontinuing CP for endemic MRSA and

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VRE. The bundled intervention included the discontinuation of CP for all carriers of MRSA and VRE, except patients with draining wounds, maintaining high hand hygiene rates, and CHG baths for nearly all patients. There was no significant increase in transmission rates, and the intervention saved the health system an estimated $643,776 and 45,277 hours per year in healthcare worker time previously spent on donning and doffing personal protective equipment.[13] Another large academic hospital published a time series approach of seven interventions to reduce healthcare-associated infections and noted no increase in MRSA or VRE transmission when CP were discontinued when combined with other horizontal preventions.[14] Results were found to be similar in a high-risk population of patients with hematologic malignancies and hematopoietic stem cell transplantation, where both surveillance and CP for VRE were discontinued and did not impact the rates of VRE bacteremia.[15]

WHY CONTACT PRECAUTIONS MAY BE HARMFUL

Multiple studies have examined the deleterious effects of CP, including a comprehensive systematic literature review of various adverse outcomes linked with CP.[16] CP decrease the amount of time that healthcare workers (HCW) spend with patients,[17] create delays at admission and discharge,[18] increase symptoms of anxiety and depression in patients,[19,20] and decrease patient satisfaction with care.[21,22] In a study conducted at the Cleveland Clinic Hospital, physician communication, staff responsiveness, patients' perception of cleanliness, and their willingness to recommend the hospital on the Hospital Consumer Assessment of Healthcare Providers and Systems survey were lower in each category for patients on CP when compared with patients not on CP.[22] Patients who are on CP are six times more likely to experience an adverse event in the hospital, including falls and pressure ulcers.[23] A recent study from a large academic medical center demonstrated that noninfectious adverse events were reduced by 72% after discontinuing CP for MRSA and VRE. These events included postoperative respiratory failure, hemorrhage or hematoma, thrombosis, wound dehiscence, pressure ulcers, and falls or trauma.[24]

The financial costs of unnecessary CP have also been studied. A recent retrospective study examining a large cohort of patients on CP for MRSA demonstrated that when compared with nonisolated patients, those on MRSA CP had a 30% increase in length of stay and a 43% increase in costs of care. Patients isolated for MRSA were 4.4% more likely than nonisolated individuals to be readmitted within 30 days after discharge, unrelated to MRSA.[25] These data contribute to the growing evidence that a conscientious, patient-centered approach to CP is preferred to overly broad policies that compromise patient safety.

WHEN CONTACT PRECAUTIONS SHOULD BE USED FOR MRSA AND VRE

Contact precautions for MRSA and VRE should be used to interrupt transmission during uncontrolled outbreaks, and in patients with open wounds, uncontained secretions, or incontinent diarrhea.

In addition, there are other commonly encountered organisms for which CP should be continued. CP should be used for active *Clostridium difficile* infection to prevent transmission. Due to the paucity of data regarding prevention of novel and highly resistant organisms and the complexity in treating these MDROs, it is reasonable to initiate CP in these cases.[26] Examples include active infection with multidrug resistance, including carbapenem-resistant *Enterobacteriaceae*, highly drug-resistant *Pseudomonas aeruginosa*, and other emerging MDROs such as vancomycin-resistant or -indeterminate *S. aureus* (VRSA or VISA) and *Candida auris*.[27] Limiting CP to instances where there is clear evidence to support will ensure patient safety and limit the harms associated with CP.

WHAT YOU SHOULD DO INSTEAD

Horizontal prevention aims to reduce the burden of all microorganisms. This includes techniques such as hand hygiene, antimicrobial stewardship, CHG bathing, and environmental cleaning methods to decrease colonization of all MDROs in hospital rooms. Compared with vertical prevention strategies that use active surveillance testing for colonization and CP, horizontal interventions are the most effective means to reduce transmission of MDROs.[28] The simplest and the most well-studied method for reducing transmission of all organisms in the hospital remains hand hygiene.[29] High institutional hand hygiene rates of at least 90% are critical to the success of any initiative that seeks to eliminate CP.

CHG bathing has also been studied across multiple patient settings for reducing MRSA and VRE acquisition, catheter-associated urinary tract infections, and central line-associated bacterial infections.[30] In addition, hospital-wide daily CHG bathing has been associated with decreased *C. difficile* infection, and the baths were well tolerated by patients.[31]

SHEA recently released recommendations for timing of discontinuation of CP for patients with MDROs and emphasized that hospital systems must take an individual approach to discontinuing CP that takes into account local prevalence, risk, and resources.[32] The decision to not place a patient on CP is one side of this high-value coin. The other side is knowing when it is appropriate to discontinue CP.

RECOMMENDATION

- Discontinue the use of CP for MRSA and VRE in hospitals with low endemic rates and high hand hygiene compliance.
- Improve horizontal preventions by promoting hand hygiene, antimicrobial stewardship, and considering CHG bathing for all patients.
- Create a systematic approach to discontinuing CP and compare transmission of MRSA and VRE rates through microbiology surveillance before and after discontinuation.

CONCLUSION

Contact precautions for MRSA and VRE are another example of a "Thing We Do for No Reason". For most patients with MRSA and VRE, CP have not been shown to effectively reduce transmission. In addition, CP are expensive and associated

with increased rates of patient adverse events. Hospitalists can lead the effort to ensure optimal hand hygiene and work with local infection control teams to reevaluate the utility of CP for patients with MRSA and VRE.

Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason?" Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other "Things We Do for No Reason" topics by emailing TWDFNR@hospitalmedicine.org.

Disclosures: There are no conflicts of interest for any authors, financial or other.

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Egad!

This icon represents the patient's case. Each paragraph that follows represents the discussant's thoughts.

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A 69-year-old woman presented to the clinic with pain in the right great toe lasting several days. She was prescribed colchicine and indomethacin empirically for gout. She took one tablet of colchicine (0.6 mg) every hour until her stools became loose after the eighth tablet. Her toe pain resolved, but two days later she developed bilateral lower extremity pruritus and paresthesia and presented to the emergency department (ED). On physical examination, no rash, weakness, or sensory deficits were observed, and she was able to ambulate without assistance. Her patellar reflexes were normal. The complete blood count was notable for an absolute lymphocyte count of 6,120/μL (normal: 1,100-4,800), and the comprehensive metabolic panel was normal. Serum creatine kinase (CK) was 341 U/L (normal: 24-170) and uric acid 7.7 mg/dL (normal: 2.4-6.4). Her lower extremity symptoms were attributed to colchicine, which was discontinued. She was prescribed diphenhydramine and discharged home.

Monoarthritis of the hallux is the classic manifestation of gout, although other considerations include pseudogout, sesamoiditis, and trauma. The typical side effects of colchicine include diarrhea and myositis. Colchicine-induced muscle injury often results in a modest elevation of CK levels and is associated with myalgia.

Paresthesia is defined as abnormal sensory symptoms that most commonly localize to the peripheral nerves or spinal cord. Acute neuropathies or myelopathies might result from vasculitis, heavy metal toxicity, vitamin deficiencies, and paraneoplastic neurologic syndromes. The normal motor, sensory, and reflex examination, however, make these unlikely.

The neuro-anatomic localization of pruritus is poorly understood but is proposed to include peripheral nerves, spinothalamic tracts, and thalami. Acute pruritus (lasting <6 weeks) typically results from a primary dermatologic process such as a drug reaction, eczema, or xerosis. Less common causes include uremia, cholestasis, and thyroid disease. Pruritus can also be seen with malignancy, most commonly hematologic or paraneoplastic syndromes, or with connective tissue diseases. At this stage, it is unclear whether her pruritus and paresthesia are part of a unifying disease process.

