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CHOOSING WISELY®: THINGS WE DO FOR NO REASON

PERSPECTIVES IN HOSPITAL MEDICINE

EDITORIALS

Leading By Example: How Medical Journals Can Improve Representation in Academic Medicine

Samir S Shah, MD, MSCE[1]*; Erin E Shaughnessy, MD, MSHCM[2]; Nancy D Spector, MD[3]

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Women and racial and ethnic minorities remain underrepresented in senior faculty roles and academic leadership positions.[1] Participation in peer review and publication in medical journals are important components of academic advancement that are emphasized in the promotion process. These efforts offer recognition of expertise and increase visibility in the scientific community, which may enhance opportunities for networking and collaboration, and provide other opportunities for career advancement. In addition, abundant evidence shows that organizations benefit from diverse teams, with better quality decisions and increased productivity resulting from diverse ideas and perspectives.[2]

Numerous studies have highlighted the prevalence and persistence of disparities in peer review and authorship.[3,4] Much of this work has focused on gender though gaps in these measures likely exist for racial and ethnic minorities. Yet, there are few examples of journals implementing strategies to address disparities and track results of such efforts.[5] While institutional barriers to advancement must be addressed, we believe that medical journals have an obligation to address unequal opportunities.

At the *Journal of Hospital Medicine*, we are committed to leading by example and developing approaches to create equity in all facets of journal leadership and authorship.[6] The first step towards progress is to assess the current representation of women and racial and ethnic minorities in our journal community, including first and senior authors, invited expert contributors, reviewers, and editorial team members. Like most journals, we have not collected demographic information from authors or reviewers. But now, as part of the journal's commitment to this cause, we request that everyone in the journal community (author, reviewer, editor) update their journal account (accessible at https://mc.manuscriptcentral.com/jhm) with demographic data, including gender, race, and ethnicity.

Inclusion of these data is voluntary. While each individual will be able to access and edit their personal demographic data, the individual data will remain private and unviewable to others. As such, it will not be available for nor will it be used in the manuscript review or decision process but rather for assessing our own inclusiveness. We will review these data in aggregate to broadly inform outreach efforts to promote diversity and inclusion in our author, invited expert contributor, reviewer, and journal leadership pools. We will report on the progress of these efforts in upcoming years.

We are committed to equity in providing opportunities for academic advancement across the journal community. Diversity and inclusion are important in raising the quality of the work that we publish. Different perspectives strengthen our journal and will help us continue to advance the field of Hospital Medicine.

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Resuming Anticoagulation following Upper Gastrointestinal Bleeding among Patients with Nonvalvular Atrial Fibrillation—A Microsimulation Analysis

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BACKGROUND: Among patients with nonvalvular atrial fibrillation (NVAF) who have sustained an upper gastrointestinal bleed (UGIB), the benefits and harms of oral anticoagulation change over time. Early resumption of anticoagulation increases recurrent bleeding, while delayed resumption exposes patients to a higher risk of ischemic stroke. We therefore set out to estimate the expected benefit of resuming anticoagulation as a function of time after UGIB among patients with NVAF.

METHODS: We created a decision-analytic model estimating discounted quality-adjusted life-years when patients with NVAF resume anticoagulation on each day following UGIB. We simulated from a health system perspective over a lifelong time horizon.

RESULTS: Peak utility for warfarin was achieved by resumption 41 days after hemostasis from the index UGIB. Resumption between days 32 and 51 produced greater than 99.9% of the peak utility. Peak utility for apixaban was achieved by resumption 32 days after the index UGIB. Resumption between days 21 and 47 produced greater than 99.9% of the peak utility. Of input parameters, results were most sensitive to underlying stroke risk. Specifically, across the range of CHA_2DS_2-Vasc scores, the optimal day of resumption varied by around 11 days for patients resuming warfarin and by around 15 days for patients resuming apixaban. Results were less sensitive to underlying risk of rebleeding.

CONCLUSIONS: For patients with NVAF following UGIB, warfarin is optimally restarted approximately six weeks following hemostasis, and apixaban is optimally restarted approximately one month following hemostasis. Modest changes to this timing based on probability of thromboembolic stroke are reasonable. *Journal of Hospital Medicine* 2019;14:394-400. Published online first April 8, 2019. © 2019 Society of Hospital Medicine

Anticoagulation is commonly used in the management of atrial fibrillation to reduce the risk of ischemic stroke. Warfarin and other anticoagulants increase the risk of hemorrhagic complications, including upper gastrointestinal bleeding (UGIB). Following UGIB, management of anticoagulation is highly variable. Many patients permanently discontinue anticoagulation, while others continue without interruption.[1-4] Among patients who resume warfarin, different cohorts have measured median times to resumption ranging from four days to 50 days.[1-3] Outcomes data are sparse, and clinical guidelines offer little direction.[5]

Following UGIB, the balance between the risks and benefits of anticoagulation changes over time. Rebleeding risk is highest immediately after the event and declines quickly; therefore, rapid resumption of anticoagulation causes patient harm.[3] Meanwhile, the risk of stroke remains constant, and delay in resumption of anticoagulation is associated with increased risk of stroke and death.[1] At some point in time following the initial UGIB, the expected harm from bleeding would equal the expected harm from stroke. This time point would represent the optimal time to restart anticoagulation.

Trial data are unlikely to identify the optimal time for restarting anticoagulation. A randomized trial comparing discrete reinitiation times (eg, two weeks vs six weeks) may easily miss the optimal timing. Moreover, because the daily probability of thromboembolic events is low, large numbers of patients would be required to power such a study. In addition, a number of oral anticoagulants are now approved for prevention of thromboembolic stroke in atrial fibrillation, and each drug may have different optimal timing.

In contrast to randomized trials that would be impracticable for addressing this clinical issue, microsimulation modeling can provide granular information regarding the optimal time to restart anticoagulation. Herein, we set out to estimate the expected benefit of reinitiation of warfarin, the most commonly used oral anticoagulant,[6] or apixaban, the direct oral anticoagulant with the most favorable risk profile,[7] as a function of days after UGIB.

METHODS

We previously described a microsimulation model of anticoagulation among patients with nonvalvular atrial fibrillation

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(NVAF; hereafter, we refer to this model as the Personalized Anticoagulation Decision-Making Assistance model, or PADMA).[8,9] For this study, we extended this model to incorporate the probability of rebleeding following UGIB and include apixaban as an alternative to warfarin. This model begins with a synthetic population following UGIB, the members of which are at varying risk for thromboembolism, recurrent UGIB, and other hemorrhages. For each patient, the model simulates a number of possible events (eg, thromboembolic stroke, intracranial hemorrhage, rebleeding, and other major extracranial hemorrhages) on each day of an acute period of 90 days after hemostasis. Patients who survive until the end of the acute period enter a simulation with annual, rather than daily, cycles. Our model then estimates total quality-adjusted life-years (QALYs) for each patient, discounted to the present. We report the average discounted QALYs produced by the model for the same population if all individuals in our input population were to resume either warfarin or apixaban on a specific day. Input parameters and ranges are summarized in Table 1, a simplified schematic of our model is shown in the Supplemental Appendix, and additional details regarding model structure and assumptions can be found in earlier work.[8,9] We simulated from a health system perspective over a lifelong time horizon. All analyses were performed in version 14 of Stata (StataCorp, LLC, College Station, Texas).

Synthetic Population

To generate a population reflective of the comorbidities and age distribution of the US population with NVAF, we merged relevant variables from the National Health and Nutrition Examination Survey (NHANES; 2011-2012), using multiple imputation to correct for missing variables.[10] We then bootstrapped to national population estimates by age and sex to arrive at a hypothetical population of the United States.[11] Because NHANES does not include atrial fibrillation, we applied sex- and age-specific prevalence rates from the AnTicoagulation and Risk Factors In Atrial Fibrillation study.[12] We then calculated commonly used risk scores (CHA_2DS_2-Vasc and HAS-BLED) for each patient and limited the population to patients with a CHA_2DS_2-Vasc score of one or greater.[13,14] The population resuming apixaban was further limited to patients whose creatinine clearance was 25 mL/min or greater in keeping with the entry criteria in the phase 3 clinical trial on which the medication's approval was based.[15]

To estimate patient-specific probability of rebleeding, we generated a Rockall score for each patient.[16] Although the discrimination of the Rockall score is limited for individual patients, as with all other tools used to predict rebleeding following UGIB, the Rockall score has demonstrated reasonable calibration across a threefold risk gradient.[17-19] International consensus guidelines recommend the Rockall score as one of two risk prediction tools for clinical use in the management of patients with UGIB.[20] In addition, because the Rockall score includes some demographic components (five of a possible 11 points), our estimates of rebleeding risk are covariant with other patient-specific risks. We assumed that the endoscopic components of the Rockall score were present in our cohort at the same frequency as in the original derivation and are independent of known patient risk factors.[16] For example, 441 out of 4,025 patients in the original Rockall derivation cohort presented with a systolic blood pressure less than 100 mm Hg. We assumed that an independent and random 10.96% of the cohort would present with shock, which confers two points in the Rockall score.

The population was replicated 60 times, with identical copies of the population resuming anticoagulation on each of days 1-60 (where day zero represents hemostasis). Intermediate data regarding our simulated population can be found in the Supplemental Appendix and in prior work.

Event Type, Severity, and Mortality

Each patient in our simulation could sustain several discrete and independent events: ischemic stroke, intracranial hemorrhage, recurrent UGIB, or extracranial major hemorrhage other than recurrent UGIB. As in prior analyses using the PADMA model, we did not consider minor hemorrhagic events.[8]

The probability of each event was conditional on the corresponding risk scoring system. Patient-specific probability of ischemic stroke was conditional on CHA_2DS_2-Vasc score.[21,22] Patient-specific probability of intracranial hemorrhage was conditional on HAS-BLED score, with the proportions of intracranial hemorrhage of each considered subtype (intracerebral, subarachnoid, or subdural) bootstrapped from previously-published data.[21-24] Patient-specific probability of rebleeding was conditional on Rockall score from the combined Rockall and Vreeburg validation cohorts.[17] Patient-specific probability of extracranial major hemorrhage was conditional on HAS-BLED score.[21] To avoid double-counting of UGIB, we subtracted the baseline risk of UGIB from the overall rate of extracranial major hemorrhages using previously-published data regarding relative frequency and a bootstrapping approach.[25]

Probability of Rebleeding Over Time

To estimate the decrease in rebleeding risk over time, we searched the Medline database for systematic reviews of recurrent bleeding following UGIB using the strategy detailed in the Supplemental Appendix. Using the interval rates of rebleeding we identified, we calculated implied daily rates of rebleeding at the midpoint of each interval. For example, 39.5% of rebleeding events occurred within three days of hemostasis, implying a daily rate of approximately 13.2% on day two (32 of 81 events over a three-day period). We repeated this process to estimate daily rates at the midpoint of each reported time interval and fitted an exponential decay function.[26] Our exponential fitted these datapoints quite well, but we lacked sufficient data to test other survival functions (eg, Gompertz, lognormal, etc.). Our fitted exponential can be expressed as:

$$P_{rebleeding} = b_0 * \exp(b_1 * day)$$

where $b_0 = 0.1843$ (SE: 0.0136) and $b_1 = -0.1563$ (SE: 0.0188). For example, a mean of 3.9% of rebleeding episodes will occur on day 10 ($0.1843 * \exp(-0.1563 * 10)$).

TABLE 1. **Summary of Model Input Parameters**

Fixed and Sampled Inputs

Input parameter	Base-case estimate	References
Age and sex of US population	US Census	11
Age- and sex-specific prevalence of atrial fibrillation	ATRIA	12
Age- and sex-specific prevalence and covariation of stroke risk factors	NHANES	10
Annual incidence of ischemic stroke	Fixed for each CHA_2DS_2-Vasc score (0.2% to 14.4%)	21,22
Annual incidence of intracranial hemorrhage	Fixed for each HAS-BLED score (0.1%-1.3%)	21,22
Annual incidence of extracranial major hemorrhage	Fixed for each HAS-BLED score (0.5% to 14.5%)	21,22
Incidence of rebleeding	Fixed for each Rockall score based on combined rates in Rockall and Vreeburg cohorts	17
Timing of rebleeding	Exponential decay model (see methods)	26
Subtypes of intracranial hemorrhage	65% intracerebral, 6% subarachnoid, 29% subdural	23,24
Trajectories of INR after reinitiation of warfarin	Sampled from clinical warfarin initiation group of COAG trial	27
Inpatient mortality following ischemic or hemorrhagic stroke	Predicted	38,39
Inpatient mortality following subdural hemorrhage	Predicted	40
Length of stay, conditioned on diagnosis	Sampled	28
Hazard ratio for long-term mortality following stroke or ICH, mRS ≤ 2	1.7	33
Hazard ratio for long-term mortality following stroke or ICH, mRS = 3 or 4	2.9	33
Hazard ratio for long-term mortality following stroke or ICH, mRS 5	8.3	33
Baseline probability of death by age	Varies	41
Future mRS following ischemic stroke	Predicted using NINDS trial data	8,9,42
Future mRS following ICH, conditional on survival to discharge	13.8% each mRS 0-2, 19.5% each mRS 3-5	30
Disutility, mRS 1	0.046	34
Disutility, mRS 2	0.212	34
Disutility, mRS 3	0.331	34
Disutility, mRS 4	0.652	34
Disutility, mRS 5	0.944	34

Continuously Varying Input Parameters

Input Parameter	Mean (Median)	sd (IQR)	Distribution	References
Incidence of rebleeding	17.8%	0.8%	Normal	17
Percentage of major extracranial hemorrhagic events that are gastrointestinal	35.2%	2.2%	Normal	25
Percentage of GI bleeds that arise from the upper GI tract	75.0%	5.1%	Normal	25
Severity of ischemic strokes (NIHSS)	16.2	7.0	Normal	38,39
Severity of intracerebral hemorrhages (NIHSS)	9	(3-19)	Normal	39
Severity of subarachnoid hemorrhages (NIHSS)	3	(0-11)	Gamma	39
In-hospital mortality following extracranial major hemorrhage	9.5%	3.4%	Normal	29,43
Discount rate	3%	1.7%	Uniform (0%-6%)	44

Abbreviations: GI, gastrointestinal; ICH, intracerebral hemmorhage; mRS, modified Rankin Score; NIHSS, NIH Stroke Scale.

TABLE 2. **Optimal Day of Warfarin or Apixaban Reinitiation by CHA_2DS_2-Vasc Score**[a]

CHA_2DS_2-Vasc	Apixaban	Warfarin
1	52 (49 - 55)	50 (48 - 52)
2	49 (46 - 52)	48 (46 - 50)
3	46 (43 - 49)	46 (44 - 47)
4	43 (40 - 46)	43 (42 - 45)
5	40 (37 - 43)	41 (39 - 43)
6	37 (34 - 40)	39 (37 - 40)
7	34 (31 - 37)	36 (35 - 38)
8	31 (28 - 34)	34 (32 - 36)
9	28 (25 - 31)	32 (30 - 34)

[a]Day 0 represents hemostasis from the index UGIB. The range of predicted days on which initiation would confer at least 99.99% of the peak QALYs is shown in parentheses

Relative Risks of Events with Anticoagulation

For patients resuming warfarin, the probabilities of each event were adjusted based on patient-specific daily INR. All INRs were assumed to be 1.0 until the day of warfarin reinitiation, after which interpolated trajectories of postinitiation INR measurements were sampled for each patient from an earlier study of clinical warfarin initiation.[27] Relative risks of ischemic stroke and hemorrhagic events were calculated based on each day's INR.

For patients taking apixaban, we assumed that the medication would reach full therapeutic effect one day after reinitiation. Based on available evidence, we applied the relative risks of each event with apixaban compared with warfarin.[25]

Future Disability and Mortality

Each event in our simulation resulted in hospitalization. Length of stay was sampled for each diagnosis.[28] The disutility of hospitalization was estimated based on length of stay.[8] Inpatient mortality and future disability were predicted for each event as previously described.[8] We assumed that recurrent episodes of UGIB conferred morbidity and mortality identical to extracranial major hemorrhages more broadly.[29,30]

Disutilities

We used a multiplicative model for disutility with baseline utilities conditional on age and sex.[31] Each day after resumption of anticoagulation carried a disutility of 0.012 for warfarin or 0.002 for apixaban, which we assumed to be equivalent to aspirin in disutility.[32] Long-term disutility and life expectancy were conditional on modified Rankin Score (mRS).[33,34] We discounted all QALYs to day zero using standard exponential discounting and a discount rate centered at 3%. We then computed the average discounted QALYs among the cohort of patients that resumed anticoagulation on each day following the index UGIB.

Sensitivity Analyses and Metamodel

To assess sensitivity to continuously varying input parameters, such as discount rate, the proportion of extracranial major hemorrhages that are upper GI bleeds, and inpatient mortality from extracranial major hemorrhage, we constructed a metamodel (a regression model of our microsimulation results).[35] We tested for interactions among input parameters and dropped parameters that were not statistically significant predictors of discounted QALYs from our metamodel. We then tested for interactions between each parameter and day resuming anticoagulation to determine which factors may impact the optimal day of reinitiation. Finally, we used predicted marginal effects from our metamodel to assess the change in optimal day across the ranges of each input parameter when other parameters were held at their medians.

RESULTS

Resuming warfarin on day zero produced the fewest QALYs. With delay in reinitiation of anticoagulation, expected QALYs increased, peaked, and then declined for all scenarios. In our base-case simulation of warfarin, peak utility was achieved by resumption 41 days after the index UGIB. Resumption between days 32 and 51 produced greater than 99.9% of peak utility. In our base-case simulation of apixaban, peak utility was achieved by resumption 32 days after the index UGIB. Resumption between days 21 and 47 produced greater than 99.9% of peak utility. Results for warfarin and apixaban are shown in Figures 1 and 2, respectively.

The optimal day of warfarin reinitiation was most sensitive to CHA_2DS_2-Vasc scores and varied by around 11 days between a CHA_2DS_2-Vasc score of one and a CHA_2DS_2-Vasc score of six (the 5th and 95th percentiles, respectively) when all other parameters are held at their medians. Results were comparatively insensitive to rebleeding risk. Varying Rockall score from two to seven (the 5th and 95th percentiles, respectively) added three days to optimal warfarin resumption. Varying other parameters from the 5th to the 95th percentile (including HAS-BLED score, sex, age, and discount rate) changed expected QALYs but did not change the optimal day of reinitiation of warfarin. Optimal day of reinitiation for warfarin stratified by CHA_2DS_2-Vasc score is shown in Table 2.

Sensitivity analyses for apixaban produced broadly similar results, but with greater sensitivity to rebleeding risk. Optimal day of reinitiation varied by 15 days over the examined range of CHA_2DS_2-Vasc scores (Table 2) and by six days over the range of Rockall scores (Supplemental Appendix). Other input parameters, including HAS-BLED score, age, sex, and discount rate, changed expected QALYs and were significant in our metamodel but did not affect the optimal day of reinitiation. Metamodel results for both warfarin and apixaban are included in the Supplemental Appendix.

DISCUSSION

Anticoagulation is frequently prescribed for patients with NVAF, and hemorrhagic complications are common. Although anticoagulants are withheld following hemorrhages, scant evidence to inform the optimal timing of reinitiation is available.

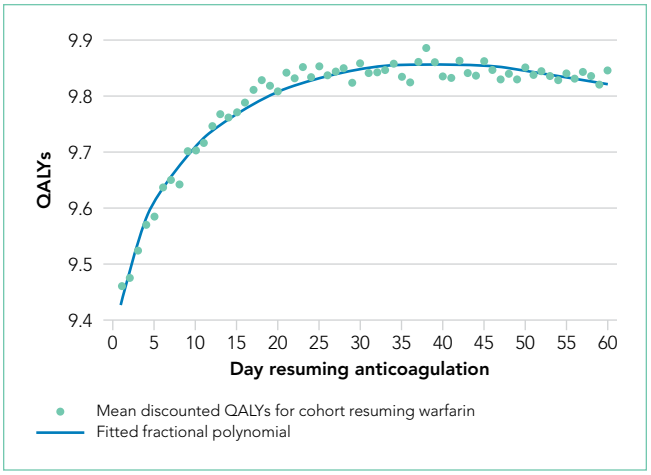

FIG 1. Expected Average QALYs Conferred as a Function of Day on which Warfarin is Resumed. Day 0 represents hemostasis of the index UGIB. The fitted line is a fractional polynomial.

Abbreviations: QALYs, quality-adjusted life-years; UGIB; upper gastrointestinal bleeding

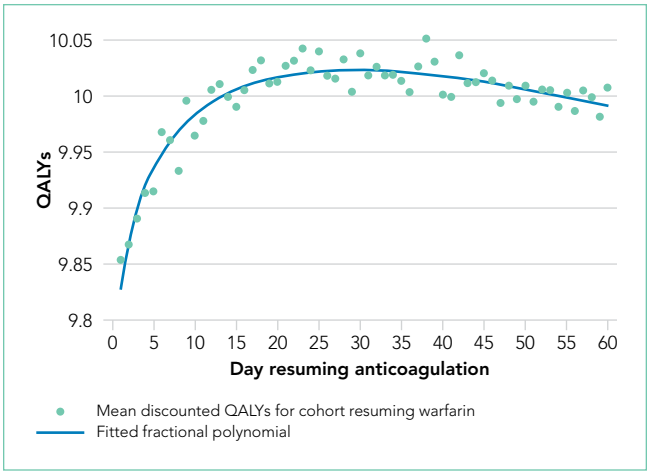

FIG 2. Expected Average QALYs Conferred as a Function of Day on which Apixaban is Resumed. Day 0 represents hemostasis of the index UGIB. The fitted line is a fractional polynomial.

Abbreviations: QALYs, quality-adjusted life-years; UGIB; upper gastrointestinal bleeding

In this microsimulation analysis, we found that the optimal time to reinitiate anticoagulation following UGIB is around 41 days for warfarin and around 32 days for apixaban. We have further demonstrated that the optimal timing of reinitiation can vary by nearly two weeks, depending on a patient's underlying risk of stroke, and that early reinitiation is more sensitive to rebleeding risk than late reinitiation.

Prior work has shown that early reinitiation of anticoagulation leads to higher rates of recurrent hemorrhage while failure to reinitiate anticoagulation is associated with higher rates of stroke and mortality.[1-4,36] Our results add to the literature in a number of important ways. First, our model not only confirms that anticoagulation should be restarted but also suggests when this action should be taken. The competing risks of bleeding and stroke have left clinicians with little guidance; we have quantified the clinical reasoning required for the decision to resume anticoagulation. Second, by including the disutility of hospitalization and long-term disability, our model more accurately represents the complex tradeoffs between recurrent hemorrhage and (potentially disabling) stroke than would a comparison of event rates. Third, our model is conditional upon patient risk factors, allowing clinicians to personalize the timing of anticoagulation resumption. Theory would suggest that patients at higher risk of ischemic stroke benefit from earlier resumption of anticoagulation, while patients at higher risk of hemorrhage benefit from delayed reinitiation. We have quantified the extent to which patient-specific risks should change timing. Fourth, we offer a means of improving expected health outcomes that requires little more than appropriate scheduling. Current practice regarding resuming anticoagulation is widely variable. Many patients never resume warfarin, and those that do resume do so after highly varied periods of time.[1-5,36] We offer a means of standardizing clinical practice and improving expected patient outcomes.

Interestingly, patient-specific risk of rebleeding had little effect on our primary outcome for warfarin, and a greater effect in our simulation of apixaban. It would seem that rebleeding risk, which decreases roughly exponentially, is sufficiently low by the time period at which warfarin should be resumed that patient-specific hemorrhage risk factors have little impact. Meanwhile, at the shorter post-event intervals at which apixaban can be resumed, both stroke risk and patient-specific bleeding risk are worthy considerations.

Our model is subject to several important limitations. First, our predictions of the optimal day as a function of risk scores can only be as well-calibrated as the input scoring systems. It is intuitive that patients with higher risk of rebleeding benefit from delayed reinitiation, while patients with higher risk of thromboembolic stroke benefit from earlier reinitiation. Still, clinicians seeking to operationalize competing risks through these two scores—or, indeed, any score—should be mindful of their limited calibration and shared variance. In other words, while the optimal day of reinitiation is likely in the range we have predicted and varies to the degree demonstrated here, the optimal day we have predicted for each score is likely overly precise. However, while better-calibrated prediction models would improve the accuracy of our model, we believe ours to be the best estimate of timing given available data and this approach to be the most appropriate way to personalize anticoagulation resumption.

Our simulation of apixaban carries an additional source of potential miscalibration. In the clinical trials that led to their approval, apixaban and other direct oral anticoagulants (DOACs) were compared with warfarin over longer periods of time than the acute period simulated in this work. Over a short period of time, patients treated with more rapidly therapeutic medications (in this case, apixaban) would receive more days of effective therapy compared with a slower-onset medication, such as warfarin. Therefore, the relative risks experienced by patients are likely different over the time period we have simulated compared with those measured over longer periods of time (as in phase 3 clinical trials). Our results for apixaban

should be viewed as more limited than our estimates for warfarin. More broadly, simulation analyses are intended to predict overall outcomes that are difficult to measure. While other frameworks to assess model credibility exist, the fact remains that no extant datasets can directly validate our predictions.[37]

Our findings are limited to patients with NVAF. Anticoagulants are prescribed for a variety of indications with widely varied underlying risks and benefits. Models constructed for these conditions would likely produce different timing for resumption of anticoagulation. Unfortunately, large scale cohort studies to inform such models are lacking. Similarly, we simulated UGIB, and our results should not be generalized to populations with other types of bleeding (eg, intracranial hemorrhage). Again, cohort studies of other types of bleeding would be necessary to understand the risks of anticoagulation over time in such populations.

