

THE Hospitalist[®]

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Dr. Mangla Gulati

Battling hospitalist burnout

Higher salaries are not sufficient

By Thomas R. Collins

Hospitalist Rahul C. Borsadia, MD, had been working with Orlando Health Inpatient Medicine Group since the year of its founding in 2011.

The salaries of the practice's physicians back then were based on relative value units (RVU) – the more patients that physicians saw, the higher their salaries. But a problem arose, Dr. Borsadia said. Physicians were trying to squeeze in two dozen or more patients a day “in a practice that is modeled for quality.”

“By the time the end of the day comes, it’s 9 or 10 p.m. and you are leaving but coming back at 6:30 the next morning. So, lack of sleep, more patients, striving to earn that higher salary,” he said. “The desire to perform quality work with that kind of patient load was not fulfilled and that led to dissatisfaction and stress, which led to irritation and exodus from the group.”

Three years ago, the practice transitioned to a throughput process with a census limit of 18 patients or fewer, without an RVU system, but with salary incentives based on patient satisfaction, billing, and documentation.

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Photograph by Christopher Lewkovich

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THE HOSPITALIST is the official newspaper of the Society of Hospital Medicine, reporting on issues and trends in hospital medicine. THE HOSPITALIST reaches more than 35,000 hospitalists, physician assistants, nurse practitioners, medical residents, and health care administrators interested in the practice and business of hospital medicine. Content for THE HOSPITALIST is provided by Frontline Medical Communications. Content for the Society Pages is provided by the Society of Hospital Medicine.

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THE HOSPITALIST (ISSN 1553-085X) is published monthly for the Society of Hospital Medicine by Frontline Medical Communications Inc., 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609. Print subscriptions are free for Society of Hospital Medicine members. Annual paid subscriptions are available to all others for the following rates:

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Single Issue: Current – \$35 (US), \$47 (Canada/Mexico), \$59 (All Other Nations) Back Issue – \$47 (US), \$59 (Canada/Mexico), \$71 (All Other Nations)

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The
Hospitalist

Laurence Wellikson, MD, MHM, announces retirement as CEO of SHM

Society recognizes Dr. Wellikson's leadership, retains Spencer Stuart for successor search

After serving as the first and only chief executive officer of the Society of Hospital Medicine since January of 2000, Laurence Wellikson, MD, MHM, has announced his retirement effective on Dec. 31, 2020. In parallel, the SHM Board of Directors has commenced a search for his successor.

"When I began as CEO 20 years ago, SHM – then known as the National Association of Inpatient Physicians – was a young national organization with approximately 500 members, and there was minimal understanding as to the value that hospitalists could add to their health communities," Dr. Wellikson said. "I am proud to say that, nearly 20 years later, SHM boasts a growing membership of more than 17,000, and hospitalists are on the front line of innovation as a driving force in improving patient care."

SHM has grown not only its mem-

bership but also its diverse portfolio of offerings for hospital medicine professionals under Dr. Wellikson's leadership. Its first annual conference welcomed approximately 300 attendees; the most recent conference, Hospital Medicine 2019, saw that number increase more than 10-fold to nearly 4,000. Its conferences, publications, online education, chapter program, advocacy efforts, quality improvement programs, and more have evolved significantly to ensure hospitalists at all stages of their careers – and those who support them – have access to resources to keep them up to date and demonstrate their value in America's health care system.

During Dr. Wellikson's tenure, SHM launched its peer-reviewed *Journal of Hospital Medicine*, the premier, ISI-indexed publication for the specialty, successfully advocated for a Focused Practice in Hospital Medicine certification option and C6

hospitalist specialty code, and earned the John M. Eisenberg Patient Safety and Quality Award for its quality improvement programs. These are just a few of the noteworthy accomplish-



Dr. Wellikson

ments that have elevated SHM as a key partner for hospitalists and their institutions.

To assist with the search for SHM's next CEO, the society has retained

Spencer Stuart, a leading global executive and leadership advisory firm. The search process is being overseen by a diverse search committee led by the president-elect of SHM's Board of Directors, Danielle B. Scheurer, MD, SFHM, MSCR.

"On behalf of the society and its members, I want to extend a sincere thank you to Larry for his years of dedication and service to SHM, its staff, and the hospital medicine professionals we serve," said Christopher Frost, MD, SFHM, president of SHM's Board of Directors. "His legacy will allow SHM to continue its growth trajectory through key programs and services supporting members' needs for years to come. Larry has taken the specialty of hospital medicine and created a movement in SHM, where the entire hospital medicine team can come for education, community, and betterment of the care we provide to our patients. We are indebted to him beyond words."

Those who are interested in leading SHM into the future as its next CEO are encouraged to contact either Jennifer P. Heenan (jheenan@spencerstuart.com) or Mark Furman, MD (mfurman@spencerstuart.com).

Hospitalist Movers and Shakers

By Matt Pesyna

Mark Williams, MD, MHM, FACP, recently was appointed chief quality and transformation officer for the University of Kentucky's UK HealthCare (Lexington). Dr. Williams, a tenured professor in the division of hospital medicine at the UK College of Medicine, will serve as chair of UK HealthCare's Executive Quality Committee. Dr. Williams will lead integration of quality improvement, safety, and quality reporting with data analytics.

Dr. Williams established the first hospitalist program at a public hospital (Grady Memorial Hospital) and academic hospitalist programs at Emory University, Northwestern University, and UK HealthCare. An inaugural member of SHM, he is a past president, was the founding editor-in-chief of the *Journal of Hospital Medicine*, and led SHM's Project BOOST.

Also at UK HealthCare, **Romil Chadha, MD, MPH, SFHM, FACP**, has been named interim chief of the division of hospital medicine and medical director of Physician Information



Dr. Chadha

Technology Services. Previously, he was associate chief of the division of hospital medicine, and he also serves as medical director of telemetry.

Dr. Chadha is the founder of the Kentucky chapter of SHM, where he is the immediate past president. He is also the codirector of the Heartland Hospital Medicine Conference.

Amit Vashist, MD, MBA, CPE, FHM, FACP, FAPA, has been named chief clinical officer at Ballad Health, a 21-hospital health system in Northeast Tennessee, Southwest Virginia, Northwest North Carolina, and Southeast Kentucky.



Dr. Vashist

In his new role, he will focus on clinical quality, value-based initiatives to improve quality while reducing cost of care, performance improvement, oversight of the clinical delivery of care, and will be the liaison to the Ballad Health Clinical Council. Dr. Vashist is a member of The Hospitalist's editorial advisory board.

Nagendra Gupta, MD, FACP, CPE, has been appointed to the American Board of Internal Medicine's Internal Medicine Specialty Board. ABIM Specialty Boards are responsible for the broad definition of the discipline across Certification and Maintenance of Certification (MOC). Special-



Dr. Gupta

ty Board members work with physicians and medical societies to develop Certification and MOC credentials to recognize physicians for their specialized knowledge and commitment to staying current in their field.

Dr. Gupta is a full-time practicing hospitalist with Apogee Physicians and currently serves as the director of the hospitalist program at Texas Health Arlington Memorial Hospital. He also serves as vice president for SHM's North Central Texas Chapter.

T. Steen Trawick Jr., MD, was named the CEO of Christus Shreveport-Bossier Health System in Shreveport, La., in August 2019.

Dr. Trawick has worked for Christus as a pediatric hospitalist since 2005 and most recently has served concurrently as associate chief medical officer for Sound Physicians. Through Sound Physicians, Dr. Trawick oversees the hospitalist and emergency medical programs for Christus and other hospitals – 14 in total – in Texas and Louisiana. He has worked in that role for the past 6 years.



Dr. Trawick

Continued on following page

Observation versus inpatient status

A dilemma for hospitalists and patients

By Isha Puri, MD, MPH

A federal effort to reduce health care expenditures has left many older Medicare recipients experiencing the sticker shock of “observation status.” Patients who are not sick enough to meet inpatient admission criteria, however, still require hospitalization, and may be placed under Medicare observation care.

Seniors can get frustrated, confused, and anxious as their status can be changed while they are in the hospital, and they may receive large medical bills after they are discharged. The Centers for Medicare & Medicaid Services’ “3-day rule” mandates that Medicare will not pay for skilled nursing facility care unless the patient is admitted as an “inpatient” for at least 3 days. Observation days do not count toward this 3-day hospital stay.

There has been an increase in outpatient services over the years since 2006. The 2018 *State of Hospital Medicine Report (SoHM)* highlights the percentage of discharges based on hospitalists’ billed Current Procedural Terminology codes. Codes 99217 (observation discharge) and 99238-99239 (inpatient discharge) were used to calculate the percentages. 80.7% of adult medicine hospitalist discharges were coded using inpatient discharge codes, while 19.3% of patients were discharged with observation discharge codes.

In the 2016 *SoHM* report, the ratio was 76.0% inpatient and 21.1% observation codes, and in the 2014 report we saw 80.3% inpatient and 16.1% observation discharges. But in both of those surveys, same-day admission/discharge codes were also separately reported, which did not occur in 2018. That makes year-over-year

comparison of the data challenging.

Interestingly, the 2017 CMS data on Evaluation and Management Codes by Specialty for the first time included separate data for hospitalists, based on hospitalists who credentialed with Medicare using the new C6 specialty code. Based on that data, as for only at inpatient (99238-99239) and observation (99217) codes, 83% of the discharges were inpatient and 17% were observation.

Physicians feel the pressure of



strained patient-physician relationships as a consequence of patients feeling the brunt of the financing gap related to observation status. Patients often feel they were not warned adequately about the financial ramifications of observation status. Even if Medicare beneficiaries have received the Medicare Outpatient Observation Notice, outlined by the Notice of Observation Treatment and Implication for Care Eligibility Act, they have no rights to appeal.

Currently Medicare beneficiaries admitted as inpatients incur only a Part A deductible; they are not liable for tests, procedures, and nursing care. On the other hand, in observation status all services are billed separately. For Medicare Part B services (which covers observation care) patients must pay 20% of services after the Part B deductible, which could result in a huge financial burden. Costs for skilled nursing facilities, when they are not covered by Medicare Part A, because of the 3-day rule, can easily go up to \$20,000 or more. Medicare beneficiaries have no cap on costs for an

observation stay. In some cases, hospitals have to apply a condition code 44 and retroactively change the stay to observation status.

I attended the 2019 Society of Hospital Medicine Annual Conference in Washington. Hospitalists from all parts of the country advocated on Capitol Hill against the “observation bill,” and “meet and greets” with congressional representatives increased their opposition to the bill. These efforts may work in favor of protecting patients from surprise medical bills. Hospital medicine physicians are on the front lines for providing health care in the hospital setting; they have demanded a fix to this legislative loophole which brings high out-of-pocket costs to our nation’s most vulnerable seniors. The observation status “2-midnight rule” utilized by CMS has increased financial barriers and decreased access to post-acute care, affecting the provision of high-quality care for patients.

My hospital has a utilization review committee which reviews all cases to determine the appropriateness of an inpatient versus an observation designation. (An interesting question is whether the financial resources used to support this additional staff could be better assigned to provide high-quality care.) Distribution of these patients is determined on very specific criteria as outlined by Medicare. Observation is basically considered a billing method implemented by payers to decrease dollars paid to acute care hospitals for inpatient care. It pertains to admission status, not to the level of care provided in the hospital. Unfortunately, it is believed that no two payers define observation the same way. A few examples of common observation diagnoses are



Dr. Puri is a hospitalist at Lahey Hospital and Medical Center in Burlington, Mass.

chest pain, abdominal pain, syncope, and migraine headache; in other words, patients with diagnoses for which it is suspected that a less than 24-hour stay in the hospital could be sufficient.