Five days later she re-presented to the ED with nausea and emesis after eating at a restaurant. Her symptoms improved with intravenous fluids, and she was discharged. Four days later she returned with difficulty ambulating, bilateral leg cramping, and continued pruritus and paresthesia. The chemistry panel was normal except for a potassium level of 2.6 mmol/L and a bicarbonate level of 32 mmol/L. She was admitted to the hospital because of severe hypokalemia and impaired ability to ambulate. Her potassium was replenished. Her CK was elevated (3,551 U/L on hospital day 7). She was given cyclobenzaprine, gabapentin, oxycodone, acetaminophen, and prednisone (40 mg); her cramping only mildly improved, and she remained unable to walk. On hospital day five she had visual hallucinations and confusion, which did not resolve with administration of haloperidol; a head CT was unremarkable. On hospital day eight the patient, with her family's support, left the hospital and presented to a different ED for a second opinion.

Difficulty ambulating often results from weakness, sensory impairment, cerebellar ataxia, extrapyramidal dysfunction (eg, parkinsonism), and pain. In this patient, leg cramping suggests pain or true weakness due to a myopathic process as a contributing factor. Symptoms of muscle disease include cramps, myalgia, and difficulty walking. Causes of elevated CK and myalgia include inflammatory myopathies, endocrinopathies, drugs, infections, and electrolyte abnormalities (eg, hypokalemia). Her age and acuity of presentation decrease the likelihood of a metabolic myopathy due to a disorder of glycogen storage, lipid metabolism, or mitochondrial function. Her hypokalemic metabolic alkalosis likely resulted from vomiting. Hypokalemic periodic paralysis is unlikely as exacerbations typically only last hours to days. As such, her difficulty ambulating, muscle cramps, and elevated CK strongly support a

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primary myopathic disorder, although additional information regarding the neurologic examination is still required.

Acute changes in mental status without corresponding changes in cranial nerve, motor, or sensory function are common in the hospital setting and frequently relate to delirium, which is the most likely explanation for her confusion. Her age and exposure to muscle relaxants, opiates, and corticosteroids increase her risk considerably. Other possible explanations for isolated changes in mental status include nonconvulsive seizures, central nervous system (CNS) infection, and strokes that involve the thalamus, nondominant parietal lobe, and reticular activating system. A shower of emboli resulting in small multifocal strokes can have the same effect.

She was re-evaluated by her new providers. Her only prior medical history was hypertension, which was treated at home with atenolol and amlodipine. She had emigrated from Nigeria to the US many years prior. She occasionally consumed alcohol and never smoked tobacco or used illicit drugs. She was unsure if she had received a tetanus booster in the past 10 years.

On physical examination, her temperature was 36°C, blood pressure 149/70 mm Hg, pulse 56 beats per minute, respiratory rate 18 breaths per minute, and oxygen saturation 98% on ambient air. She was diaphoretic and appeared anxious, grabbing both bedrails out of fear of falling. Cardiovascular, pulmonary, abdominal, and skin examinations were normal. She was alert and oriented to her identity, her location, and the time. Cranial nerves II to XII were normal. Tone was normal in her upper extremities but markedly increased in her lower extremities and back. There were spontaneous and stimulus-induced painful spasms, predominantly involving her axial muscles and distal lower extremities. Muscle bulk was normal. Strength was normal in the upper extremities and could not be assessed in the lower extremities due to rigidity. Reflexes were 2+ and symmetric throughout with downgoing toes on Babinski testing. A sensory examination was normal. Gait could not be tested because of the severe muscle spasms. The patient was admitted to the hospital.

Localized muscle spasms may be caused by muscle overuse, but more generalized spasms are associated with systemic diseases such as electrolyte disturbances, toxidromes, tetanus, peripheral nerve hyperexcitability syndromes (including Isaacs syndrome and Morvan syndrome), or stiff person syndrome (SPS). Hypokalemia is unlikely the cause as its correction did not improve her symptoms. Although tetanus is rare in the United States, it remains endemic in the developing world and can cause focal as well as generalized stimulus-induced spasms. The patient should be asked about potential exposure to *Clostridium tetani* infection, such as incurring a puncture wound. It is also important to consider neuroleptic malignant syndrome and serotonin syndrome, which can cause confusion, elevated CK, and increased muscle tone. Her confusion, however, was transient and the elevated CK preceded the administration of haloperidol.

SPS and progressive encephalomyelitis with rigidity and myoclonus (PERM) provide better explanations for her presentation. Both diseases cause severe spasms, impaired ambulation, and stiffness. They differ in their acuity of onset, accompanying symptoms, antibody associations, and responses to treatment. The rapid onset, paresthesia, and confusion seen in this patient are atypical of SPS. SPS usually presents with subacute-to-chronic stiffness or soreness of muscles in the back and lower extremities, followed by the upper extremities. Rigidity, stimulation-provoked spasms, hyperlordosis, and difficulty ambulating are typically later-stage findings. Her rapid escalation of symptoms is more consistent with PERM, which is often more acute and progressive than typical SPS; however, unlike this patient, PERM commonly causes widespread CNS dysfunction, including persistent encephalopathy, cranial neuropathies, hyperreflexia, and autonomic instability. Both are rare diagnoses that can manifest as a paraneoplastic neurologic syndrome.

Blood tests showed a leukocyte count of 17,350/μL, neutrophils 8,720/μL (normal: 1,500–7,800), lymphocytes 6,130/μL, hemoglobin 11.3 g/dL, and platelets 231,000/μL. The basic metabolic panel was normal. Serum total protein was 6.7 g/dL with albumin 3.5 g/dL. Aspartate aminotransferase (AST) was 94 U/L (normal: 0-31), alanine aminotransferase (ALT) 56 U/L (normal: 0-31), alkaline phosphatase 45 U/L, and total bilirubin 1.1 mg/dL. Vitamin B12 was 868 pg/mL. Hemoglobin A1c and thyrotropin levels were normal. Creatine kinase was 3,757 U/L and lactate dehydrogenase (LDH) 435 U/L (normal: 122-220). The syphilis treponemal test and hepatitis B surface antigen were negative. HIV and hepatitis C antibodies were nonreactive. The anti-nuclear antibody screen was negative and complement C3 and C4 were normal.

Neutrophilia likely reflects glucocorticoid-induced demargination, as opposed to an infectious process, given the temporal association with steroid administration. Persistent mild lymphocytosis is nonspecific but more likely to reflect a reactive rather than a clonal process. Elevated LDH and CK, as well as a greater increase of AST relative to ALT, suggest muscle injury, although mild concomitant hepatic injury cannot be excluded. Normal or negative serum studies for TSH, HIV, ANA, peripheral blood smear, and creatinine eliminate many of the systemic causes of her pruritus, but malignancy and associated paraneoplastic etiologies remain considerations.

The initial work-up for SPS includes electromyography (EMG) which would show spontaneous muscle activity. Her poorly localized sensory abnormalities, transient vestibular symptoms, and confusion warrant an MRI of the brain and spine to evaluate for inflammation (eg, encephalomyelitis), which could be consistent with PERM.

An MRI of the brain and cervicothoracic spine without contrast was significantly limited by motion artifact but without obvious intracranial or cord signal abnormalities.