Higher-quality data regarding risk of rebleeding over time would improve our estimates. Our literature search identified only one systematic review that could be used to estimate the risk of recurrent UGIB over time. These data are not adequate to interrogate other forms this survival curve could take, such as Gompertz or Weibull distributions. Recurrence risk almost certainly declines over time, but how quickly it declines carries additional uncertainty.

Despite these limitations, we believe our results to be the best estimates to date of the optimal time of anticoagulation reinitiation following UGIB. Our findings could help inform clinical practice guidelines and reduce variation in care where current practice guidelines are largely silent. Given the potential ease of implementing scheduling changes, our results represent an opportunity to improve patient outcomes with little resource investment.

In conclusion, after UGIB associated with anticoagulation, our model suggests that warfarin is optimally restarted approximately six weeks following hemostasis and that apixaban is optimally restarted approximately one month following hemostasis. Modest changes to this timing based on probability of thromboembolic stroke are reasonable.

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The Current State of Advanced Practice Provider Fellowships in Hospital Medicine: A Survey of Program Directors

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BACKGROUND: Postgraduate training for advanced practice providers (APPs) is a growing field in hospital medicine. As hospital programs continue to benefit from highly trained physician assistants (PAs) and nurse practitioners (NPs), fellowship programs have become more prevalent. However, little is known about the number of active programs or how they prepare trainees.

OBJECTIVES: To describe the existing APP fellowships in hospital medicine, with a focus on program characteristics, rationale, curricula, and learner assessment.

METHODS: An electronic survey was distributed by e-mail to hospital medicine program directors in May 2018. The survey consisted of 25 multiple choice and short answer questions. Descriptive statistics were calculated utilizing Stata 13 for data analysis.

RESULTS: Of the 11 fellowships identified, 10 (91%) of directors responded to the survey. Eighty percent of programs accept both NPs and PAs and 80% are between 12 and 13 months long. All programs cite "training and retaining" as the main driver for their creation and 90% were founded in institutions with existing physician residencies. Ninety percent of program curricula are informed by Society of Hospital Medicine resources. Despite these similarities, there was wide variation in both curricular content and APP fellow assessment.

CONCLUSION: APP fellowships in hospital medicine are quickly growing as a means to train and retain nonphysician hospitalists. While most programs accept similar types of applicants and share a common rationale for program development, there is little standardization in terms of curriculum or assessment. Further research may be valuable to characterize the best practices to guide the future of these fellowships. *Journal of Hospital Medicine* 2019;14:401-406. Published online first April 8, 2019. © 2019 Society of Hospital Medicine

Postgraduate training for physician assistants (PAs) and nurse practitioners (NPs) is a rapidly evolving field. It has been estimated that the number of these advanced practice providers (APPs) almost doubled between 2000 and 2016 (from 15.3 to 28.2 per 100 physicians) and is expected to double again by 2030.[1] As APPs continue to become a progressively larger part of the healthcare workforce, medical organizations are seeking more comprehensive strategies to train and mentor them.[2] This has led to the development of formal postgraduate programs, often called APP fellowships.

Historically, postgraduate APP fellowships have functioned to help bridge the gap in clinical practice experience between physicians and APPs.[3] This gap is evident in hours of clinical training. Whereas NPs are generally expected to complete 500-1,500 hours of clinical practice before graduating,[4] and PAs are expected to complete 2,000 hours,[5] most physicians will complete over 15,000 hours of clinical training by the end of residency.[6] As increasing patient complexity continues to challenge the healthcare workforce,[7] both the NP and the PA leadership have recommended increased training of graduates and outcome studies of formal postgraduate fellowships.[8,9] In 2007, there were over 60 of these programs in the United States,[10] most of them offering training in surgical specialties.

First described in 2010 by the Mayo Clinic,[11] APP fellowships in hospital medicine are also being developed. These programs are built to improve the training of nonphysician hospitalists, who often work independently[12] and manage medically complex patients.[13] However, little is known about the number or structure of these fellowships. The limited understanding of the current APP fellowship environment is partly due to the lack of an administrative body overseeing these programs.[14] The Accreditation Review Commission on Education for the Physician Assistant (ARC-PA) pioneered a model in 2007 for postgraduate PA programs, but it has been held in abeyance since 2014.[15] Both the American Nurses Credentialing Center and the National Nurse Practitioner Residency and Fellowship Training Consortium have fellowship accreditation review processes, but they are not specific to hospital medicine.[16] The Society of Hospital Medicine (SHM) has several resources for the training of APPs;[17] however, it neither reviews nor accredits fellowship programs. Without standards, guidelines, or active

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TABLE. **Characteristics of APP Hospital Medicine Fellowships**

Program		A	B	C	D	E	F	G	H	I	J
Years active		**1**	**2**	**2**	**3**	**3**	**4**	**5**	**5**	**9**	**>10**
Program context	Hospital beds	403	338	452	400	681	350	455	900	765	213
	MD residency at institution?	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
	Learn with residents?	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
Program features	Duration (months)	12	12	12	18	6	12	12	12	13	12
	Use SHM core competencies?	No	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes
	What organization accredited the fellowship?	None	None	None	None	None	None	None	None	None	ARC-PA
	Starting salary (in dollars)	>70K	>70K	55-60K	55-60K	>70K	>70K	60-65K	65-70K	60-65K	55-60K
Fellow characteristics	Eligible APPs	NP/PA	NP/PA	NP/PA	PA	NP/PA	NP/PA	NP/PA	NP/PA	NP/PA	PA
	Fellows per class	>5	2	2	2	>5	>5	4	2	>5	3
	Total alumni in the past five years	3	3	3	2	20	6	12	>20	>20	14
	Female fellows in the past five years (%)	100	80	100	100	85	67	70	78	79	65
Postfellowship employment	Is it implied that successful graduates will be retained?	No	Yes	No	No	Yes	Yes	No	Yes	No	No
	Salary/bonus contingent on retention?	Yes	Yes	No	Yes	No	Yes	No	Yes	No	No
	Alumni in last five years hired for full-time position (%)	100	75	100	100	96	100	75	71	86	90
Main driver(s) for fellowship creation	Train and retain applicants	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Build interprofessional team	✓	✓						✓	✓	✓
	Manage patient volume	✓	✓						✓		
	Reduce overhead		✓				✓		✓		

Abbreviations: APP, advanced practice provider; ARC-PA, Accreditation Review Commission on Education for the Physician Assistant; IM, internal medicine; K, thousand; NP, nurse practitioner; PA, physician assistant; SHM, Society of Hospital Medicine.

accrediting bodies, APP fellowships in hospital medicine are poorly understood and are of unknown efficacy. The purpose of this study was to identify and describe the active APP fellowships in hospital medicine.

METHODS

This was a cross-sectional study of all APP adult and pediatric fellowships in hospital medicine, in the United States, that were identifiable through May 2018. Multiple methods were used to identify all active fellowships. First, all training programs offering a *Hospital Medicine Fellowship* in the ARC-PA and Association of Postgraduate PA Programs databases were noted. Second, questionnaires were given out at the NP/PA forum at the national SHM conference in 2018 to gather information on existing APP fellowships. Third, similar online requests to identify known programs were posted to the SHM web forum Hospital Medicine Exchange (HMX). Fourth, Internet searches were used to discover additional programs. Once those fellowships were identified, surveys were sent to their program directors (PDs). These surveys not only asked the PDs about their fellowship but also asked them to identify additional APP fellowships beyond those that we had captured. Once additional programs were identified, a second round of surveys was sent to their PDs. This was performed in an iterative fashion until no additional fellowships were discovered.

The survey tool was developed and validated internally in the AAMC Survey Development style[18] and was influenced by prior validated surveys of postgraduate medical fellowships.[10,19-21] Each question was developed by a team that had expertise in survey design (Wright and Tackett), and two survey design team members were themselves PDs of APP fellowships in hospital medicine (Kisuule and Franco). The survey was revised iteratively by the team on the basis of meetings and pilot testing with PDs of other programs. All qualitative or descriptive questions had a free response option available to allow PDs to answer the survey accurately and exhaustively. The final version of the survey was approved by consensus of all authors. It consisted of 25 multiple choice questions which were created to gather information about the following key areas of APP hospital medicine fellowships: fellowship and learner characteristics, program rationales, curricula, and methods of fellow assessment.

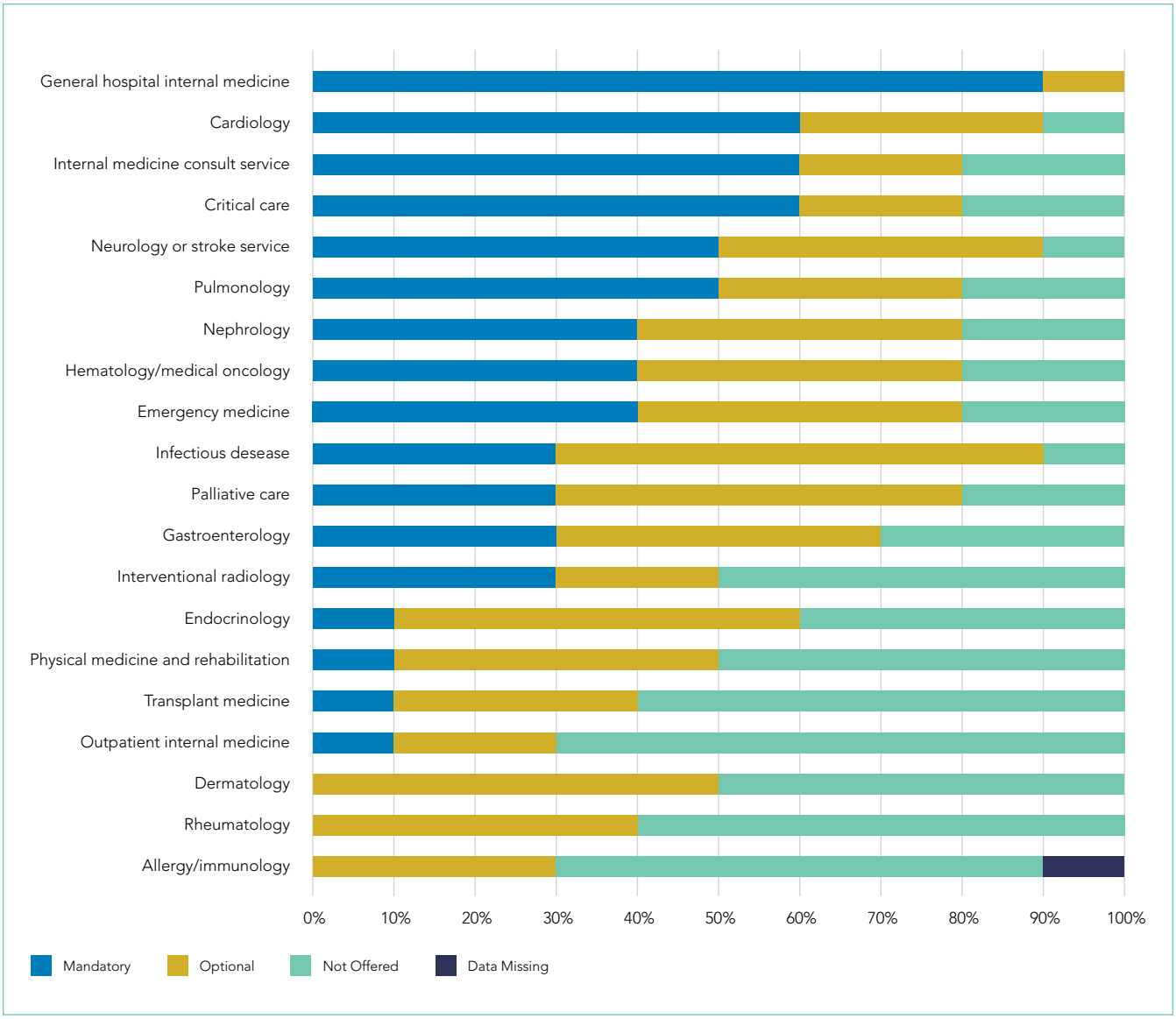

FIG 1. Educational Experiences for Advanced Practice Provider Hospital Fellowships: Clinical Rotations

A web-based survey format (Qualtrics) was used to distribute the questionnaire e-mail to the PDs. Follow up e-mail reminders were sent to all nonresponders to encourage full participation. Survey completion was voluntary; no financial incentives or gifts were offered. IRB approval was obtained at Johns Hopkins Bayview (IRB number 00181629). Descriptive statistics (proportions, means, and ranges as appropriate) were calculated for all variables. Stata 13 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, Texas. StataCorp LP) was used for data analysis.

RESULTS

In total, 11 fellowships were identified using our multimethod approach. We found four (36%) programs by utilizing existing online databases, two (18%) through the SHM questionnaire and HMX forum, three (27%) through internet searches, and the remaining two (18%) were referred to us by the other PDs who were surveyed. Of the programs surveyed, 10 were adult programs and one was a pediatric program. Surveys were sent to the PDs of the 11 fellowships, and all but one of them (10/11, 91%) responded. Respondent programs were given alphabetical designations A through J (Table).

Fellowship and Individual Characteristics

Most programs have been in existence for five years or fewer. Eighty percent of the programs are about one year in duration; two outlier programs have fellowship lengths of six months and 18 months. The main hospital where training occurs has a mean of 496 beds (range 213 to 900). Ninety percent of the hospitals also have physician residency training programs. Sixty percent of programs enroll two to four fellows per year while 40% enroll five or more. The salary range paid by the programs is $55,000 to >$70,000, and half the programs pay more than $65,000.

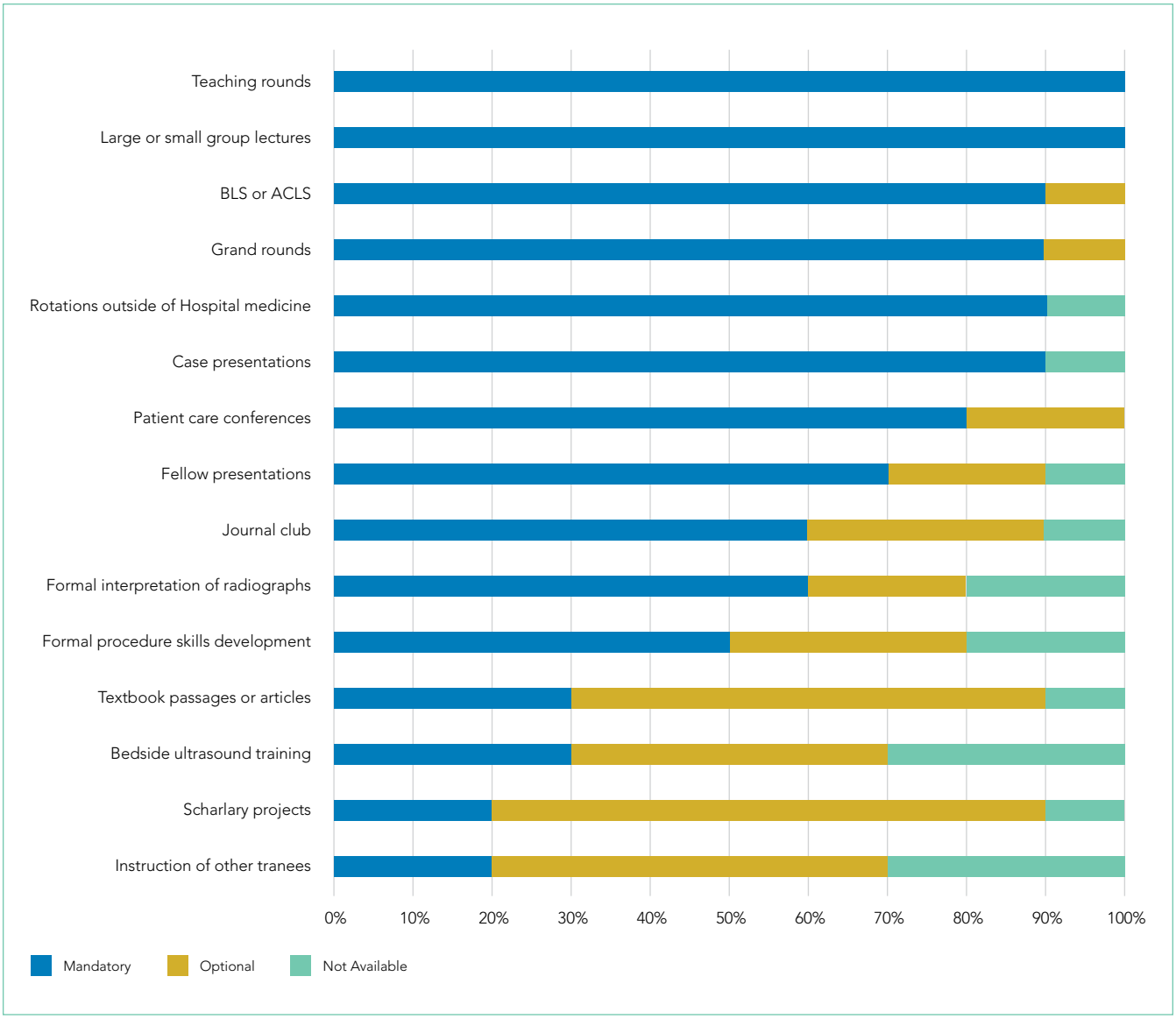

FIG 2. Educational Experiences for Advanced Practice Provider Hospital Fellowships: Learning Formats

The majority of fellows accepted into APP fellowships in hospital medicine are women. Eighty percent of fellows are 26-30 years old, and 90% of fellows have been out of NP or PA school for one year or less. Both NP and PA applicants are accepted in 80% of fellowships.

Program Rationales

All programs reported that training and retaining applicants is the main driver for developing their fellowship, and 50% of them offer financial incentives for retention upon successful completion of the program. Forty percent of PDs stated that there is an implicit or explicit understanding that successful completion of the fellowship would result in further employment. Over the last five years, 89% (range: 71%-100%) of graduates were asked to remain for a full-time position after program completion.

In addition to training and retention, building an interprofessional team (50%), managing patient volume (30%), and reducing overhead (20%) were also reported as rationales for program development. The majority of programs (80%) have fellows bill for clinical services, and five of those eight programs do so after their fellows become more clinically competent.

Curricula

Of the nine adult programs, 67% teach explicitly to SHM core competencies and 33% send their fellows to the SHM NP/PA Boot Camp. Thirty percent of fellowships partner formally with either a physician residency or a local PA program to develop educational content. Six of the nine programs with active physician residencies, including the pediatric fellowship, offer shared educational experiences for the residents and APPs.

There are notable differences in clinical rotations between the programs (Figure 1). No single rotation is universally required, although general hospital internal medicine is required in all adult fellowships. The majority (80%) of programs offer at least

one elective. Six programs reported mandatory rotations outside the department of medicine, most commonly neurology or the stroke service (four programs). Only one program reported only general medicine rotations, with no subspecialty electives.

There are also differences between programs with respect to educational experiences and learning formats (Figure 2). Each fellowship takes a unique approach to clinical instruction; teaching rounds and lecture attendance are the only experiences that are mandatory across the board. Grand rounds are available, but not required, in all programs. Ninety percent of programs offer or require fellow presentations, journal clubs, reading assignments, or scholarly projects. Fellow presentations (70%) and journal club attendance (60%) are required in more than half the programs; however, reading assignments (30%) and scholarly projects (20%) are rarely required.

Methods of Fellow Assessment

Each program surveyed has a unique method of fellow assessment. Ninety percent of the programs use more than one method to assess their fellows. Faculty reviews are most commonly used and are conducted in all rotations in 80% of fellowships. Both self-assessment exercises and written examinations are used in some rotations by the majority of programs. Capstone projects are required infrequently (30%).

DISCUSSION

We found several commonalities between the fellowships surveyed. Many of the program characteristics, such as years in operation, salary, duration, and lack of accreditation, are quite similar. Most fellowships also have a similar rationale for building their programs and use resources from the SHM to inform their curricula. Fellows, on average, share several demographic characteristics, such as age, gender, and time out of schooling. Conversely, we found wide variability in clinical rotations, the general teaching structure, and methods of fellow evaluation.

There have been several publications detailing successful individual APP fellowships in medical subspecialties,[22] psychiatry,[23] and surgical specialties,[24] all of which describe the benefits to the institution. One study found that physician hospitalists have a poor understanding of the training PAs undergo and would favor a standardized curriculum for PA hospitalists.[25] Another study compared all PA postgraduate training programs in emergency medicine;[19] it also described a small number of relatively young programs with variable curricula and a need for standardization. Yet another paper[10] surveyed postgraduate PA programs across all specialties; however, that study only captured two hospital medicine programs, and it was not focused on several key areas studied in this paper—such as the program rationale, curricular elements, and assessment.

It is noteworthy that every program surveyed was created with training and retention in mind, rather than other factors like decreasing overhead or managing patient volume. Training one's own APPs so that they can learn on the job, come to understand expectations within a group, and witness the culture is extremely valuable. From a patient safety standpoint, it has been documented that physician hospitalists straight out of residency have a higher patient mortality compared with more experienced providers.[26] Given the findings that on a national level, the majority of hospitalist NPs and PAs practice autonomously or somewhat autonomously,[12] it is reasonable to assume that similar trends of more experienced providers delivering safer care would be expected for APPs, but this remains speculative. From a retention standpoint, it has been well described that high APP turnover is often due to decreased feelings of competence and confidence during their transition from trainees to medical providers.[27] APPs who have completed fellowships feel more confident and able to succeed in their field.[28] To this point, in one survey of hospitalist PAs, almost all reported that they would have been interested in completing a fellowship, even it meant a lower initial salary.[29]

Despite having the same general goals and using similar national resources, our study reveals that APP fellows are trained and assessed very differently between programs. This might represent an area of future growth in the field of hospitalist APP education. For physician learning, competency-based medical education (CBME) has emerged as a learner centric, outcomes-based model of teaching and assessment that emphasizes mastery of skills and progression through milestones.[30] Both the ACGME[31] and the SHM[32] have described core competencies that provide a framework within CBME for determining readiness for independent practice. While we were not surprised to find that each fellowship has its own unique method of determining readiness for practice, these findings suggest that graduates from different programs likely have very different skill sets and aptitude levels. In the future, an active accrediting body could offer guidance in defining hospitalist APP core competencies and help standardize education.

Several limitations to this study should be considered. While we used multiple strategies to locate as many fellowships as possible, it is unlikely that we successfully captured all existing programs, and new programs are being developed annually. We also relied on self-reported data from PDs. While we would expect PDs to provide accurate data, we could not externally validate their answers. Additionally, although our survey tool was reviewed extensively and validated internally, it was developed de novo for this study.

CONCLUSION

APP fellowships in hospital medicine have experienced marked growth since the first program was described in 2010. The majority of programs are 12 months long, operate in existing teaching centers, and are intended to further enhance the training and retention of newly graduated PAs and NPs. Despite their similarities, fellowships have striking variability in their methods of teaching and assessing their learners. Best practices have yet to be identified, and further study is required to determine how to standardize curricula across the board.

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Prevalence and Postdischarge Outcomes Associated with Frailty in Medical Inpatients: Impact of Different Frailty Definitions

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We compared prevalence estimates and prognostication if frailty were defined using the face-to-face Clinical Frailty Scale (CFS) or the administrative-data-derived Hospital Frailty Risk Score (HFRS). We evaluated 489 adults from a prospective cohort study of medical patients being discharged back to the community; 276 (56%) were deemed frail (214 [44%] on the HFRS and 161 [33%] on the CFS), but only 99 (20%) met both frailty definitions (kappa 0.24, 95% CI 0.16-0.33). Patients classified as frail on the CFS exhibited significantly higher 30-day readmission/death rates, 19% versus 10% for those not frail (aOR [adjusted odds ratio] 2.53, 95% CI 1.40-4.57) and 21% versus 6% for those aged >65 years (aOR 4.31, 95% CI 1.80-10.31). Patients with HFRS-defined frailty exhibited higher 30-day readmission/death rates that were not statistically significant (16% vs 11%, aOR 1.62 [95% CI 0.95-2.75] in all adults and 14% vs 11%, aOR 1.24 [95% CI 0.58-2.83] in those aged >65 years). *Journal of Hospital Medicine* 2019;14:407-410. Published online first March 20, 2019. © 2019 Society of Hospital Medicine

Frailty is associated with adverse outcomes in hospitalized patients, including longer length of stay, increased risk of institutionalization at discharge, and higher rates of readmissions or death postdischarge.[1-4] Multiple tools have been developed to evaluate frailty and in an earlier study,[4] we compared the three most common of these and demonstrated that the Clinical Frailty Scale (CFS)[5] was the most useful tool clinically as it was most strongly associated with adverse events in the first 30 days after discharge. However, it must be collected prospectively and requires contact with patients or proxies for the evaluator to assign the patient into one of nine categories depending on their disease state, mobility, cognition, and ability to perform instrumental and functional activities of daily living. Recently, a new score has been described which is based on an administrative data algorithm that assigns points to patients having any of 109 ICD-10 codes listed for their index hospitalization and all hospitalizations in the prior two years and can be generated retrospectively without trained observers.[6] Although higher Hospital Frailty Risk Scores (HFRS) were associated with greater risk of postdischarge adverse events, the kappa when compared with the CFS was only 0.30 (95% CI 0.22-0.38) in that study.[6] However, as the HFRS was developed and validated in patients aged ≥75 years within the UK National Health Service, the authors themselves recommended that it be evaluated in other healthcare systems, other populations, and with comparison to prospectively collected frailty data from cumulative deficit models such as the CFS.