Observation care is increasing and can sometimes contribute to work-flow impediments and frustrations in hospitalists; thus, hospitalists are demanding reform. It has been proposed that observation could be eliminated altogether by creating a payment blend of inpatient/outpatient rates. Another option could be to assign lower Diagnosis Related Group coding to lower acuity disease processes, instead of separate observation reimbursement.

Patients and doctors lament that “Once you are in the hospital, you are admitted!” I don’t know the right answer that would solve the observation versus inpatient dilemma, but it is intriguing to consider changes in policy that might focus on the complete elimination of observation status.

Continued from previous page

Scott Shepherd, DO, FACP, has been selected chief medical officer of the health data technology company Verinovum in Tulsa, Okla. Dr. Shepherd is the medical director for hospitalist medicine with St. John Health System in Tulsa, and also medical director of the Center for Health Systems Innovation at his alma mater, Oklahoma State University in Stillwater.

Amanda Logue, MD, has been elevated to senior vice president and chief medical officer at Lafayette (La.) General Hospital. A hospitalist/internist by training, Dr. Logue has worked at Lafayette

General in a variety of clinical leadership roles since 2009.

Rina Bansal, MD, MBA, recently was appointed full-time president of Inova Alexandria (Va.) Hospital, after serving as acting president since November 2018. Dr. Bansal has been at Inova since 2008, when she started as a hospitalist at Inova Fairfax (Va.).

Dr. Bansal created and led Inova’s Clinical Nurse Services Hospitalist program through its department of neurosciences and has done stints as Inova Fairfax’s associate chief medical officer, medical director of Inova Telemedicine,

and chief medical officer at Inova Alexandria.

James Napoli, MD, has been named chief medical officer for Blue Cross and Blue Shield of Arizona, after serving in an interim role since March. He assumed those duties on top of his role as BCBSAZ’s enterprise medical director for health care ventures and innovation.

Dr. Napoli served previously as director of hospitalist services at Abrazo Arrowhead Campus (Glendale, Ariz.).



Dr. Napoli

Introducing SHM's president-elect

By Danielle B. Scheurer, MD, SFHM, MSCR

It is with great pleasure that I enter my president-elect year for the Society of Hospital Medicine! I am hopeful that this year will allow me time to get to know the organization even better than I already do, and truly understand the needs of our members so I can focus on meeting and exceeding your expectations!

I have been a hospitalist now for 17 years and have practiced in both academic tertiary care and community hospital settings. As a chief quality officer, I also work with improving quality and safety in all health care settings, including ambulatory, nursing homes, home health, and surgical centers. As such, I hope I can bring a broad lens of the medical industry to this position, improving the lives and careers of hospitalists and the patients and families they serve.

The demands placed on hospitalists are greater than ever. With shortening length of stay, rising acuity and complexity, increasing

administrative burdens, and high emphasis on care transitions, our skills (and our patience) need to rise to these increasing demands. As a member-based society, SHM (and the board of directors) seeks to ensure we are helping hospitalists be the very best they can be, regardless of type or practice setting.

The good news is that we are still in high demand. There has been an explosive growth in the need for hospitalists, as we now occupy almost every hospital setting in the United States. But as a current commodity, it is imperative that we continue to prove the value we are adding to our patients and their families, the systems in which we work, and the industry as a whole. That is where our board and SHM come into play – to provide the resources you need to improve health care.

These resources come in the form of education and training; leadership and professional development; practice management assistance; advocacy work; mentored quality improvement; networking and project work (through special interest

groups, local chapter meetings, and committee work); stimulation of research, new knowledge, and innovation; and promotion of evidence-based practice through our educational resources, publications, and other communications. The purpose of our existence is to provide you what you need to improve your work lives and your patients' health.

SHM has always fostered a "big-tent" philosophy, so we will continue to explore ways to expand membership beyond "the core" of internal medicine, family medicine, and pediatrics, and reach a better understanding of what our constituents need and how we can add value to their work lives and careers. In addition to expanding membership within our borders, other expansions already include working with international chapters and members, with an "all teach, all learn" attitude to better understand mutually beneficial partnerships with international members. Through all these expansions, we will come closer to truly realizing our mission at SHM, which is to "promote exceptional



Dr. Scheurer is chief quality officer and professor of medicine at the Medical University of South Carolina, Charleston. She is the medical editor of The Hospitalist, and president-elect of SHM.

care for hospitalized patients."

My humble hope, as it is with any of my leadership positions, is to leave SHM better than I found it. Please contact me if you have ideas or suggestions on how we can better help you be successful in improving the care for your patients, your systems, and health care as a whole.

Webinar series: Effective documentation and coding

Hospitalists cannot bill for everything they do, but they can document and code to obtain appropriate reimbursements. It is important to know the factors that influence coding to ensure accuracy and compliance.

SHM developed the Clinical Documentation & Coding for Hospitalists webinar series (formerly known as CODE-H) to provide the latest information on best practices in coding, documentation, and compliance from nationally recognized experts, along with the opportunity to claim CME.

The Hospitalist spoke with Carol Pohlig, BSN, RN, CPC, ACS, course director of the series and a coding and documentation expert at the University of Pennsylvania Medical Center in Philadelphia.

What inspired the creation of Clinical Documentation & Coding for Hospitalists?

Providers are so busy trying to keep up with regulations for their institution, such as malpractice and quality issues, that the focus isn't always on documentation required for reimbursement. The series rose out of a need for providers to understand key issues related to documentation and billing and some of the hurdles that they need to overcome – or need to be aware of.

What are some challenges that hospitalists encounter when coding, and how does this series help to address these challenges?

Some common challenges relate to concurrent

care or comanagement. Hospitalists are hired to be the gatekeepers – the ones overseeing patient care. When other consultants are on board, they wind up sharing responsibilities, which can muddy the waters, especially with billing and coding. It is important for hospitalists to understand their role in comanagement and, in turn, how the payers view their role.

We highlight everything – including requirements for history, exam, and medical decision making – and review each component in depth. We also discuss billing based on these key components or, when appropriate, billing based on time. However, when billing time-based services, you have to meet certain qualifications because it is different from the standard way of reporting.

Related to mitigating risk, EMRs and their copy and paste function is another topic we delve into. It's easy to pull forward information from a previous note to help save time. However, it is important to understand the ramifications. Each copied and pasted encounter must be modified to make it applicable to the current day's patient and ensure care is not being misrepresented.

We believe that each of the eight modules in the series offers something unique that will help improve documentation and coding practices.

How can this series go beyond the HM care team and affect the institution as a whole?

Hospitalists are involved in a number of differ-

ent categories of services, including observation and same-day admission/discharge. The series reviews rules and challenges specific to those sites of service, which impact not only providers in other service lines but also those who work in the revenue cycle at the parent institution. How each of these parties understands the nuances explained in the series can directly affect the successful processing of the submitted claims.

Interpretation of rules when it comes to coding and documentation can vary at a local level. We raise awareness of local interpretations to ensure everyone involved in the documentation and coding process knows things to look out for when reading rules. Everyone involved with billing and coding can reflect on the implications that incorrect coding may have on their hospital.

Who would benefit from this series?

Although we primarily had hospitalists of all types in mind during the development of course content, anyone who works as a practice manager, biller, coder, or internal auditor has the potential to benefit from the series. If they understand broader challenges in coding, it could help them proactively prevent issues throughout the process with more accurate documentation that could reduce claims denials.

For more information, visit hospitalmedicine.org/coding.

Burnout

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"We've not had anybody leave the hospital because of burnout or dissatisfaction" since the new system was put into place, Dr. Borsadia said. "Less burnout means more people are happy."

Although symptoms of burnout still seem to be rampant across hospital medicine, hospitalists are putting potential solutions into place. And – sometimes – they are making progress, through tweaks in schedules and responsibilities, incentives suited to different goals, and better communication.

Scheduling problems

The need for continuing efforts to improve the work experience for hospitalists is apparent, said Henry Michtalik, MD, MPH, MHS, assistant professor of general internal medicine at Johns Hopkins, Baltimore, who led a workshop on the topic at the 2019 Annual Conference of the Society of Hospital Medicine (HM19).

A 2016 survey of academic general internal medicine clinicians – including about 600 hospitalists and outpatient physicians – found that 67%

reported high stress, 38% said they were "burned out," 50% said they felt they had "low control" over their work, and 60% said they felt high documentation pressures. Still, 68%



Dr. Michtalik

said they were satisfied with the values of their departments. Hospitalists surveyed were actually less likely to say they were burned out, compared with outpatient internists – 52%, compared with 55% – but they were more likely to score low on a scale measuring personal accomplishments, compared with the outpatient clinicians – 20% versus 10%. The survey found no significant difference between the two groups in depression or suicidality. But with 40% reporting depression and 10% reporting thoughts of suicide, the numbers virtually cry out for solutions.

Hospitalists in the HM19 workshop, as in other sessions at the

Annual Conference, questioned whether the standard 7-days-on, 7-days-off work schedule – seven 12-hour shifts followed by 7 days off – allows hospitalists to pair their work lives with their personal lives in a sustainable way. They described the way that the stress and fatigue of such an intense work period bleeds into the days off that follow after it.

"By the end of seven 12's, they're bleary eyed, they're upset, they go home (for) 2 days of washout before they even start to enjoy whatever life they have left," said Jonathan Martin, MD, director of medicine at Cumberland Medical Center in Crossville, Tenn. "It's hard to get hospitalists to buy in, which increases their dissatisfaction."

Dr. Michtalik had a similar perspective. "You just shut the rest of your life down completely for those 7 days and then, on your 7 days off, you've scheduled your life," he said. "But that last off day – day number 7 – you feel that pit in your stomach, that the streak is coming." He joked

that the feeling was similar to the dread inspired by the phrase "winter is coming" in the popular HBO series "Game of Thrones."

Systematic reviews of the literature have found that it's mostly changes at the organization level – rather than changes that an individual physician makes on his or her own – that tend to make significant differences. Changes to structure, communication, and scheduling tend to work better than working on mindfulness, education, or trying to improve resilience, Dr. Michtalik said.

In one study discussed at the HM19 workshop, researchers compared a schedule in which an intensivist works in-house for 7 days, with home call at night, to a schedule in which the intensivist is completely off at night, with an in-house intensivist covering the night shift. The schedule in which the intensivist was truly off for the night significantly reduced reports of burnout, while not affecting length of stay or patient-experience outcomes.

Dr. Michtalik said that another study compared 4-week rotations to 2-week rotations for attending physicians. Researchers found that the

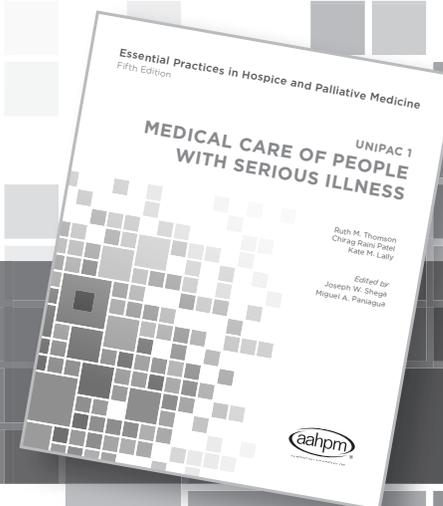
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Continued from previous page

2-week version resulted in lower reports of burnout, with readmissions and patient experience unaffected, although they noted that residents tended to prefer 4-week schedules because they felt it resulted in better relationships with the attending physician.