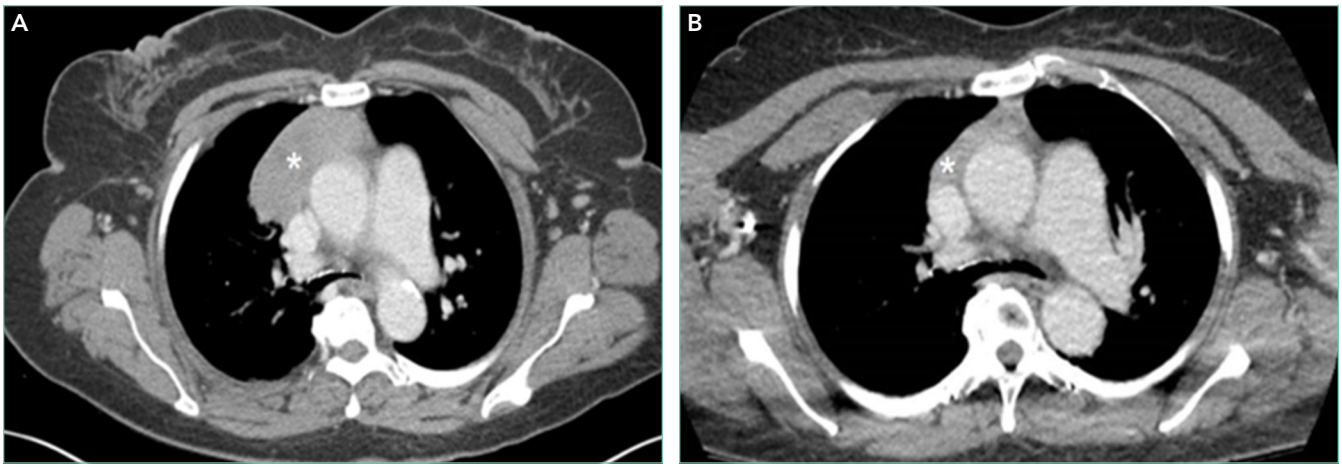

FIG 1. Chest CT with contrast showed a 3.9 × 8.0 × 7.0 cm anterior mediastinal mass (Panel A, asterixis), which shrunk to 1.7 × 6.5 × 5.2 cm after chemotherapy (Panel B, asterixis).

Electromyography demonstrated spontaneous muscle activity in both lower extremities with co-contraction of agonist and antagonist muscles (hamstrings and quadriceps as well as medial gastrocnemius and tibialis anterior). Sensory and motor nerve conductions were normal. Cerebral spinal fluid (CSF) contained six leukocytes (96% lymphocytes) and three red blood cells per microliter; glucose was 67 mg/dL and protein 24 mg/dL. There were two oligoclonal bands unique to the CSF. Cytology was negative for malignant cells.

The EMG narrows the differential diagnosis considerably. Co-contraction of opposing flexor and extensor groups (with predominance of extensors) on EMG is a diagnostic criterion for SPS and explains the myalgia and elevated CK. Her normal MRI studies effectively ruled out any focal lesion and did not show signs of encephalitis. Oligoclonal bands in the CSF are a sensitive marker of intrathecal inflammation, although not specific to one diagnosis. The mildly elevated cell count also supports CNS inflammation. In the setting of a lymphocytic pleocytosis and unique oligoclonal bands, it is important to consider infectious, neoplastic, autoimmune, and paraneoplastic causes of neuroinflammatory disorders.

Serum analyses, including antiglutamic acid decarboxylase 65 (GAD65) antibody and anti-amphiphysin antibody, should be ordered. The anti-GAD65 antibody is most commonly elevated in the setting of autoimmune diabetes mellitus; the titer, however, is usually dramatically higher in SPS. The CSF titer of anti-GAD65 antibodies is more specific than the serum titer for SPS. Antibodies against amphiphysin are typically elevated in paraneoplastic SPS, and anti-glycine receptor antibodies are associated with PERM, which commonly does not have elevated anti-GAD65 antibodies.

The serum GAD65 antibody level was greater than 265,000 × 10^3 IU/μL (normal <5,000), and the CSF level was 11.2 nmol/L (normal: ≤0.02). Serum amphiphysin antibody testing was negative.

Significantly elevated serum and CSF anti-GAD65 antibody levels are highly suggestive of SPS. Stiff person syndrome with rapidly progressive clinical symptoms raises the concern of a paraneoplastic neurologic syndrome. Although anti-amphiphysin antibody – the antibody classically associated with breast cancer and SPS – was negative, anti-GAD65 antibody has been implicated in paraneoplastic SPS with thymoma, lymphoma, and thyroid carcinoma. Paraneoplastic neurologic syndrome can predate a detectable malignancy by several years. As SPS and lymphoma are associated with pruritus and lymphocytosis, imaging is indicated to search for malignancy. Antiglycine receptor antibody, associated with PERM, is not routinely available commercially.

Computed tomography of the chest, abdomen, and pelvis with intravenous contrast revealed a 3.9 × 8.0 × 7.0 cm anterior mediastinal mass (Figure 1, Panel A). Biopsy of the mass demonstrated a thymoma. Given that the patient exhibited no further signs of CNS involvement, her initial transiently altered mental status was attributed to opioids and steroids. As she did not meet the clinical criteria for PERM, testing of antiglycine antibodies was not pursued.

She received scheduled baclofen and diazepam with as needed cyclobenzaprine for continued muscle spasms. Over the next several days, her stiffness, spasms, and myoclonic jerks slowly improved, and she was able to attempt physical therapy (Appendix Video 1; https://youtu.be/d0gLpTgqaCs). She subsequently received intravenous immunoglobulin (IVIG) with further improvement. After five months of scheduled diazepam and baclofen, she was able to ambulate with minimal assistance (Appendix Video 2; https://youtu.be/I00i638u00o). Given the absence of safe tissue planes for resection, the patient received neoadjuvant chemotherapy with four cycles of cyclophosphamide, doxorubicin, and cisplatin. Tumor size decreased to 1.7 × 6.5 × 5.2 cm (Figure 1, Panel B), and she subsequently underwent resection (Figure 2). Pathological analysis demonstrated a type B1 thymoma.

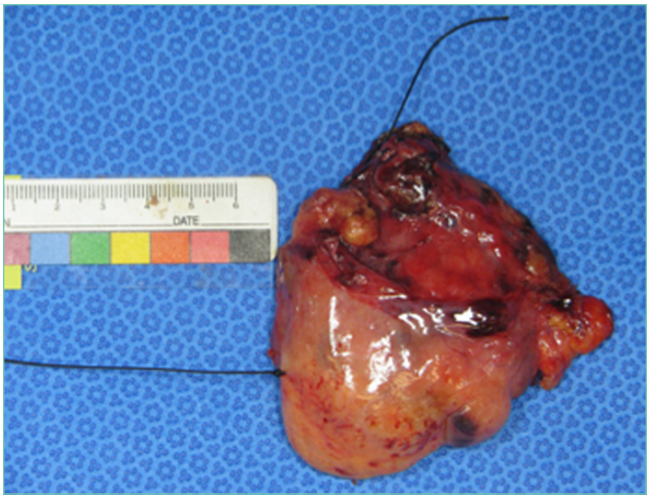

FIG 2. Surgical resection revealed a 2.1 × 7.0 × 7.9 cm firm mass (short stitch denotes apex of the thymus; long stitch denotes the lateral aspect).

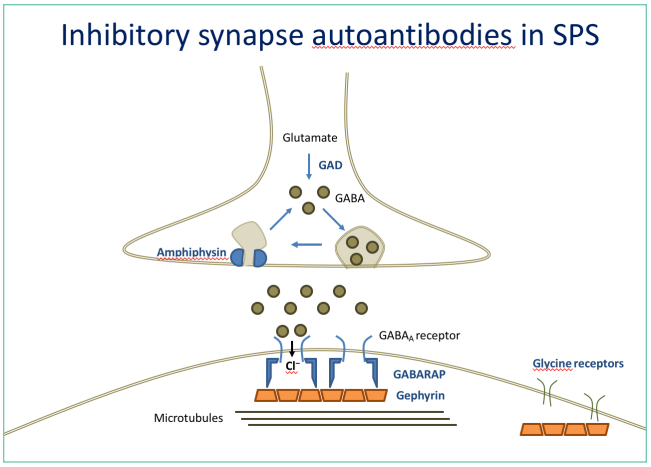

FIG 3. The primary inhibitory neurotransmitter, gamma-aminobutyric acid (GABA), is produced from glutamate in a reaction catalyzed by glutamic acid decarboxylase (GAD). GABA is loaded into secretory vesicles for release into the synaptic space through fusion of the vesicles with the plasma membrane. Amphiphysin, gephyrin, $GABA_A$ receptor-associated protein (GABARAP), and glycine receptors are important to this signal transduction pathway.