The aim of this study was to compare frailty assessments using the CFS and the HFRS in a population of adult patients hospitalized on general medical wards in North America to determine the impact on prevalence estimates and prediction of outcomes within the first 30 days after hospital discharge (a timeframe highlighted in the Affordable Care Act and used by Centers for Medicare & Medicaid Services as an important hospital quality indicator).

METHODS

As described previously,[7] we performed a prospective cohort study of adults without cognitive impairment or life expectancy less than three months being discharged back to the community (not to long-term care facilities) from general medical wards in two teaching hospitals in Edmonton, Alberta, between October 2013 and November 2014. All patients provided signed consent, and the University of Alberta Health Research Ethics board (project ID Pro00036880) approved the study.

Trained observers assessed each patient's frailty status within 24 hours of discharge based on the patient's best status in the week *prior* to becoming ill with the reason for the index hospitalization. The research assistant classified patients into one of the following nine CFS categories: very fit, well, managing well, vulnerable, mildly frail (need help with at least one instrumental activities of daily living such as shopping, finances, meal preparation, or housework), moderately frail (need help with one or two activities of daily living such as bathing and dressing), severely frail (dependent for personal care), very severely frail (bedbound), and terminally ill. According to the CFS

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TABLE 1. **Baseline Characteristics of Cohort Patients**

	Not Frail on CFS or HFRS Models, n = 213	Frail on the CFS only, n = 62	Frail on the HFRS only, n = 115	Frail on CFS and HFRS, n = 99	*P* Value Comparing the Columns
Age, y, mean (95% CI)	57.8 (55.4, 60.2)	73.8 (70..0, 77.7)	61.4 (57.9, 64.8)	72.6 (69.7, 75.5)	<.01
Sex, female, no (%)	95 (44.6)	39 (62.9)	48 (41.7)	64 (64.7)	<.01
No. of comorbidities, mean (95% CI)	3.6 (3.3, 3.9)	6.0 (5.3, 6.6)	5.3 (4.8, 5.8)	6.4 (5.9, 7.0)	.01
Charlson comorbidity score, mean (95% CI)	2.0 (1.7, 2.2)	3.2 (2.7, 3.7)	3.3 (2.9, 3.8)	3.8 (3.4, 4.2)	.16
No. of patients hospitalized in prior 12 months, no (%)	47 (22.1)	23 (37.1)	72 (62.6)	73 (73.7)	<.01
Preadmission living situation, no (%)					<.01
Living at home independently	169 (79.3)	20 (32.3)	73 (63.5)	23 (23.2)	
Living at home with help	43 (20.2)	35 (56.5)	34 (29.6)	54 (54.6)	
Assisted living or lodge	1 (0.5)	7 (11.3)	8 (7.0)	22 (22.2)	
EQ-5D overall score, /100, mean (95% CI)	65.7 (63.4, 68.1)	60.7 (55.6, 65. 9)	65.1 (61.8, 68.4)	60.0 (54.8, 63.2)	.06
Goals of care in the hospital, no (%) Resuscitation/ICU					<.01
ICU but no resuscitation	179 (87.8)	26 (47.3)	86 (77.5)	43 (46.7)	
No ICU, no resuscitation	13 (6.4)	12 (21.8)	9 (8.1)	21 (22.8)	
Comfort care	12 (5.9)	17 (30.9)	15 (13.5)	28 (30.4)	
	0 (0)	0 (0)	1 (0.9)	0 (0)	
Timed Up and Go Test, s, mean (95% CI)	12.9 (11.2, 14.7)	23.2 (18.9, 27.5)	13.2 (12.1, 14.3)	25.4 (21.9, 28.9)	<.01
Grip Strength, KG, mean (95% CI)	31.8 (30.1, 33.5)	12.8 (19.6, 24.0)	28.5 (26.4, 30.6)	20.0 (18.3, 21.6)	<.01
Serum albumin, g/L, mean (95% CI)	35.0 (33.5, 36.5)	35.8 (33.6, 38.0)	31.5 (29.6, 33.4)	33.0 (31.5, 34.5)	<.01
No. of prescription medications at discharge, mean (95% CI)	4.6 (4.1, 5.0)	9.0 (8.1, 9.9)	6.0 (5.4, 6.6)	8.2 (7.5, 8.9)	<.01
Length of stay, d, median, [IQR]	7.2 (3.8, 10.7)	6.9 (5.4, 8.4)	7.6 (6.6, 8.6)	10.4 (8.5, 12.5)	<.01

Definitions of frailty: scoring ≥5 on the Clinical Frailty Scale (CFS), ≥5 on the Hospital Frailty Risk Score (HFRS)

validation studies, the last five categories were defined as frail for the purposes of our analyses.

Independent of the trained observer's assessments, we calculated the HFRS for each participant in our cohort by linking to Alberta administrative data holdings within the Alberta Health Services Data Integration and Measurement Reporting unit and examining all diagnostic codes for the index hospitalization and any other hospitalizations in the prior two years for the 109 ICD-10 codes listed in the original HFRS paper and used the same score cutpoints as they reported (HFRS <5 being low risk, 5-15 defined as intermediate risk, and >15 as high risk for frailty; scores ≥5 were defined as frail).[6]

All patients were followed after discharge by research personnel blinded to the patient's frailty assessment. We used patient/caregiver self-report and the provincial electronic health record to collect information on all-cause readmissions or mortality within 30 days.

We have previously reported[4,7] the association between frailty defined by the CFS and unplanned readmissions or death within 30 days of discharge but in this study, we examined the correlation between CFS-defined frailty and the HFRS score (classifying those with intermediate or high scores as frail) using chance-corrected kappa coefficients. We also compared the prognostic accuracy of both models for predicting death and/or unplanned readmissions within 30 days using the C statistic and the integrated discrimination improvement index and examined patients aged >65 years as a subgroup.[8] We used SAS version 9.4 (SAS Institute, Cary, North Carolina) for analyses, with *P* values of <.05 considered as statistically significant.

RESULTS

Of the 499 patients in our original cohort,[7] we could not link 10 to the administrative data to calculate HFRS, and thus this study sample is only 489 patients (mean age 64 years, 50% women, 52% older than 65 years, a mean of 4.9 comorbidities, and median length of stay five days).

Overall, 276 (56%) patients were deemed frail according to at least one assessment (214 [44%] on the HFRS [35% intermediate risk and 9% high risk] and 161 [33%] on the CFS), and 99 (20%) met both frailty definitions (Appendix Figure). Among the 252 patients aged >65 years, 66 (26%) met both frailty

TABLE 2. **Predictive Ability of Different Frailty Assessment Methods Adjusted for Age and Sex**

Frailty Definition Met	Adjusted Odds Ratio for 30-Day Readmission/Death	95% CI	C Statistics for Model Predicting 30-day Readmission/Death, Including Age, Sex, and Frailty Definition (95% CI)
Entire cohort			
CFS (whether they also met the HFRS definition or not)	2.53	1.40-4.57	0.64 (0.56-0.70)
CFS and HFRS	2.38	1.30-4.41	0.60 (0.52-0.68)
CFS only (but not HFRS)	1.35	0.63-2.89	0.54 (0.46-0.61)
HFRS (whether they also met the CFS definition or not)	1.62	0.95-2.75	0.58 (0.50-0.65)
HFRS only (but not CFS)	0.85	0.44- 1.60	0.55 (0.47- 0.63)
Patients aged ≥65 years			
CFS (whether they also met the HFRS definition or not)	4.31	1.80-10.31	0.68 (0.59-0.79)
CFS and HFRS	2.17	0.97-4.83	0.62 (0.51-0.72)
CFS only (but not HFRS)	2.33	0.99-5.47	0.59 (0.46-0.71)
HFRS (whether they also met the CFS definition or not)	1.24	0.58-2.63	0.55 (0.45-0.65)
HFRS only (but not CFS)	0.47	0.17- 1.42	0.58 (0.47-0.69)

Adjusted odds ratios are for patients meeting the definition of frailty described for that row compared to those not meeting that frailty definition.
Abbreviations: CFS, clinical frailty scale; HFRS, hospital frailty risk score.

definitions and 166 (66%) were frail according to at least one assessment. Agreement between HFRS and the CFS (kappa 0.24, 95% CI 0.16-0.33) was poor. The CFS definition of frailty was 46% sensitive and 77% specific in classifying frail patients compared with HFRS-defined frailty.

As we reported earlier,[4] patients deemed frail were generally similar across scales in that they were older, had more comorbidities, more prescriptions, longer lengths of stay, and poorer quality of life than nonfrail patients (all $P < .01$, Table 1). However, patients classified as frail on the HFRS only but not meeting the CFS definition were younger, had higher quality of life, and despite a similar Charlson Score and number of comorbidities were much more likely to have been living independently prior to admission than those classified as frail on the CFS.

Death or unplanned readmission within 30 days occurred in 13.3% (65 patients), with most events being readmissions (62, 12.7%). HFRS-defined frail patients exhibited higher 30-day death/readmission rates (16% vs 11% for not frail, $P = .08$; 14% vs 11% in the elderly, $P = .5$), which was not statistically significantly different from the nonfrail patients even after adjusting for age and sex (aOR [adjusted odds ratio] 1.62, 95% CI 0.95-2.75 for all adults; aOR 1.24, 95% CI 0.58-2.63 for the elderly). CFS-defined frail patients had significantly higher 30-day readmission/death rates (19% vs 10% for not frail, aOR 2.53, 95% CI 1.40-4.57 for all adults and 21% vs 6% in the elderly, aOR 4.31, 95% CI 1.80-10.31).

Adding the HFRS results to the CFS-based predictive models added little new information, with an integrated discrimination improvement of only 0.009 that was not statistically significant ($P = .09$, Table 2). In fact, the HFRS was not an independent predictor of postdischarge outcomes after adjusting for age and sex. Although predictive models incorporating the CFS demonstrated the best C statistics, none of the models had high C statistics (ranging between 0.54 and 0.64 for all adults and between 0.55 and 0.68 for those aged >65 years). Even when the frailty definitions were examined as continuous variables, the C statistics were similar as for the dichotomized analyses (0.64 for CFS and 0.58 for HFRS) and the correlation between the two remained weak (Spearman's correlation coefficient 0.34).

DISCUSSION

We have demonstrated that the prevalence of frailty in patients being discharged from medical wards was high, with the HFRS (44%) being higher than the CFS (33%), and that only 46% of patients deemed frail on the HFRS were also deemed frail on the CFS. We confirm the report by the developers of the HFRS that there was poor correlation between the CFS cumulative deficit model and the administrative-data-based HFRS model in our cohort, even among those older than 65 years.

Previous studies have reported marked heterogeneity in prevalence estimates between different frailty instruments.[2,9] For example, Aguayo et al. found that the prevalence of frailty in the English Longitudinal Study of Aging varied between 0.9% and 68% depending on which of the 35 frailty scales they tested were used, although the prevalence with comprehensive geriatric assessments (the gold standard) was 14.9% (and 15.3% on the CFS).[9] Although frail patients are at higher risk for death and/or readmission after discharge, other investigators have also reported similar findings to ours that frailty-based risk models are surprisingly modest at predicting postdischarge readmission or death, with the C statistics ranging between 0.52 and 0.57, although the CFS appears to correlate best with the gold standard of comprehensive geriatric assessment.[10-14] This is not surprising since the CFS is multidimensional and as a cumulative deficit model, it incorporates assessment of the patient's underlying diseases, cognition, function, mobility, and mood in the assignment of their CFS level. Regardless, others[15]

have pointed out the need for studies such as ours to compare the validity of published frailty scales.

Despite our prospective cohort design and blinded endpoint ascertainment, there are some potential limitations to our study. First, we excluded long-term care residents and patients with foreshortened life expectancy – the frailest of the frail – from our analysis of 30-day outcomes, thereby potentially reducing the magnitude of the association between frailty and adverse outcomes. However, we were interested only in situations where clinicians were faced with equipoise about patient prognosis. Second, we assessed only 30-day readmissions or deaths and cannot comment on the impact of frailty definitions on other postdischarge outcomes (such as discharge locale or need for home care services) or other timeframes. Finally, although the association between the HFRS definition of frailty and the 30-day mortality/readmission was not statistically significant, the 95% confidence intervals were wide and thus we cannot definitively rule out a positive association.

In conclusion, considering that it had the strongest association with postdischarge outcomes and is the fastest and easiest to perform, the most useful of the frailty assessment tools for clinicians at the bedside still appears to be the CFS (both overall and in those patients who are elderly). However, for researchers who are analyzing data retrospectively or policy planners looking at health services data where the CFS was not collected, the HFRS holds promise for risk adjustment in population-level studies comparing processes and outcomes between hospitals.

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Comparison of Parent Report with Administrative Data to Identify Pediatric Reutilization Following Hospital Discharge

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Healthcare providers rely on historical data reported by parents to make medical decisions. The Hospital to Home Outcomes (H2O) trial assessed the effects of a one-time home nurse visit following pediatric hospitalization for common conditions. The H2O primary outcome, reutilization (hospital readmission, emergency department visit, or urgent care visit), relied on administrative data to identify reutilization events after discharge. We sought to compare parent recall of reutilization events two weeks after discharge with administrative records. Agreement was relatively high for any reutilization (kappa 0.74); however, this high agreement was driven by agreement between sources when no reutilization occurred (sources agreed 98%-99%). Agreement between sources was lower when reutilization occurred (48%-76%). Some discrepancies were related to parents misclassifying the site of care. The possibility of inaccurate parent report of reutilization has clinical implications that may be mitigated by confirmation of parent-reported data through verification with additional sources, such as electronic health record review. *Journal of Hospital Medicine* 2019;14:411-414. Published online first April 8, 2019. © 2019 Society of Hospital Medicine

Prior healthcare utilization predicts future utilization;[1] thus, providers should know when a child has had a recent healthcare visit. Healthcare providers typically obtain this information from parents and caregivers, who may not always provide accurate information.[2-4]

The Hospital to Home Outcomes study (H2O) was a randomized controlled trial conducted to assess the effects of a one-time home nurse visit following discharge on unplanned healthcare reutilization.[5] We assessed reutilization through two sources: parent report via a postdischarge telephone call and administrative data. In this analysis, we sought to understand differences in reutilization rates by source by comparing parent report with administrative data.

METHODS

The H2O trial included children (<18 years) hospitalized on the hospital medicine (HM) or neuroscience (Neurology/Neurosurgery) services at Cincinnati Children's Hospital Medical Center (CCHMC) from February 2015 to April 2016; they had an English-speaking parent and were discharged to home without skilled nursing care.[6] For this analysis, we restricted the sample to children randomized to the control arm (discharge without a home visit), which reflects typical clinical care.

We used administrative data to capture 14-day reutilization (unplanned hospital readmissions, emergency department [ED] visits, or urgent care visits). CCHMC is the only pediatric admitting facility in the region and includes two pediatric EDs and five urgent care centers. We supplemented hospital data with a dataset (The Health Collaborative[7]) that included utilization at other regional facilities. Parent report was assessed via a research coordinator phone call 14-23 days after discharge. Parents were asked: "I'm going to [ask] about your child's health since [discharge date]. Has s/he been hospitalized overnight? Has s/he been taken to the Emergency Room/Emergency Department (didn't stay overnight)? Has s/he been taken to an urgent care?" We report 14-day reutilization rates by source (parent and/or administrative) and visit type.

We considered administrative data the gold standard for documentation of reutilization events for two reasons. First, all healthcare encounters generate billing and are therefore documented with verifiable coding. Second, we had access to data from our center and other regional healthcare facilities. Any parent-reported utilization to a facility not documented in either dataset was considered an unverifiable event (eg, outside our catchment region). Agreement between administrative and parent report of 14-day reutilization was summa-

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TABLE 1. **Discrepancies and Agreement Indices between Parent Report and Administrative Data Documentation of Reutilization**[a]

		Administrative		Agreement			
Type	Parent	Yes	No	Positive (%)	Negative (%)	Overall (%)	Kappa (95% CI)
Any	Yes	48	15	76.2	97.7	95.9	0.74 (0.65, 0.83)
	No	15	645				
Hospital Readmission	Yes	19	3	74.5	99.1	98.2	0.74 (0.60, 0.87)
	No	10	691				
Emergency Department Visit	Yes	24	8 (including 3 unverifiable)	75.0	98.8	97.8	0.74 (0.62, 0.86)
	No	8	683				
Urgent Care Visit	Yes	5	6 (including 4 unverifiable)	47.6	99.2	98.5	0.47 (0.20, 0.73)
	No	5	707				

[a]n = 723.

rized as positive agreement (reutilization documented in both administrative and parent report), negative agreement (no reutilization reported in either administrative or parent report), and overall agreement (combination of positive and negative agreement). We classified discrepancies as reutilization events in administrative data without parent report of reutilization or vice versa. We performed medical record review of discrepancies in our institutional data.

We summarized agreement by using the Cohen's kappa statistic by reuse type (hospital readmission, ED, and urgent care visit) and overall (any reutilization event). Strength of agreement based on the kappa statistics was classified as poor (<0.20), fair (0.21-0.40), moderate (0.41-0.60), good (0.61-0.80), and very good (0.81-1.00).[8] We used McNemar's test to evaluate marginal homogeneity.

RESULTS

Of 749 children randomized to the standard of care arm, 723 parents completed the 14-day follow-up call and were included in this analysis. The median child age was two years (interquartile range: 0.4, 6.9), the median length of stay (LOS) was two days (1, 3), and the majority were white (62%). Payer mix varied, with 44% privately insured and 54% publicly insured. Most patients (83%) were admitted to the HM service, and the most common diagnoses groups for index admission were respiratory (35%), neurologic (14%), and gastrointestinal (9%) diseases.

Administrative data showed 63 children with any reutilization event; parents reported 63 with any reutilization event; 48 children had events reported by both sources. The overall agreement was high, ranging from 95.9% to 98.5% (Table 1) depending on visit type. The positive agreement (ie, parent and administrative data indicated reutilization) ranged from 47.6% to 76.2%. Negative agreement (ie, parent and administrative data agreed no reutilization) was very high, 97.7% to 99.2%. Parents reported three ED visits and four urgent care visits that were unverifiable due to lack of access to administrative data (sites of care reported were not included in our datasets).

The kappa statistics indicated good agreement between parent report and administrative data for hospital readmission, ED visit, and composite any type of reutilization but moderate agreement for urgent care visit (Table 1).

Discrepancies were noted between parent report and administrative data (Table 2). In 15 children, a parent reported no reutilization when the administrative data included one; in 15 children, a parent reported a reutilization (including seven unverifiable events) when the administrative data revealed none. However, a few discrepancies were due to the incorrect site of care report (Table 2). Chart review of discrepancies involving CCHMC locations verified the accuracy of administrative data except in one case. In this case, a child's ED revisit appeared to be a separate encounter but actually led to a hospital readmission.

The 14-day reutilization rates by type (any, hospital readmission, ED visit, and urgent care visit) and data source (administrative data only, parent report only, and administrative or parent report) are depicted in the Appendix. Reutilization rates were similar when computed using administrative only or parent report only. However, reutilization rates increased slightly if a composite measure of any administrative data or parent report was utilized. No significant difference was found between administrative data and parent report in the marginal reuse proportions, with McNemar's test *P* values all >.05 for hospital readmission, ED visit, and urgent care visit evaluated separately.

DISCUSSION

By comparing parent report of reutilization after hospital discharge through postdischarge phone calls with administra-

TABLE 2. **Discrepancies in Recall at CCHMC**

Number of Patients	Parent Report	Administrative Data
2	Hospital Readmission	No visit
7[a]	ED Revisit	No visit
6[b]	Urgent Care Revisit	No visit
1	ED Revisit	Hospital Readmission & Separate ED Revisit
3[c]	Hospital Readmission	ED Revisit & Separate Hospital Readmission
1	ED Revisit	Urgent Care Revisit
1	Hospital Readmission	Urgent Care Revisit
1	No visit	ED Revisit & Separate Hospital Readmission
1	No visit	Urgent Care Revisit & Separate Hospital Readmission
7	No visit	Hospital Readmission
4	No visit	ED Revisit
2	No visit	Urgent Care Revisit

[a]Includes three unverifiable events.
[b]Includes four unverifiable events.
[c]Medical record review identified administrative data inconsistency (ED revisit appeared to be a separate encounter but actually resulted in hospital readmission).
Abbreviation: CCHMC, Cincinnati Children's Hospital Medical Center; ED, emergency department.

tive data, we demonstrated high overall agreement between sources (95.9%); this finding is similar to prior research investigating the relationship between an established medical home and reutilization.[9] However, this agreement is largely due to both sources reporting no reutilization. When revisits did occur, the agreement was notably lower, especially with regard to urgent care visits.

Discrepancies between sources have several possible explanations. First, parents may be confused by the framing of reutilization questions, perhaps lacking clarity around which visit we were referencing. Second, parents may experience limitations in health literacy[10,11] with a lack of familiarity with healthcare language, such as the ability to delineate location types (for example, a parent may identify an urgent care visit as an ED visit, given their close proximity at our facility). Finally, our prior work identified that the "fog" of hospitalization,[12] which is often a stressful and disruptive time for families, may linger after admission and could lead to difficulty in recalling detailed events.

Our findings have implications for effective care in a complex healthcare system where parent report may be the most practical method to obtain historical information, both within clinical care and in the context of research or quality measures, such as postdischarge utilization. Given that one of the greatest risk factors for readmission is prior utilization,[1] the knowledge that a patient experienced a reutilization after a prior discharge might prompt the inpatient provider to better prepare families for subsequent transition to home.

To apply our findings practically, it is important to realize that a parent report may be sufficient when reporting that no revisit occurred, if there is also no record of a visit in accessible administrative data (such as an electronic health record). However, further questions or investigation should be considered when parents report a visit did occur or when administrative data indicate a visit occurred that the parent does not recall. Providers and researchers alike should remember to use health literacy universal precautions with all families, employing plain language without medical jargon.[13] As linked electronic health record use becomes more prevalent, administrative data may be accessible in real-time, allowing for verification of family interview information. Administrative data beyond a single hospital system should be considered to effectively capture reutilization for research or quality efforts.

Our study has several limitations. Similar to most studies using reutilization outcomes, our data may miss a few unverifiable reuse events. By supplementing with additional regional data,[7] we likely captured most events. Second, we did not include patients with limited English proficiency, although it is unclear how this might have biased our results. Third, while relatively few families did not complete the calls, it is possible that more discrepancies would have been noted in nonresponders. Fourth, research coordinators administering the calls followed a script to determine reutilization information; in clinical practice, a practitioner might not ask questions as clearly, which could negatively impact recall or might add clarifying follow-up questions to enhance recall. Finally, the analysis occurred in the setting of a randomized controlled trial that included children with relatively noncomplex health conditions with short LOS;[6] thus, the results may not apply to other populations.

In conclusion, parent report and administrative data of reutilization following hospital discharge were usually in agreement

when no reutilization occurred; however, discrepancies were noted more often when reutilizations occurred and may have care implications.

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Leadership & Professional Development: Sponsored—Catapulting Underrepresented Talent off the Cusp and into the Game

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"When you've worked hard, and done well, and walked through that doorway of opportunity, you do not slam it shut behind you. You reach back and you give other folks the same chances that helped you succeed."

—Michelle Obama

We are at a point in time where awareness around the existing disparities in gender equity in academic medicine couldn't be higher. It is time for us to take this knowledge and move swiftly into action. What's one of the best ways to do this? Become a sponsor or be sponsored. "Sponsorship can effectively catapult nascent talent from unknown to rising-star status."[1]

Catapult—an excellent and fitting word to describe the effect sponsorship can have on careers. Women start out behind and often remain behind men, even with mentoring.[2] With the catapult of sponsorship, however, high-level career advancement is attainable. Studies show that sponsorship is significantly associated with success: 72.5% of men and 59.0% of women who reported sponsorship were successful, compared with 57.7% and 44.8% who did not report sponsorship.[3] For women and underrepresented minorities, sponsorship is especially important and can "dramatically overcome many of the tripwires to achievement."[4]

Sponsorship is a two-way proposition—and both the sponsor and protégé have responsibility to make the relationship successful. Want to be sponsored? Here's what to do: (1) Broadcast your achievements. You don't have to be a braggart, but you don't need to be humble—celebrate and share your achievements within and outside your network. (2) Seek out leaders of different backgrounds—sponsors don't need to be just like you. Varied viewpoints bring broader perspectives to the challenges ahead as you climb the leadership ladder. (3) Clearly spell out your leadership goals for yourself and a potential sponsor. Then work to achieve your shared goals in a timely way.

Consider how you can be a sponsor, particularly for junior faculty and those from under-represented groups. Ask yourself: Who have you sponsored this week? Whose success have you celebrated this quarter? Who will you nominate for an award or recognition this year?