Perhaps the dominant factor in job satisfaction that's been identified in surveys is how physicians, patients, and administrators relate to one another, Dr. Michtalik said.

"The important concept here is that relationships were really important in driving job satisfaction, whether that be with our colleagues, our patients, or with the staff that you're working with," he said. "It's always easier to decline a consultation or have a bad interaction with someone over the phone than it is if you actually know them or you are communicating face to face. That's why it's important to develop these kinds of relationships, which also put a face to what's going on."

Beyond salary adjustments

Hospitalists attending the HM19 workshop said they thought that participating in administration committees at their own institutions



Dr. Rahul C. Borsadia

helps keep hospitalists involved in hospital matters, limiting the effects of burnout and improving workplace satisfaction.

Kevin McAninch, DO, a hospitalist with Central Ohio Primary Care in Westerville, said a shift in work responsibilities has made an improvement at his hospital. There is now an "inpatient support center" – which has a physician and a

nurse in an office taking calls from 6 p.m. to 7 a.m., so that rounders can stop taking floor calls during that time.

The system "takes the pressure off our admitters at night and our nurses because they're not getting floor calls anymore, so they're just taking care of the admissions from the ER," he said.

A recurring theme of the discussion was that salary alone seems universally incapable of eradicating feelings of burnout. One hospitalist said that in surveys, higher-paid physicians insist that monetary compensation is their main driver, but still often complain of burnout because they must work extra shifts to earn that higher level of pay.

Instead, burnout and satisfaction indicators tend to have more to do with time, control, and support, Dr. Michtalik noted.

Mangla Gulati, MD, SFHM, chief quality officer at the University of Maryland Medical Center in Baltimore, said that there's no big secret about what hospitalists want from their places of employment. They want things like getting patients to service faster so they can make diagnoses, making sure patients get the care they need, fixing the problems associated with electronic medical records, and having a work-life "integration."

"The question is – how do we get there?" Dr. Gulati wondered. She suggested that hospitalists have to be more assertive and explanatory in their interactions with members of the hospital C-suite.

"I think it's really important for you to understand or ask your C-suite, 'Where are you in this whole journey? What is your perception of wellness? Tell me some of the measures of staff wellness,'" she said.

If the C-suite says "we have no money" to make improvements, hospitalists must be willing to say, "Well, you're going to have to invest a little bit." Dr. Gulati said. "What is the ROI [return on investment] on the turnover of a physician? Because when you turn a physician over, you have to recruit and hire new staff."

Dr. Gulati said that hospitalists should provide C-suite leaders with a detailed walk-through of their actual workflows – what their workdays look like – because "it's not something they're familiar with."

Aside from improving relations with hospital administration, Dr. Gulati suggested creating CME pro-

grams for wellness, offering time and funding for physician support meetings, supporting flexibility in work hours, and creating programs specifically to help clinicians with burnout symptoms.

She also touted the benefits of "Schwartz Rounds," in which several medical disciplines gather to talk about a case that was particularly challenging, clinically complex, and emotionally draining for everyone involved.

At Cumberland Medical Center, Dr. Martin said he has two meetings a month with executives in the hospital's C-suite. One is with his hospitalist group, TeamHealth, and

"By the time the end of the day comes, it's 9 or 10 p.m. and you are leaving but coming back at 6:30 the next morning. So, lack of sleep, more patients, striving to earn that higher salary. The desire to perform quality work with that kind of patient load was not fulfilled and that led to dissatisfaction and stress, which led to irritation and exodus from the group."

one is more direct, between himself and hospital administrators. It's just 2 hours a month, but these conversations have undoubtedly helped, he said, although he cautioned that "the meetings themselves don't have as much meaning if you aren't communicating effectively," meaning hospitalists must understand how the C-suite thinks and learn to speak in terms they understand.

"When I go to the administration now and I say 'Hey, this is a problem that we're having. I need your help in solving it,' the executives are much more likely to respond to me than if they'd never seen me, or only see me rarely," Dr. Martin said.

As a result, a collaborative approach to such conversations tends to be more effective.

"If you go to the C-suite and say, 'Here's our issue, how can you help us?' – as opposed to telling the administration, 'This is what I need' – they are more likely to work with you to generate a solution."

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Key Clinical Question

Managing alcohol withdrawal in the hospitalized patient

Symptom-triggered therapy has multiple benefits

By Veevek Agrawal, DO; Svetlana Chernyavsky, DO; Patricia Dharapak, MD; Erica Grabscheid, MD; Eve Merrill, MD; Kamana Pillay MD; and Dahlia Rizk, DO, MPH

Case

A 57-year-old man with a history of alcohol abuse (no history of seizures) presents to the ED “feeling awful.” He claims his last drink was 1 day prior. Initial vital signs are: T = 99.1°F, HR 102 bpm, BP 162/85 mm Hg, respirations 18/minute, and 99% oxygen saturation. He is tremulous, diaphoretic, and has an unsteady gait. What is the best way to manage his symptoms while hospitalized?



HIPANOSTIC/GETTY IMAGES

Brief overview of the issue

With over 15 million people with alcohol use disorder (AUD) in the United States alone, alcohol dependence and misuse remain significant issues among hospitalized patients.¹ It is estimated that over 20% of admitted patients meet DSM-5 criteria for AUD and that over 2 million will withdraw each year.^{2,3} Acute withdrawal includes a spectrum of symptoms ranging from mild anxiety and diaphoresis to hallucinations, seizures, and delirium tremens. Onset of these symptoms ranges from 24 hours up to 5 days.

Severe alcohol withdrawal syndrome (SAWS) attributable to abrupt discontinuation of alcohol leads to increased morbidity and mortality; therefore, early detection and prevention in the acute care setting is critical. Several factors can help predict who may withdraw, and once detected, pharmacological treatment is necessary.⁴ Thorough evaluation and treatment can help reduce mortality from the most severe forms of alcohol withdrawal including delirium tremens, which has up to 40% mortality if left untreated.⁵

Overview of the data

How do we use benzodiazepines to treat alcohol withdrawal? Benzodiazepines are the mainstay of alcohol withdrawal treatment. Benzodiazepines work by stimulating the gamma-aminobutyric acid (GABA) receptor resulting in a reduction of neuronal activity. This leads to a sed-

ative effect and thus slows the progression of withdrawal symptoms.

Long-acting benzodiazepines, such as chlordiazepoxide and diazepam, are the preferred choices for most patients. Their active metabolites have a rapid onset of action and their long half-lives allow for a lower incidence of breakthrough symptoms and rebound phenomena such as seizures.⁶ Benzodiazepines with shorter half-lives, such as lorazepam and oxazepam, are preferred in patients with liver dysfunction and those prone to respiratory depression.

Intravenous administration has a rapid onset of action and is the standard administration route of choice in patients with acute severe withdrawal, delirium tremens, and seizure activity. In patients with mild withdrawal symptoms or those in the outpatient setting, oral administration is generally effective.⁶

The Clinical Institute Withdrawal Assessment (CIWA) is one commonly used titration model that requires calculation of a symptom-based withdrawal score. Data have consistently demonstrated that a symptom-triggered method results in administration of less total benzodiazepines over a significantly shorter duration, thereby reducing cost and duration of treatment and minimizing side effects. This regimen may also reduce the risk of undermedicating or overmedicating a patient since the dosing is based upon an individual's symptoms.^{7,8}

The efficacy of symptom-trig-

gered regimens, however, depends on the reliability and accuracy of the patient assessment. A fixed-interval benzodiazepine-dosing approach where benzodiazepines are administered regardless of symptoms is useful when frequent monitoring and reassessment are not feasible or are unreliable.

What about phenobarbital?

Phenobarbital has similar pharmacokinetics to the benzodiazepines frequently used for alcohol withdrawal, including simultaneous effects on gamma-aminobutyric acid (GABA) and *N*-methyl-D-aspartate (NMDA) receptors, and has been proposed as a treatment option for delirium tremens.

In 2019, as reported in the American Journal of Emergency Medicine, Nelson et al. found that incorporating phenobarbital into a benzodiazepine-based protocol or as sole agent led to similar rates of ICU admission, length of stay, and need for mechanical ventilation in patients treated for alcohol withdrawal in the emergency department.⁹ The authors concluded that “phenobarbital (was) a safe and effective treatment alternative for alcohol withdrawal.” The systematic review by Hammond et al. in 2017 found that phenobarbital, either as

monotherapy or in conjunction with benzodiazepines, could have comparable or superior results in comparison to other treatments, including benzodiazepines monotherapy.¹⁰ Further studies are needed to determine dosing and the most effective way to incorporate the use of phenobarbital in treatment of alcohol withdrawal syndrome (AWS).

Should gabapentin or any other medications be added to his treatment regimen?

Chronic alcohol use induces a reduction in GABA activity (the major inhibitory neurotransmitter in the brain) and alcohol cessation results in decreased inhibitory tone. This physiologic imbalance contributes to the syndrome of alcohol withdrawal. As such, gabapentin has emerged as a promising treatment option in AWS and may help reduce the need for benzodiazepines.

Gabapentin has few drug-drug interactions and is safe for use in patients with impaired liver function; however, dosage adjustment is required for renal dysfunction (CrCl less than 60 mL/min). Gabapentin's neuroprotective effects may also help decrease the neurotoxic effects associated with AWS. Common side

Continued on following page

Key Points

- Alcohol use disorder and alcohol withdrawal are significant problems in hospitalized patients; early detection and treatment are crucial in preventing high morbidity and mortality.
- Long-acting benzodiazepines with active metabolites such as chlordiazepoxide and diazepam are the preferred treatment for alcohol withdrawal except for patients with advanced liver disease or those prone to respiratory depression.
- Symptom-triggered therapy decreases the amount of medication, shortens treatment duration, and decreases inpatient length of stay, compared with fixed-schedule dosing.
- Gabapentin may be effective in the treatment of mild to moderate AWS but cannot yet be routinely recommended as monotherapy in severe withdrawal, in patients with seizure history, or in patients who are at high risk for progression to delirium tremens.
- Thiamine deficiency is common in chronic alcohol use disorders; thiamine repletion should be considered for patients at risk or when Wernicke's encephalopathy and Korsakoff's syndrome are suspected.



Dr. Agrawal



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Dr. Dharapak



Dr. Grabscheid



Dr. Merrill



Dr. Pillay



Dr. Rizk

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Continued from previous page

effects of gabapentin include dizziness, drowsiness, ataxia, diarrhea, nausea, and vomiting. The potential for misuse has been reported.

In several small studies, gabapentin monotherapy was found to be comparable to benzodiazepines in the treatment of mild to moderate AWS. Gabapentin is efficacious in reducing cravings as well as improving mood, anxiety, and sleep, and showed an advantage over benzodiazepines in preventing relapse with no difference in length of hospital stay.^{6,11} Given the small sample sizes of these studies and the differing methods, settings, and inclusion/exclusion criteria used, the generalizability of these findings to patients with significant medical and/or

psychiatric comorbidities remains limited. Additional studies are needed to standardize dosing protocols and treatment strategies for both inpatients and outpatients.