COMMENTARY

SPS is a condition of muscle stiffness and spasticity. Diagnosis is difficult and often delayed due to its rarity, with an approximate prevalence of one to two cases per million people.[1] SPS typically occurs in middle age, and women are diagnosed twice as often as men. Classic SPS is characterized by axial and limb muscle stiffness, episodic spasms precipitated by tactile or auditory stimuli, continuous motor unit activity in agonist and antagonist muscles on EMG, high-titer antibody to GAD65 or amphiphysin, and the absence of an alternate diagnosis.[2] Variant syndromes have been described, including a milder variant limited to the limbs, a severe variant with brainstem and spinal cord involvement, and a paraneoplastic variant.[3] This patient's clinical presentation, EMG findings, and extraordinarily high anti-GAD titers in the serum and CSF were diagnostic of SPS.

The pathophysiology of SPS is associated with autoantibodies targeting proteins such as GAD65, amphiphysin, gephyrin, and $GABA_A$ receptor-associated protein (GABARAP). These proteins are critical to gamma-aminobutyric acid (GABA) signaling, the primary inhibitory neurotransmitter pathway in the CNS (Figure 3).[4] The formation of GABA from glutamate is catalyzed by GAD65. Gamma-aminobutyric acid is loaded into secretory vesicles, and amphiphysin facilitates vesicle recycling from the synaptic space.[5] In the postsynaptic neuron, GABA binds the $GABA_A$ receptor, leading to neuronal hyperpolarization and resistance to excitation. The $GABA_A$ receptor is clustered on the plasma membrane through a scaffold formed by gephyrin. GABARAP facilitates this clustering, in part by linking $GABA_A$ receptors and gephyrin.[6] Autoantibodies to these proteins may be pathogenic; however, the direct effects on their targets are unclear. The end result is decreased GABAergic activity, leading to continuous activation of opposing muscle groups. The resulting stiffness is characteristic of this disorder. Colchicine is known to antagonize $GABA_A$ receptor signaling, and this may have brought the underlying diagnosis of SPS to clinical attention.[7,8]

Symptomatic treatment of SPS targets the GABAergic system. Typically, high doses of scheduled benzodiazepines[9] and baclofen[10] are necessary. When symptoms are not controlled by GABAergic drugs, immunosuppression with corticosteroids and IVIG has been used, as have plasmapheresis and rituximab.[11] The efficacy of the latter, however, was not supported by a randomized, placebo-controlled trial.[12] This patient experienced significant improvement with benzodiazepines, baclofen, IVIG, and neoadjuvant chemotherapy prior to thymoma resection. The pruritus, paresthesia, and lymphocytosis also resolved with medical therapy. Interestingly, GABA signaling suppresses itch, suggesting that loss of $GABA_A$ signaling may have contributed to the development of pruritus.

SPS occasionally occurs as a paraneoplastic neurologic syndrome. Breast cancer is the most commonly associated malignancy, although associations between thymomas and SPS[13] with anti-GAD65 antibodies[14] have also been described. The presentation of thymomas is variable, with approximately one-third discovered incidentally on imaging, one-third producing symptoms of local compression, and one-third identified in the setting of another syndrome, most commonly myasthenia gravis. In addition to myasthenia gravis, thymomas have been associated with conditions such as hypogammaglobulinemia, pure red cell aplasia, and agranulocytosis. Stiff person syndrome is a known, albeit infrequently associated, condition.[15]

A critical step in arriving at the relevant differential diagnosis requires correctly framing the patient's case.[16] The treatment team's initial frame was "a 69-year-old woman with weakness and elevated CK," which prioritized causes of weakness and myositis. Stiff person syndrome does not cause weakness, but rather impaired movement from marked stiffness and spasms. The patient's elevated CK was a result of continual muscle contractions. The physical exam and lack of motor deficit on EMG

led the treatment team to reframe as "a 69-year-old woman with severe stiffness and spasms." Egad! This correct frame was the key to diagnosis and confirmed by EMG and GAD65 antibody testing.

KEY LEARNING POINTS

- Classic SPS is characterized by axial and limb muscle stiffness, episodic spasms precipitated by tactile or auditory stimuli, continuous motor unit activity in agonist and antagonist muscles on EMG, and high-titer antibody to GAD65 or amphiphysin.
- SPS typically occurs in middle age, and women are diagnosed twice as often as men.
- Symptomatic treatment of SPS targets the GABAergic system. Typically, high doses of scheduled benzodiazepines and baclofen are necessary.
- SPS occasionally occurs as a paraneoplastic neurologic syndrome, most commonly in association with breast cancer.

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Appendix Video 1: This video was taken during a physical therapy session after 1 week of scheduled benzodiazepine and 2 days of intravenous immunoglobulin. It was difficult for the patient to stand without assistance due to severe stiffness. (https://youtu.be/d0gLpTgqaCs)

Appendix Video 2: This video was taken 5 months after scheduled diazepam and baclofen, and 1 week prior to thymectomy. (https://youtu.be/I00i638u00o)

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The Complex Problem of Women Trainees in Academic Medicine

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Despite media attention to gender inequality in multiple professions, medicine has only recently begun to identify disparities facing women in academic medicine, focusing primarily on women faculty rather than trainees. Because of the unique and poorly understood juxtaposition of forces affecting their experience, focusing on women medical trainees may provide a representative framework to understand the larger, complex problem of gender equity in medicine. Rather than being a complicated problem with component parts that can be separately addressed, gender equity in medicine is a complex problem—one composed of a myriad of interrelated human and systemic factors. Such a complex problem demands innovative, open-minded, user-centered interventions. Here, we outline some of the factors unique to women trainees, including lack of female role models in leadership, gender bias, sexual harassment, work-life imbalance, and few formal leadership training programs. We propose one potential strategy, leadership programs specifically targeted to women residents and fellows. We recently implemented this strategy at our institution in the form of a day-long symposium of skill-building sessions for women residents and fellows.

Although women have achieved equal representation in several medical training programs, there is still a dearth of women in high-profile leadership positions within academic medicine. Although women comprised 46% of United States medical school applicants and residents in 2015-2016, underrepresentation persists at the level of associate professor (35% women), full professor (22%), department chair (14%), and dean (16%).[1] Many potential women leaders may not self-identify as such due to the limited exposure to women role models in positions of power and may in fact be ready for leadership roles earlier but not apply until later in their careers as compared with men.[2,3] The lack of role models with a shared background is an even more severe problem for women of color and all of these factors contribute to the "leaky pipeline" phenomenon.[4] We aimed to address this mindset and help women see themselves as leaders by overcoming "second-generation gender bias" through our work.[2]

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Due to the intense and inflexible nature of residency and fellowship training programs, many women choose to defer milestones such as childbearing.[5] Women trainees are more likely than their male colleagues to avoid having a child during residency due to perceived threat to their career and negative perceptions of colleagues.[5,6] Women who are in a domestic partnership often bear the brunt of the household work regardless of the careers of the two partners, a phenomenon termed the "second shift."[7] This work-life imbalance has been shown to correlate with depressive symptoms in women internal medicine trainees.[8]

Recently, a trainee published on the experience of medical residents being asked whether they were ever called "nurse." All the women in the room put up their hands; none of their male colleagues did.[9] At issue is not the relative importance of the professions of medicine and nursing, but rather the gender stereotypes in medicine that lead to automatic categorization of women into one group. Although the majority of women residents likely have had personal experiences with bias and microaggressions, few are explicitly taught the tools to address these. Beyond microaggressions, women trainees are also subject to more sexual harassment than their male colleagues.[10] In addition, women living at the intersections of race, ethnicity, and gender are faced with even higher rates of harassment.[11] Reporting sexual assault and harassment can be particularly difficult as a trainee because of the risk of retaliation, fear of poor evaluations from superiors, and lack of confidence in the reporting process.[10]

Finally, women trainees often receive little training about the skills required for career advancement to achieve parity with their male colleagues. Women are less likely to negotiate due to concerns about backlash or due to general lack of awareness about the importance of negotiation.[12] Women are asked to volunteer for "nonpromotable" tasks more often than men by colleagues of both sexes, a barrier to women reaching their full career potential and a difficult workplace scenario to navigate.[13] Unlike the fields of business, law, and technology, for example, women in medicine do not routinely have training courses that incorporate skills such as navigating difficult conversations, conflict resolution, curriculum vitae writing, and negotiation. Various solutions have been offered to address some of the barriers facing women in medicine (such as the Association of American Medical Colleges and Executive Leadership in Academic Medicine leadership courses), but typically these focus on faculty rather than trainees. Given that women physicians practicing in the inpatient setting have been shown

to have better patient outcomes[14] and organizations with female leadership outperform those led by men,[15] equipping our women trainees to thrive in the clinical and leadership environments is an essential step in fulfilling our mission as high-quality training programs.