Sponsorship is an essential component of good leadership. Individual leaders and academic health centers (AHCs) must take a step forward toward equity by making sponsorship an expectation and strategic priority. Set the expectation that senior leaders will act as sponsors, set clear goals to work toward (ie, more female chairs, increasing recruitment and retention of underrepresented minorities, etc.), and track metrics.[2] While "pay it forward" may seem cliché, sponsorship can truly be a remarkable opportunity for growth for both the sponsor and the protégé, and a winning proposition for the institution.

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Methods for Research Evidence Synthesis: The Scoping Review Approach

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Research evidence synthesis involves the aggregation of available information using well-defined and transparent methods to search, summarize, and interpret a body of literature, frequently following a systematic review approach. A scoping review is a relatively new approach to evidence synthesis and differs from systematic reviews in its purpose and aims.[1] The purpose of a scoping review is to provide an overview of the available research evidence without producing a summary answer to a discrete research question.[2] Scoping reviews can be useful for answering broad questions, such as "What information has been presented on this topic in the literature?" and for gathering and assessing information prior to conducting a systematic review.[1]

In this issue of the *Journal of Hospital Medicine*, Fan et al. used a scoping review to identify information available in the literature on contributors to loss and theft of controlled drugs in hospitals and the safeguards that have been suggested to address these diversions.[3] The authors followed Arksey and O'Malley's framework for scoping reviews and the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) checklist in reporting findings.[2,4]

PURPOSE OF A SCOPING REVIEW

Scoping reviews describe existing literature and other sources of information and commonly include findings from a range of different study designs and methods.[5] The broad scope of the collected information makes using formal meta-analytic methods difficult, if not impossible. Results of a scoping review often focus on the range of content identified, and quantitative assessment is often limited to a tally of the number of sources reporting a particular issue or recommendation. In contrast, systematic reviews commonly select the information sources by requiring specific study types, such as randomized controlled trials, and imposing quality standards, such as adequate allocation concealment, and place their emphasis on synthesizing data to address a specific research question. (Table) By focusing on specific studies, the synthesis component in a systematic review often takes the form of a meta-analysis in which the results of multiple scientific studies are combined to develop a summary conclusion, such as a common effect estimate, along with an evaluation of its heterogeneity across studies.

A scoping review can be a particularly useful approach when the information on a topic has not been comprehensively reviewed or is complex and diverse.[6] Munn et al. proposed several objectives that can be achieved utilizing the scoping review framework, including identifying types of existing evidence in a given field, clarifying key concepts or definitions in the literature, surveying how research is conducted on a certain topic, identifying key characteristics related to a certain topic, and identifying knowledge gaps.[1] When choosing to use a scoping review approach, it is important that the objective of the review align with the review's indication or purpose.

METHODOLOGICAL FRAMEWORK OF SCOPING REVIEWS

Scoping reviews, like systematic reviews, require comprehensive and structured searches of the literature to maximize the capture of relevant information, provide reproducible results, and decrease potential bias from flawed implementations. The methodological framework for scoping reviews was developed by Arksey and O'Malley[1] and further refined by Levac et al.[7] and the Joanna Briggs Institute.[6,8] Arksey and O'Malley's framework for scoping reviews consists of the following six steps:

- Step 1: Identify the research question—the research question should be clearly defined and usually broad in scope to provide extensive coverage.
- Step 2: Identify relevant studies—the search strategy should be thorough and broad in scope and typically include electronic databases, reference lists, hand searches, and gray literature (ie, substantive or scholarly information that has not been formally published and often is not peer-reviewed), including conference abstracts, presentations, regulatory data, working papers, and patents.
- Step 3: Study selection—the study selection process can include post hoc, or modified, inclusion and exclusion criteria as new ideas emerge during the process of gathering and reviewing information.
- Step 4: Chart the data—the data extraction process in a scoping review is called data charting and involves the use of a data charting form to extract the relevant information from the reviewed literature.
- Step 5: Collate, summarize, and report the results—the description of the scope of the literature is commonly presented in tables and charts according to key themes.
- Optional Step 6: Consultation exercise—in this optional

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TABLE. **Characteristics of Systematic and Scoping Reviews**

	Systematic Review	Scoping Review
Purpose	Provide empirical evidence that meets prespecified criteria	Provide a narrative or descriptive account of available information
Research question	Specific, focused on a single issue	Broadly defined
Study protocol	A priori	A priori and post hoc
Search strategy	Explicit and transparent	Explicit and transparent
Study selection	Restricted to certain study types, meeting quality standards	All study types, nonstandard sources of information
Inclusion/exclusion criteria	Developed at the protocol stage before the review is conducted	Informed by the review process, applied at the study selection stage
Data extraction	Well-defined process for extracting information relevant to evidence synthesis	Data charting according to key general themes
Bias assessment	Mandatory critical appraisal	Optional (but desirable)
Results	Formal synthesis of findings	Overview of the literature and general themes emerging from the review

step, stakeholders outside the study review team are invited to provide their insights to inform and validate findings from the scoping review.

Since the number of studies included in a scoping review can be substantial, several study team members may participate in the review process. When multiple reviewers are employed, the team ought to conduct a calibration exercise at each step of the review process to ensure adequate interrater agreement. In addition, the PRISMA-ScR guidelines should be followed when reporting findings from scoping reviews to facilitate complete, transparent, and consistent reporting in the literature.[4]

LIMITATIONS OF THE SCOPING REVIEW APPROACH

The scoping review approach has several limitations. Scoping reviews do not formally evaluate the quality of evidence and often gather information from a wide range of study designs and methods. By design, the number of studies included in the review process can be sizable. Thus, a large study team is typically needed to screen the large number of studies and other sources for potential inclusion in the scoping review. Because scoping reviews provide a descriptive account of available information, this often leads to broad, less defined searches that require multiple structured strategies focused on alternative sets of themes. Hand searching the literature is therefore necessary to ensure the validity of this process. Scoping reviews do not provide a synthesized result or answer to a specific question, but rather provide an overview of the available literature. Even though statements regarding the quality of evidence and formal synthesis are avoided, the scoping review approach is not necessarily easier or faster than the systematic review approach. Scoping reviews require a substantial amount of time to complete due to the wide coverage of the search implicit in the approach.

Like other studies, scoping reviews are at risk for bias from different sources. Critical appraisal of the risk of bias in scoping reviews is not considered mandatory, but some scoping reviews may include a bias assessment. Even if bias is not formally assessed, that does not mean that bias does not exist. For example, selection bias may occur if the scoping review does not identify all available data on a topic and the resulting descriptive account of available information is flawed.

WHY DID THE AUTHORS USE THE SCOPING REVIEW METHOD?

Fan et al. used the scoping review approach to examine the available information on contributors to and safeguards against controlled-drug losses and theft (drug diversion) in the hospital setting.[3] The authors addressed the following questions: (1) "What clinical units, health professions, or stages of the medication-use process are commonly discussed?" (2) "What are the identified contributors to diversion in hospitals?" and (3) "What safeguards to prevent or detect diversion in hospitals have been described?" Part of the rationale for using a scoping review approach was to permit the inclusion of a wide range of sources falling outside the typical peer-reviewed article. The authors comment that the stigmatized topic of drug diversion frequently falls outside the peer-reviewed literature and emphasize the importance of including such sources as conferences, news articles, and legal reports. The search strategy included electronic research databases, such as Web of Science, as well as an extensive gray literature search. Multiple reviewers were included in the process and a calibration exercise was conducted to ensure consistency in the selection of articles and to improve interrater agreement. The scoping review identified contributors to controlled-drug diversion and suggested safeguards to address them in the hospital setting.

OTHER CONSIDERATIONS

Methodological approaches to evidence synthesis vary, and new methods continue to emerge to meet different research objectives, including evidence mapping,[9] concept analysis,[10] rapid reviews,[11] and others.[12] Choosing the right approach may not be straightforward. Researchers may need to seek guidance from methodologists, including epidemiologists, statisticians, and information specialists, when choosing an appro-

priate review approach to ensure that the review methods are suitable for the objectives of the review.

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Diversion of Controlled Drugs in Hospitals: A Scoping Review of Contributors and Safeguards

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Drug losses and theft from the healthcare system are accelerating; hospitals are pressured to implement safeguards to prevent drug diversion. Thus far, no reviews summarize all known risks and potential safeguards for hospital diversion. Past incidents of hospital drug diversion have impacted patient and staff safety, increased hospital costs, and resulted in infectious disease outbreaks. We searched MEDLINE, Embase, PsycINFO, CINAHL, Scopus, and Web of Science databases and the gray literature for articles published between January 2005 and June 2018. Articles were included if they focused on hospital settings and discussed either: (1) drug security or accounting practices (any drug) or (2) medication errors, healthcare worker substance use disorder, or incident reports (only with reference to controlled drugs). We included 312 articles and extracted four categories of data: (1) article characteristics (eg, author location), (2) article focus (eg, clinical areas discussed), (3) contributors to diversion (eg, factors enabling drug theft), and (4) diversion safeguards. Literature reveals a large number of contributors to drug diversion in all stages of the medication-use process. All health professions and clinical units are at risk. This review provides insights into known methods of diversion and the safeguards hospitals must consider to prevent them. Careful configuration of healthcare technologies and processes in the hospital environment can reduce the opportunity for diversion. These system-based strategies broaden the response to diversion beyond that of individual accountability. Further evidence is urgently needed to address the vulnerabilities outlined in this review and prevent harm. *Journal of Hospital Medicine* 2019;14:419-428. Published online first June 12, 2019. © 2019 Society of Hospital Medicine

The United States (US) and Canada are the two highest per-capita consumers of opioids in the world;[1] both are struggling with unprecedented opioid-related mortality.[2,3] The nonmedical use of opioids is facilitated by diversion and defined as the transfer of drugs from lawful to unlawful channels of use[4,5] (eg, sharing legitimate prescriptions with family and friends[6]). Opioids and other controlled drugs are also diverted from healthcare facilities;[4,5,7,8] Canadian data suggest these incidents may be increasing (controlled-drug loss reports have doubled each year since 2015[9]).

The diversion of controlled drugs from hospitals affects patients, healthcare workers (HCWs), hospitals, and the public. Patients suffer insufficient analgesia or anesthesia, experience substandard care from impaired HCWs, and are at risk of infections from compromised syringes.[4,10,11] HCWs that divert are at risk of overdose and death; they also face regulatory censure, criminal prosecution, and civil malpractice suits.[12,13] Hospitals bear the cost of diverted drugs,[14,15] internal investigations,[4] and follow-up care for affected patients,[4,13] and can be fined in excess of $4 million dollars for inadequate safeguards.[16] Negative publicity highlights hospitals failing to self-regulate and report when diversion occurs, compromising public trust.[17-19] Finally, diverted drugs impact population health by contributing to drug misuse.

Hospitals face a critical problem: how does a hospital prevent the diversion of controlled drugs? Hospitals have not yet implemented safeguards needed to detect or understand how diversion occurs. For example, 79% of Canadian hospital controlled-drug loss reports are "unexplained losses,"[9] demonstrating a lack of traceability needed to understand the root causes of the loss. A single US endoscopy clinic showed that $10,000 of propofol was unaccounted for over a four-week period.[14] Although transactional discrepancies do not equate to diversion, they are a potential signal of diversion and highlight areas for improvement.[15] The hospital medication-use process (MUP; eg, procurement, storage, preparation, prescription, dispensing, administration, waste, return, and removal) has multiple vulnerabilities that have been exploited. Published accounts of diversion include falsification of clinical documents, substitution of saline for medication, and theft.[4,20-23] Hospitals require guidance to assess their drug processes against known vulnerabilities and identify safeguards that may improve their capacity to prevent or detect diversion.

In this work, we provide a scoping review on the emerging topic of drug diversion to support hospitals. Scoping reviews can be a "preliminary attempt to provide an overview of exist-

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ing literature that identifies areas where more research might be required."[24] Past literature has identified sources of drugs for nonmedical use,[6,25,26] provided partial data on the quantities of stolen drug,[7,8] and estimated the rate of HCW diversion.[5,27-29] However, no reviews have focused on system gaps specific to hospital MUPs and diversion. Our review remedies this knowledge gap by consolidating known weaknesses and safeguards from peer- and nonpeer-reviewed articles. Drug diversion has been discussed at conferences and in news articles, case studies, and legal reports; excluding such discussion ignores substantive work that informs diversion practices in hospitals. Early indications suggest that hospitals have not yet implemented safeguards to properly identify when diversion has occurred, and consequently, lack the evidence to contribute to peer-reviewed literature. This article summarizes (1) clinical units, health professions, and stages of the MUP discussed, (2) contributors to diversion in hospitals, and (3) safeguards to prevent or detect diversion in hospitals.

METHODS

Scoping Review

We followed Arksey and O'Malley's six-step framework for scoping reviews,[30] with the exception of the optional consultation phase (step 6). We addressed three questions (step 1): what clinical units, health professions, or stages of the medication-use process are commonly discussed; what are the identified contributors to diversion in hospitals; and what safeguards have been described for prevention or detection of diversion in hospitals? We then identified relevant studies (step 2) by searching records published from January 2005 to June 2018 in MEDLINE, Embase, PsycINFO, CINAHL, Scopus, and Web of Science; the gray literature was also searched (see supplementary material for search terms).

All study designs were considered, including quantitative and qualitative methods, such as experiments, chart reviews and audit reports, surveys, focus groups, outbreak investigations, and literature reviews. Records were included (step 3) if abstracts met the Boolean logic criteria outlined in Appendix 1. If no abstract was available, then the full-text article was assessed. Prior to abstract screening, four reviewers (including R.R.) independently screened batches of 50 abstracts at a time to iteratively assess interrater reliability (IRR). Disagreements were resolved by consensus and the eligibility criteria were refined until IRR was achieved (Fleiss kappa > 0.65). Once IRR was achieved, the reviewers applied the criteria independently. For each eligible abstract, the full text was retrieved and assigned to a reviewer for independent assessment of eligibility. The abstract was reviewed if the full-text article was not available. Only articles published in English were included.

Reviewers charted findings from the full-text records (steps 4 and 5) by using themes defined a priori, specifically literature characteristics (eg, authors, year of publication), characteristics related to study method (eg, article type), variables related to our research questions (eg, variations by clinical unit, health profession), contributors to diversion, and safeguards to detect or prevent diversion. Inductive additions or modifications to the themes were proposed during the full-text review (eg, reviewers added a theme "name of drugs diverted" to identify drugs frequently reported as diverted) and accepted by consensus among the reviewers.

RESULTS

Scoping Review

The literature search generated 4,733 records of which 307 were duplicates and 4,009 were excluded on the basis of the eligibility criteria. The reviewers achieved 100% interrater agreement on the fourth round of abstract screening. Upon full-text review, 312 articles were included for data abstraction (Figure).

Literature Characteristics

Table 1 summarizes the characteristics of the included literature. The articles were published in a mix of peer-reviewed (137, 44%) and nonpeer-reviewed (175, 56%) sources. Some peer-reviewed articles did not use research methods, and some nonpeer-reviewed articles used research methods (eg, doctoral theses). Therefore, Table 1 categorizes the articles by research method (if applicable) and by peer-review status. The articles primarily originated in the United States (211, 68%) followed by Canada (79, 25%) and other countries (22, 7%). Most articles were commentaries, editorials, reports or news media, rather than formal studies presenting original data.

Literature Focus by Clinical Unit, Health Profession, and Stage of Medication-Use Process

Most articles did not focus the discussion on any one clinical unit, health profession, or stage of the MUP. Of the articles that made explicit mention of clinical units, hospital pharmacies and operating rooms were discussed most often, nurses were the most frequently highlighted health profession, and most stages of the MUP were discussed equally, with the exception of prescribing which was mentioned the least (Supplementary Table).

Contributors to Diversion

The literature describes a variety of contributors to drug diversion. Table 2 organizes these contributors by stage of the MUP and provides references for further discussion.

The diverse and system-wide contributors to diversion described in Table 2 support inappropriate access to controlled drugs and can delay the detection of diversion after it occurred. These contributors are more likely to occur in organizations that fail to adhere to drug-handling practices or to carefully review practices.[34,44]

Diversion Safeguards in Hospitals

Table 3 summarizes published recommendations to mitigate the risk of diversion by stage of the MUP.

DISCUSSION

This review synthesizes a broad sample of peer- and nonpeer-reviewed literature to produce a consolidated list of

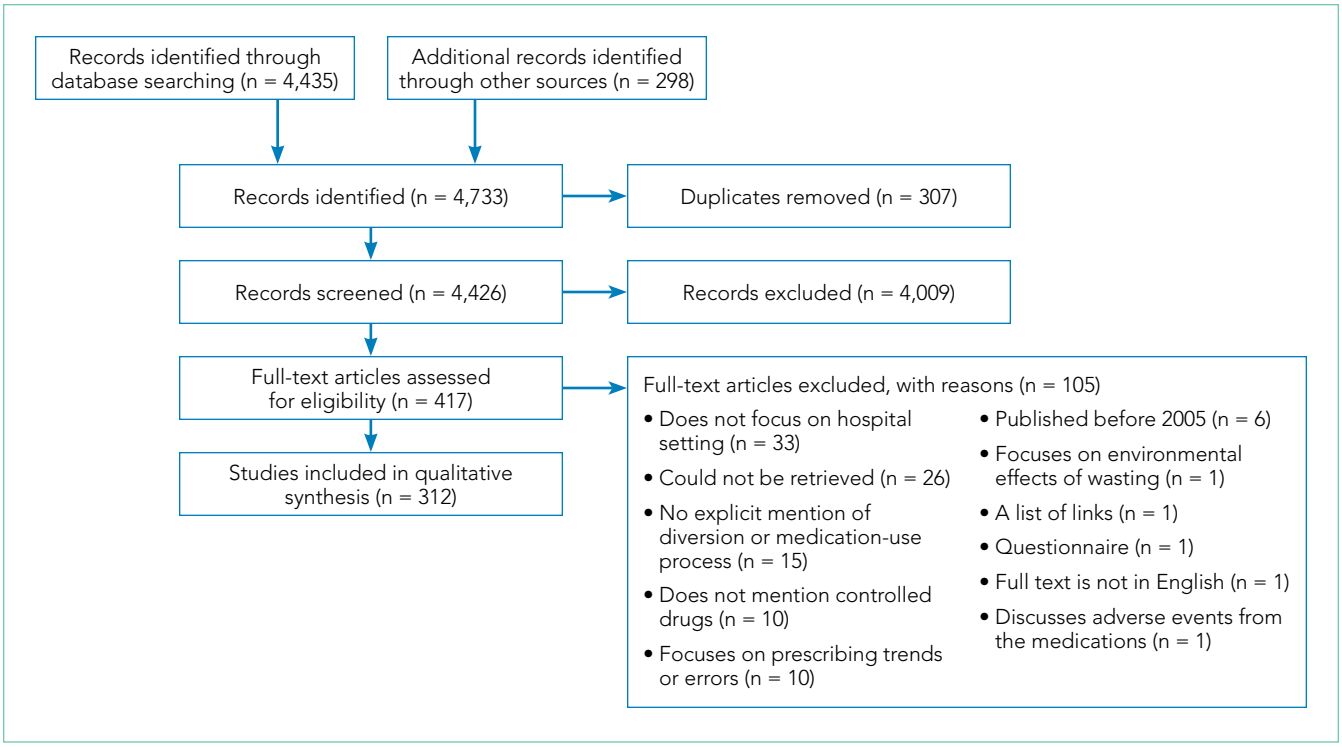

FIG. Flow Diagram of Inclusion and Exclusion of Identified Articles.

known contributors (Table 2) and safeguards against (Table 3) controlled-drug diversion in hospitals. The literature describes an extensive list of ways drugs have been diverted in all stages of the MUP and can be exploited by all health professions in any clinical unit. Hospitals should be aware that nonclinical HCWs may also be at risk (eg, shipping and receiving personnel may handle drug shipments or returns, housekeeping may encounter partially filled vials in patient rooms). Patients and their families may also use some of the methods described in Table 2 (eg, acquiring fentanyl patches from unsecured waste receptacles and tampering with unsecured intravenous infusions).

Given the established presence of drug diversion in the literature,[5,7-9,96,97] hospitals should assess their clinical practices against these findings, review the associated references, and refer to existing guidance to better understand the intricacies of the topic.[7,31,51,53,60,79] To accommodate variability in practice between hospitals, we suggest considering two underlying issues that recur in Tables 2 and 3 that will allow hospitals to systematically analyze their unique practices for each stage of the MUP.

The first issue is falsification of clinical or inventory documentation. Falsified documents give the opportunity and appearance of legitimate drug transactions, obscure drug diversion, or create opportunities to collect additional drugs. Clinical documentation can be falsified actively (eg, deliberately falsifying verbal orders, falsifying drug amounts administered or wasted, and artificially increasing patients' pain scores) or passively (eg, profiled automated dispensing cabinets [ADC] allow drug withdrawals for a patient that has been discharged or transferred over 72 hours ago because the system has not yet been updated). Falsification of inventory documentation can involve deliberate miscounting of drug inventory, removing records of drug procurement and intercepting the shipment when it arrives, and forging signatures on drug deliveries from the pharmacy to the care unit. Prevention safeguards include constraining clinical choices, decreasing delays to documentation updates, increasing traceability, and improving verification of transactions. For example, standardizing ordering protocols constrains clinical choices so that minimal controlled drug is dispensed, leading to reduced risk of dispensing more than the patient needs (eg, order sets that avoid dose ranges or limit as needed [PRN] doses). An example of decreasing delays to documentation updates are ADC profiles that rapidly remove discharged patients, so that it is not possible to dispense drugs for a transferred patient. Examples of increasing traceability include biometric (eg, fingerprint) signatures or using cameras in select areas which deter forgery and support auditing. Verification of the transactions listed in the documentation has typically relied upon a real-time witness, but may not always be possible. For example, it is infeasible to require a witness to verify all drug administration to patients. Therefore, future work may be needed to develop other strategies to verify physical transactions (eg, weight sensors and computer vision). Detection safeguards for documentation rely on auditing, therefore electronic systems can be an important asset to employ. For example, electronic systems support monitoring of unusual trends (eg, prescribing activity by care unit or HCW; number of unverified verbal orders; dispensing activity by ADC, care unit, drug, or HCW; variations in patient pain scores between HCWs; drug

TABLE 1. **Summary of Literature Characteristics[1] (n = 312 Articles Included in the Analysis)**

Article type		**n (%)**	
Location of article		**312 (100)**	
United States		211 (68)	
Canada		79 (25)	
Other[2]		22 (7)	
Article Type[3]	**Total n (%)**	**Nonpeer Reviewed n (%)**	**Peer Reviewed n (%)**
Commentary, editorial or report	94 (29)	33 (35)	61 (65)
News media, magazine article or press release	44 (14)	44 (100)	–
Legislative or regulatory document	27 (8)	27 (100)	–
Case study or case report	25 (8)	3 (12)	22 (88)
Chart review or medication records review (eg, audit of medication records)	21 (7)	4 (19)	17 (81)
Survey or database review (eg, law enforcement data)	16 (5)	3 (19)	13 (81)
Literature analysis (eg, systematic review or study with less rigorous method)	13 (4)	5 (38)	8 (62)
Guidance from professional organizations	9 (3)	6 (67)	3 (33)
Case law (hearings or decisions)	7 (2)	7 (100)	–
Outbreak investigation	4 (1)	–	4 (100)
Focus group and/or interview study	4 (1)	–	4 (100)
Drug assay	4 (1)	1 (25)	3 (75)
Direct observation or in-person clinical audit	4 (1)	1 (25)	3 (75)
Experimental study	3 (1)	–	3 (100)
Cohort study or analysis	2 (1)	–	2 (100)
Randomized controlled trial	1 (0)	–	1 (100)
Other (eg, newsletter, patent, article supplement)	45 (14)	45 (100)	–

[1]All categories are listed by descending frequency (highest to lowest count), with the exception of the "Other" category.
[2]Including Australia, Brazil, Finland, France, Japan, Korea, Malaysia, Nepal, New Zealand, South Africa, Spain, Thailand, United Kingdom
[3]Some articles were assigned to more than one category, therefore the total count of articles will exceed 312.

wastage amounts). If data from multiple systems can be integrated (eg, electronic health records and ADCs), then hospitals can more easily identify discrepancies among the drug amount ordered, dispensed, administered, and wasted or disposed for each patient. Hospitals can also compare purchased inventory against financial records to identify discrepancies. Clinical outcomes can also highlight potential drug discrepancies (eg, uncontrolled pain could be a signal for partial or absent administration of drugs).

The second issue involves failure to maintain the physical security of controlled drugs, thereby allowing unauthorized access. This issue includes failing to physically secure drug stock (eg, propping doors open to controlled-drug areas; failing to log out of ADCs, thereby facilitating unauthorized access; and leaving prepared drugs unsupervised in patient care areas) or failing to maintain accurate access credentials (eg, staff no longer working on the care unit still have access to the ADC or other secure areas). Prevention safeguards require adherence to existing security protocols (eg, locked doors and staff access frequently updated) and limiting the amount of controlled drugs that can be accessed (eg, supply on care unit should be minimized to what is needed and purchase smallest unit doses to minimize excess drug available to HCWs). Hospitals may need to consider if security measures are actually feasible for HCWs. For example, syringes of prepared drugs should not be left unsupervised to prevent risk of substitution or tampering; however, if the responsible HCW is also expected to collect supplies from outside the care area, they cannot be expected to maintain constant supervision. Detection safeguards include the use of tamper-evident packaging to support detection of compromised controlled drugs or assaying drug waste or other suspicious drug containers to detect dilution or tampering.