Alternative agents such as antipsychotics (e.g., haloperidol), centrally acting α_2 agonists (e.g., clonidine), beta-blockers, and an agonist of the GABA-B receptor (e.g., baclofen) may also attenuate the symptoms of withdrawal. Since these all have limited evidence of their efficacy and have potential for harm, such as masking symptoms of progressive withdrawal and lowering seizure threshold, these agents are not routinely recommended for use. Valproic acid/divalproex, levetiracetam, topiramate, and zonisamide have also showed some efficacy in reducing symptoms of alcohol withdrawal in limited studies. The data on prevention of withdrawal seizures or delirium tremens when used as monotherapy are less robust.¹²

A daily multivitamin and folate are ordered. What about thiamine? Does the route matter?

Alarming, 80% of people who chronically abuse alcohol are thiamine deficient.¹³ This deficiency is attributable to several factors including inadequate oral intake, malabsorption, and decreased cellular utilization. Thiamine is a crucial factor in multiple enzymatic and metabolic pathways. Its deficiency can lead to free radical production, neurotoxicity, impaired glucose metabolism, and ultimately, cell death.¹⁴ A clinical concern stemming from thiamine deficiency is the development of Wernicke's encephalopathy (WE), which is potentially reversible with prompt recognition and treatment, in comparison to its irreversible amnesic sequela, Korsakoff's syndrome.

Wernicke's encephalopathy had been defined as a triad of ataxia, ophthalmoplegia, and global confusion. However, Harper et al. discovered that only 16% of patients presented with the classic triad and 19% had none of these signs.¹⁵ Diagnosis is clinical since thiamine serology results do not accurately represent brain storage.

Currently, there are no consistent guidelines regarding repletion of thiamine administration in the treatment or prevention of WE attributable to alcohol overuse. Thiamine has a safe toxicity profile as excess thiamine is excreted in the urine. Outside of rare reports of anaphylactoid reactions involving large parenteral doses, there is no concern for overtreatment. As Wernicke-Korsakoff syndrome is associated with significant morbidity and mortality, high doses such as 200-500 mg are recommended to ensure blood-brain barrier passage. The intravenous route is optimal over oral administration to bypass concerns of gastrointestinal malabsorption. Thiamine 100 mg by mouth daily for ongoing supplementation can be considered for patients who are at risk for WE. It is also important to recognize that magnesium and thiamine are intertwined in several key enzymatic pathways. For the responsiveness of thiamine repletion to be optimized, magnesium levels should be tested and repleted if low.

Application of the data to our patient

Nurses are able to frequently monitor the patient so he is started on symptom-triggered treatment with chlorthalidone using the CIWA protocol. This strategy will help limit the amount of benzodiazepines he receives and shorten his treatment duration. Given the ataxia, the patient is also started on high-dose IV thiamine three times a day to treat possible Wernicke's encephalopathy. Gabapentin is added to his regimen to help manage his moderate alcohol withdrawal syndrome.

Bottom line

Long-acting benzodiazepines using symptom-triggered administration when feasible are the mainstay of treating alcohol withdrawal. Other medications such as gabapentin, carbamazepine, and phenobarbital can be considered as adjunctive agents. Given the high rate of thiamine deficiency and the low risk of over-replacement, intravenous thiamine can be considered for inpatients with AWS.



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Quiz

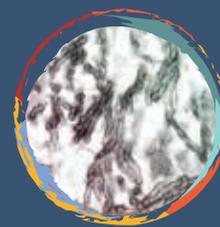


A 51-year-old female with a history of hypertension and continuous alcohol abuse presents to the hospital with fever and cough. She is found to have community-acquired pneumonia and is admitted for treatment. How else would you manage this patient?

- A. Start scheduled benzodiazepines and oral thiamine.
- B. Start CIWA protocol using a long-acting benzodiazepine and oral thiamine.
- C. Start scheduled benzodiazepines and IV thiamine.
- D. Start CIWA protocol using a long-acting benzodiazepine and consider IV or oral thiamine.

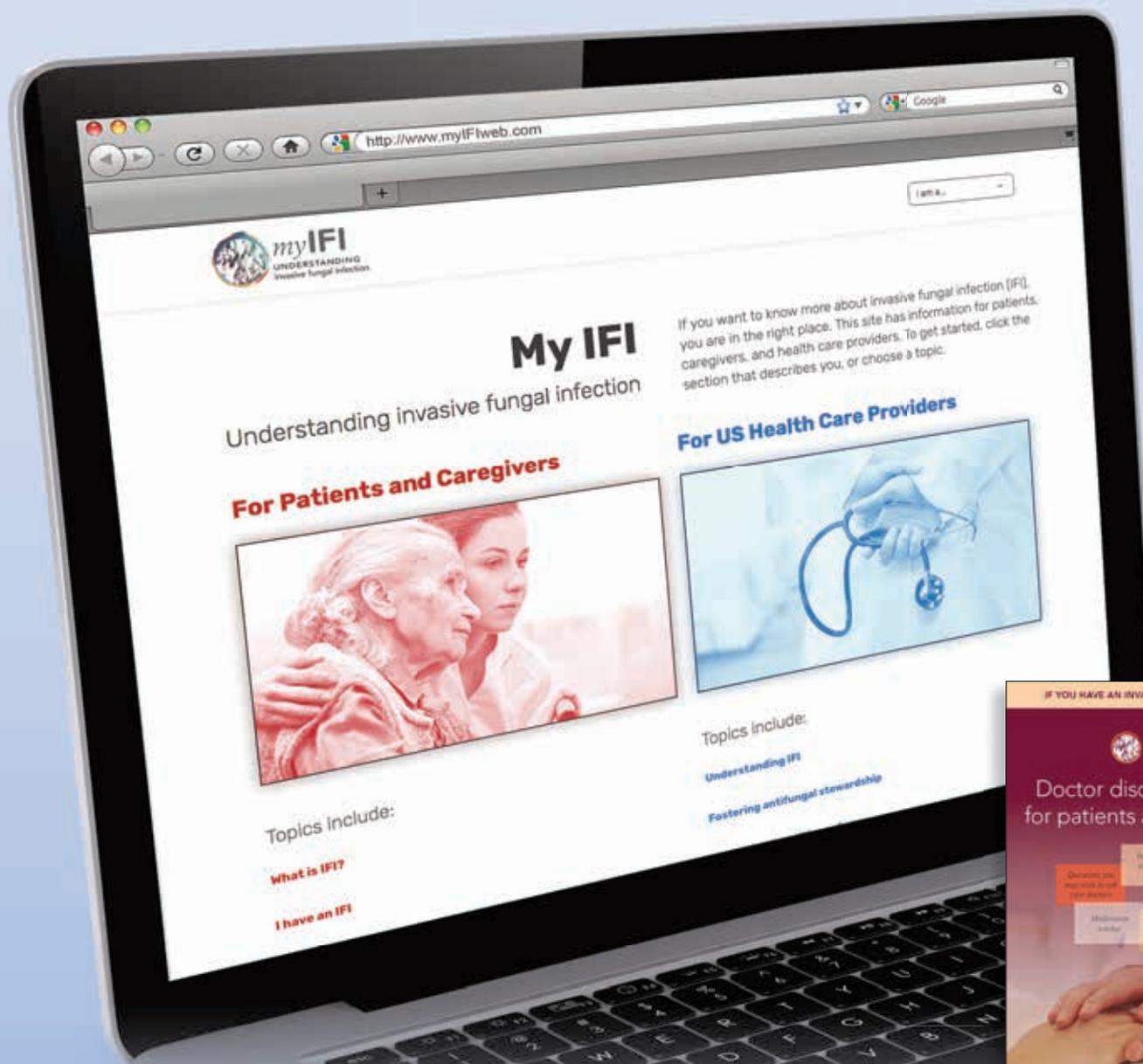
Answer: D. Symptom-triggered benzodiazepine therapy is favored as is consideration for thiamine repletion in the treatment of AWS.

Treating patients with invasive fungal infection (IFI), or at risk for one?

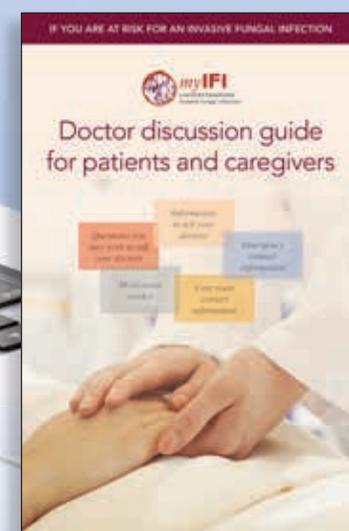
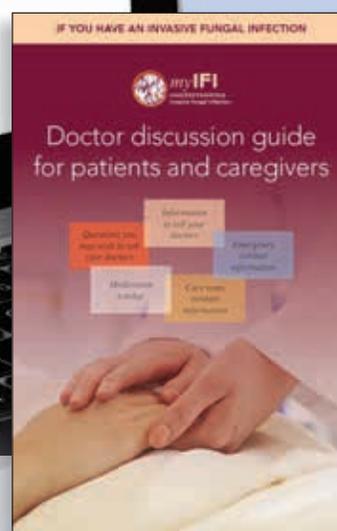


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Clinician reviews of HM-centric research

By Steven Deitelzweig, MD, SFHM, MMM; Halle Field, MD; Caley McIntyre, MD; Ryan Nelson, MD; Jeremiah Newsom, MD, MSPH; and Kristen Rogers, MD, MPH

Ochsner Health System, New Orleans

IN THIS ISSUE

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By Steven Deitelzweig, MD, SFHM, MMM

1 No rise in major hemorrhagic events with antiplatelet therapy after ICH

CLINICAL QUESTION: Does the risk of increased recurrent intracerebral hemorrhage (ICH) exceed the benefits of decreased vaso-occlusive events for patients resuming antiplatelet therapy following an ICH?

BACKGROUND: Antiplatelet agents reduce the risk of major vascular events in patient with established vaso-occlusive disease, but they may increase the risk of ICH. Patients with prior ICH are at risk for both vaso-occlusive and hemorrhagic events. Clarification of the relative risk and benefit of antiplatelet agent use in this clinical scenario would serve to guide therapy.

STUDY DESIGN: Prospective, open-label, randomized parallel group trial.

SETTING: 122 hospitals located in the United Kingdom.

SYNOPSIS: The study included 537 adult patients with imaging-confirmed, nontraumatic intracerebral hemorrhage who were previously prescribed antithrombotic medications were randomized in 1:1 fashion to either start or avoid antiplatelet therapy. Participants were followed up on an annual basis with postal questionnaires both to the participants and their primary care



Dr. Deitelzweig

providers. No significant difference was identified in rates of recurrent ICH (adjusted hazard ratio, 0.51; 95% confidence interval, 0.25-1.03), major hemorrhagic events (aHR, 0.71; 95% CI, 0.39-1.30), or major occlusive vascular events (aHR, 1.02; 95% CI, 0.65-1.60) between groups.

Hospitalists should be aware that these data suggest that the risk assessment for resumption of antiplatelet agents should not be affected by a history of nontraumatic intracerebral hemorrhage when weighed against the benefit of these medications in patients with occlusive vascular disease.

BOTTOM LINE: Resumption of antiplatelet agents following intracerebral hemorrhage showed no evidence of increased risk of recurrent intracerebral hemorrhage or major hemorrhagic events.

CITATION: RESTART Collaboration. Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (RESTART): A randomized, open-label trial. *Lancet*. 2019. doi: 10.1016/S0140-6736(19)30840-2.

Dr. Deitelzweig is system department chair of hospital medicine at Ochsner Health System, New Orleans.

By Halle Field, MD

2 Hospital vs. outpatient management comparable for elderly syncope patients

CLINICAL QUESTION: Is there a difference in risk of post-ED serious adverse events at 30 days in older adults with unexplained syncope when managed as an outpatient versus with hospitalization?