At our institution, we recognized the need for training in leadership skills for women medical trainees and designed a day-long symposium for internal medicine women residents and fellows. Before developing the curriculum, we conducted a needs assessment to ascertain which skills women wanted to develop; women overwhelmingly wanted to learn about public speaking skills, work-life integration, and mentoring. Based on these responses, a group spanning multiple levels of training (residency, fellowship, and faculty) designed a combination of large-group lectures and small-group workshops termed "Women in Leadership Development" (WILD). The day-long curriculum included sessions on public speaking skills, women as change agents, mentorship, conflict resolution, and addressing microaggressions and concluded with a networking event for women faculty and trainees (Table).

In total, 77 medicine residents and fellows voluntarily participated in the symposium in 2017 and 2018. The public speaking skills session received the highest reviews, with 98% of participants reporting that they identified ways to change public speaking styles to project confidence. This session was facilitated by an outside consultant in public speaking, highlighting the benefit of seeking experts outside of academic medicine. Another novel session focused on responding to microaggressions, defined as subtle and sometimes unintentional actions that express prejudice toward marginalized groups, in the clinical and academic environments. Microaggressions can undermine the recipient's confidence, feeling of belonging, and effectiveness at work.[16] At our institution, trainees in graduate medical education report the largest single source of microaggressions as patients (greater than attendings, fellow trainees, or staff), with gender bias being responsible for the greatest number of microaggressions (Schaeffer, unpublished data). Navigating these situations to ensure good patient care and strong patient-provider relationships, while also establishing a climate of mutual respect, can be challenging for all women physicians, in particular for trainees who are just beginning to experience the clinical environment independently. Our session on microaggressions was purposefully led by a national expert in patient-provider communication and offered an opportunity for women trainees to reflect on their past experiences being the target of microaggressions, to name them as such, and then to brainstorm possible responses as a group. The result was a "toolkit" of resources for responding to microaggressions.[17]

Of the attendees of WILD 2017 and 2018, 91% strongly agreed that participation in the symposium was a useful experience. One attendee reflected that they "feel more empowered to discuss women-related issues in academics with peers, mentors, mentees" and another stated that as a result of WILD, they would "sponsor peers and mentors, speak out more about gender bias, seek out leadership positions." Challenges for our symposium included obtaining protected curricular time from busy trainee schedules. Supportive leadership at all levels was critical to our success; carving out dedicated curricular time will be essential for the sustainability of this leadership symposium. Our group has recently received funding to expand to a longitudinal course open to all women residents and fellows across graduate medical education.

TABLE. **WILD Symposium Agenda**[a]

Topic	Core Competency
Introduction to Issues Facing Women in Medicine	Shaping Leadership Identity Advocacy and Empowerment
"Culture Box" Group Share	Community Building
"Honing Your Voice as a Leader" Public Speaking Seminar	Leadership Skills Shaping Leadership Identity
Women as Change Agents in Academic Medicine	Advocacy and Empowerment
"Advocacy in Action" Brainstorming Session	Advocacy and Empowerment
Peer Networking Lunch	Community Building
Addressing Microaggressions and Ally Skill Building	Leadership Skills
Building your Mentorship Team	Mentoring and Sponsorship
Navigating Difficult Conversations and Conflict	Leadership Skills
Mentor/Mentee Relationships Panel	Mentoring and Sponsorship
Networking with Faculty Reception	Community Building Mentoring and Sponsorship

[a]Sessions for the WILD Symposium are listed under "Topic." The corresponding core competencies that each "Topic" item fulfills are listed under "Core Competency."

Although the complex and unique problems facing women medical trainees are unlikely to be comprehensively addressed by a leadership course, we urge other institutions to adopt and expand on our model for teaching vital leadership skills. In addition to leadership skills, academic medical centers should adopt a multipronged approach to support their female trainees, including clear and confidential reporting practices of sexual harassment without fear of retaliation, training for all staff on harassment and bias, involvement of men as allies, and mentorship programs for women trainees. Further research is needed to better understand this complex problem, its impact on career outcomes, and a path to achieving gender equality in medicine.

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The socio-adaptive (or "nontechnical") aspects of healthcare including leadership, followership, mentorship, culture, teamwork, and communication are not formally taught in medical training. Yet, they are critical to our daily lives as hospitalists. The LPD series features brief "pearls of wisdom" that highlight these important lessons.

Leadership & Professional Development: Know Your TLR

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"Better to remain silent and be thought a fool than to speak and remove all doubt.."

—Abraham Lincoln

Have you ever been in a meeting with a supervisor wondering when you will get a chance to speak? Or have you walked away from an interview not knowing much about the candidate because you were talking all the time? If so, it might be time to consider your TLR: Talking to Listening Ratio. The TLR is a leadership pearl of great value. By keeping track of how much you talk versus how much you listen, you learn how and when to keep quiet.

As Mark Goulston wrote, "There are three stages of speaking to other people. In the first stage, you are on task, relevant and concise . . . the second stage (is) when it feels so good to talk, you don't even notice the other person is not listening. The third stage occurs after you have lost track of what you were saying and begin to realize you might need to reel the other person back in." Rather than finding a way to re-engage the other person by giving them a chance to talk while you listen, ". . . the usual impulse is to talk even more in an effort to regain their interest."[1]

When you are talking, you are not listening—and when you are not listening, you are not learning. Executives who do all the talking at meetings do not have the opportunity to hear the ideas of others. Poor listening can make it appear as if you don't care what others think. Worse, being a hypocompetent listener can turn you into an ineffective leader—one who does not have the trust or respect of others.

The TLR is highly relevant for hospitalists: physicians and nurses who do all the talking are not noticing what patients or families want to say or what potentially mistaken conclusions they are drawing. Similarly, quality improvement and patient safety champions who do all the talking are not discovering what frontline clinicians think about an initiative or what barriers need to be overcome for success. They are also not hearing novel approaches to the problem or different priorities that should be addressed instead.

Your goal: ensure that your TLR is less than 1. How? Make it a habit to reflect on your TLR after an encounter with a patient, colleague, or supervisor and ask yourself, "Did I listen well?" In addition to its value in monitoring your own talkativeness, use the TLR to measure others. For example, when interviewing a new hire, apply TLR to discover how much patience would be required to work with a candidate. We once interviewed a physician whose TLR was north of 20 . . . we passed on hiring them. The TLR is also helpful for managing meetings. If you find yourself in one with an over-talker (TLR >5), point to the agenda and redirect the discussion. If it's a direct report or colleague that's doing all the talking, remind them that you have another meeting in 30 minutes, so they will need to move things along. Better yet: share the TLR pearl with them so that they can reflect on their performance. If you're dealing with an under-talker (eg, TLR<0.5), encourage them to voice their opinion. Who knows—you might learn a thing or two.