TABLE 2. **Contributors to Diversion at Each Stage of the Medication-Use Process with Associated List of References**

Stage of Medication-Use Process	Contributors to Diversion	Description, Examples, and Associated References
Procurement	Excess ordering	Excess drug can be ordered and diverted by removing the purchase order and packing slip, thereby obscuring evidence of any diversion at all.[20,31]
Storage[a]	Unsupervised access to drug storage areas	High levels of personnel traffic can lead to poor practices (eg, doors may be propped open[32,33]), which may obscure who has accessed drug storage areas.[20,34] When unsupervised, drugs can be vulnerable to tampering, while the product container appears intact (eg, removing a few pills from a 1000-count bottle, drinking cough syrup directly from the bottle[23,35]). Individuals may also substitute saline for diverted drug to obscure tampering.[11,22,31,36] Intentional miscounts of received drug while restocking can also obscure diversion.[37,38]
Prescribing	Unverified verbal orders	Verbal orders can be falsified to grant inappropriate access to controlled drug.[12,31]
	Flexible ordering	Although there are legitimate reasons for allowing flexible dose orders (eg, as-needed doses, a dosing range), they allow access to more drug than may be needed and can facilitate diversion[39,40] (eg, maximum doses recorded as administered, but excess actually diverted).
	Forgery	If prescription pads are not kept physically secured and strictly supervised, written orders can be altered, forged or reused.[23,31,36]
Preparation	Compounding and repackaging	Procuring drugs that require compounding or repackaging (eg, not purchasing unit doses) provides opportunities for diversion (eg, diversion from overfill,[15,31] "extra" withdrawals from multidose containers, tampering/substitution of drug in solutions).[31,41]
Dispensing	Typical doses smaller than stocked drugs	When drug doses are purchased in formats that exceed the typical doses used on the clinical unit, and are not compounded or repackaged to unit doses, HCWs at the bedside gain reliable access to excess drug when prescribed.[42]
	Poor verification of dispensing to clinical units	When drugs are transferred from pharmacy to a clinical unit, the delivery person can forge the co-signature of an individual "verifying" receipt.[35] Unsupervised inventory checks when replenishing unit inventory can open the door to intentional miscounts.[37,43]
	Reduced pharmacy oversight of dispensing with introduction of technology	Implementation of ADCs[44] and computerized physician order entry can reduce awareness of drug use (eg, hydromorphone previously available only from pharmacy may become available in the emergency department's ADC[45]).
Dispensing and administration	Loopholes in the intended use of ADCs	HCWs may cancel or perform null transactions, such that the ADC does not record a change in inventory, despite a quantity of drug having been taken,[38,46-48] or they may withdraw both injectable and oral drugs at the same time (eg, a duplicate dose) to obscure diversion of an extra dose.[34] HCWs may withdraw drugs for patients who have been discharged or transferred, or for surgical cases that have been cancelled.[31,47,49,50]
Administration	Prepared drugs are unsupervised and unsecured	Prepared drugs left unsecured in clinical areas[51] are prone to diversion (eg, unlabeled prepared syringes may be replaced with syringes of saline). Drugs can also be withdrawn from active IV infusions (eg, patient-controlled analgesia (PCA) pumps).[33,48]
	Unsupervised access to drug stock in patient care areas	HCWs may not lock drug inventory (eg, an anesthesiologist may leave the room without locking the drug cart,[52] nurses may forget to log out of the ADC[46]).
	ADC may not be optimally configured, updated, or monitored	ADCs may allow users to perform a "critical override" when the pharmacy is closed,[46,53] granting access to drugs normally requiring pharmacy review; if this access is not regularly reviewed the override feature can be abused. Access privileges to the ADC may not be revoked, providing access to some HCWs longer than appropriate.[49] ADCs may not automatically log out within a short enough timeframe, falsely tying subsequent withdrawals to the original user.[46] ADCs, if not rapidly updated, can dispense drugs for patients that have already been discharged or transferred.[46,47]
	Flexibility in administration	HCWs may be given a high degree of autonomy[10] and flexibility, which can create opportunities for diversion (eg, flexible ordering [see 'Prescribing']) can increase latitude for unnecessary dispensing,[39] delays between dispensing and wasting facilitates diversion of partial doses,[44] sloppy recordkeeping can obscure traceability[49,50,54]). Intravenous infusions can be prematurely replaced, or fentanyl patches reused, to make additional drug available for diversion.[47]
	Falsification of patient documentation	HCWs may document complete administration of a drug when some or all of the dose was diverted,[4,22,31,37,39,41,50] and/or may falsely report pain scores to support apparently higher dose administration.[48,55,56]
Wastage, returns and disposal	Visual confirmation of wasting cannot detect drug content	Individuals diverting drugs may replace the contents of a syringe with saline before requesting a witness.[12,57]
	Falsification of drug expiry	Prematurely expiring valid drugs allows them to be transferred to a separate area;[20] these drugs may then be less frequently audited thereafter, and at higher risk of diversion.
	Presence of partially administered drugs on clinical units	Drugs yet to be fully administered (eg, unfinished infusions[10]) may be left unmonitored in clinical areas and diverted.[19,32,51] Overfill in an injectable vial can be diverted.[58]
	Unsecured waste receptacles	Drugs may be removed from sharps receptacles.[4,21,34,47,54,59,60] Expired drugs may be diverted from holding areas.[23,31,35]
	Complacency in the enforcement of wasting procedures	Optimal practices may not be regularly reinforced (eg, drugs accidentally taken home in HCWs' pockets,[46] lack of adherence to proper drug wasting procedure[12]).
	Falsification of witnessing	HCWs may verify wastage without actually witnessing it.[4,42,50] A colleague's credentials can be used to document that wastage was witnessed, without their presence.[22,31]

[a]For convenience, storage is placed after the procurement stage of the medication-use process because the largest storehouse of controlled drug likely exists in the hospital pharmacy. However, storage occurs elsewhere (eg, in patient areas, delivery trucks) and readers should be cognizant that storage risks occur at multiple stages of the medication-use process, rather than as a discrete step as it may appear in the table.

Abbreviations: ADC, automated dispensing cabinet; HCW, healthcare worker; PCA, patient-controlled analgesia.

TABLE 3. **Diversion Safeguards at Each Stage of the Medication-Use Process with Associated List of References**[a]

Stage of Medication-Use Process	Safeguard	Description, Examples, and Associated References
Procurement	Separate purchasing and receiving roles	Regularly rotate healthcare workers (HCWs) associated with inventory control roles (eg, purchase, discrepancy resolution, auditing).[35] Provide the minimum information necessary for a purchaser to generate orders to replenish controlled drugs.[35]
	Periodically audit and reconcile vault inventory against purchasing and receiving records	Periodically audit inventory, particularly controlled drugs stored in the pharmacy vault.[31,35] Reconcile financial statements and wholesale purchase history with inventory; this may identify cases where the purchase orders and packing slips (as a pair) have been removed.[31,40,61] Maintain a separate log of all purchase orders so they can be reconciled against the vault records.[35] Establish a process to identify unusual peaks in quantity or frequency of controlled-drug purchases.[31]
Storage[b]	Improve detection of drug tampering	Purchase drugs with tamper-evident packaging (eg, seals that break upon opening).[11,40,62] Regularly inspect inventory for tampering,[31,34] particularly after discrepancies have been identified.[31,33]
	Enable processes in the pharmacy that enforce documentation and traceability of controlled-drug inventory and all who have accessed it	Establish clear audit trails for all controlled-drug access (ie, who accessed substances and when, what changes were made).[63] Cameras recording critical areas (eg, controlled-drug vault) will help identify who has accessed inventory.[11,21,35,40,61] Blind counts should be used in the pharmacy when accessing controlled drugs; and users should identify how much is to be removed before gaining access.[40] Establish dedicated human resources to audit access reports and known risk points (eg, repackaged products).[35] Ensure that expiry dates are accurate in inventory documentation, and eliminate other sources of discrepancies (eg, labeling on products differing from product records in electronic system).[64] Audit multi-dose or bulk transactions to account for each milligram of drug.[35]
	Maximize security of drugs within the pharmacy	Limit access to inventory areas to appropriate HCWs (and only on days when they are scheduled to work), and minimize unnecessary traffic (eg, personal belongings never kept in drug storage areas).[10,61] Secure multidose vials when not in use (eg, in a locked refrigerator).[35] Ensure that key/code access is tightly controlled, and establish a process to update keys/codes regularly.[38,40,52]
Prescribing	Establish processes to identify unusual or inappropriate prescribing	Do not allow prescribers to prescribe drug for themselves or for friends/family.[40,] Identify unusual prescribing trends or patterns (eg, variance compared to peers).[31] Audit compliance with verbal order policy;[65] large numbers of rejected verbal orders may be cause for suspicion.[33,47]
	Reduce range orders	Where feasible, restrict the use of dosing ranges;[40] this prevents HCWs seeking to divert from preferentially documenting larger doses to facilitate their diversion. Frequent assessments of the patient's sedation may reduce the amount of drug administered[66] and therefore the amount available for diversion.
	Avoid forged prescriptions	Ensure that prescription pads/papers are kept secure and are tamper-resistant; ensure that electronic order entry/e-prescribing systems are secure.[21,31,32,35,36,40]
Preparation	Avoid compounding and repackaging	Purchase unit-dose drugs where possible, to minimize requirements for repackaging of drugs in pharmacy and thus minimize opportunities for diversion.[40]
Dispensing	Log drug movement into and out of the pharmacy	Log drugs entering or leaving the pharmacy to support auditing, with identification and resolution of discrepancies daily, ideally by a HCW who is not routinely involved in handling controlled drugs.[35] Include in the log: dispensation by hand, dispensation to unit automated dispensing cabinets (ADCs), and other deliveries.[40,67] Deliveries to non-ADC areas should be co-signed by the delivery person and the receiver, and the drugs should be immediately secured on the unit.[40]
	Reduce unnecessary supply and access to controlled drugs on clinical units	Limit quantities of drugs stocked in the unit, and restock frequently; use unit doses where possible, to reduce drug waste susceptible to diversion.[68] Avoid placing controlled drugs in matrix-type drawers that accommodate multiple products (wherever possible, access should be limited to only the desired drugs).[68] When the pharmacy is closed, limit the supply of controlled drugs for urgent orders. For surgical teams, consider limiting the supply of narcotics (per procedure or daily), to maximize individual accountability and simplify the audit trail; reconciliation of the administration record with the dispensing record and wastage should occur immediately to identify and resolve discrepancies.[69] Controlled-drug inventory levels are routinely reviewed, and orders are based on usage to minimize excess stock.[31]

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Hospitals may also consider monitoring whether staff access controlled-drug areas when they are not scheduled to work to detect security breaches.

Safeguards for both issues benefit from an organizational culture reinforced through training at orientation and annually thereafter. Staff should be aware of reporting mechanisms (eg, anonymous hotlines), employee and professional assistance programs, self-reporting protocols, and treatment and rehabilitation options.[10,12,29,47,72,91] Other system-wide safeguards described in Table 3 should also be considered. Detection of transactional discrepancies does not automatically indicate diversion, but recurrent discrepancies indicate a weakness in controlled-drug management and should be rectified; diversion prevention is a responsibility of all departments, not just the pharmacy.

Hospitals have several motivations to actively invest in safeguards. Drug diversion is a patient safety issue, a patient privacy issue (eg, patient records are inappropriately accessed to identify opportunities for diversion), an occupational health issue given the higher risks of opioid-related SUD faced by HCWs, a regulatory compliance issue, and a legal issue.[31,41,46,59,78,98,99] Although individuals are accountable for drug diversion itself, hospitals should take adequate measures to prevent or detect diversion and protect patients and staff from associated harms. Hospitals should pay careful attention to the configuration of healthcare technologies, environments, and processes in their institution to reduce the opportunity for diversion.

Our study has several limitations. We did not include articles prior to 2005 because we captured a sizable amount of literature with the current search terms and wanted the majority of the studies to reflect workflow based on electronic

TABLE 3. **Diversion Safeguards at Each Stage of the Medication-Use Process with Associated List of References[a] (continued)**

Stage of Medication-Use Process	Safeguard	Description, Examples, and Associated References
Administration	Minimize the use of critical override function	ADCs may allow users to access specific drugs when the pharmacy is closed or in critical emergent situations (typically via a "critical override"). Eliminate this function, or institute tight control with co-signatures and frequent auditing.[40,68] Other approaches to override controls (eg, in the case of power outages, system failures) should also be audited and evaluated for security.[46,68] Avoid the need for nonpharmacists to have access to the pharmacy by properly stocking night cabinets, drug carts or ADCs during pharmacy off-hours.[68]
	Ensure clinical documentation is accurate to enable detection of abnormal patterns in drug access	Ensure records accurately capture which HCWs are accessing what drugs and when to ensure that the amount of drug ordered, administered, and wasted is clinically appropriate.[21,56,63,70] The number of discrepancies should be tracked, and resolved within 24 hours, and 72 hours at most.[15,31,46] Electronic systems (eg, ADCs) may support accurate documentation and trigger alerts (eg, HCWs withdrawing more drug than their peers will be flagged).[71] After-hours drug access and repeating pairs of co-signers should also be identified.[10,31,43,72] Nonclinical systems (eg, key-card access and shift schedules) should also be consulted to identify HCWs: accessing drugs or documentation when not on duty, accessing ADCs outside their work area, or associating with patients who have been affected by outbreaks of blood-borne pathogens (eg, hepatitis C virus).[11,53] For patient-controlled analgesia, institute a co-signature process for pump cartridges, keep such cartridges secure in a locked infusion pump;[10,21] require that a witness observe the waste disposal process once the cartridge is removed from the pump.[31] Where possible, use portless intravenous infusion tubing for controlled-drug infusions, lock pump interfaces (to limit manipulation of infusion rate and/or volume) and clearly document volumes infused, infusion rate and boluses for reconciliation at shift change.[10]
	Minimize credential sharing between HCWs and ensure access privileges are updated frequently	Passwords and/or identification badges should never be shared between HCWs;[38,56] the use of biometric access may reduce the risk of credential sharing.[37,40,61,73,74] Ensure that ADCs are updated regularly to capture staffing changes, and changes to patient profiles (eg, discharged patients should not appear in the ADC patient list).[46]
	Support drug-handling procedures that promote accountability and security	Maximize the security of dispensed drug: provide containers for carrying drugs to the bedside to minimize risk of being left unattended;[68] such containers help to secure controlled drug before and after administration, before disposal of waste. However, these containers should only be accessible to authorized personnel when not in use.[31] Limit amount of dispensed drug: limit drug retrieval to the current doses required for a single patient.[56] Prohibit withdrawal of more than a single dose of a controlled drug into a syringe, so that partial doses are not vulnerable to diversion.[21] Maximize accountability for dispensed drug: the HCW retrieving the drug should be the person who administers, to optimize accountability.[33,40] Assigning patients to specific HCWs may increase accountability and traceability of drug administration.[33,55]
	Reduce opportunities for diversion between drug withdrawal and administration	Define a specific interval within which drugs should be administered after retrieval.[40] Ensure that the number, size and location of ADCs is appropriate for the clinical unit (ie, no more than 30 m from patients' rooms) to support usability, efficiency and compliance.[75] HCWs should use ADCs only in their primary work area. Account for nurses' requirements and concerns, which may differ from those of the pharmacy (eg, nursing workflow may require more counter space and multi-tasking across multiple medical devices than pharmacists would consider).[75] Label any syringes containing drugs that are not administered immediately, in accordance with institutional policy.[10,40,52,62]
Wastage, returns, and disposal	Audit wasted drugs using assay technologies	Consider random assays of drugs returned to the pharmacy via refractometry or ultraviolet spectroscopy, with recognition that each approach has its limitations (eg, accuracy and cost).[4,31,35,49,69,76,77]
	Reinforce the need for appropriate witnessing	Establish processes to ensure that all waste is witnessed in real time with visual line of sight; witnessing after the fact is unacceptable.[21,56] Some guidelines suggest wasting occur at time of withdrawal from secure storage.[78] The transfer of controlled drugs to a destruction company should also be witnessed and co-signed.[65]
	Secure wasted and expired drugs	Frequently remove expired items to prevent accumulation of drug.[21,23,35] Sharps/waste receptacles should prevent drugs and waste from being shaken out or attempts to forcibly reach into openings.[21] If larger containers must be used, video cameras may be helpful to monitor their status.[21] Lock waste receptacles to the wall or other stationary equipment so that they cannot be easily removed from a clinical unit; keys allowing replacement of containers should be limited to a few designated HCWs.[21]
	Audit and reconcile documentation to verify wastage	Verify and audit the return of drugs intended for disposal to the pharmacy (eg, require co-signatures from the responsible HCW and the recipient in the pharmacy). All other wastage should be witnessed and co-signed.[21,31,56] Where possible, correlate quantities administered with quantities dispensed (eg, dispensations per surgical case). Reconcile the list of controlled drugs sent for disposal against reports from the destruction company, to ensure that all items are accounted for.[4,65]

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TABLE 3. **Diversion Safeguards at Each Stage of the Medication-Use Process with Associated List of References[a] (continued)**

Stage of Medication-Use Process	Safeguard	Description, Examples, and Associated References
System-wide[c]	Pre-employment screening	Reference and background checks should be conducted[10,12,18,60,62,70] to prevent hiring HCWs with known or suspected drug diversion histories.[17,51] High-risk roles (eg, pharmacy staff), should be rescreened on an annual basis after hire.[20] Consider existing regulations where available. For example, the US Drug Enforcement Agency (DEA) suggests specific questions regarding the candidate's criminal history during pre-employment screens.[10,60] Question references with knowledge of candidate's clinical behavior rather than purely administrative details.[10] Note, employers can be reluctant to disclose poor job performance due to liability risks.[19,51,53] Reforms have been suggested to improve disclosure from employers.[51,79]
	Implement a drug testing program	Drug testing of HCWs has been used in three capacities: pre-employment screening, random testing on an ongoing basis, and when there is reason to suspect impairment (ie, "for cause" drug testing).[18,20,27,60,80-89] Some authors caution against random drug testing.[86,87,90] Drug testing is connected with issues of legal discovery and confidentiality, which vary according to local and federal regulations; review the provided references and refer to local statutes and counsel.
	Educate staff	Educating HCWs is essential to diversion prevention;[4,10,12,31,91] preferably during orientation and annually thereafter.[4,38,74] Key concepts include: raising awareness that diversion occurs in all facilities where controlled drugs are handled,[12] identifying drugs that are prone to diversion, describing characteristics of individuals seeking to divert drugs, ensuring that drug-handling policies and procedures are understood, explaining the importance of reporting and how to do so, and deterring diversion by explaining detection practices that are in place.[42,43] Random in-person audits of clinical units (eg, compliance checks) can assess staff awareness of preferred practices and reinforce adherence.[32,60]
	Establish dedicated diversion investigation teams	Commit staff resources to prevent, detect and respond to diversion.[4,10,31,44,46-49,56,74] Staff may monitor data from a variety of sources: ADCs and associated analytics,[10,12,21,37,57,67-69,71,73,78,92,93] video surveillance[11,21] (while being mindful of patient privacy[94]), drug assaying technologies (to verify the contents of wasted drugs), [4,35,49,69,76,77] and biometric access.[37,40,61,73,74] Diversion teams audit high-risk drugs (eg, narcotics, benzodiazepines, propofol, gabapentin) and follow-up on cues that may indicate potential diversion, such as reports of HCW behaviors,[10,12,22,34,56,79,81] patients' reports of untreated pain,[10,31] or outbreaks where multiple patients are infected with the exact same strain (an outcome consistent with a single infectious HCW who may be self-injecting in the course of their diversion).[11,52,62] These teams can use a standard investigation protocol to ensure HCW confidentiality, equal treatment of all employees, optimize evidence-handling procedures, and minimize legal criticisms of how investigations were handled.[60,92,95]

[a]Table 3 is not intended to provide a direct one-to-one mapping with the contributors to diversion described in Table 2.

[b]For convenience, storage is placed after the procurement stage of the medication-use process because the largest storehouse of controlled drug likely exists in the hospital pharmacy. However, storage occurs elsewhere (eg, in patient areas, delivery trucks) and readers should be cognizant that storage risks occur at multiple stages of the medication-use process, rather than as a discrete step as it may appear in the table.

[c]System-wide refers to safeguards that apply to multiple stages of the medication-use process.

Abbreviations: ADC, automated dispensing cabinet; DEA, drug enforcement agency; HCW, healthcare worker.

health records and medication ordering, which only came into wide use in the past 15 years. Other possible contributors and safeguards against drug diversion may not be captured in our review. Nevertheless, thorough consideration of the two underlying issues described will help protect hospitals against new and emerging methods of diversion. The literature search yielded a paucity of controlled trials formally evaluating the effectiveness of these interventions, so safeguards identified in our review may not represent optimal strategies for responding to drug diversion. Lastly, not all suggestions may be applicable or effective in every institution.

CONCLUSION

Drug diversion in hospitals is a serious and urgent concern that requires immediate attention to mitigate harms. Past incidents of diversion have shown that hospitals have not yet implemented safeguards to fully account for drug losses, with resultant harms to patients, HCWs, hospitals themselves, and the general public. Further research is needed to identify system factors relevant to drug diversion, identify new safeguards, evaluate the effectiveness of known safeguards, and support adoption of best practices by hospitals and regulatory bodies.

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Aspiration Pneumonia in Older Adults

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Aspiration pneumonia refers to an infection of the lung parenchyma in an individual that has inhaled a bolus of endogenous flora that overwhelms the natural defenses of the respiratory system. While there are not universally agreed upon criteria, the diagnosis can be made in patients with the appropriate risk factors and clinical scenario, in addition to a radiographic or an ultrasonographic image of pneumonia in the typical dependent lung segment. Treatment options for aspiration pneumonia vary based on the site of acquisition (community-acquired aspiration pneumonia [CAAP] versus healthcare-associated aspiration pneumonia [HCAAP]), the risk for multidrug-resistant (MDR) organisms, and severity of illness. Hospitalized CAAP patients without severe illness and with no risk for MDR organisms or Pseudomonas aeruginosa (PA) can be treated with standard inpatient community-acquired pneumonia therapy covering anaerobes. Patients with CAAP and either of the following—risk factors for MDR pathogens, septic shock, need for an intensive care unit (ICU) admission, or mechanical ventilation—can be considered for broader coverage against anaerobes, methicillin-resistant Staphylococcus aureus (MRSA), and PA. Severe aspiration pneumonia that originates in a long-term care facility or HCAAP with one or more risk factors for MDR organisms should be considered for similar treatment. HCAAP with one or more risk factors for MDR organisms or PA, plus septic shock, need for ICU admission or mechanical ventilation should receive double coverage for PA in addition to coverage for MRSA and anaerobes. Multiple gaps in current understanding and management of aspiration pneumonia require future research, with a particular focus on antibiotic stewardship. *Journal of Hospital Medicine* 2019;14:429-435. Published online first February 20, 2019. © 2019 Society of Hospital Medicine

Aspiration pneumonia refers to an infection of the lung parenchyma in an individual who has inhaled a bolus of endogenous flora that overwhelms the natural defenses of the respiratory system. It primarily affects older adults with almost 80% of cases occurring in those 65 years and older.[1] Compared with nonaspiration pneumonia, aspiration pneumonia (whether community acquired or healthcare associated) results in more ICU stays, mechanical ventilation, increased length of hospital stay, and higher mortality.[2]

The etiology of aspiration pneumonia comes from aspirated bacteria from the oropharynx or stomach.[3] However, aspiration alone is a common occurrence and does not always lead to clinical pneumonia. Indeed, one study demonstrated that 45% of "normal subjects" aspirate in their sleep,[4] illustrating that our bodies have evolved defense mechanisms to protect us from aspirated bacteria. Thus, it is only when these systems are overwhelmed, after compromise of both glottic closure and the cough reflex in addition to dysphagia,[3] that an infection manifests.

ASPIRATION PNEUMONITIS

Aspiration pneumonitis refers to a significant inflammation of the lung parenchyma that results from inhalation of regurgitated gastric contents.[5] It can produce fever, cough, wheezing, shortness of breath, hypoxemia, leukocytosis, and a pulmonary infiltrate as well as lead to severe acute respiratory distress syndrome and even death. In the past, the use of antibiotics shortly after aspiration in patients who develop a fever, leukocytosis, or a pulmonary infiltrate was discouraged.[5] Empiric antibiotics were recommended only for patients who aspirate gastric contents and who have conditions associated with colonization of gastric contents, such as small-bowel obstruction.[5] Yet, it is difficult to distinguish aspiration pneumonitis from pneumonia[6] and there are no randomized trials in older adults to help guide their management.