BACKGROUND: In the United States,

there are over 1 million visits to EDs for syncope with a greater than 50% hospitalization rate for older adult patients. There remains uncertainty around which patients without an identified cause for the syncope could be discharged from the ED and managed as an outpatient.

STUDY DESIGN: Propensity score analysis.

SETTING: EDs from 11 nonprofit academic hospitals.

SYNOPSIS: Prospective data for 2,492 patients aged 60 years and older who did not have an identified cause in the ED for their presenting complaint of syncope were included in the propensity score analysis resulting in a sample size of 1,064 with 532 patients in each of the discharged and hospitalized groups. There was no significant difference in risk of 30-day post-ED serious adverse events between the hospitalized patients (4.89%; 95% confidence interval, 3.06%-6.72%) and discharged patients (2.82%; 95% CI, 1.41%-4.23%; risk difference 2.07%; 95% CI, -0.24% to 4.38%). There was also no statistically significant difference in 30-day mortality post-ED visit.

These results show no clinical benefit in hospitalization for older adults with unexplained syncope after ED evaluation suggesting that it would be reasonable to proceed with outpatient management and evaluation of these patients.

BOTTOM LINE: Consider discharging older patients home from the ED who do not have high risk factors and no identified cause of their syncope.

CITATION: Probst MA et al. Clinical benefit of hospitalization for older adults with unexplained syncope: A propensity-matched analysis. *Ann Emerg Med*. 2019 Aug;74(2):260-9.

3 Order errors not reduced with limiting number of open records

CLINICAL QUESTION: What is the risk of wrong-patient orders in an EHR limiting clinicians to one open record versus allowing up to four open records concurrently?

BACKGROUND: An estimated 600,000 patients in U.S. hospitals had

an order placed in their record that was meant for another patient in 2016. The Office of the National Coordinator for Health Information Technology and the Joint Commission



Dr. Field

recommend that EHRs limit the number of open records to one at a time based on expert opinion only. There is wide variation in the number of open records allowed among EHRs

across the United States currently.

STUDY DESIGN: Randomized clinical trial.

SETTING: Large health system in New York.

SYNOPSIS: There were 3,356 clinicians (inpatient, outpatient, ED) randomized in a 1:1 ratio into either a restricted group (one open record at a time) or an unrestricted group (up to four open records at a time). In this study, 12,140,298 orders, in 4,486,631 order sessions, were analyzed with the Wrong-Patient Retract-and-Reorder (RAR) measure to identify wrong-patient orders. The proportion of wrong-patient order sessions were 90.7 vs. 88.0 per 100,000 order sessions for the restricted versus unrestricted groups (odds ratio, 1.03; 95% confidence interval, 0.90-1.20). There were no statistically significant differences in wrong-patient order sessions between the restricted and unrestricted groups in any clinical setting examined (inpatient, outpatient, ED).

Despite the ability to have up to four open records at one time in the unrestricted group, 66% of the order sessions were completed with only one record open in that group. This limited the power of the study to detect a difference in risk of order errors between the restricted and unrestricted groups.

BOTTOM LINE: Limiting clinicians to only one open record did not reduce the proportion of wrong-patient orders, compared with allowing up to four open records concurrently.

CITATION: Adelman JS et al. Effect of restriction of the number of concurrently open records in

an electronic health record on wrong-patient order errors: A randomized clinical trial. *JAMA*. 2019;32(18):1780-7.

Dr. Field is a hospitalist at Ochsner Health System, New Orleans.

By Caley McIntyre, MD

4 Patent foramen ovale linked with increased risk of ischemic stroke in PE

CLINICAL QUESTION: Is patent foramen ovale (PFO) associated with increased risk of ischemic stroke in patients diagnosed with acute pulmonary embolism (PE)?

BACKGROUND: Studies have demonstrated the increased risk for ischemic stroke in patients diagnosed with acute PE, and data support the mechanism of paradoxical embolism via PFO. However, the frequency of this phenomenon is unknown and the strength of the association between PFO and ischemic stroke in patients with PE is unclear.

STUDY DESIGN: Prospective cohort study.

SETTING: Four French hospitals.

SYNOPSIS: 315 patients aged 18 years and older presenting with acute symptomatic PE were evaluated at the time of diagnosis for PFO

with contrast transthoracic echocardiography and for ischemic stroke with cerebral magnetic resonance imaging. The overall frequency of ischemic stroke at the time of PE diagnosis was high (7.6%), and was nearly four times higher in the PFO group than the non-PFO group (21.4% vs. 5.5%; difference in proportions, 15.9 percentage points; 95% confidence interval, 4.7-30.7).



Dr. McIntyre

This study adds to the growing body of data which supports the association of ischemic stroke with PFO and PE. Given the moderate indication for indefinite anticoagulation in patients at high risk for recurrent PE and stroke, there may be a role for screening for PFO in patients with acute PE so that they can be appropriately risk stratified.

BOTTOM LINE: The presence of ischemic stroke in patients with acute pulmonary embolism is high, and there is a strong association with PFO.

CITATION: Le Moigne E et al. Patent Foramen Ovale and Ischemic Stroke

in Patients With Pulmonary Embolism: A Prospective Cohort Study. *Ann Intern Med*. 2019;170:756-63.

5 Restrictive IV fluid strategy comparable to usual care for severe sepsis, septic shock

CLINICAL QUESTION: Will restrictive IV fluid resuscitation yield similar clinical outcomes for severe sepsis and septic shock similar to those of usual-care resuscitation?

BACKGROUND: Since the advent of early goal-directed therapy (EGDT), studies have challenged the notion that high-volume IV fluid resuscitation improves clinical outcomes in sepsis and septic shock. The optimal IV fluid resuscitation strategy for severe sepsis and septic shock remains unclear.

STUDY DESIGN: Prospective randomized controlled trial.

SETTING: Two critical care units in one academic system.

SYNOPSIS: The Restrictive IV Fluid Trial in Severe Sepsis and Septic Shock (RIFTS) randomized 109 participants ages 54-82 years to a restrictive (less than 60 mL/kg) or to usual care (no prespecified limit) IV fluid resuscitation strategy for the first 72 hours of ICU admission. The primary out-

come of 30-day mortality was similar between groups (odds ratio, 1.02; 95% confidence interval, 0.41-2.53).

Limitations to RIFTS include its small sample size, single-system design, and inadequate power to detect noninferiority or superiority. While larger, multicenter trials are required for further investigation, hospitalists should note a trend toward conservative IV fluid administration in severe sepsis and septic shock.

BOTTOM LINE: Restrictive IV fluid resuscitation for severe sepsis and septic shock may result in mortality rates similar to those of usual care, but larger, multicenter studies are needed to confirm noninferiority.

CITATION: Corl KA et al. The restrictive IV fluid trial in severe sepsis and septic shock (RIFTS): A randomized pilot study. *Crit Care Med*. 2019;47(7):951-9.

Dr. McIntyre is a hospitalist at Ochsner Health System, New Orleans.

By Ryan Nelson, MD

6 A dedicated mobility technician improves inpatient mobility

CLINICAL QUESTION: Does providing a dedicated mobility technician

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to assist older inpatients with regular ambulation improve functional status and outcomes?

BACKGROUND: Studies have shown improved hospital outcomes in patients who ambulate regularly. Many assisted mobility protocols aimed at ambulating patients multiple times daily are nurse centered. However, implementation is difficult because of the large number of nursing duties and difficulty finding time away from other competing responsibilities.



Dr. Nelson

STUDY DESIGN: Single-blind randomized controlled trial.
SETTING: Single-center 1,440-bed tertiary care hospital.
SYNOPSIS: This study randomized 102 moderately impaired adult inpatients aged 60 years and older with Activity Measures for Post-Acute Care mobility scores of 16-20 to either dedicated regular ambulation sessions with mobility technicians or usual care with hospital nurse-driven protocol. Patients who achieved greater than 400 steps were more likely to discharge to home rather than post-acute care (71% vs. 46%; $P = .01$). Assisted ambulation did not decrease length of stay or affect the discharge disposition, but it did increase the total daily number of steps taken by patients (1,182 vs. 726; $P = .02$, per-protocol analysis) and the patients' mobility scores (18.90 vs. 18.27, $P = .04$).

BOTTOM LINE: A dedicated mobility technician to provide assisted ambulation for older inpatients can improve patient mobility.

CITATION: Hamilton AC et al. *Increas-*

ing mobility via in-hospital ambulation protocol delivered by mobility technicians: A pilot randomized controlled trial. *J Hosp Med.* 2019;14:272-7.

Dr. Nelson is a hospitalist at Ochsner Health System, New Orleans.

By Jeremiah Newsom, MD, MSPH

7 Successful bowel preps linked with modifiable risk factors

CLINICAL QUESTION: What are modifiable risk factors associated with inadequate bowel preparation (IBP), and what is the association in hospitalized patients?

BACKGROUND: IBP is very common and associated with increased length of stay and cost of care. Many nonmodifiable risk factors have been identified such as socioeconomic status, male gender, and increased age, but no studies have



Dr. Newsom

been done to look at modifiable risk factors such as medication use, timing of colonoscopy, and diet before colonoscopy. Furthermore, no studies have been done to assess the effects of these

modifiable factors on IBP.

STUDY DESIGN: Retrospective cohort study using multivariate logistic regression analysis.

SETTING: Cleveland Clinic Hospitals in Ohio and Florida.

SYNOPSIS: Records of 8,819 patients (aged greater than 18 years) undergoing colonoscopy at Cleveland Clinic between January 2011 and June 2017 were reviewed. They found that 51% had IBP. Modifiable risk factors, in-

cluding opiate use within 3 days of colonoscopy, colonoscopy performed before noon, and solid diet the day before colonoscopy, were associated with IBP. After adjustment for these variables, they found the rates of IBP were reduced by 5.6%. They also found that patients who had IBP had increased length of stay by 1 day (6 days vs. 5 days; P less than .001). This translates into 494 unnecessary hospital days or approximately \$1 million dollars in unnecessary costs based on the number of patients (almost 9,000).

This study was performed in a single institution so it may be difficult to extrapolate to other institutions. Further studies need to be performed using multicenter institutions to assess accuracy of data.

BOTTOM LINE: Liquid diet or nothing by mouth (NPO) 1 day prior to colonoscopy, performing colonoscopy before noon, and avoiding opioids 3 days prior to colonoscopy are modifiable risk factors that may decrease the rate of inadequate bowel preparations in hospitalized patients.

CITATION: Garber A et al. Modifiable factors associated with quality of bowel preparation among hospitalized patients undergoing colonoscopy. *J Hosp Med.* 2019;5:278-83.

Dr. Newsom is a hospitalist at Ochsner Health System, New Orleans.

By Kristen Rogers, MD, MPH

8 Continued extension of time for thrombolysis in stroke

CLINICAL QUESTION: Is thrombolysis beneficial between 4.5 and 9 hours after onset of stroke in patients with hypoperfused but salvageable regions of brain detected on automated perfusion imaging?

BACKGROUND: Current guidelines

for ischemic stroke recommend the time to thrombolysis be within 4.5 hours after onset of stroke. Guidelines are based on noncontrasted CT, but CT perfusion and perfusion-diffusion MRI may show salvageable brain tissue beyond the 4.5 hours. Studies have shown better outcomes in patients who were chosen for reperfusion based on tissue viability rather than time from onset of



Dr. Rogers

stroke. This has resulted in a disparity between the time windows used for thrombolysis.