The most surprising aspect to us about TLR is how oblivious people tend to be about it. High TLR'ers have little idea about the effect they have on people while those with an extremely low TLR (less than 0.2) wonder why they didn't get picked for a project or promotion. Aim for a TLR between 0.5 and 0.7. Doing so will make you a better leader and follower.

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Treatment of Inpatient Asymptomatic Hypertension: Not a Call to Act but to Think

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Your pager beeps. Your patient, Mrs. Jones, who was admitted with cellulitis and is improving, now has a blood pressure of 188/103 on routine vitals. Her nurse reports that she is comfortable and asymptomatic, but she met the "call parameters." You review her chart and find that since admission her systolic blood pressure (SBP) has ranged from 149 to 157 mm Hg and her diastolic blood pressure (DBP) from 84 to 96 mm Hg. Her nurse asks how you would like to treat her.

While over half of inpatients have at least one hypertensive episode during their stay, evidence suggests that nearly all such episodes—estimates are between 98% and 99%[1,2]—should be treated over several days with oral antihypertensives, not acutely with intravenous medications.[3-6] Current guidelines recommend that intravenous medications should be reserved for severe hypertensive episodes (SBP > 180, DBP > 120) with acute end-organ damage,[7,8] but such "hypertensive emergencies" are rare on the general medicine wards. Still, hospitalists regularly face the dilemma posed by Mrs. Jones, and evidence shows they often prescribe intravenous antihypertensives.[1,4,5] This unnecessary use can lead to unreliable drops in blood pressure and exposes our patients to potential harm.[5,6]

In this issue of the *Journal of Hospital Medicine*, two papers describe the frequency of inappropriate intravenous antihypertensive use in their hospitals and the subsequent quality improvement efforts implemented to reduce this practice. The first, by Jacobs et al., found that over a 10-month period, 11% of patients who experienced "asymptomatic hypertension" on an urban academic hospital medicine service were treated inappropriately with intravenous antihypertensives,[9] with 14% of those experiencing an adverse event. The second paper, by Pasik et al., found that in their urban academic medical center there were 8.3 inappropriate intravenous antihypertensive orders placed per 1,000 patient days,[10] with nearly half of those treated experiencing an adverse event. Based on these findings, each group then led interventions to reduce the use of intravenous antihypertensives.

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While both groups engaged physicians and nurses as primary stakeholders, Pasik et al.[10] worked to further expand nursing staff roles by empowering them to assess for underlying causes of hypertension, such as pain or anxiety, as well as end-organ damage via specific guided algorithms prior to contacting physicians. In doing so, they reduced intravenous antihypertensive use by 60% during the postintervention period, with a proportional reduction in adverse events. In addition to their educational initiative, Jacobs et al. aimed to limit calls by liberalizing the "ceiling" on standard nursing call parameters for blood pressure from 160/80 to 180/90. Following their intervention, intravenous antihypertensive orders were reduced by 40%, with the mean orders per patient with asymptomatic hypertension decreasing from 11% to 7% .

While these results are admirable, some caution in their interpretation is needed. For example, Jacobs et al. used electronic health record data to retrospectively identify hypertension as "symptomatic" or "asymptomatic" using laboratory, electrocardiogram, and imaging diagnostics as surrogate markers for "provider concern for end-organ damage." Although it appropriately focused on concern for end-organ damage as justification for intravenous antihypertensives, this approach potentially underappreciated true hypertensive emergencies, thereby overestimating the amount of inappropriate use of intravenous antihypertensives. Pasik et al. utilized chart review of patients prescribed intravenous antihypertensives and therefore did not explore how often symptomatic hypertension occurred in patients who did not receive intravenous antihypertensives. Subsequently, this limited their ability to evaluate unintended harms of their initiative. To address this limitation, the authors followed a group of 111 patients who had elevated hypertension but did not receive intravenous antihypertensives and found no adverse outcomes.[10] Because both studies were retrospective in nature, they were subject to biases from providers choosing intravenous antihypertensives for reasons that were neither captured by their datasets nor adjusted for. Additionally, neither study reported downstream impacts such as an increase in symptomatic hypertensive episodes or more rare events such as kidney injury, stroke, or myocardial infarction.

Given that guidelines discourage using intravenous antihypertensives, why were the efforts of Jacobs et al.[9] and Pasik et al.[10] needed in the first place? In a recent installment of *Choosing Wisely: Things We Do For No Reason*, Breu et al.[11] cite two primary reasons: first, providers have unfounded fears that asymptomatic hypertension will quickly progress to cause organ

damage; second, providers lack understanding of the potential harms from overtreatment. It is fitting, therefore, that both groups of authors focused on these topics in their education initiatives for physicians and nurses. Yet, as good quality improvement requires steps beyond education, it was promising to see that both authors additionally focused on intervening to change the systems and culture that existed around physician and nursing communication.

In the age of electronic health records, there has been a sustained focus on creating standardized order sets. While the value of these order sets has been widely demonstrated, there are downsides. For example, nursing call parameters in admission order sets are rarely patient-specific but account for a significant portion of nursing and physician communication. These one-size-fits-all orders limit nurses from using their clinical training and create unnecessary tensions as nurses are obligated to call covering hospitalists to address "abnormal" but clinically insignificant findings. Regular monitoring of vital signs is an integral part of caring for acutely ill inpatients but for most inpatients, the importance of vitals is to detect clinically meaningful changes, not to treat risk factors like hypertension that should be treated safely over the long term.

When inpatients become febrile, tachycardic, or hypoxic, hospitalists use critical thinking to diagnose the underlying causes. Unfortunately, high blood pressure is a vital sign that is treated differently. Many hospitalists see it as a number to fix, not a potential sign of a new underlying problem such as uncontrolled pain, anxiety, or medication side effects.[8] Both groups of authors took the important first step of educating physicians to think critically when called about high blood pressure. Even more importantly, they took steps to change the system and culture in which providers make these decisions in the first place. Future work in this area would be wise to follow in these footsteps, by encouraging collaboration between hospitalist and nurses to create more logical and patient-specific call parameters that could potentially improve nursing-physician communication, and subsequently, patient care.

Changing the culture to limit the use of intravenous antihypertensives will not be easy, but it is necessary. We encourage readers to investigate intravenous antihypertensives in their own hospitals and consider how better communication between nurses and physicians could change their practice. Recalling Mrs. Jones above, the provider should engage her nurse to help confirm that her hypertension is "asymptomatic" and then consider underlying causes such as pain, anxiety, or withholding her home medications as reasons for her elevated blood pressure. After all, if nothing else, it seems clear that a call about inpatient hypertension is not a call to act, but to think.

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The Critical Role of Hospitalists for Successful Hospital-SNF Integration
Hospitalists and Hospital/SNF Integration

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In 2015, the Centers for Medicare and Medicaid Services (CMS) tied 42% of Medicare payments to a value-based model of care.[1] Many of these models are designed to expand the scope of hospitals' accountability to include care provided to patients postdischarge (eg, readmission penalties, bundled payments, accountable care organizations). With such a significant change in organizational incentives, one would expect to see activity as it relates to hospital-skilled nursing facility (SNF) integration, potentially including shared risk among providers.[2,3]

Hospitals can choose from several different strategies when contemplating SNF integration, such as vertical integration with SNFs, which would involve acquiring and owning SNFs. However, despite the high level of incentive alignment and financial integration achieved through SNF acquisition, this strategy has not been widely adopted. Perhaps this is because hospitals can often attain a shorter length of stay and lower readmission rates without taking on the additional risk of owning a facility, except under particular market conditions.[4] Hospitals can alternatively pursue *virtual* integration by developing preferred provider networks through contractual relationships or other formal processes, attempting to direct patients to SNF providers that have met predefined criteria, as described by Conway and colleagues in this issue of the *Journal of Hospital Medicine®*.[5] While hospitals have adopted this form of integration more widely than vertical integration, only those with additional financial motivations, such as those employing bundled payments, engaged in accountable care organizations (ACOs) or forward-thinking organizations preparing for looming global models of payment, have implemented such action. Finally, hospitals can focus on relational coordination through informal person-to-person communication and transition management. Given the high number of patients discharged to SNFs, the strategies above are not mutually exclusive, and enhanced relational coordination is most likely going to occur regardless of the type of—and perhaps even without—organizational-level integration.