PRESENTATION OF ASPIRATION PNEUMONIA

Pneumonia in older adults can present in an atypical fashion. In one study of community-acquired pneumonia (CAP), the combination of cough, fever, and dyspnea is present in only 31% of patients, although separately, they are present in 67%, 64%, and 71% of patients, respectively. The same study also showed that delirium was present in 45% of patients with CAP.[7] Nonrespiratory symptoms were present during the initial presentation of CAP in 55% of patients, with confusion in 42%, and falls in 16% of cases.[8] The same is true of aspiration pneumonia where altered mental status is seen in approximately 30% of community-acquired aspiration pneumonia (CAAP) patients and in 19% of continuing care facility patients with aspiration pneumonia.[2] Another study that compared CAP, CAAP, and healthcare-associated aspiration pneumonia (HCAAP) showed that confusion is present in 5.1%, 12.7%, and 18.6%, respec-

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tively.[9] The absence of fever in older adults is shown in studies where fever, defined as greater than or equal to 37.5°C, is absent in 32% of the very old[10] and in 40% of patients 65 years or older when it was defined as greater than 37°C.[8] The inconsistencies regarding typical symptoms of pneumonia in the older adult population are also confirmed in nursing home residents.[11] Ultimately, it is important to remember that any infection in older adults, especially in those residing in long-term care facilities, may present with subtle findings such as an acute change in cognitive and functional status.[12]

Risk Factors for Aspiration Pneumonia

Risk factors for aspiration pneumonia, while not universally agreed upon, are important to recognize as they increase the probability of the diagnosis when present. A 2011 systematic review identified age, male gender, lung disease, dysphagia, and diabetes mellitus (level 2a), as well as severe dementia, angiotensin I-converting enzyme deletion/deletion genotype, and poor oral health (level 2b) as risk factors.[13] In 2016, a panel of experts reached a consensus (modified Delphi Method) on the following risk factors for the diagnosis of aspiration pneumonia in nursing home residents: history of dysphagia, choking incident, tube feeding, neurologic disease, and cognitive impairment. The presence of one or more of these risk factors in the appropriate clinical setting may suggest a diagnosis of aspiration pneumonia.[14]

Radiographic/Ultrasonographic Imaging

In the appropriate scenario, the diagnosis of aspiration pneumonia is supported with an image representative of pneumonia. The pulmonary segment involved in aspiration pneumonia depends on the position of the patient during the aspiration event. If the aspiration event occurs while the patient is in the recumbent position, development of pneumonia is more common in the posterior segments of the upper lobes and the apical segments of the lower lobes; whereas if it occurs while the patient is in an upright position, the location changes to the basal segments of the lower lobes.[3]

Overall, the sensitivity of a chest X-ray to diagnose pneumonia ranges between 32%-77.7%,[15-17] suggesting that a significant proportion of patients suspected of having pneumonia in past research studies, may have been misdiagnosed. Studies using lung ultrasound to identify pneumonia demonstrate a higher sensitivity, but additional research is needed to validate these findings.[17-19] Noncontrast CT scans of the chest remain the reference standard for diagnosing pneumonia and currently tend to have the largest impact on diagnosis and subsequent treatment decisions.[15,16,20,21] As a result, if radiation exposure risks are not a concern for the patient, we recommend utilizing noncontrast CT imaging whenever the diagnosis is in doubt until future research elucidates the most appropriate approach to imaging.

Diagnosis

Diagnosing aspiration pneumonia is difficult, in part because there is no universal definition or set of diagnostic criteria. The diagnosis of aspiration pneumonia is supported by the fulfillment of three criteria. First, appropriate risk factors for aspiration, as documented above, should be present. Second, there should be evidence of clinical signs and symptoms of pneumonia (typical or atypical). Third, radiographic representation of pneumonia in a dependent pulmonary segment confirms the diagnosis. Once these criteria are met, it is important to distinguish between CAAP and HCAAP with particular attention to risk factors for multidrug-resistant (MDR) organisms and Pseudomonas aeruginosa (PA).

MICROBIOLOGY

Many studies have tried to determine the exact bacterial etiology of aspiration pneumonia as documented in the Table.

Even when an ideal method is used to obtain a good sample, however, the results are limited by other variables in the study. For example, in studies that use protected brush specimens and protected bronchoalveolar lavage to acquire samples for culture, many patients received antibiotics prior to sampling, and the studies are small (Table). Although anaerobes have traditionally been implicated in aspiration pneumonia, only El-Solh et al.[22] were able to culture a significant proportion of anaerobes. The study, however, was limited to institutionalized older adults requiring mechanical ventilation and it did not require the typical radiographic location for aspiration pneumonia. Even under the best circumstances, it is difficult to determine causality because the antibiotics used to treat these cases of aspiration pneumonia cover a broad range of organisms. Based on the studies in the Table, causative organisms may include Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, and gram-negative rods in addition to traditional organisms classically thought to cause aspiration pneumonia-anaerobes. Microbiologic etiology, however, may also be insinuated from the studies discussed in the therapeutic strategies section below as some include antibiotics with limited antimicrobial activity.

Therapeutic Strategies

The management of aspiration pneumonia has evolved significantly since it was first studied in the 1970s because of the development of antibiotic resistance patterns, newer antibiotics, and increasing information on the diversity of pathogens involved in each subset of aspiration syndromes. The antimicrobial treatment of aspiration pneumonia was classically directed against anaerobic pathogens; treatment of these infections, however, was extrapolated from studies of pulmonary abscesses and other anaerobic pulmonary infections.

A randomized controlled trial in the mid-1980s comparing penicillin and clindamycin demonstrated a significantly improved cure rate in the clindamycin group.[23] A follow-up study in 1990 implicated a significant number of penicillin-resistant Bacteroides infections—the majority of these infections were subsequently reclassified as Prevotella melaninogenica—as the cause for high rates of penicillin resistance in lung abscesses and necrotizing pneumonias, further supporting

TABLE. **Determining Bacterial Etiology of Aspiration Pneumonia**

Study	Radiographic Criteria for Diagnosis	Microbiology	Limitations
Mier et al.[49] (1993) Prospective	Alveolar opacity	Blood culture: Streptococcus pneumoniae (1 patient) Staphylococcus aureus (1 patient) Protected brush specimen isolates: Staphylococcus aureus 22% Streptococcus pneumonia 15% Pseudomonas aeruginosa 11% Haemophilus influenzae 7.4% Escherichia coli 7.4% Proteus mirabilis 7.4% Streptococcus sp. 7.4% Klebsiella pneumoniae 3.7% Enterobacter cloacae 3.7% Serratia marcescens 3.7% Streptococcus viridans 3.7% Morganella morgannii 3.7% Candida albicans 3.7%	Small sample size; only ICU patients[a]; alveolar opacity did not have to be in a dependent lobe; antibiotics were administered before protected brush specimen (PBS) cultures were obtained
Marik et al.[50] (1999) Prospective	Alveolar infiltrate	Protected specimen brush sampling and mini-bronchoalveolar lavage isolates: Enterobacter spp 17.6% Streptococcus pneumoniae 11.7% Methicillin-sensitive Staphylococcus aureus (MSSA) 11.7% Haemophilus influenzae 11.7% Klebsiella pneumoniae 11.7% Escherichia coli 11.7% Flavobacterium spp 11.7% Serratia spp 5.8% V paravula 5.8%	Small sample size; all patients required mechanical ventilation; infiltrate did not have to be in dependent lobes; 48% of patients received an antibiotic with anaerobic coverage in the 24 hours prior to microbiologic sampling
El-Solh et al.[22] (2003) Prospective	Infiltrate compatible with pneumonia	Blood culture: Streptococcus pneumoniae (1 patient) Staphylococcus aureus (1 patient) Klebsiella pneumonia (1 patient) Protected bronchoalveolar lavage isolates: Anaerobes 20.5% (Prevotella spp 11%, Fusobacterium spp 5.5%, Bacteroides spp 2%, Peptostreptococcus 2%) Escherichia coli 20% Klebsiella pneumoniae 15% Staphylococcus aureus 15% Serratia spp 13% Proteus mirabilis 11% Streptococcus spp 11% Streptococcus pneumoniae 9% Haemophilus influenzae 4% Pseudomonas aeruginosa 4% Enterobacter cloacae 2%	Only institutionalized older adults requiring mechanical ventilation; small sample size; infiltrate did not have to be in dependent lobes; does not specify when antibiotics were administered in relation to protected bronchoalveolar lavage cultures, although cultures were taken within 4 hours of presentation to the emergency department
Kadowaki et al.[33] (2005) Randomized prospective	Infiltrate in the posterior segments of the lower lobes	Sputum culture isolates: Klebsiella pneumoniae 30.8 % Methicillin-resistant Staphylococcus aureus (MRSA) 14.1% MSSA 11.5% Enterobacter 7.7% Haemophilus influenzae 6.4% Streptococcus pneumonia 6.4% Serratia 5.1% Pseudomonas aeruginosa 5.1% Escherichia coli 3.8% Citrobacter 2.6%	Sputum cultures are less reliable than PBS; the study did not document the time antibiotics were administered in relation to sputum acquisition; did not specify whether sputum cultures were processed for anaerobes

Continued on page 432

TABLE. **Determining Bacterial Etiology of Aspiration Pneumonia (continued)**

Study	Radiographic Criteria for Diagnosis	Microbiology	Limitations
Shariatzadeh et al.[2] (2006) Prospective	Pulmonary infiltrate	CAAP: Blood culture[b]: Staphylococcus aureus 35.7% Streptococcus pneumoniae 21.4% Escherichia coli 14.3% Sputum culture[c]: Gram-negative bacilli 45% Streptococcus pneumoniae 20% Haemophilus influenzae 20% Continuing care facility aspiration pneumonia: Blood culture[d]: Gram-negative bacilli 40% Streptococcus pneumoniae 20% Staphylococcus aureus 20% Sputum culture[e]: Pseudomonas aeruginosa 43% Gram-negative bacilli 29% Staphylococcus aureus 21%	Infiltrate did not have to be in dependent lobes; sputum cultures are less reliable than PBS; sputum and blood cultures were not performed on all patients; the study did not specify when antibiotics were administered in relation to the acquisition of cultures; sputum culture was not processed for anaerobes
Lanspa et al.[9] (2013) Retrospective	Radiographic evidence of pneumonia	CAAP & HCAAP[f]: Streptococcus pneumoniae 2.5% Enteric organisms 2.2% MRSA 1.9% Haemophilus sp, 1.8% MSSA 1.6% Pseudomonas 1.0% Beta-hemolytic strep 0.7% M. catarrhalis 0.3% Neisseria sp. 0.7% Other 1.6% HCAAP patients had statistically significant increased rates of enteric bacteria causing infection.	Retrospective design; no clear definition of aspiration pneumonia; only 7.8% of patients had positive cultures (blood/tracheal); HCAP aspiration patients lacked full criteria for HCAP; PBS was not used to obtain culture samples; tracheal aspirate was the most common method used for recovering an organism; the study did not specify when antibiotics were administered in relation to the acquisition of cultures; recovery of anaerobic organisms was limited to blood and pleural fluid
Marumo et al.[32] (2014) Prospective cohort	New infiltrate	NHCAP (all cultures[g]): Streptococcus pneumoniae 22% MSSA 10% Haemophilus influenza 6% Escherichia coli 1.7% Pseudomonas aeruginosa 1.7% MRSA 0.9%	Infiltrate did not have to be in dependent lobes; NHCAP differed slightly from standard HCAP definitions; only NHCAP patients with no risk factors for MDR pathogens were evaluated; bacterial diagnosis was established in only 47% of patients; PBS or protected bronchoalveolar lavage was not used to obtain culture samples; the study did not specify when antibiotics were administered in relation to the acquisition of cultures; anaerobic culture media was not used.

All isolates are expressed as a percentage of positive isolates (except for Lanspa et al. and Marumo et al.).

[a] 50% of patients had altered consciousness from a drug overdose, and an additional 15% aspirated because of intestinal obstruction; 72% of sterile PBS cultures were from drug overdose patients. Most patients were not older adults.

[b] Blood cultures were positive in only 12% of CAAP patients who had blood cultures drawn.

[c] Sputum cultures were positive in 44% of CAAP patients who had sputum cultures.

[d] Blood cultures were positive in only 5% of continuing care facility patients who had blood cultures drawn.

[e] Sputum cultures were positive in 48% of continuing care facility patients who had sputum cultures.

[f] Expressed as a percentage of patients, rather than of isolates, who were carrying the pathogen.

[g] Expressed as a percentage of patients, rather than of isolates, who were carrying the pathogen.

clindamycin as the treatment of choice for these infections.[24] Amoxicillin-clavulanic acid (IV and PO regimens), studied in the treatment of community-acquired necrotizing pneumonia/lung abscess, shows good efficacy as well.[25] This study also attempted to elucidate the underlying causative organisms in these patients. Organisms associated with CAP as well as anaerobic organisms were isolated, giving more credence to the idea of broader coverage for aspiration pneumonia.

Community-Acquired Aspiration Pneumonia/Healthcare-Associated Aspiration Pneumonia

The importance of making a diagnostic distinction between CAAP versus HCAAP is critical for management strategies. A prospective population-based study demonstrated that ICU length of stay and 30-day mortality is highest for HCAAP, followed by CAAP, and lastly for those with CAP.[9] Although some studies use different nomenclature for identifying aspiration

pneumonia patients at risk for a wider array of microorganisms, we attempt to standardize the language by using HCAAP. The literature on nonaspiration pneumonia is changing from terms such as CAP and healthcare-associated pneumonia (HCAP) to pneumonia with the risk of MDR organisms. One study proposed a new treatment algorithm for CAP based on the presence or absence of the following six risk factors: prior hospitalization of greater than or equal to two days in the preceding 90 days, immunosuppression, previous antibiotic use within the preceding 90 days, use of gastric acid-suppressive agents, tube feeding, and nonambulatory status.[26] A similar approach proposed years earlier for HCAP patients found the following to be risk factors for MDR organisms: hospitalization in the past 90 days, antibiotic therapy in the past six months, poor functional status as defined by activities of daily living score, and immune suppression.[27] Other factors, such as structural lung disease, that increase the risk of organisms resistant to standard antibiotic treatment regimens[28-31] should be considered in aspiration pneumonia as well. Aspiration pneumonia is following a similar trajectory where the risk of MDR organisms is taking precedence over the environment of acquisition. The final nomenclature will allow the healthcare provider to understand the organisms that need to be targeted when choosing an appropriate antibiotic treatment regimen.

There is evidence supporting the premise that CAAP and nursing home patients with no risk factors for MDR organisms can be treated with standard regimens used for patients with CAP. A prospective cohort study in 2014 did not show any statistically significant differences in clinical outcomes in nursing and healthcare-associated aspiration pneumonia patients (with no risks of MDR organisms) treated with azithromycin versus ampicillin/sulbactam. However, only 36 patients were included in the azithromycin arm, and the therapeutic choices were made by the treating physician.[32]

A prospective study of 95 long-term care residents reported that of those patients admitted to the ICU with severe aspiration pneumonia, the causative organisms are gram-negative enteric bacilli in 49% of isolates, anaerobes in 16%, and Staphylococcus aureus in 12%.[22] This study mentioned that six of seven anaerobic pneumonia cases had inadequate anaerobic coverage yet were effectively treated; based on the organisms represented, however, the antibiotics administered did provide some coverage.[22] Prevotella was one of the common anaerobic organisms that could be treated by levofloxacin or ceftriaxone/azithromycin, possibly explaining the success of azithromycin in the study quoted previously.[22,32] Therefore, although anaerobic organisms still need to be considered, some may be treated by traditional CAP coverage.[22]

In a 2005 randomized prospective study of 100 patients aged 71 to 94 years, clindamycin was found to have clinical efficacy equivalent to ampicillin-sulbactam and panipenem in the treatment of mild-to-moderate aspiration pneumonia.[33] Most patients in this study are nursing home residents, and 53% of sputum cultures in the clindamycin arm grew gram-negative rods. In contrast to the previous study, the significance of gram-negative rod infections in this population of patients, with less severe infections, is called into question, as clindamycin has no coverage against these organisms. This premise is supported by a more recent study using azithromycin in nursing and healthcare-associated aspiration pneumonia patients, mentioned previously.[32] Taken together, these three studies suggest that the severity of aspiration pneumonia may be a risk factor that needs to be taken into account when considering broad-spectrum antimicrobial coverage.

While further research is needed to validate treatment approaches, based on the current literature we propose the following:

CAAP requiring hospitalization but without any of the following-risk for PA or MDR organisms, septic shock, the need for ICU admission, or mechanical ventilation-can be treated with standard CAP therapy that covers anaerobes.[26,32-34] Patients with CAAP and either of the following—risk factors for MDR organisms, septic shock, need for ICU admission, or mechanical ventilation—should be considered for broader coverage with vancomycin or linezolid, antipseudomonal antibiotics, and anaerobic coverage. CAAP with specific risk for a PA infection should be considered for two antipseudomonal antibiotics (where only one can be a beta-lactam antibiotic, and one has anaerobic coverage).

Severe HCAAP without risk for MDR organisms or PA but with any of the following-septic shock, ICU admission, or mechanical ventilation-can be treated based on the 2016 Infectious Diseases Society of America guideline recommendation for hospital-acquired pneumonia, with a regimen that also provides adequate anaerobic coverage.[35] If patients have HCAAP with one or more risk factors for MDR organisms, no septic shock, and no need for ICU admission or mechanical ventilation, provide coverage with a similar regimen. In contrast, HCAAP with risk factors for PA or severe HCAAP causing septic shock, requiring ICU admission, or needing mechanical ventilation, which occurs in the setting of one or more risk factors for MDR organisms, or structural lung disease, should receive two antipseudomonal antibiotics (where only one can be a beta-lactam antibiotic and one has anaerobic coverage) in addition to vancomycin or linezolid.

A recent systematic review demonstrates the paucity of studies of ideal methodologic design which complicates the ability to recommend, with confidence, one guideline-based antimicrobial regimen over another.[36] Future studies may determine that despite the severity of the infection, if patients do not carry any risk for MDR pathogens or PA, they may only require CAAP coverage. When a patient presents with an acute infection, it is prudent to review previous cultures, and although it may be necessary to treat with broad-spectrum antibiotics initially, it is always important to narrow the spectrum based on reliable culture results. If future studies support the results of many studies cited in this article, we may be using fewer antibiotics with narrower spectrums in the near future.

Prevention

Although the healthcare system has practices in place to prevent aspiration pneumonia, the evidence supporting them

are either inconclusive or not of ideal methodological design. Two systematic reviews failed to show statistically significant decreases in rates of aspiration pneumonia or mortality using the standard of care positioning strategies or thickened fluids in patients with chronic dysphagia.[37,38] One study showed a decreased incidence of all pneumonia in dysphasic patients with dementia or Parkinson disease when a chin-down posture (with thin liquids) or thickened fluids in a head-neutral position was used. The study, however, has significant limitations, including a lack of a "no treatment" group for comparison, which did not allow investigators to conclude that the decreased incidence was from their interventions.[39]

There are preventive strategies that show a decreased risk of aspiration pneumonia. Poor oral hygiene seems to be a modifiable risk factor to establish better control of oral flora and decrease aspiration pneumonia. A systematic review of five studies, evaluating the effects of oral healthcare on the incidence of aspiration pneumonia in frail older people, found that tooth brushing after each meal along with cleaning dentures once a day and professional oral healthcare once a week decreases febrile days, pneumonia, and dying from pneumonia.[40] A two-year historical cohort study using aromatherapy with black pepper oil, followed by application of capsaicin troches, and finally menthol gel, as the first meal, leads to a decreased incidence of pneumonia and febrile days in older adults with dysphagia.[41] Well-designed validation studies may establish these practices as the new standard of care for preventing pneumonia in patients with dysphagia.

Feeding Tubes

Multiple studies show that in older adults with advanced dementia there is no survival benefit from percutaneous endoscopic gastrostomy (PEG) tube placement[42-44] and more recent systematic reviews also conclude that there is currently no evidence to support the use of PEG tubes in this specific population.[45,46] In February 2013, as part of the American Board of Internal Medicine Foundation Choosing Wisely® campaign, the American Geriatrics Society advised providers not to recommend percutaneous feeding tubes in patients with advanced dementia, rather, "offer assisted oral feeding."[47] It is worth noting, however, that none of the studies reviewed were of ideal methodological design, so opinions may change with future studies.

A more recent study compared liquid feeds versus semisolid feeds in patients with PEG tubes. The study shows a 22.2% incidence of aspiration pneumonia in the liquid feed group, which is comparable to prior studies, but the incidence of aspiration pneumonia is only 2.2% in the semisolid feed group ($P < .005$).[48] A benefit of this size warrants future studies for validation.

CONCLUSION

Aspiration pneumonia leads to increased mortality when compared with CAP and HCAP.[2] Until future studies validate or refute the current understanding surrounding its management, the following should provide some guidance: aspiration pneumonia should be suspected in any individual with risk factors of aspiration who presents with typical or atypical symptoms of pneumonia. Confirmation of the diagnosis requires an image representative of pneumonia in the typical dependent lung segment on chest X-ray, lung ultrasound, or noncontrast CT scan of the chest. Treatment of aspiration pneumonia should take into account the site of acquisition, severity of illness, and risk for MDR organisms as the causative organisms may include Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, and gram-negative rods, in addition to the traditional organisms classically thought to cause aspiration pneumonia-anaerobes.

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Updates in Pediatric Hospital Medicine: Six Practical Ways to Improve the Care of Hospitalized Children

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BACKGROUND: As pediatric hospital medicine continues to grow, it is important to keep abreast of the current literature. This article provides a summary of six of the most impactful articles published in 2018.

METHODS: The authors reviewed articles published between January 2018 and December 2018 for the 2019 Society of Hospital Medicine national conference presentation of Top Articles in Pediatric Hospital Medicine, where the top 10 articles of 2018 were presented. Six of the 10 articles are highlighted in this review based on article quality and their applicability to change practices in the hospital setting or prompt further research.

RESULTS: Key findings from the articles include: multiple interventions aimed at providers can improve compliance with bronchiolitis guidelines; a developed calculator can improve testing for urinary tract infections in children aged 2-24 months; nonmedical costs of hospitalizations are underappreciated and disproportionately affect those with a lower socioeconomic status; a progress note template in an electronic health record can lead to higher quality and shorter notes; for febrile infants aged 60 days and younger, most blood and cerebrospinal fluid culture pathogens can be identified within 24 hours and nearly all by 36 hours; and the development of a high-value care tool can help to bring concepts of high-value care into family-centered rounds.

CONCLUSION: The six selected articles highlight findings pertinent to pediatric hospital medicine. *Journal of Hospital Medicine* 2019;14:436-440. Published online first June 12, 2019. © 2019 Society of Hospital Medicine

The field of pediatric hospital medicine has seen tremendous growth in scholarship in the past decade. To obtain a wide view of advancements in the field from the current literature, the authors selected 18 English-language journals (Table 1) across four domains believed to be relevant to the practice of pediatric hospital medicine, including hospital medicine, pediatrics, emergency care, and medical education. The median Hirsch index (h-index) of the selected journals was 131. A goal of 10, a number that could maximally benefit consumers of the finished product, was set as the final number of articles to be selected.

Guiding principles for the initial selection included novelty of hypotheses, study design, significance of results, and likelihood to change pediatric hospital medicine practice from both the community and academic hospital perspectives. Journals were assigned randomly to each author for review and assignments were switched after six months to limit potential bias in coverage. A three-stage review process was employed. The authors initially independently reviewed titles and abstracts from 13,296 articles published between January 2018 and December 2018 and rated them according to their likelihood to be included in the final set of 10 articles and their broad applicability to pediatric hospital medicine. This resulted in 99 studies that were selected for further review. Next, the authors were assigned a subset of the 99 articles for further review;

TABLE 1. **List of Journals Reviewed**

Academic Medicine
Academic Pediatrics
Annals of Emergency Medicine
Archives of Disease in Childhood
British Medical Journal
British Medical Journal - Paediatrics
Hospital Pediatrics
Journal of Graduate Medical Education
Journal of Hospital Medicine
Journal of Pediatrics
Journal of the American Medical Association
Journal of the American Medical Association Pediatrics
The Lancet
The Lancet Child and Adolescent Health
New England Journal of Medicine
Pediatric Emergency Care
Pediatric Infectious Disease Journal
Pediatrics

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TABLE 2. **Key Findings from the Selected Articles**

1. Novel interventions, such as a real-time data dashboard of provider performance, can improve compliance with clinical practice guidelines for bronchiolitis.
2. UTICalc is a calculator that evaluates the pre- and posttest probability of urinary tract infections in children aged 2-24 months with excellent sensitivity and specificity.
3. Nonmedical costs of hospitalizations can cause significant financial burdens for families, with a median household losing 45% of their daily household income during a hospitalization. This loss is more significant for those already facing social and financial hardships.
4. An electronic health record progress note template using best-practice guidelines can lead to higher quality, shorter, and earlier-completed notes.
5. For febrile infants aged ≤60 days with bacteremia or meningitis, 88%-89% of the pathogens present are detected by 24 hours, and 95% are detected by 36 hours; well-appearing infants could be considered for discharge after 24 hours.
6. A newly developed, validated rounding tool focusing on high-value care items can be incorporated into family-centered rounds.

each author rated the articles independently based on their likelihood of inclusion in the final 10-article set. At this stage, 75 articles were excluded. Finally, all remaining 24 articles were reviewed independently and in depth by both authors.

Ten articles were selected by consensus formation, and the authors presented their findings at the 2019 Society for Hospital Medicine annual meeting. From these 10 articles, six were determined to be most impactful to current practice; these articles are presented below. After discussing the study background, an overview, key results, limitations of the study, important findings (Table 2), and implications for practice and future research are presented.