STUDY DESIGN: Multicenter, randomized, placebo-controlled trial.

SETTING: Hospitalized patients with acute ischemic stroke from 16 centers in Australia, 10 centers in Taiwan, 1 center in New Zealand, and 1 center in Finland.

SYNOPSIS: 225 patients (aged 18 years and older) with acute ischemic stroke with hypoperfused but salvageable areas of brain detected on CT perfusion imaging or perfusion-diffusion MRI were randomly assigned to receive IV alteplase or placebo between 4.5 and 9 hours after onset of stroke or on awakening with stroke. Primary outcome measured on modified Rankin scale was 0 (no neurologic deficit) or 1. Before the trial was fully enrolled, it was terminated because of a loss of equipoise based on positive results from a previous trial. Of the patients enrolled, the primary outcome occurred in 35.4% of the alteplase group and 29.5% in the placebo group (adjusted risk ratio, 1.44). Symptomatic intracerebral hemorrhage was experienced in 6.2% of the patients in the alteplase group and 0.9% of patients in the placebo group (adjusted risk ratio, 7.22).

Not all centers may have access to perfusion imaging, so the study's findings may not be applicable to multiple sites.

BOTTOM LINE: Diffusion-perfusion imaging may be useful in determining salvageable brain tissue in acute ischemic stroke that may benefit from thrombolysis after the standard 4.5-hour window, but further studies need to be conducted before guidelines are changed.

CITATION: Ma H et al. Thrombolysis guided by perfusion imaging up to 9 hours after onset of stroke. *N Engl J Med.* 2019;380(19):1795-803.

Dr. Rogers is a hospitalist at Ochsner Health System, New Orleans.

SHORT TAKES

Routine serial TB screening for health care workers no longer recommended

A systematic review of literature for 2006-2017 reviewed by the National Tuberculosis Controllers Association-CDC work group led to a 2019 update of the CDC screening guidelines for tuberculosis (previously updated in 2005). One notable change is a recommendation against routine serial screening in health care workers in the absence of recognized exposure or symptoms.

CITATION: Sosa LE et al. Tuberculosis screening, testing, and treatment of U.S. healthcare personnel: Recommendations for the

National Tuberculosis Controllers Association and CDC, 2019. *MMWR.* 2019;68(19):439-43.

Fewer endotracheal tube dislodgements with securement device

Randomized control trial shows that overall incidence of primary outcome (lip ulcers, facial skin tears, and endotracheal tube dislodgment) decreased by 30 per 1,000 ventilator-days when using endotracheal tube fastener rather than adhesive tape.

CITATION: Landsperger JS et al. The effect of adhesive tape versus endotracheal tube fastener in crit-

ically ill adults: The endotracheal tube securement (ETTS) randomized controlled trial. *Critical Care.* 2019;23:161.

SGLT2 inhibitors associated with Fournier gangrene

Review of the FDA Adverse Event Reporting System database identified 55 unique cases of Fournier gangrene in diabetic patients taking SGLT2 Inhibitors.

CITATION: Bersoff-Matcha S et al. Fournier gangrene associated with sodium-glucose cotransporter-2 inhibitors: A review of spontaneous postmarketing cases. *Ann Intern Med.* 2019 Jun 4;170(11):764-70.

Study: Cardiac biomarkers predicted CV events

Change in usual practice needed to cut cardiovascular CAP complications

By Jeff Craven

MDedge News

Cardiac biomarkers were used to predict the likelihood of cardiovascular events at day 1 and day 30 in patients with community-acquired pneumonia, in a recently conducted study.

These biomarkers were also used to predict late cardiovascular events at day 30 of community-acquired pneumonia (CAP) in patients who did not have a history of cardiovascular disease, according to Rosario Menéndez, MD, from the Hospital Universitario y Politécnico La Fe and Instituto de Investigación Sanitaria La Fe in Valencia, Spain, and colleagues.

“Some patients have still high levels of inflammatory and cardiac biomarkers at 30 days, when they are usually referred to primary care without receiving any specific additional recommendations,” Dr. Menéndez and colleagues wrote in *CHEST* (2019 Aug 2. doi: 10.1016/j.chest.2019.06.040). “Our results suggest that a change in usual practice is needed to reduce current and further cardiovascular CAP complications.”

Dr. Menéndez and colleagues prospectively followed 730 patients for 1 year who were hospitalized for CAP, measuring the cardiac biomarkers proadrenomedullin (proADM), pro b-type

natriuretic peptide (proBNP), proendothelin-1, and troponin T, and the inflammatory biomarkers interleukin 6 (IL-6), C-reactive protein (CRP), and procalcitonin (PCT). The researchers also collected data on age, gender, smoking status, and vaccination history, as well as whether patients had any cardiac, renal, pulmonary, neurological, or diabetes-related comorbidities.

“Patients who experienced both early and late cardiovascular events had significantly higher initial levels of proADM, proendothelin-1, troponin, proBNP, and IL-6.”

Overall, 95 patients experienced early cardiovascular events, 67 patients had long-term cardiovascular events, and 20 patients experienced both early and late events. In hospital, the mortality rate was 4.7%; the 30-day mortality rate was 5.3%, and the 1-year mortality rate was 9.9%.

With regard to biomarkers, patients who experienced both early and late cardiovascular events had significantly higher initial levels of proADM, proendothelin-1, troponin, proBNP, and IL-6. Patients who experienced later events had consistent levels of these biomarkers until

day 30, except for a decrease at day 4 or day 5.

After adjustment for age, sepsis, previous cardiac disease, and a partial pressure of oxygen in the alveoli to fractional inspired oxygen ratio ($\text{PaO}_2/\text{FiO}_2$) of less than 250 mm Hg, cardiac biomarkers proendothelin-1 (odds ratio, 2.25; 95% confidence interval, 1.34-3.79), proADM (OR, 2.53; 95% CI, 1.53-4.20), proBNP (OR, 2.67; 95% CI, 1.59-4.49), and troponin T (OR, 2.70; 95% CI, 1.62-4.49) significantly predicted early cardiovascular events, while proendothelin-1 (OR, 3.13; 95% CI, 1.41-7.80), proADM (2.29; 95% CI, 1.01-5.19), and proBNP (OR, 2.34; 95% CI, 1.01-5.56) significantly predicted late cardiovascular events. For day 30 results, when researchers added IL-6 levels to proendothelin-1, the odds ratio for late events increased to 3.53, and when they added IL-6 levels to proADM, the odds ratio increased to 2.80.

Researchers noted the limitations of the study included that they did not analyze cardiac biomarkers to predict specific cardiovascular events, did not identify the cause for mortality at 1 year in most patients, and did not include a control group.

This study was supported in part by funding from Instituto de Salud Carlos III, Sociedad Española de Neumología y Cirugía Torácica, and the Center for Biomedical Research Network in Respiratory Diseases. The authors reported no relevant conflicts of interest.

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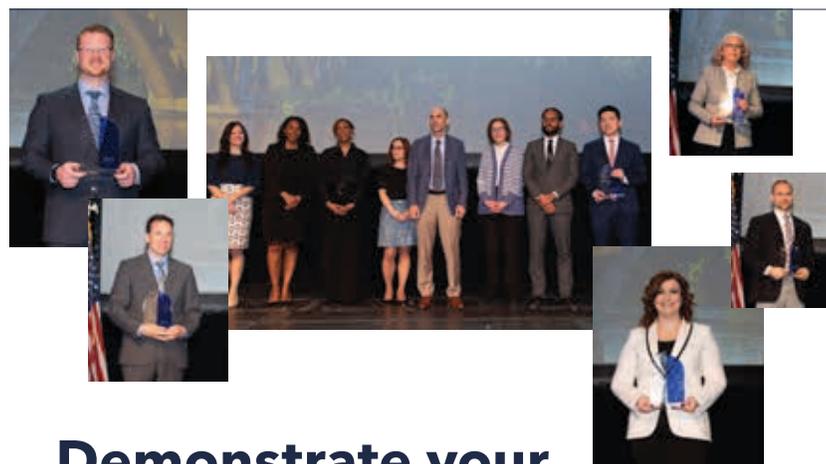
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IV fluid weaning unnecessary after gastroenteritis rehydration

By M. Alexander Otto

MDedge News

SEATTLE – Intravenous fluids can simply be stopped after children with acute viral gastroenteritis are rehydrated in the hospital; there's no need for a slow wean, according to a review at the Connecticut Children's Medical Center, Hartford.

Researchers found that children leave the hospital hours sooner, with no ill effects. "This study suggests that slowly weaning IV fluids may not be necessary," said lead investigator Danielle Klima, DO, a University of Connecticut pediatrics resident.

The team at Connecticut Children's noticed that weaning practices after gastroenteritis rehydration varied widely on the pediatric floors, and appeared to be largely provider dependent, with "much subjective decision making." The team wanted to see if it made a difference one way or the other, Dr. Klima said at the 2019 Pediatric Hospital Medicine Conference.

During respiratory season, "our pediatric floors are surging. Saving even a couple hours to get these kids out" quicker matters, she said, noting that it's likely the first time the issue has been studied.

The team reviewed 153 children aged 2 months to 18 years, 95 of whom had IV fluids stopped once physicians deemed they were fluid resuscitated and ready for an oral feeding trial; the other 58 were weaned, with at least two reductions by half before final discontinuation.

There were no significant differences in age, gender, race, or insurance type between the two



Dr. Danielle Klima

The team at Connecticut Children's noticed that weaning practices after gastroenteritis rehydration varied widely on the pediatric floors, and appeared to be largely provider dependent, with "much subjective decision making."

groups. The mean age was 2.6 years, and there were slightly more boys. The ED triage level was a mean of 3.2 points in both groups on a scale of 1-5, with 1 being the most urgent. Children with serious comorbidities, chronic diarrhea, feeding

tubes, severe electrolyte abnormalities, or feeding problems were among those excluded.

Overall length of stay was 36 hours in the stop group versus 40.5 hours in the weaning group ($P = .004$). Children left the hospital about 6 hours after IV fluids were discontinued, versus 26 hours after weaning was started (P less than .001).

Electrolyte abnormalities on admission were more common in the weaning group (65% versus 57%), but not significantly so ($P = .541$). Electrolyte abnormalities were also more common at the end of fluid resuscitation in the weaning arm, but again not significantly (65% vs 42%, $P = .077$).

Fluid resuscitation needed to be restarted in 15 children in the stop group (16%), versus 11 (19%) in the wean arm ($P = .459$). One child in the stop group (1%) versus four (7%) who were weaned were readmitted to the hospital within a week for acute viral gastroenteritis ($P = .067$).

"I expected we were taking a more conservative weaning approach in younger infants," but age didn't seem to affect whether patients were weaned or not, Dr. Klima said.

With the results in hand, "our group is taking a closer look at exactly what we are doing," perhaps with an eye toward standardization or even a randomized trial, she said.

She noted that weaning still makes sense for a fussy toddler who refuses to take anything by mouth.

There was no external funding, and Dr. Klima had no disclosures. The conference was sponsored by the Society of Hospital Medicine, the American Academy of Pediatrics, and the Academic Pediatric Association.

In newborns, concentrated urine helps rule out UTI

By M. Alexander Otto

MDedge News

SEATTLE – The more concentrated urine is in newborns, the more you can trust negative nitrite tests to rule out urinary tract infections, according to investigators at the University of Texas Health Science Center, Houston.