For those hospitals choosing not to pursue integration with SNFs, there are several reasons to maintain the status quo. First, hospitals have different interpretations of provider choice ("beneficiary freedom to choose"), whereby many do not believe they can provide information to patients outside of facility names and addresses. As such, they will refrain from developing a SNF network due to their interpretation of hazy federal rules.[6] Second, it is possible that the incremental benefit of establishing a network is viewed by many hospitals as not worth the cost, measured by the time and effort required and the potential risk of not adhering to choice requirements. This could be especially true for hospitals without additional financial motivations, such as participation in an ACO or bundled payment program.

As the landscape continues to evolve, more successful systems will embrace a more concordant partnership with local and regional SNF providers, and several market factors will support the trend. First, the Medicare Payment Advisory Commission (MedPAC) is discussing the idea of choice in the context of postacute discharge, potentially leading to hospitals relaxing their strict interpretations of choice and the level of information provided to patients.[7] Second, the evidence supports better patient outcomes when hospitals develop SNF networks.[8,9] Finally, continued penetration of value-based payment models combined with CMS decisions regarding choice will continue to provide the additional motivation hospitals may need to change the cost-benefit calculation in favor of developing a network.

IMPLICATIONS FOR HOSPITALISTS

Traditionally, primary care physicians followed their patients through the acute- and postacute care continuum, but a variety of changes led to the growth of hospital medicine as fewer primary care physicians saw patients in the hospital.[10,11] This shift has challenged efforts to ensure continuity of care across settings, especially since most hospitalists have ceded control of postdischarge placement to case managers and therapists. Further, there has been little incentive to connect hospitalists to any other component or provider along the range of care, and compensation models rarely, if at all, consider any accountability for patient outcomes outside the hospital. Several factors can change this reality for hospitalists.

First, as more providers adopt team-based care approaches and as alternative payment models expand the scope of accountability, hospitalists will become an even more central component of the risk evaluation process for hospitalized pa-

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tients as it relates to their discharge profile. This could mean that hospitalists are more involved in the postdischarge follow-up of patients sent home, to make sure patients adhere to discharge instructions. Alternatively, hospitalists may need to increase the level of physician-to-physician communication with SNF medical directors for patients discharged to SNF. This, in turn, could result in an increasing number of hospitalist groups recruiting SNFists to join their group or potentially assigning existing hospitalists or physician assistants to round on patients in the SNF. The 2018 Society of Hospital Medicine report showed an increase in activity among hospital medicine groups performing services in postacute-care facilities outside the hospital from 13% in 2016 to 25% in 2018.[12] Similarly, a 2017 study in *JAMA Internal Medicine* reported a 48.2% increase in the number of physicians classified as SNFists from 2007 to 2014.[13]

Second, hospitalists will be more involved in the discharge planning process through internal interdisciplinary team communications. Whereas case managers and therapists owned the discharge planning process historically, new teams will include hospitalists, case managers, physical therapists, and pharmacists. System leaders will task them with identifying the appropriate discharge destination (eg, SNF, home health), finalizing the medication reconciliation, scheduling follow-up appointments, and completing a warm handoff.

Finally, as the field matures and hospitalists learn more about postacute-care connections, they will continue to be held more accountable for patient outcomes postdischarge. Many hospitalists have already connected to community providers through checklists and use evidence-based discharge programs like ProjectRed or Project BOOST.[14,15] Organizations will need a similar strategy for SNFs, developing process measures, with the input of hospitalists, around those noteworthy areas that hospitalists can control. This will require greater alignment among constituents around overall organizational goals and, more importantly, entail the hospitalist to be attuned to overall patient goals beyond the care provided in the hospital setting.

As payment and care models continue to evolve, the status quo cannot be sustained. We anticipate that hospitalists will become more integrated into the patient discharge process, especially as it relates to discharge to SNFs before patients reconnect to their community physicians. Hospital systems will accelerate integration through the development of preferred SNF networks, and hospitalists stand to play a critical role in the success of these arrangements by enriching the benefits they create through these outward relationships.

For organizations engaged in embedded networks, they can realize gains via incentive alignment, trust, information transfer, mutual support, and coordination through virtual integration, without requiring vertical ownership.[3,16] Thus, the opportunity exists for hospitalists to be critical drivers of network success, serving as intermediaries from which information, collaboration, and shared problem-solving flow between hospitals, SNFs, patients, and the entire care team. Opportunities to rebuild our system are long past; however, like all changing sectors in healthcare, the disaggregate acute and postacute settings must move in lockstep. Hospitals and postacute care facilities must find ways to alter their thinking to eradicate the obstructive and injurious invisible wall.

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Things We Do For Good Reasons: Contact Precautions for Multidrug-resistant Organisms, Including MRSA and VRE

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Contact precautions (CP), the use of gowns and gloves as personal protective equipment when caring for patients who are colonized or infected with one or more multidrug-resistant organisms (MDROs), is an important infection prevention intervention utilized to prevent pathogens from being transmitted among patients in healthcare settings. Recently, certain healthcare facilities have taken steps to limit the use of CP for patients colonized or infected with MDROs that are considered to be endemic, namely methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant Enterococci (VRE). In this issue of the *Journal of Hospital Medicine*, authors Young et al. argue that CP for MRSA and VRE is an intervention that should be eliminated as part of the Choosing Wisely® campaign because it is a "thing we do for no reason."[1] We respectfully disagree with this characterization of CP for MRSA and VRE, and we assert instead that CP are a necessary practice that should be continued.

Young et al. refer to published studies and a recent meta-analysis that did not conclusively show a benefit of CP for MRSA and VRE.[2] The quasi-experimental studies cited have major methodological flaws that limit their ability to demonstrate the effect of CP. Most importantly, these studies fail to account for the fact that among patients who develop an infection following hospital-acquired MRSA colonization, approximately 70% of the infections are identified after discharge.[3] When such studies do not restrict their outcome measure to include only those infections occurring among patients with hospital-acquired colonization, and do not take steps to accurately identify postdischarge infections that occur in such patients, their results are biased toward the null and difficult to interpret. Due to several serious challenges to study feasibility, including the need for an extremely large sample size, a very long period of follow-up, and the need to control for a variety of other concurrent infection prevention measures, there may never be a study that conclusively proves that CP, apart from other infection prevention interventions, has a significant impact. However, despite these limitations, one of the recent multicenter randomized controlled trials, cited by the authors as evidence against the use of CP, was able to demonstrate a significant reduction in MRSA transmission using universal gowns and gloves for all intensive care unit patients, even in sites that utilized other effective strategies, including chlorhexidine bathing.[4,5]

In this issue of the *Journal of Hospital Medicine®*, Young et al. acknowledge that CP are generally utilized as part of a comprehensive package of infection prevention approaches that also includes hand hygiene, environmental cleaning, antimicrobial stewardship, and evidence-based interventions to prevent device- and procedure-related infections. This multifaceted approach makes it more difficult to determine the attributable effect of CP alone. However, there is a strong rationale for using CP to prevent transmission, and there are numerous examples where the use of bundled approaches that include CP was associated with success. In the Netherlands, CP were part of an aggressive "search and destroy" approach to MRSA associated with almost total elimination of MRSA from hospitals in that country. The United Kingdom achieved an 80% decrease in MRSA bacteremia following a series of aggressive intervention policies designed to prevent MRSA transmission, including use of screening and CP.[6] In the United States, the Veterans Affairs system utilizes this type of approach and reported a 62% decrease in MRSA rates. Subsequent analysis showed that the downward trend of hospital-onset MRSA infections was observed only among patients who were not carrying MRSA at the time of admission, suggesting that preventing transmission was an important contributor to the overall trends.[7,8] More broadly, healthcare-associated MRSA rates in the United States have decreased dramatically over the past decade,[9,10] a period during which more than 81% of hospitals reported using CP for patients colonized or infected with MRSA as part of the bundle of infection prevention approaches.[11] Given these decreases, and the potential role that CP played in achieving these results, we, along with others,[12] urge caution about the dangers of abandoning CP prematurely and without data to indicate that it is safe to stop.