SELECTED PUBLICATIONS

Interventions to Reduce Over-Utilized Tests and Treatments in Bronchiolitis. Tyler A, et al. *Pediatrics.* 2018;141(6):e20170485.[1]

Background

The American Academy of Pediatrics (AAP) published clinical practice guidelines (CPG) for bronchiolitis in 2014.[2] However, unnecessary tests and interventions continue to be ordered and used on children with bronchiolitis that are not recommended by the guidelines. In this quality improvement project, the authors sought to increase compliance with the AAP CPG for bronchiolitis by reducing chest x-rays (CXR) to <20%, respiratory viral testing (RVT) to <15%, and use of bronchodilators to <20%.

Study Overview and Results

This project took place at a free-standing children's hospital and included urgent care locations. Authors obtained pre-intervention data through two bronchiolitis seasons in 2013 and 2014 for patients aged 1-23 months with a primary or secondary diagnosis of bronchiolitis and who did not require admission to the Intensive Care Unit (ICU). The intervention period was from December 2015 to April 2016. All sites simultaneously implemented their interventions, which included education of care team members and families, updated order sets, and electronic health record (EHR)-generated e-mails that provided data looking at peer ranking statistics for each intervention, CXR, RVT, and bronchodilator usage. A data dashboard was created to display real-time utilization of the studied interventions. Providers were also asked to sign a pledge that they would reduce unnecessary testing and treatment. As balancing measures, the numbers of patients presenting to the Emergency Room (ER) or readmitted within seven days of an ED visit or admission for bronchiolitis were tracked; patients who required ICU levels of care during their first admission or on readmission were also tracked. Statistically significant decreases in CXR ordering from 39.5% to 27.2%, RVT ordering from 31.9% to 26.3%, and any bronchodilator usage from 34.2% to 21.5% were noted. No difference pre- and postintervention in patients readmitted to the ICU was found, and length of stay (LOS) between groups was not statistically significant.

Limitations

As all interventions were initiated simultaneously, identifying which individual or subset of interventions was responsible for changing provider behavior was impossible. More patients postintervention were admitted under observation status and under a milder All Patient Refined Diagnosis Related Groups (APR DRGs) severity index, which may indicate a less-sick cohort of patients in this group. Since the LOS and number of patients readmitted to the ICU were similar in both groups, it is unlikely that the postintervention group represented a less-sick cohort.

Important Findings and Implications

This QI project highlighted novel ways to implement and emphasize the importance of compliance to CPG. A provider pledge may be helpful in reinforcing to all providers the idea that the institution is committed to guideline implementation. Comparing individual provider data and having a real-time dashboard with group performance can help reinforce goals and progress toward them at the group, site, and individual patient population levels.

Development and Validation of a Calculator for Estimating the Probability of Urinary Tract Infection in Young Febrile Children. Shaikh N, et al. *JAMA Pediatrics.* 2018;172(6):550-556.[3]

Background

The prevalence of urinary tract infections (UTIs) in children under 2 years of age that present to the emergency department

(ED) with fever is about 7%.[4] After clinical examination, providers obtaining a urinalysis must then determine if empirical antibiotics are warranted for a suspected UTI. This study describes the development of a novel calculator, UTICalc that estimates the pretest probability of a UTI based on clinical findings and the posttest probability of a UTI based on laboratory results.

Study Overview and Results

This study features a single-center, nested, case-control design that looked retrospectively at 542 children aged 2-24 months who presented to the ED from January 2007 to April 2013 with fever and had a catheterized urinalysis obtained. Patients were then matched with randomly selected children without a UTI to create a training database. Five models using different variables were developed, including one with only clinical characteristics and four that combined clinical characteristics with differing laboratory values. The area under the curve of the "clinical model" was 0.80, while those of the remaining four models ranged from 0.97 to 0.98. The clinical model showed a sensitivity of 95% and specificity of 35% in the training database, while the four other models showed sensitivities ranging from 93% to 96% and specificities ranging from 91% to 93%. The models were then validated using a cohort of children aged 2-24 months who presented to the ED with fever from July 2015 to December 2016; the UTI prevalence in this cohort was 7.8%. Finally, using a hypothetical cohort of 1,000 children being evaluated for a UTI, the authors showed that UTICalc reduced the numbers of urine samples obtained by 8.1% and missed UTIs from 3 to 0 compared with following AAP guidelines.[5]

Limitations

The training database was created retrospectively at a single institution and is subject to local practice patterns. The proposed calculator creates an algorithm that is meant to be used in a setting where the pretest probability for a UTI is reasonably high based on criteria from the AAP UTI guidelines.

Important Findings and Implications

UTICalc could be a great tool for providers to guide testing for UTIs in children aged 2-24 months presenting with a fever. Given further study at multiple sites and settings, including outpatient clinics, UTICalc could have significant implications for reducing unnecessary testing and treatment in febrile children.

Lost Earnings and Nonmedical Expenses of Pediatric Hospitalizations. Chang LV, et al. *Pediatrics.* 2018;142(3):e20180195.[6]

Background

Although medical expenses related to hospitalization can be significant for many families, nonmedical costs, such as transportation, parking, meals, and lost earnings from missed days at work, are also important to consider. These hardships can lead to challenges in postdischarge follow-up and adherence to discharge instructions, both of which lead to hospital readmissions. This article presents a cross-sectional analysis at a large, free-standing children's hospital that participated in the Hospital-to-Home Outcomes Study (H2O). The authors sought to determine whether families with more financial or social hardships are affected disproportionately by nonmedical costs related to hospitalizations.

Study Overview and Results

A total of 1,372 children were included and children with lengths of stay >13 days were excluded. Face-to-face parental surveys were conducted and included questions on parental education, employment status, sick leave flexibility, and measures of financial and social hardship. The study authors calculated a total cost burden (TCB) based on nonmedical costs estimated at the time of the survey, including lost wages and expenses during the hospitalization. A daily cost burden (DCB) based on length of hospital stay and daily cost burden as a percentage of daily income (DCBi) were also calculated. The median TCB was $112.80, and the median DCB was $51.40. The median DCBi showed that the median household had 45% of their daily income depleted by nonmedical expenses related to their hospitalization. Those who reported more financial or social hardships had a higher median DCBi; if ≥3 financial hardships were reported, 86% of the daily household income was depleted.

Limitations

The study was conducted at a single institution with a number of existing support systems in place to help unburden families of hospitalized children. Non-English-speaking families were excluded. A face-to-face survey may have influenced parental responses regarding social and financial hardships.

Important Findings and Implications

Nonmedical costs of hospitalized children can be quantified and disproportionately affect those experiencing financial and social hardships. Hospitalists should be aware of these findings and find ways within their hospital systems to provide support for families both during and after hospitalizations.

A Prescription for Note Bloat: An Effective Progress Note Template. Kahn D, et al. *Journal of Hospital Medicine.* 2018;13(6):378-382.[7]

Background

Although electronic health records (EHRs) have improved the speed and legibility of documentation, the harm of "note bloat," defined as multiple pages of nonessential information which leaves key aspects buried or lost, is prevalent. In this prospective, quality improvement study across four internal medicine residency programs, the authors investigated a bundled intervention consisting of didactic teaching and an electronic progress note template on note quality, length, and timeliness.

Study overview and results

Notes pre- and postintervention were graded using a tool that considered the general impression of the note, its score on the validated Physician Documentation Quality Instrument (PDQI-9),[8] and a questionnaire based on the Accreditation Council for

Graduate Medical Education competency note checklist.[9] Analyzing 200 preintervention and 199 postintervention notes, significant improvement was seen in general impression scores, all PDQI-9 domains, and 6 of 13 note competency questionnaire items. The mean number of lines in the note decreased by 25%, and the mean completion time when the note was signed was 1 hour and 15 minutes earlier. The greatest impact on shortening notes involved a reduction in the auto-population of laboratory and imaging studies.

Limitations

The study was unblinded. The authors attempted to minimize bias with an objective questionnaire and employed multiple graders per note; however, poor interrater reliability was obtained. Postintervention, 70% of all residents used the template. At one of the four institutions, evidence of note quality improvement despite low template use was found. At another institution, no improvement in note quality was reported despite relatively high template uptake. Local culture and institutional buy-in may be factors affecting these results. In addition, pre- and postintervention notes were examined in the same academic year; thus, the effects seen may be due, in part, to resident maturation. Generalizability to nonacademic institutions and the durability of the intervention are additional concerns.

Important Findings and Implications

Resident education on documentation and an EHR progress note template incorporating best practices can effectively combat "note bloat" and lead to higher quality and shorter notes that are completed earlier in the day. This solution has significant implications for improving transitions of care, handoffs, and patient safety.

Time to Pathogen Detection for Non-Ill Versus Ill-Appearing Infants ≤60 Days Old with Bacteremia and Meningitis. Aronson PL, et al. *Hospital Pediatrics* 2018;8(7):379-384.[10]

Background

The routine evaluation of febrile infants aged ≤60 days old often involves blood and cerebrospinal (CSF) fluid evaluations, and many infants are hospitalized while waiting for culture results. A previous study of febrile infants showed that 91% of the pathogenic organisms could be identified on blood culture within 24 hours and that 96% could be identified within 36 hours; 81% of the bacterial pathogens present were detected on CSF culture within 36 hours.[11]

Study Overview and Results

In this large, multicenter study of infants presenting to the Emergency Departments (EDs) of 10 children's hospitals over a five-year study period, the authors investigated the time to pathogen detection in blood and CSF for infants aged ≤60 days with bacteremia and/or bacterial meningitis; whether the time to detection differed for non-ill and ill infants was also examined. Ill- versus non-ill-appearance was determined by a medical record review of the physical exam looking for one of 13 key words (eg, "ill-appearing," "toxic," "lethargic," etc.). A total of 381 infants were included. Overall, 88% of the pathogens present were detected in blood culture within 24 hours and 95% were detected within 36 hours. In CSF, 89% of the pathogens present were detected within 24 hours, and 95% were detected within 36 hours. In infants with bacteremia who were non-ill-appearing, 85% of the blood pathogens were detected within 24 hours.

Limitations

The median time to detection for blood culture pathogens for ill-appearing versus non-ill-appearing infants was shorter by just one hour, but 15% of the non-ill infants had a positive blood culture after 24 hours. However, the prevalence of bacteremia and meningitis in non-ill-appearing infants is likely low; the authors did not report the total number of febrile infants evaluated by EDs in the study.

Important Findings and Implications

Most positive blood and/or CSF cultures for infants aged ≤60 days will yield results by 24 hours; 95% of the pathogens present could be detected within 36 hours. Sending a non-ill-appearing febrile infant home at 24 hours may miss 15% of the instances of bacteremia, but the overall low prevalence of invasive bacterial infection in infants should be considered.

The High-Value Care Rounding Tool: Development and Validity Evidence. McDaniel CE, et al. *Academic Medicine*. 2018;93(2):199-206.[12]

Background

Providing high-value care (HVC) to patients is a struggle for physicians and healthcare systems. Although physicians teaching trainees HVC practices could be an effective way to increase cost-conscious care, the best practices for teaching HVC remain unknown. To fill this gap, the authors developed a tool to measure the frequency and content of observable HVC teaching and evaluated the validity of the tool within a pediatric inpatient setting.

Study Overview and Results

The HVC rounding tool was developed through several phases from conception to validation. The research group used a modified Delphi method to construct the tool using a consensus building process based on opinions from content experts in the field of HVC, from a variety of specialties, experience levels, and geographic areas of the United States. Each item of the HVC instrument was rated by these experts, and, from their evaluations and surveys, an 11-item HVC tool was constructed. A pilot of the tool was performed to establish internal validity and interrater reliability based on observations of 148 patient encounters. From this process, a final 10-item HVC rounding tool emerged, including domains in quality, cost, and patient values. A few items included giving positive feedback for not doing an unnecessary test, discussing whether a patient needs to stay inpatient or meets discharge criteria, and customizing a care plan to align with family values and goals. The final iteration of the tool had

no rater disagreements within the quality and patient values domain and only one disagreement within the cost domain.

Limitations

This tool was validated at a single pediatric institution, and, thus, the generalizability of the tool has not been established. The authors note that the Delphi panelists used for the construction of the tool were from a medical subspecialty background and not surgical backgrounds, which limits its applicability from a surgical perspective. The tool does not allow for differentiation between lengthy discussions or brief comments presented during rounds.

Important Findings and Implications

The HVC rounding tool is both innovative and timely. Pediatric hospitalists are leaders in family-centered care, and this tool allows assessment of whether important concepts of high-value care are discussed at the bedside. A multisite educational study using this tool would be welcome.

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Things We Do for No Reason: Neuroimaging for Hospitalized Patients with Delirium

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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.

CLINICAL SCENARIO

A 67-year-old woman with a history of hypertension and osteoarthritis was hospitalized for fever, flank pain, and dysuria with pyuria on urinalysis. She was diagnosed with acute pyelonephritis and started ceftriaxone, ondansetron for nausea, and oxycodone for pain. On hospital day two, she developed acute confusion that waxed and waned in severity throughout the day. On examination, she appeared mildly agitated, inattentive, and was noted to pick at her linens and garment. She was oriented to person only and had a nonfocal neurologic examination. Her nurse reported no recent falls or trauma. As part of the patient's evaluation, her attending physician ordered a head computed tomography (CT) scan.

BACKGROUND

Delirium is commonly diagnosed in hospitalized patients. It has a prevalence of 29%-64% and is associated with longer lengths of stay, higher mortality, and costs of over $164 billion per year in the United States.[1] While a number of practice guidelines have been created to help guide delirium diagnosis and management, there is not a clear consensus on when neuroimaging should be performed during the evaluation.[2-4] It should also be noted that numerous guidelines for delirium management exist, with variable quality and a heavy reliance on expert opinion.[5] Perhaps due to this lack of consensus, neuroimaging is performed in 33% to 67% of hospitalized patients with delirium.[6,7]

WHY YOU MAY THINK NEUROIMAGING IS HELPFUL IN EVALUATING UNDIFFERENTIATED HOSPITALIZED PATIENTS WITH DELIRIUM

Delirium is known to be associated with intracranial processes. For example, delirium occurs in 13% to 48% of patients with acute stroke[8] and conversely 7% of patients with new confusion evaluated in emergency departments or inpatient settings were found to have an acute stroke.[9] The inclusion of neuroimaging as part of a delirium evaluation is supported in certain circumstances, such as in patients with recent falls, focal neurologic signs (including papilledema), systemic anticoagulation,[2] or increased risk of intracranial processes such as metastatic malignancy.[4]

WHY NEUROIMAGING IS NOT HELPFUL IN EVALUATING UNDIFFERENTIATED HOSPITALIZED PATIENTS WITH DELIRIUM

A number of studies have evaluated the diagnostic yield of neuroimaging in hospitalized patients with delirium (Table).[6,7,10,11] Two studies included patients with delirium that developed after hospitalization[10,11] and two included patients with delirium at admission.[6,7]

Theisen-Toupal et al. conducted a retrospective study of 220 hospitalized general medical patients who underwent head CT scans for an indication of delirium, altered mental status, confusion, encephalopathy, somnolence or unresponsiveness.[10] Patients were excluded if they had a history of falls, head trauma, or new neurologic deficits in the preceding two weeks or if the admitting diagnosis was stroke or cerebral hemorrhage. Additionally, the authors limited patients to those who developed delirium 24 hours or more after admission. There were 6/220 (2.7%) patients identified with an acute intracranial process. Of these six patients, three were receiving anticoagulation. An additional 4/220 (1.8%) head CT scans were identified as equivocal, prompting further neuroimaging, which ultimately showed chronic findings.

Vijayakrishnan et al. performed a retrospective review of 400 hospitalized patients who underwent inpatient CT scans, then limited to those with new delirium.[11] They identified 36 patients, of which four (11%) had acute findings on CT: one case each of acute hemorrhage, subdural hematoma, brain metastases, and septic emboli. The authors state "all the four patients had preimaging clinical symptoms and signs, which warranted imaging as per guidelines suggested by the British Geriatrics Society and the Australian and New Zealand Society for Geriatric Medicine," though they do not provide further details. The strength of this paper is that it isolated patients

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TABLE. **Studies of Neuroimaging for Hospitalized Patients with Delirium**

Lead Author	Year	Study Design	Population (n)	Setting	Methods	Definition of Positive Neuroimaging	Outcome Measures	Results
Lai[6]	2010	Case Control	Adult patients admitted to a delirium unit over an 18-month period (300 patients, 200 with head CT)	Single teaching hospital in Australia	CAM used by geriatricians to identify patients. Then chart review for additional predictive risk factors. Two clinicians reviewed the clinical significance of CT results.	Intracranial abnormalities accountable for a cause of delirium that resulted in a change in patient's management.	The yield of true positive CT findings showing an intracranial cause of delirium.	29/200 (14.5%) true positive CT findings, 13 with ischemic stroke, 7 with SDH, 9 with ICH. 3/200 (1.5%) had none of the three risk factors: focal neurologic deficits, recent falls, or deterioration in consciousness.
Thiesen-Toupal[10]	2014	Retrospective Cohort	Adult patients who underwent CT head scans on multiple medical floors over a 35-month period (1,714 head CT studies, 220 scans for delirium)	Single tertiary care center in the Northeast	Indications for scans were delirium, AMS, confusion, encephalopathy, or unresponsiveness. CT scans had to be done 24 hours after admission. Patients excluded if known fall, head trauma, or new neurologic deficit in the previous two weeks or admitted diagnosis of intracranial pathology.	Defined as an intracranial process that could explain delirium. "Equivocal" scans had findings of unclear significance.	Diagnostic yield of head CT imaging for identifying the cause of non-resolving or new-onset delirium.	6/220 (2.7%) positive scans and 4/220 (1.8%) equivocal. 3/6 positive scans were in anticoagulated patients.
Vijayakrishnan[11]	2015	Retrospective Cohort	Adult hospitalized patients who had CT head scans for mental status changes over a 12-month period (400 patients, 36 with an indication of delirium)	Single tertiary care center in the Northeast	Radiology logs reviewed using keywords: confusion, delirium, agitation, and AMS. Charts reviewed to include patients who developed AMS while inpatient. Patients with long-standing AMS with no worsening during inpatient stay were excluded.	Acute changes: new stroke, hemorrhage, infection, or neoplasm.	Acute CT scan findings that altered management.	4/36 (11%) CT scans with acute changes in patients with inpatient delirium. All 4 met imaging guidelines for recent falls, new neurologic deficits. or anticoagulation.
Hijazi[7]	2015	Retrospective Cohort	Adult patients diagnosed with delirium either at or during admission over a 20-month period (1653 patients with delirium, 538 with CT and/or MRI imaging)	Single tertiary care center in Australia	Patients selected by using ICD-10 codes for delirium or disorientation, disorientation NOS, other delirium, and delirium NOS. Delirium must have been documented prior to imaging request.	Acute/subacute stroke, hemorrhage, abscess, neoplasm, vasculitis, PRES, encephalitis, acute demyelination, or fat embolism.	The yield of CT and/or MRI imaging in patients with possible delirium.	78/538 (14.5%) positive CT head or MRI brain scans. Patient exam findings or risk factors for intracranial processes not described.

Abbreviations: AMS, altered mental status; CAM, Confusional Assessment Method; CT, computed tomography; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging; NOS, not otherwise specified; PRES, posterior reversible encephalopathy, syndrome; SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage.

who developed delirium while hospitalized; however, conclusions were limited by the small sample size.

Lai et al.'s case-control study evaluated 300 consecutive patients admitted to a delirium unit over 18 months.[6] Of these 300 patients, 200 (67%) had CT performed; 29/200 (14.5%) had intracranial findings on CT that explained their delirium, including 13 ischemic strokes, seven subdural hemorrhages, nine intracerebral hemorrhages, and three additional ischemic strokes that evolved on follow-up imaging but were not present on the initial scans. The authors performed univariate and multivariate analyses to identify risk factors for an intracranial cause of delirium. Only 3/29 patients with a positive scan did not have one of three main risk factors the authors identified: a fall in the preceding two weeks, new neurologic findings, or sudden deterioration of consciousness. It should be noted that authors did not define "deterioration of consciousness" and that all patients had confusion on admission to the unit, rather than developing during hospitalization.

Hijazi et al. conducted a retrospective cohort study over a 20-month period of 1,653 patients with delirium at the time of admission or during their hospitalization. Patients with delirium due to drug or medication withdrawal or "psychiatric reasons" were excluded. Overall, 538 (32.5%) patients underwent CT, MRI or both, and 78 (14.5%) patients had a positive finding on neuroimaging. This study's 14.5 % overall yield matches that of Lai et al. Unfortunately, the study included all patients with delirium and did not report the rates of fall, neurologic deficits, and/or use of anticoagulation among those with positive neuroimaging. This limits the generalizability of the findings to a cohort of patients without intracranial pathology risk factors.

The reported yield of neuroimaging for hospitalized patients with delirium ranged from 2.7% to 14.5% across studies. However, in studies taking into account specific patient risk factors; the reported yields in patients without focal neurologic findings, new decline in mental status, systemic anticoagulation, or recent falls were 0%,[11] 1.4%,[10] and 1.5%.[6] While a rate of 1.5% may appear high for a serious outcome such as stroke or intracranial bleeding, it is comparable to rates reported for missed major cardiac events in clinical algorithms for evaluating chest pain.[12] It should also be noted that neuroimaging is imperfect

for acute stroke, and thus the positive or negative predictive value may be poor in the setting of low prevalence. For example, for detection of any acute stroke, the sensitivity/specificity of MRI and CT are 83%/97% and 26%/98% respectively.[13]

Neuroimaging is expensive and has risks. The average charge for a head CT is approximately $1,400 at academic institutions.[14] Moreover, computed tomography exposes patients to significant radiation and up to 2% of malignancies in the United States may be attributable to prior tomography exposure.[15] Additionally, there are non-negligible rates of incidental findings during neuroimaging, 1% for CT[16] and 2.7%-13.7% for MRI,[17,18] which may result in further evaluation or treatment that causes significant patient anxiety. Obtaining neuroimaging on delirious patients can be time consuming and labor intensive, which could delay care to other patients. Additionally, sedating medications are often administered to agitated patients prior to imaging, which risk worsening delirium. Ordering neuroimaging for all patients with acute delirium, therefore, exposes the large majority to unnecessary costs and potential harms.

WHEN NEUROIMAGING TO EVALUATE DELIRIUM IN HOSPITALIZED PATIENTS COULD BE REASONABLE

The diagnostic yield of head CT in the evaluation of delirium is significantly higher in patients with specific risk factors. Lai et al. found adjusted odds ratios for abnormal CT of 18.2 in patients with new focal deficits, 5.6 with a fall in the preceding two weeks and 4.6 in patients with deterioration in consciousness. Patients with systemic anticoagulation had higher unadjusted, (OR 2.4) though not adjusted odds of having an abnormal CT.[6] Thiesen-Toupal et al. excluded patients with recent falls or neurologic deficits but reported that three out of six delirious patients with abnormal neuroimaging were anticoagulated.[10] Vijayakrishnan et al. found that all four delirious patients with intracranial findings met guideline criteria for neuroimaging.[11] Thus, current recommendations for neuroimaging in delirious patients with falls, focal neurologic deficits, or systemic anticoagulation are appropriate. In situations when a provider lacks an accurate history and is unable to determine if risk factors are present (for example a confused patient found sitting on the floor next to the bed), it may also be reasonable to consider neuroimaging.

Data are limited, but some authors advocate for neuroimaging in cases of delirium that do not improve with treatment.[6] Additionally, it may be reasonable to consider neuroimaging in delirium patients with predispositions to embolic or metastatic intracranial processes such as endovascular infections and certain malignancies.[4]

WHAT YOU SHOULD DO INSTEAD OF NEUROIMAGING TO EVALUATE DELIRIUM IN HOSPITALIZED PATIENTS

Hospitalized patients with acute confusion should be assessed for delirium with a validated instrument such as the Confusion Assessment Method (CAM).[19,20] The original CAM included several components: acute change in mental status with a fluctuating course and inattention, plus either disorganized thinking and/or altered level of consciousness. Multiple delirium assessment tools have been created and validated, all of which include inattention as a required feature. A recent hospital-based study using a two-item bedside test asking the patient to name the day of the week and list the months of the year backwards detected delirium with a sensitivity of 93% and specificity of 64%.[21] Once the diagnosis of delirium is established, evaluation should begin with a careful history and physical examination focused on the identification of risk factors such as physical restraints, indwelling urinary catheters, and drugs known to precipitate delirium, particularly those with withdrawal potential, anticholinergic properties, and sedative-hypnotic agents.[22-24] Delirium may be the first harbinger of serious medical illness and specific testing should be guided by clinical suspicion. In general, a thorough physical examination should look for focal neurologic deficits, hypoxia, signs of infection, and other inflammatory or painful processes that could precipitate delirium.[25] Targeted laboratory evaluation may include a basic metabolic panel to identify electrolyte (including calcium) and metabolic derangements, complete blood count, and urinalysis if infection is suspected.

RECOMMENDATIONS

- Use a validated instrument such as CAM to evaluate hospitalized patients who develop altered mental status.
- Delirious patients should undergo a thorough history including a review of medications, physical exam, and targeted laboratory testing aimed at identifying common risk factors and precipitants of delirium that should be addressed.
- Perform neuroimaging if there is a history of fall or head trauma in the preceding two weeks, any new focal abnormalities on neurologic exam or if the patient is receiving systemic anticoagulation.
- It may be reasonable to consider neuroimaging for patients with an atypical course of delirium, such as a sudden decline in the level of consciousness, persistence despite addressing identified factors, or if there is a high degree of suspicion for embolic or metastatic processes.