The researchers found that urine testing negative for nitrites with a specific gravity above 1.015 in children up to 2 months old had a sensitivity of 53% for ruling out UTIs, but that urine with a specific gravity below that mark had a sensitivity of just 14%. The finding "should be taken into account when interpreting nitrite results ... in this high-risk population," they concluded.

Bacteria in the bladder convert



Dr. Raymond Parlar-Chun

nitrites to nitrites, so positive results are pretty much pathognomonic for UTIs, with a specificity of nearly 100%, according to the researchers.

Negative results, however, don't

reliably rule out infection, and are even less reliable in infants because they urinate frequently, which means they usually flush out bacteria before they have enough time to make the conversion, which takes several hours, they said.

The lead investigator Raymond Parlar-Chun, MD, an assistant professor of pediatrics at the University of Texas McGovern Medical School in Houston, said he had a hunch that negative results might be more reliable when newborns urinate less frequently and have more concentrated urine.

He and his team reviewed data collected on 413 infants up to 2 months old who were admitted for fever work-up and treated for UTIs both in the hospital and after discharge. Nitrite results were stratified by urine concentration.

A specific gravity of 1.015 was used as the cutoff between concentrated and dilute urine, which was "midway between the parameters reported" in every urinalysis, Dr. Parlar-Chun said.

Although the sensitivity of concentrated urine was only 53%, "it's a stark difference from" the 14% in dilute urine, he said. "You should take a look at specific gravity to interpret nitrites. If urine is concentrated, you have [more confidence] that you don't have a UTI if you're negative. It's better than taking [nitrites] at face value."

The subjects were 31 days old, on average, and 62% were boys; 112 had a specific gravity above 1.015, and 301 below.

There was no external funding, and Dr. Parlar-Chun didn't have any disclosures.



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Too many blood cultures ordered for pediatric SSTIs

By M. Alexander Otto

MDedge News

SEATTLE – Blood cultures were ordered for over half of pediatric skin infection encounters across 38 children's hospitals, with rates varying from about 20% to 80% between hospitals, according to a review of almost 50,000 encounters in the Pediatric Health Information System database.

It was a surprising finding, because current guidelines from the Infectious Diseases Society of America do not recommend blood cultures as part of the routine evaluation of uncomplicated pediatric skin and soft-tissue infections (SSTIs), meaning infections in children who are otherwise healthy without neutropenia or other complicating factors.

Just 0.6% of the cultures were positive in the review, and it's likely some of those were caused by contamination. After adjustment for demographics, complex chronic



Dr. John Stephens

conditions, and severity of illness, culture draws were associated with a 20% increase in hospital length of stay (LOS), hospital costs, and 30-day readmission rates.

“Our data provide more evidence

that [routine] blood cultures for children with SSTI represents low-value practice and should be avoided,” said lead investigator John Stephens, MD, a pediatrics professor and hospitalist at the University of North Carolina at Chapel Hill.

Dr. Stephens became curious about how common the practice was across hospitals after he and a friend penned an article about the issue for the Journal of Hospital

Medicine’s “Things We Do for No Reason” series. The single-center studies they reviewed showed similarly high rates of both testing and negative cultures (J Hosp Med. 2018 Jul;13[7]:496-9).

Dr. Stephens and his team queried the Pediatric Health Information System database for encounters in children aged 2 months to 18 years with the diagnostic code 383, “cellulitis and other skin infections,” from 2012 to 2017, during which time “there really wasn’t a change” in IDSA guidance, he noted. Transfers, encounters with ICU care, and immunocompromised children were excluded.

Hospital admissions were included in the review if they had an additional code for erysipelas, cellulitis, impetigo, or other localized skin infection. The rate of positive cultures was inferred from subse-

quent codes for bacteremia or septicemia.

Across 49,291 encounters, the median rate of blood culture for skin infection was 51.6%, with tremendous variation between hospitals. With blood cultures, the hospital LOS was about 1.9 days, the hospital cost was \$4,030, and the 30-day readmission rate was 1.3%. Without cultures, LOS was 1.6 days, the cost was \$3,291, and the readmission rate was 1%.

Although infrequent, it’s likely that positive cultures triggered additional work-up, time in the hospital, and other measures, which might help account for the increase in LOS and costs.

As for why blood testing was so common, especially in some hospitals, “I think it’s just institutional culture. No amount of clinical variation in patient population could explain” a 20%-80% “variation across hospitals. It’s really just ingrained habits,” Dr. Stephens said at the 2019 Pediatric Hospital Medicine Conference.

“The rate of positive blood culture was really low, and the association was for higher cost and utilization. I think this really reinforces the IDSA guidelines. We need to focus on quality improvement

efforts to do this better,” he said, noting that he hopes to do so at his own institution.

“I’d also like to know more on the positives. In the single-center studies, we know more than half of them are contaminants. Often, there’s more contamination than true positives,” he said at the meeting sponsored by the Society of Hospital Medicine, the American Academy of Pediatrics, and the Academic Pediatric Association.

Instead of routine blood culture, Dr. Stephens recommended in his article to send pus for a Gram stain and culture and sensitivity, while noting that blood cultures remain reasonable for complicated infections, immunocompromised patients, and neonates.

There was no external funding, and Dr. Stephens didn’t report any disclosures.



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Procalcitonin advocated to help rule out bacterial infections

By M. Alexander Otto

MDedge News

SEATTLE – Procalcitonin, a marker of bacterial infection, rises and peaks sooner than C-reactive protein (CRP), and is especially useful to help rule out invasive bacterial infections in young infants and pediatric community-acquired pneumonia due to typical bacteria, according to a presentation at the 2019 Pediatric Hospital Medicine Conference.

It's "excellent for identifying low-risk patients" and has the potential to decrease lumbar punctures and antibiotic exposure, but "the specificity isn't great," so there's the potential for false positives, said Russell McCulloh, MD, a pediatric infectious disease specialist at the University of Nebraska Medical Center, Omaha.

There was great interest in procalcitonin at the meeting. Testing is available in many U.S. hospitals, but a large majority of audience members, when polled, said they don't currently use it in clinical practice, and that it's not a part of diagnostic algorithms at their institutions.

Levels of procalcitonin, a calcitonin precursor normally produced by the thyroid, are low or undetectable in healthy people, but inflammation, be it from infectious or noninfectious causes, triggers production by parenchymal cells throughout the body.

Levels began to rise as early as 2.5 hours af-



(From left) Dr. Marie Wang, Dr. Russell McCulloh, and Dr. Nivedita Srinivas

ter healthy subjects in one study were injected with bacterial endotoxins, and peaked as early as 6 hours; CRP, in contrast, started to rise after 12 hours, and peaked at 30 hours. Procalcitonin levels also seem to correlate with bacterial load and severity of infection, said Nivedita Srinivas, MD, a pediatric ID specialist at Stanford (Calif.) University (*J Pediatr Intensive Care*. 2016 Dec;5[4]:162-71).

The presenters focused their talk on community-acquired pneumonia (CAP) and invasive bacterial infections (IBI) in young infants, meaning essentially bacteremia and meningitis.

Different studies use different cutoffs, but a procalcitonin below, for instance, 0.5 ng/mL is "certainly more sensitive [for IBI] than any single biomarker we currently use," including CRP, white blood cells, and absolute neutrophil count (ANC). "If it's negative, you're really confident it's negative," but "a positive test does not necessarily indicate the presence of IBI," Dr. McCulloh said.

"Procalcitonin works really well as part of a validated step-wise rule" that includes, for instance, CRP and ANC; "I think that's where its utility is. On its own, it is not a substitute for you examining the patient and doing your basic risk stratification, but it may enhance your decision making incrementally above what we currently have," he said.

In a study of 532 children a median age of 2.4 years with radiographically confirmed CAP, procalcitonin levels were a median of 6.1 ng/mL in children whose pneumonia was caused by *Streptococcus pneumoniae* or other typical bacteria, and no child infected with typical bacteria had a level under 0.1 ng/mL (*J Pediatric Infect Dis Soc*. 2018 Feb 19;7[1]:46-53).

Below that level, "you can be very sure you do not have typical bacteria pneumonia," said Marie Wang, MD, also a pediatric ID specialist at Stanford. As procalcitonin levels went up, the likelihood of having bacterial pneumonia increased.

Short-course azithromycin no benefit in pediatric asthma admissions

By M. Alexander Otto

MDedge News

SEATTLE – Adding a 3-day course of azithromycin to treatment regimens of children hospitalized with asthma did not shorten length of stay or bring other benefits in a randomized, blinded trial of more than 150 youngsters at the Children's Hospital at Montefiore, New York.

In recent years, some pediatricians at Montefiore had begun giving short-course azithromycin to hospitalized children who were not recovering as quickly as they had hoped, spurred by outpatient reports of reduced exacerbations and other benefits with long-term azithromycin (e.g., *Lancet*. 2017 Aug 12;390(10095):659-68).

"We had no evidence for doing that at all" in the hospital, and it might be going on elsewhere, said senior investigator Alyssa Silver,

MD, assistant professor of pediatrics at Montefiore and Albert Einstein College of Medicine, New York. She and her colleagues, including primary investigator Lindsey Douglas, MD, assistant professor of pediatrics at the Icahn School of Medicine at Mount Sinai, New York, took a closer look.

The negative results mean that "we can stop doing this, giving kids unnecessary things. Word is starting to get out" at Montefiore. "People are not using it as much," she said at the 2019 Pediatric Hospital Medicine Conference, sponsored by SHM, the American Academy of Pediatrics, and the Academic Pediatric Association.

The team had expected azithromycin to shorten length of stay (LOS) by about half a day, because of its anti-inflammatory effects, but that's not what was found when they randomized 80 children aged

4-12 years with persistent asthma to oral azithromycin 10 mg/kg per day for 3 days within 12 hours of admission, and 79 to placebo.

LOS was 1.86 days in the placebo arm, and 1.69 days in the azithromycin group ($P = .23$). One placebo child was transferred to the pediatric ICU, versus none in the azithromycin arm ($P = .50$). The study was stopped short of its 214 subject enrollment goal because of futility, but even so, it was well powered to detect a difference in LOS, the primary outcome, Dr. Silver said.

At 1-week phone follow-up, 7 placebo children and 11 in the azithromycin arm had persistent asthma symptoms ($P = .42$), and 1 placebo child and 2 azithromycin children had been readmitted (P greater than .99). There were no differences in days of school missed, or workdays missed among parents and guardians.

At 1 month, 23 placebo and 18 azithromycin children had persistent asthma symptoms ($P = .5$); 7 placebo and 6 azithromycin children had returned to the ED ($P = .75$).

In short, "we really found no difference" with short-course azithromycin. "Clinicians should consider [these] data before prescribing azithromycin [to] children hospitalized with asthma," Dr. Silver and her team concluded.

Subjects were an average of about 7 years old, and about two-thirds were boys. They were not on azithromycin or other antibiotics prior to admission. About half had been admitted in the previous year, and about a quarter had at least one previous pediatric ICU admission. Over two-thirds had been on daily asthma medications. There were about 2 days of symptoms prior to admission.

Dr. Silver had no disclosures.