Although some studies report adverse events associated with CP, including a reduced number of visits from healthcare personnel and increased anxiety and depression, these studies rarely control for important confounding variables such as the severity of illness or the presence of anxiety and depression at the time of hospital admission.[13-15] The highest-quality evidence in studies that control for severity of illness and the presence of depression at the time of admission suggests

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that CP are not associated with an increased incidence of adverse events.[16,17]

Interestingly, Young et al. acknowledge that CP are important and should be continued for patients infected or colonized with certain MDROs, including carbapenem-resistant Enterobacteriaceae, multidrug-resistant *Pseudomonas aeruginosa*, and *Candida auris*. They even suggest continuing CP for patients with certain types of antimicrobial-resistant *Staphylococcus aureus* isolates that are resistant or intermediate to vancomycin (Vancomycin-resistant *Staphylococcus aureus* [VRSA] or Vancomycin-intermediate *Staphylococcus aureus* [VISA]) and for which transmission has rarely been documented in the United States. It is unclear why they believe that CP are indicated and useful to prevent transmission of these multidrug-resistant pathogens while advocating that CP are not useful or indicated to prevent transmission of MRSA and VRE. One must consider whether it makes sense to use such a selective approach to using CP for patients with some, but not all, MDROs.

The authors state that CP should be employed to help interrupt outbreaks and for patients with high-risk situations such as open wounds, uncontained secretions, or incontinent diarrhea. We agree that there is appeal to a risk-based approach in which CP are applied based on the likelihood that an individual patient may be carrying and shedding an MDRO. However, to our knowledge, there are no validated algorithms available for this purpose, and it appears likely that using such algorithms would result in an increase in the proportion of patients cared for using CP, rather than a decrease.

The use of CP when caring for patients colonized or infected with an MDRO is considered to be a standard of care. Based on experimental, clinical, and epidemiologic studies and a strong theoretical rationale, the use of CP is currently recommended by the United States Centers for Disease Control and Prevention (CDC), the Healthcare Infection Control Practices Advisory Committee (HICPAC),[18] the Society for Healthcare Epidemiology of America (SHEA),[19] and the Infectious Diseases Society of America.[20] Many healthcare facilities continue to employ CP for patients with a wide array of MDROs, including MRSA and VRE, and many infection prevention experts continue to support and utilize this approach. In response to the growing movement to discontinue CP, the CDC recently reaffirmed its support and recommendation for the use of CP when caring for patients colonized or infected with MRSA.[21]

In summary, a bundled, multifaceted approach to infection prevention and transmission of MDROs is extremely important, and we caution against stopping CP for MRSA and VRE before data are available on the potential harm of that approach. Study limitations make it difficult to demonstrate the individual contribution of CP, but CP are an important component of a comprehensive infection prevention MDRO bundle that has successfully reduced healthcare-associated MRSA. Well-designed studies that control for confounders such as the severity of illness at the time of admission suggest that CP are not associated with an increased incidence of adverse events. Currently available data do not support a selective approach to utilizing CP for some MDROs while not using CP for others. Current guidelines call for the use of CP for preventing MDRO transmission, including MRSA and VRE. Healthcare facilities need to focus on how to implement CP in a patient-centered manner, rather than abandoning CP for some MDROs.

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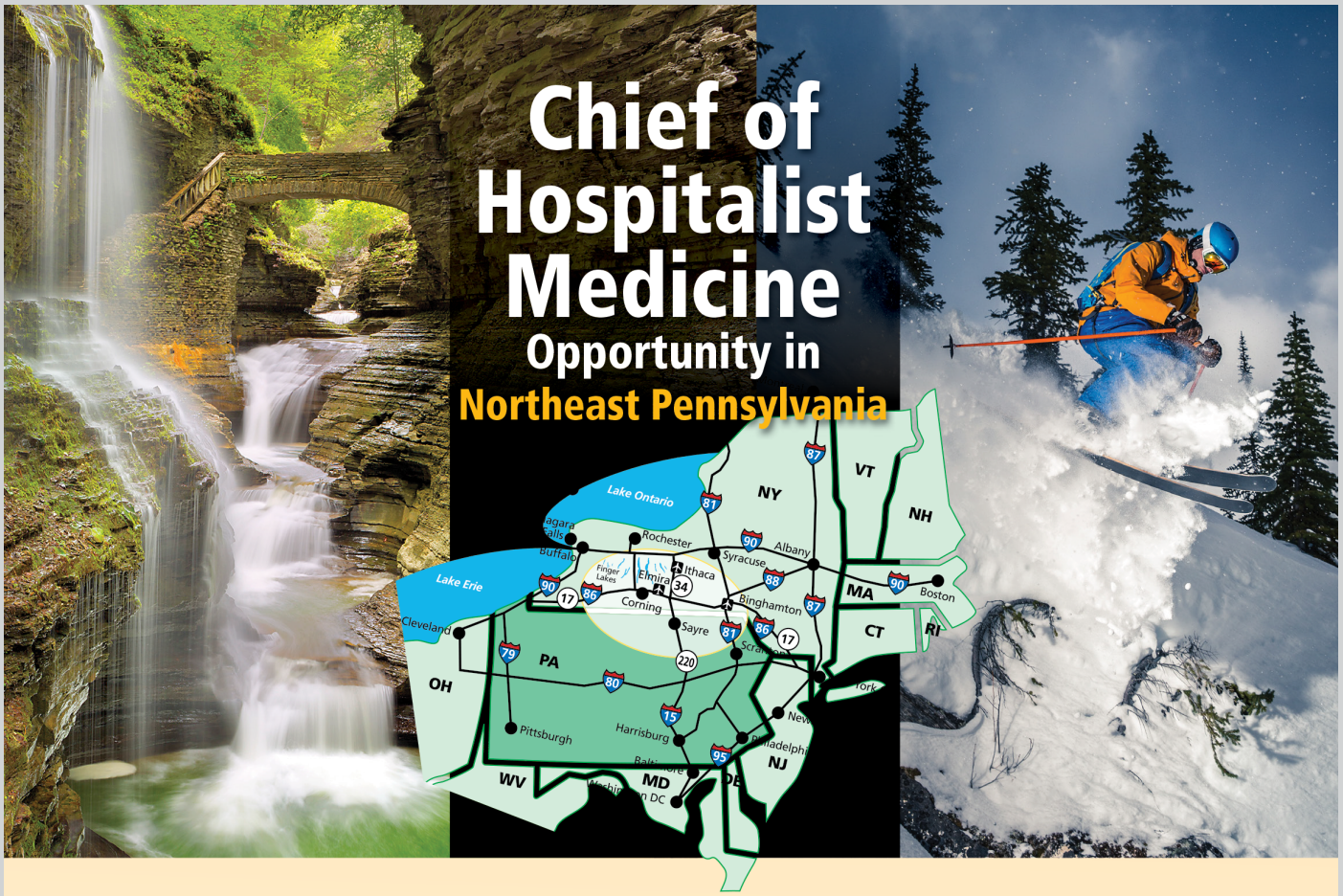

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- Ensures coverage of shifts.

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- Participates in strategic plan for hospital medicine group, including marketing, growth/recruiting, service, and quality.
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