CONCLUSIONS

Performing neuroimaging in undifferentiated patients who develop delirium while hospitalized has a low diagnostic yield, is costly, and is potentially harmful. Neuroimaging should be reserved for those with identified risk factors for intracranial pathology. For the patient described in the initial vignette with no risk factors for intracranial cause, neuroimaging would be unlikely to contribute to her care. To change provider beliefs and behaviors regarding neuroimaging, prospective studies evaluating guideline implementation are needed. However, based on the current evidence, neuroimaging should be reserved for those with identified risk factors.

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 e-mailing TWDFNR@hospitalmedicine.org.

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Early Warning Systems: The Neglected Importance of Timing

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Automated early warning systems (EWSs) use data inputs to recognize clinical states requiring time-sensitive intervention and then generate notifications through different modalities to clinicians. EWSs serve as common tools for improving the recognition and treatment of important clinical states such as sepsis. However, despite the early enthusiasm, these warning systems have often yielded disappointing outcomes. In sepsis, for example, EWSs have shown mixed results in clinical trials, and concerns regarding the overuse of EWSs in diagnosing sepsis have grown.[1-4] We argue that inattention to the importance of timing in EWS training and evaluation provides one reason that EWSs have underperformed. Thus, to improve care, a warning system must not only identify the clinical state accurately, but it must also do so in a sufficiently timely manner to implement the associated interventions, such as administration of antibiotics for sepsis. Although the literature has occasionally highlighted the importance of timing in electronic surveillance systems, no one has linked the temporal dependence of performance metrics and intervention feasibility to the failure of such warning systems and explained how to operationalize timing in their development.[5-8] Using sepsis as an example, we explain why timing is important and propose new metrics and strategies for training and evaluating EWS models. EWSs are divided into two types: detection systems that recognize critical illnesses at a particular moment and prediction systems that estimate risk of deterioration over varying time frames.[9] We focus primarily on detection systems, but our analysis is also important for prediction systems, which we will discuss in the last section.

CLINICAL TIME ZERO AND POSITIVE PREDICTIVE VALUE

EWS metrics have evolved from focusing on crude measures of discrimination to more clinically relevant metrics, such as the positive predictive value (PPV). The common performance metrics, including the c-statistic, evaluate the performance of EWSs in distinguishing events from nonevents, such as the presence or absence of sepsis in hospitalized patients. However, the c-statistic does not account for disease prevalence. A given c-statistic is compatible with a wide range of PPVs; a low PPV may limit an EWS's usefulness to promote interventions and generate increased alert fatigue.[10]

However, the PPV, although important, provides no information on the timing of state recognition in relation to clinical time zero. Time zero is the first moment at which a critical state can be recognized based on available data and current medical science. Different approaches, including laboratory values, clinical assessments, retrospective chart reviews, triage times, and others, have been used to measure time zero.[8,11-13] All these approaches feature advantages and disadvantages; the evaluation of timing will exhibit sensitivity to the approach used.[14] Further work is needed to gain additional insights into the measurement of time zero.

Just as the same c-statistic is consistent with varying PPVs, so too is the same PPV consistent with different timing in relation to clinical time zero (Figure). An alert-level PPV of 50% indicates that 50% of the alerts signify true cases of sepsis. However, such a value could also indicate any of the following:

a) 50% true cases of sepsis, with a mean time of 35 minutes after clinical time zero;
b) 50% true cases, with a mean time of 60 minutes before clinical time zero (prediction EWS);
c) 50% true cases of sepsis, with a mean time of 1.3 days since clinical time zero, but with 70% of these cases undiagnosed at the time of EWS detection;
d) 50% true cases of cases, with mean time of 1.3 days since clinical time zero, that is, all cases among those promptly detected and treated through routine clinician oversight.

Each of these situations features differing clinical utility to help meet the hospital objective of increasing early administration of antibiotics. More generally, three dimensions of timing are important for detection systems. The first dimension is the timing of detection relative to time zero. The second is the timing relative to "real-world" clinician detection. The third is timing with respect to the associated clinical objective. For a given PPV, an EWS performs better when detecting a state (1) at, near, or in advance of time zero, (2) prior to clinician detection, and (3) sufficiently in advance of an operational objective to promote change. On the other hand, when an EWS consistently sends alerts after clinician action, it serves a lesser purpose and risks causing alert fatigue; such cases have been described in studies.[15]

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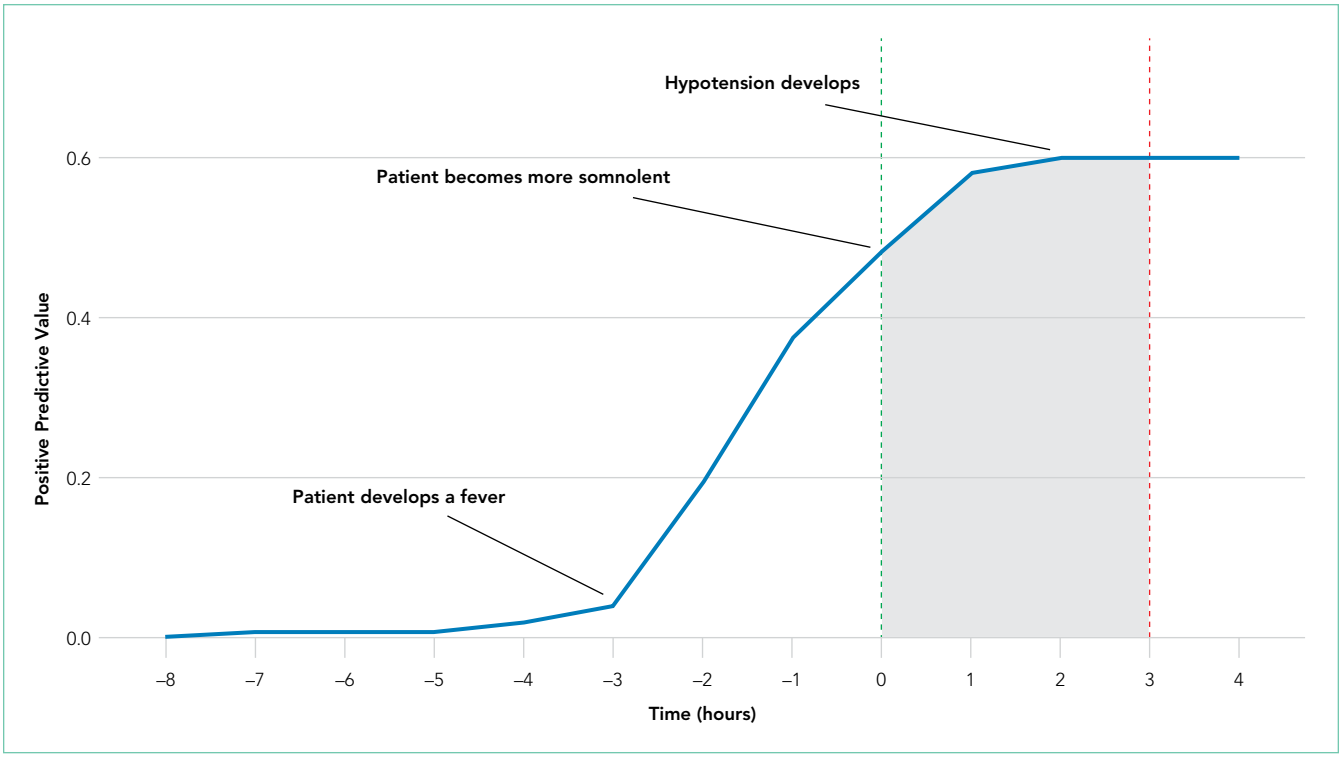

FIG. The Positive Predictive Value Relative to the Evolution of Sepsis. The PPV changes with sepsis evolution, as more information becomes available. The green dotted line depicts clinical time zero, that is, the first point at which sepsis could be recognized based on available data and current medical science. The red dotted line depicts the end of a "clinically important window" based on the operational objective associated with the early warning system.

OPERATIONALIZING TIMING IN EWS TRAINING AND EVALUATION

Acknowledging the importance of timing features implications for researchers and health system leaders. Researchers who develop EWS should include how these systems perform relative to both time zero and critical milestones in the clinical course. Operational leadership should understand the trade-offs that occur between alert fatigue (through lower PPV at the margin with earlier detection) and lead time to implement an intervention. Navigating these trade-offs involves a complex organizational decision. The "number needed to evaluate" is one way to quantify this fatigue factor.[16] Such a measure gives a sense of the number of cases a clinician will need to evaluate per event. Collaborations between clinical leadership, operational leadership, and data scientists are needed to determine how to evaluate individual systems.

A good metric should capture the three important dimensions of timing while retaining intuitiveness to clinicians and leadership. One graphical option involves plotting the PPVs over time and relative to the clinical state evolution (Figure). This PPV-over-time curve shows when true positives occur relative to the time course of sepsis, including the three major dimensions of timing. This curve can also show a clinically important window (CIW), which is bounded on the right by the latest point in time when recognition could still meet the clinical objective. For sepsis, the curve might be bounded at 2.5 hours to meet an objective of antibiotics within three hours, with the assumption that 0.5 hour is needed for a response. For detection systems, the window would be bounded on the left by clinical time zero. The graph can also designate the point when most cases of sepsis have been recognized clinically with historical data. The Figure depicts an example curve for a detection model.

The metrics derived from this curve may be used alongside the PPV for training and evaluation. Often, adjusting the PPV for its relationship to time zero and the CIW will aid in recognizing the existence of a time beyond which detection fails to help achieve the intended intervention. Detection beyond the window should not credited as a true positive if it fails to facilitate the objective. One option is to credit detection at or before time zero as one and discount later detection by the delay from time zero. More specifically, a true positive could be discounted by the difference between the end of the CIW and the moment of detection divided by the CIW length. This discounted PPV could be displayed alongside the PPV to gauge the temporal dimension of performance and be used for training.

The use of timing places additional demands on validation owing to the need for a time-based gold standard. In such a case, the unit of analysis in system development might not be the patient encounter but rather the patient-hour or patient-15-minute epoch, depending on how frequently the EWS updates risk information and may alert. By contrast, the sepsis detection models used in administrative databases rely on an encounter-level PPV, which provides more limited information compared with real-time EWSs.[17] When time zero cannot be measured, alternatives may be used to capture several dimensions of timing; these alternatives include measurement

of the percentage of cases that recognize the event prior to clinicians.[15]

MOVING TOWARD PREDICTION

Detection systems face the limitation that they lack the capability to identify a state before its occurrence. Prediction systems are more likely to be actionable, as they provide more lead time for intervention, but accurate prediction models are also more difficult to develop. With a predictive system, an additional dimension of timing becomes important: the time horizon for prediction. Prediction models may be trained to recognize a state within a specific time frame (eg, 6, 12, or 24 hours), and test characteristics, including PPV, may vary with the window.[18] A given PPV (of eventual development of sepsis) is compatible with varying time windows and thus again lacks important information on performance.

The timing relative to clinical time zero remains important for prediction. For a predictive EWS, the graph in the figure may be expected to shift to the left. Models with good performance will occasionally send an alert after time zero. For a prediction system with a time horizon of six hours, it is more useful to have alerts occur a mean time of four hours prior to time zero than four minutes prior.

CONCLUSION

Improving the clinical utility of EWSs requires better measurement of timing. Researchers should incorporate timing into system development, and operational leaders should be cognizant of timing during implementation. Specific steps should include devising better strategies to estimate the relationship of state recognition to clinical time zero and developing methods to discount recognition when it occurs too late to be actionable.

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Restarting Anticoagulants after a Gastrointestinal Hemorrhage—Between Rockall and a Hard Place

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Anticoagulant use to prevent ischemic strokes in patients with atrial fibrillation (AF) continues to be one of the most challenging decisions facing patients and their physicians, in large part due to significant patient-to-patient variation in both AF-related stroke risk and anticoagulant-associated hemorrhage risk. Now, add a layer of complexity—.how should one approach anticoagulant use following an adverse event such as an acute upper gastrointestinal (GI) hemorrhage? On the one side, the risk of ischemic stroke, and on the other, the risk of recurrent bleeding, either of which can lead to death or disability. Making this decision requires humility, clinical acumen, shared decision-making, and data.

Data on this subject are sparse.[1,2] Observational studies show that patients who restart anticoagulants after GI hemorrhage experience fewer ischemic strokes. These studies also show that patients who restart anticoagulant therapy are healthier than those who do not—in measurable ways and, importantly, in unmeasurable ways. Thus far, observational studies have not sufficiently dealt with confounding by indication; that is, patients who restart anticoagulants are fundamentally different than patients who do not.

In this issue of the *Journal of Hospital Medicine®*, Pappas et al. focus on the optimal timing of resuming oral anticoagulation in patients who have sustained acute upper GI bleeds while receiving oral anticoagulation for AF.[3] They use a microsimulation modeling approach to address this question, by creating a synthetic population of patients reflective of age, gender, and comorbidities in a United States population of patients with AF. Using data from epidemiologic studies that describe the risk of rebleeding, hemorrhagic complications, and ischemic stroke as well as the quality of life associated with each of these events, the authors have constructed a decision analytic model to determine the optimal day to restart anticoagulation. This modeling approach mitigates confounding by indication, a limitation of observational studies. They report that the optimal day to restart anticoagulant therapy is in the range of 32-51 days. As one would predict, when using direct-acting anticoagulants and for patients with high stroke risk, the investigators find that restarting therapy earlier is associated with greater benefit. These findings help to untangle a knot of risk and benefits facing patients with AF following an acute GI hemorrhage.

Interpreting the results relies on an understanding of the strengths and weaknesses of simulation modeling and the data used in the analysis. Like any research method, the devil is in the details. Stitching together event rates and outcomes from multiple studies, the results of a simulation model are only as good as the studies the model draws from. In particular, assumptions regarding the time-dependent decline in rebleeding risk are a critical component of determining the optimal time to resume anticoagulation. The authors had to make multiple assumptions to project the 24-hour risk of rebleeding determined from the Rockall score to estimate the risk of rebleeding over the next days to months.[4] Consequently, the results are likely overly precise. Practically, 30-50 days or four to eight weeks may better reflect the precision of the study findings.

Results on optimal timing of resuming anticoagulation therapy are most applicable for patients when the decision to restart anticoagulants has already been made. We part ways with the authors in their conclusion that these results confirm that anticoagulants should be restarted. There are multiple appropriate reasons why anticoagulant therapy should not be restarted following an acute upper GI hemorrhage. For example, in observational studies, patients not restarted on anticoagulant therapy were more likely to have a history of falls and to have had severe bleeds.[1] Furthermore, patients who do not restart therapy are more likely to die in follow-up. It is tempting to use this fact to support restarting anticoagulants. However, when the causes of death are examined, the vast majority of deaths were unrelated to thrombosis or hemorrhage.[2] Patients with AF are older and have multiple comorbidities and life-limiting conditions. Accordingly, the results of this study are better used to engage patients in shared decision-making and contextualized in the broader picture of patients' health and goals.[5]

Restarting anticoagulants after a GI hemorrhage is a difficult and high-stakes clinical decision. The study by Pappas et al. uses a simulation model to advance our understanding about the optimal timing to restart anticoagulants. By integrating the dynamic risk of ischemic stroke and recurrent hemorrhage following GI hemorrhage, they estimate the maximal benefit when anticoagulants are restarted between 30 days and 50 days after hemorrhage. The results of their analysis are best used to inform timing among patients where the decision to restart anticoagulants has already been made. The analysis also provides a useful starting point for shared decision-making by highlighting that the optimal net benefit is influenced by

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patient-to-patient variation in the underlying AF-related stroke risk and anticoagulant-associated rebleeding risk.

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Frailty Tools are Not Yet Ready for Prime Time in High-Risk Identification

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In this issue of the *Journal of Hospital Medicine®*, McAlister et al.[1] compared the ability of the Clinical Frailty Scale (CFS) and the Hospital Frailty Risk Score (HFRS) to predict 30-day readmission or death. The authors prospectively assessed adult patients aged ≥18 years without cognitive impairment being discharged back to the community after medical admissions. They demonstrated only modest overlap in frailty designation between HFRS and CFS and concluded that CFS is better than HFRS for predicting the outcomes of interest.

Before a prediction rule is widely adopted for use in routine practice, robust external validation is needed.[2] Factors such as the prevalence of disease in a population, the clinical competencies of a health system, the socioeconomic status, and the ethnicity of the population can all affect how well a clinical rule performs, but may not become apparent until a prospective validation in a different population is attempted.

In developing the HFRS, Gilbert et al. aimed to create a low-cost, highly generalizable method of identifying frailty using International Classification of Diseases (ICD) 10 billing codes.[3] The derivation and validation cohorts for HFRS included older adults aged >75 years in the United Kingdom, many of whom had cognitive impairment. Therefore, it is not surprising that the tool behaved very differently in the younger Canadian cohort described by McAlister et al. where persons with cognitive impairment were excluded. That the HFRS had less predictability in the Canadian cohort may simply indicate that it performs better in an older population with cognitive vulnerabilities; given the frailty constructs of the CFS, it may provide less insights in older populations.

We applaud the efforts to find a way to better identify high-risk groups of adults. We also appreciate the increasing attention to function and other frailty-related domains in risk prediction models. Nevertheless, we recommend caution in using any of the many existing frailty indices[4] in risk prediction tools unless it is clear what domains of frailty are most relevant for the predicted outcome and what population is the subject of interest.

One of the challenges of choosing an appropriate frailty tool is that different tools are measuring different domains or constructs of frailty. Most consider frailty either as a physical phenotype[5] or as a more multifaceted construct with impairments in physical and mental health, function, and social interaction.[6] There is often poor overlap between those individuals identified as frail by different measures, highlighting that they are in fact identifying different people within the population studied and have different predictive abilities.

An ideal frailty tool for clinical use would allow clinicians to identify high-risk patients relative to specific outcome(s) in real time prior to discharge from hospital or prior to a sentinel event in the community. CFS can be calculated at the bedside, but HFRS calculation can only be done retrospectively when medical records are coded for claims after discharge. This makes HFRS more suited to research or post hoc quality measure work and CFS more suited to clinical use as the authors describe.

Although using a frailty indicator to help determine those at high risk of early readmission is an important objective, the presence of frailty accounts for only part of a person's risk for readmission or other untoward events. Reasons for readmissions are complex and often heavily weighted on a lack of social and community supports. A deeper understanding of the reasons for readmission is needed to establish whether readmission of these complex patients has more to do with frailty or other drivers such as poor transitions of care.

The prevalence of frailty will continue to increase as our population ages. Definitions of frailty vary, but there is a broad agreement that frailty, regardless of how it is constructed, increases with age, results in multisystem changes, and leads to increased healthcare utilization and costs. Preventing the development of frailty, identifying frailty, and developing interventions to address frailty in and out of the hospital setting are all vital. We welcome further research regarding the biopsychosocial constructs of frailty, how they overlap with the frailty phenotype, and how these constructs inform both our understanding of frailty and the use of frailty tools.

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Who Will Guard the Guardians? Preventing Drug Diversion in Hospitals

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The patient safety field rightly focuses on identifying and addressing problems with systems of care. From the patient's perspective, however, underlying systems issues might be less critical than another unspoken question: can I trust the people who are taking care of me? Last year, a popular podcast[1] detailed the shocking story of Dallas neurosurgeon Christopher Duntsch, who was responsible for the death of two patients and severe injuries in dozens of other patients over two years. Although fellow surgeons had raised concerns about his surgical skill and professionalism almost immediately after he entered practice, multiple hospitals allowed him to continue operating until the Texas Medical Board revoked his license. Duntsch was ultimately prosecuted, convicted, and sentenced to life imprisonment, in what is believed to be the first case of a physician receiving criminal punishment for malpractice.

Only a small proportion of clinicians repeatedly harm patients as Duntsch did, and the harm they cause accounts for only a small share of the preventable adverse events that patients experience. Understandably, cases of individual clinicians who directly harm patients tend to capture the public's attention, as they vividly illustrate how vulnerable patients are when they entrust their health to a clinician. As a result, these cases have a significant effect on the patient's trust in healthcare institutions.

In this issue of the *Journal of Hospital Medicine®*, Fan and colleagues[2] describe the problem of controlled-substance diversion in hospitals and review the contributors and potential solutions to this issue. Their thorough and insightful review highlights a growing problem that is probably invisible to most hospitalists. Diversion of controlled substances can happen at any stage of the medication use process, from procurement to disposal, and drugs can be diverted by healthcare workers, nonclinical staff, patients, and caregivers. Perhaps most concerning to hospitalists, diversion at the prescribing and administration stages can directly affect patient care. Strategies used to individualize pain control, such as using flexible dose ranges for opioids, can be manipulated to facilitate diversion at the expense of the patient's suffering.

The review presents a comprehensive summary of safeguards against diversion at each stage of the medication use process and appropriately emphasizes system-level solutions. These include analyzing electronic health record data to identify unusual patterns of controlled substance use and developing dedicated diversion investigation teams. These measures, if implemented, are likely to be effective at reducing the risk of diversion. However, given the complexity of medication use, eliminating this risk is unrealistic. Opioids are used in more than half of all nonsurgical hospital admissions;[3] although this proportion may be decreasing due to efforts to curb opioid overprescribing, many hospitalized patients still require opioids or other controlled substances for symptom control. The opportunity to divert controlled substances will always be present.

Eliminating the problem of drug diversion in hospitals will require addressing the individuals who divert controlled substances and strengthening the medication safety system. The term "impaired clinician" is used to describe clinicians who cannot provide competent care due to illness, mental health, or a substance-use disorder. In an influential 2006 commentary, Leape and Fromson made the case that physician performance impairment is often a symptom of underlying disorders, ranging from short-term, reversible issues (eg, an episode of burnout or depression) to long-term problems that can lead to permanent consequences (eg, physical illness or substance-use disorders).[4] In this framework, a clinician who diverts controlled substances represents a particularly extreme example of the broader problem of physicians who are unable to perform their professional responsibilities.

Leape and Fromson called for proactively identifying clinicians at risk of performance failure and intervening to remediate or discipline them before patients are harmed. To accomplish this, they envisioned a system with three key characteristics:

- Fairness: All physicians should be subject to regular assessment, and the same standards should be applied to all physicians in the same discipline.
- Objectivity: Performance assessment should be based on objective data.
- Responsiveness: Physicians with performance issues should be identified and given feedback promptly, and provided with opportunities for remediation and assistance when underlying conditions are affecting their performance.

Some progress has been made toward this goal, especially in identifying underlying factors that predispose to performance problems.[5] There is also greater awareness of underlying factors that may predispose to more subtle performance deterioration. The recent focus on burnout and well-being among physicians is long overdue, and the recent Charter on Physician Well-Being[6] articulates important principles for healthcare or-

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ganizations to address this epidemic. Substance-use disorder is a recognized risk factor for performance impairment. Physicians have a higher rate of prescription drug abuse and a similar overall rate of substance-use disorders compared to the general population. While there is limited research around the risk factors for drug diversion by physicians, qualitative studies[7] of physicians undergoing treatment for substance-use disorders found that most began diverting drugs to manage physical pain, emotional or psychiatric distress, or acutely stressful situations. It is plausible that many burned out or depressed clinicians are turning to illicit substances to self-medicate increasing the risk of diversion.

However, 13 years after Leape and Fromson's commentary was published, it is difficult to conclude that their vision has been achieved. Objectivity in physician performance assessment is still lacking, and most practicing physicians do not receive any form of regular assessment. This places the onus on members of the healthcare team to identify poorly performing colleagues before patients are harmed. Although nearly all states mandate that physicians report impaired colleagues to either the state medical board or a physician rehabilitation program, healthcare professionals are often reluctant[8] to report colleagues with performance issues, and clinicians are also unlikely[9] to self-report mental health or substance-use issues due to stigma and fear that their ability to practice may be at risk.

Even when colleagues do raise alarms—as was the case with Dr. Duntsch, who required treatment for a substance-use disorder during residency—existing regulatory mechanisms either lack evidence of effectiveness or are not applied consistently. State licensing boards play a crucial role in identifying problems with clinicians and have the power to authorize remediation or disciplinary measures. However, individual states vary widely[10] in their likelihood of disciplining physicians for similar offenses. The board certification process is intended to ensure that only fully competent physicians can practice medicine independently. However, there is little evidence that the certification process ensures that clinicians maintain their skills, and significant controversy has accompanied efforts to revise the maintenance of certification process. The medical malpractice system aims to improve patient safety by ensuring compensation when patients are injured and by deterring substandard clinicians from practicing. Unfortunately, the system often fails to meet this goal, as malpractice claims are rarely filed even when patients are harmed due to negligent care.[11]

Given the widespread availability of controlled substances in hospitals, comprehensive solutions must incorporate the systems-based solutions proffered by Fan and colleagues and address individual clinicians (and staff) who divert drugs. These clinicians are likely to share some of the same risk factors as clinicians who cannot perform their professional responsibilities for other reasons. Major system changes are necessary to minimize the risk of short-term conditions that could affect physician performance (such as burnout) and develop robust methods to identify clinicians with longer-term issues affecting their performance (such as substance-use disorders).

Although individual clinician performance problems likely account for a small proportion of adverse events, these issues strike at the heart of the physician-patient relationship and have a profound impact on patients' trust in the healthcare system. Healthcare organizations must maintain transparent and effective processes for addressing performance failures such as drug diversion by clinicians, even if these processes are rarely deployed.

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