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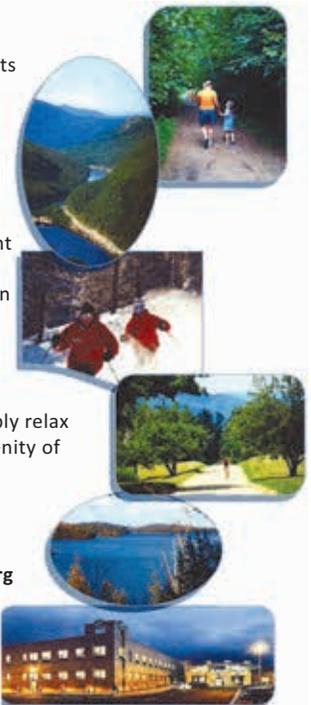
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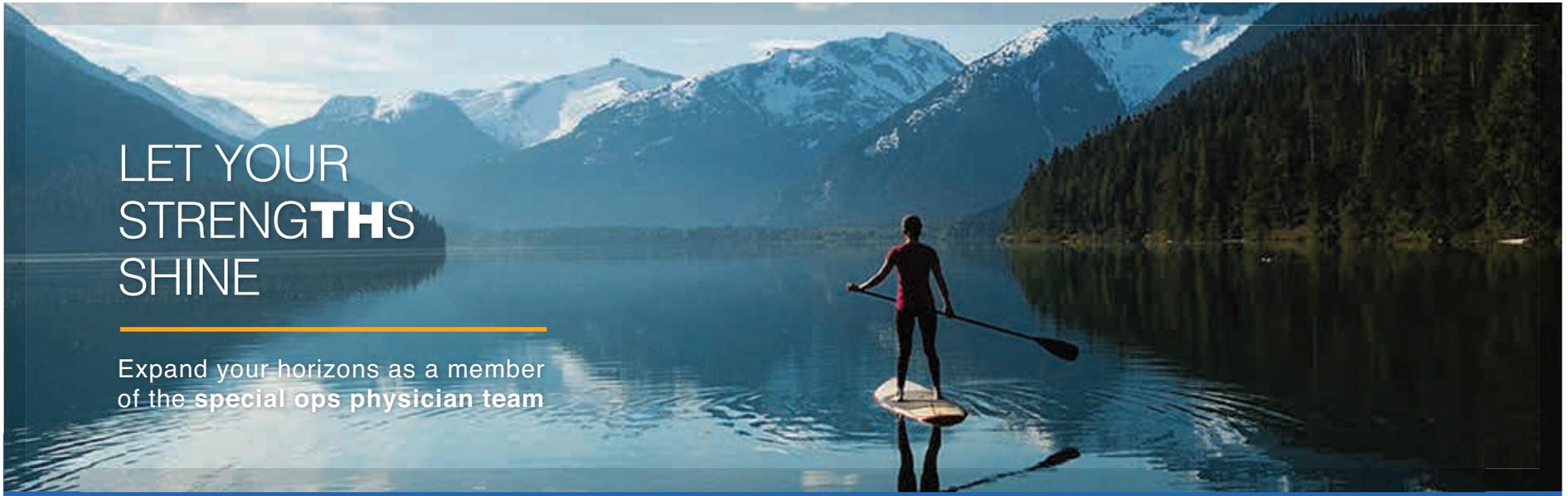
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THE Hospitalist

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CONTACT:
Heather Gonroski
 973.290.8259
hgonroski@mdedge.com
 or
Linda Wilson
 973.290.8243
lwilson@mdedge.com

Hospitalist/Nocturnist Cambridge Health Alliance

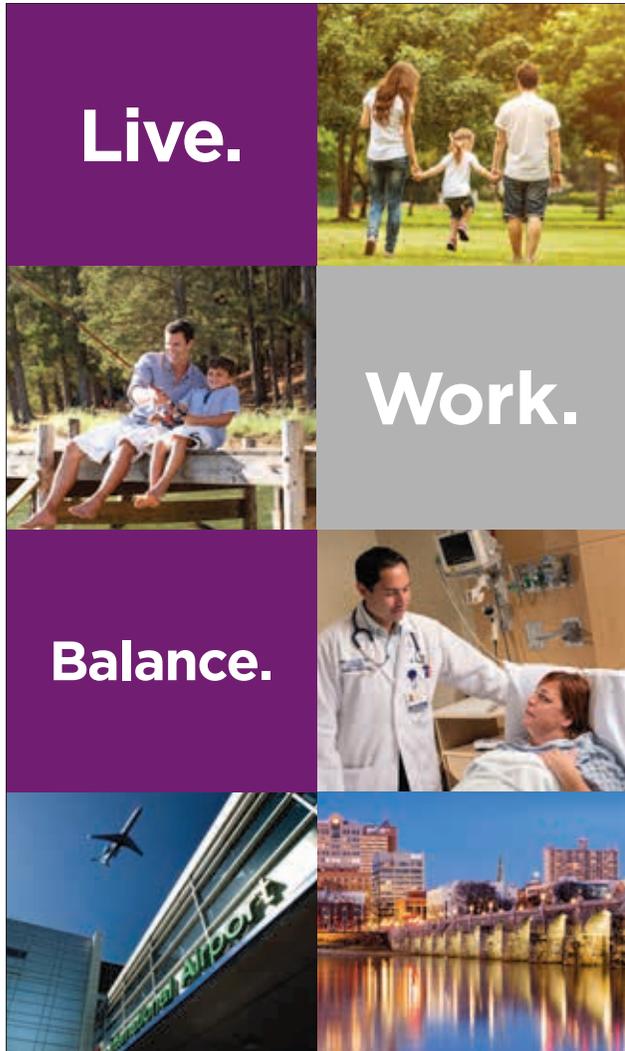
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For more information please contact:
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Reversal agents for direct-acting oral anticoagulants

Summary of guidelines published in the Journal of Hospital Medicine

By Matthew Tuck, MD, MEd, FACP

When on call for admissions, a hospitalist receives a request from a colleague to admit an octogenarian man with an acute uncomplicated deep vein thrombosis to start heparin, bridging to warfarin. The patient has no evidence of postphlebotic syndrome, pulmonary embolism, or right-sided heart strain. The hospitalist asks her colleague if he had considered treating the patient in the ambulatory setting using a direct-acting oral anticoagulant (DOAC). After all, this would save the patient an unnecessary hospitalization, weekly international normalized ratio checks, and other important lifestyle changes. In response, the colleague voices con-

risk of major bleeding with DOACs over warfarin but no difference in overall mortality when used to treat venous thromboembolism (see Table 2). Because of these combined advantages, DOACs are increasingly prescribed, accounting for approximately half of all oral anticoagulant prescriptions in 2014.

Although DOACs have been shown to be as good if not superior to VKAs and heparins in these circumstances, there are situations where a DOAC should not be used. There are limited data on the safety of DOACs in patients with mechanical heart valves, liver failure, and chronic kidney disease with a creatinine clearance less than 30 mL/min. Therefore, warfarin is still the preferred agent in these settings. There are some data that apixaban may be safe in patients with a creatinine clearance of greater

cizumab for patients on dabigatran and use of prothrombin complex concentrate (PCC) or recombinant coagulation factor Xa (andexanet alfa) for patients on apixaban or rivaroxaban for the treatment of life-threatening bleeding (see Table 3).

Idarucizumab is a monoclonal antibody developed to reverse the effects of dabigatran, the only DOAC that directly inhibits thrombin. In 2017, researchers reported on a cohort of subjects receiving idarucizumab for uncontrolled bleeding or who were on dabigatran and about to undergo an urgent procedure. Of those with uncontrolled bleeding, two-thirds had confirmed bleeding cessation within 24 hours. Periprocedural hemostasis was achieved in 93.4% of patients undergoing urgent procedures. However, it should be noted that use of idarucizumab conferred an increase risk (6.3%) of thrombosis within 90 days. Based on these findings, guidelines recommend use of idarucizumab in patients experiencing life-threatening bleeding, balanced against the risk of thrombosis.

In 2018, the Food and Drug Administration approved recombinant coagulation factor Xa for treatment of life-threatening or uncontrolled bleeding in patients on apixaban or rivaroxaban. The approval came after a study by the ANNEXA-4 investigators showed that recombinant coagulation factor Xa quickly and effectively achieved hemostasis. Full study results were published in April 2019, demonstrating 82% of patients receiving the drug attained clinical hemostasis. However, as with idarucizumab, up to 10% of patients had a thrombotic event in the follow-up period. Use of recombinant coagulation factor Xa for treatment of life-threatening bleeding related



Dr. Tuck is associate section chief for hospital medicine at the Veterans Affairs Medical Center in Washington, D.C.

Table 1. Comparison of mortality and bleeding-related mortality in patients with atrial fibrillation on DOACs or warfarin

Outcome	Event rates per year		Risk ratio	NNT/NNH*
	Warfarin	DOACs	DOAC vs. VKA	per year
All-cause mortality	4.87%	4.46%	0.90 (P <.0001)	244
Fatal hemorrhage	0.38%	0.19%	0.49 (P <.00001)	526

*Number needed to treat/number needed to harm

Source: J Am Coll Cardiol. 2016;68:2508-21

cern that the “new drugs don’t have antidotes.”

DOACs have several benefits over vitamin K antagonists (VKAs) and heparins. DOACs have quicker onset of action, can be taken by mouth, in general do not require dosage adjustment, and have fewer

than 10 mL/min, but long-term safety studies have not been performed in patients with end-stage renal disease on hemodialysis. Finally, in patients requiring concomitant inducers or inhibitors of the P-glycoprotein or cytochrome P450 enzymes like anti-epileptics and protease inhibitors,

VKAs and heparins are favored.

Notwithstanding their advantages, when DOACs first hit the market there were concerns that reversal agents were not available. In the

August issue of the *Journal of Hospital Medicine's* Clinical Guideline Highlights for the Hospitalist, Emily Gottenborg, MD, and Gregory Misky, MD, summarized guideline recommendations for reversal of the newer agents. This includes use of idaru-

Table 2. Mortality, major bleeding compared for DOACs or warfarin in venous thromboembolism

Outcome	Hazard ratio	Confidence interval
All-cause mortality	0.99	0.84-1.16
Major bleeding	0.92	0.82-1.03

Source: BMJ. 2017;359:j4323

dietary and lifestyle modifications, compared with VKAs and heparins. In atrial fibrillation, DOACs have been shown to have lower all-cause and bleeding-related mortality than warfarin (see Table 1). Observational studies also suggest less

to betrixaban and edoxaban is considered off label but is recommended by guidelines. Studies on investigational reversal agents for betrixaban and edoxaban are ongoing.

Both unactivated and activated PCC contain clotting factor X. Their use to control bleeding related to DOAC use is based on observational studies. In a systematic review of the nonrandomized studies, the efficacy of PCC to stem major bleeding was 69% and the risk for thromboembolism was 4%. There are no head-to-head studies comparing use of recombinant coagulation factor Xa and PCC. Therefore, guidelines are to use either recombinant factor Xa or PCC for the treatment of life-threatening bleeding related to DOAC use.

As thrombosis risk heightens after use of any reversal agent, the recommendations are to resume anticoagulation within 90 days if the patient is at moderate or high risk for recurrent thromboembolism.

After discussion with the hospitalist about the new agents available to reverse anticoagulation, the colleague decided to place the patient on a DOAC and keep him in his nursing home. The patient did not thereafter experience sustained bleeding necessitating use of these reversal agents. More importantly for the patient, he was able to stay in the comfort of his home.

Table 3. Reversal agent(s) for direct oral anticoagulants

Anticoagulant	Reversal Agent(s)
Apixaban	PCC or recombinant coagulation factor Xa
Betrixaban*	
Edoxaban*	
Rivaroxaban	Idarucizumab
Dabigatran	

*Off-label recommendation to use recombinant coagulation factor Xa in these drugs

Source: Dr. Tuck

For a complete list of references, see the online version of this article at www.the-hospitalist.org.

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