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## A VICIOUS CYCLE WITH SIGNIFICANT BURDEN

WHAT COULD BE THE CONSEQUENCES OF RECURRENT *C. DIFFICILE* INFECTION?

## Learn why it requires aggressive action



THE CDC ACKNOWLEDGES C. DIFFICILE INFECTION AS A MAJOR AND URGENT THREAT.<sup>1</sup>



IT RECURS IN UP TO 35% OF CASES WITHIN 8 WEEKS AFTER INITIAL DIAGNOSIS.<sup>2,3</sup>



THE CONSEQUENCES OF RECURRENCE ARE SIGNIFICANT, **POTENTIALLY DEADLY**.<sup>2</sup>

Now is the time to learn how Ferring is shedding light on the link between disease and disruptions in the gut microbiome, exploring the potential for repopulating its diversity and restoring hope to patients.

**References: 1.** Centers for Disease Control and Prevention. 2019 Antibiotic Resistance Threats Report: *Clostridioides Difficile*. https://www.cdc. gov/drugresistancxqe/pdf/threats-report/clostridioides-difficile-508.pdf. Accessed April 8, 2021. **2.** Lessa FC, Mu Y, Bamberg WM, et al. Burden of *Clostridium difficile* infection in the United States. *N Engl J Med*. 2015;372(9):825-834. **3.** Cornely OA, Miller MA, Louie TJ, Crook DW, Gorback SL. Treatment of first recurrence of *Clostridium difficile* infection: fidaxomicin versus vancomycin. *Clin Infect Dis*. 2012;55(suppl 2):s154-s161.





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## **Hospitalists: Leading** into the Future

By Rachel Thompson, MD, MPH, SFHM, SHM president

February of 2019, I wrote The Amazing Work We *Get To Do* 10 months before the first case of COVID-19 at Providence Everett in Washington was diagnosed. In that article, I

wrote of the evolving health care landscape in our country, the opportunities ahead, and how "our hospital

medicine



Dr. Thompson workforce is innovative, diverse,

tech-savvy, and poised for leading." It's unreal to think about what's happened since then. On a personal note, I moved back to my home state in the Northwest to develop an acute care division. Within a year, it was facing previously unimaginable events head-on. We were at the epicenter of a pandemic in the U.S. There was a new disease. We were afraid. Did we have enough N95s? Would these protect us? How could we help our patients? Were there enough ventilators? Would we have to just watch patients die? And at the ends of our days, when we came home weary, we wondered if we were risking our families' lives.

We all experienced it. We saw the death. We saw our teams suffering trying to care for people with what felt like few resources. Across the country, we saw halls lined with ventilated patients. We saw colleagues fall sick with COVID-19. One colleague, exposed at work, transferred in with severe COVID-19. He almost died. Through some miracle (and possibly extracorporeal membrane oxygenation), he managed to survive. Others did not.

In the chaos, we turned to innovation. Could we prone a patient to improve outcomes? Was this similar to acute respiratory distress syndrome? Would steroids help? Could we monitor patients remotely to prevent admissions and reduce overcrowding? We built teams and infrastructures and innovative staffing models to brace for volumes beyond capacity. We talked of rationing resources and readied models for the day they would be needed. We deployed remote home oxygen monitoring to avoid hospitalization in lower-risk COVID-19 patients. We became experts at consent for emergency use authorization. Our colleagues led trials to evaluate new treatments. My teams published on decreasing COVID mortality over time and on the duration of treatment with remdesivir.

COVID-19 mutated and hit from another direction—sowing more fear in our hearts and minds.

Political voices influenced health care, telling us how to practice, how to treat, and whether to even be concerned. Celebrated as heroes early on, we were accused, by some, of being government drones refusing to treat with ivermectin or injecting nano-bots into the arms of our communities. One colleague's team faced people accusing them of *prescribing* fake therapies and refusing to provide appropriate care in their lobby. On the radio, some of us were berated daily. We suffered. We struggled to find our footing. Some of us lost our way. We lost our tempers. We lost our perspective. We lost hope. We lost a colleague to death by suicide. He was not the only one to fall to the stress of our profession.

Through it all, our teams kept showing up. We covered for each other; we took extra shifts. We continued our tradition of innovation. We installed hospitalist robots to spread our clinicians across the country, harnessing some of the most efficient models of care imaginable. Where there were no robots, we used iPads. We leveraged telerounding—seeing patients in ICUs across the country, rounding from home while in isolation, and attending to patients in pop-up COVID-19 hospitals. We developed teams across competitor health systems, prioritizing serving patients. We developed geographic care models on units and in isolated hospitals to treat COVID-19—to create transitions units when discharges seemed impossible. We dissolved archaic med-staff rules preventing advanced practice providers from working independently at top-of-license. We learned to come together on Zoom, Teams, and webinars. We learned how to unmute.

What made us *the* profession poised to lead the U.S. into the future of health care in 2019 is exactly what made us *the* profession to lead through 27 months of the pandemic. For all the negatives we have experienced, for all the pain we have endured, we stand today altogether stronger.

Our communities and our country see us now; they understand our value. Being a hospitalist continues to be about serving people, connecting, and improving care. Touring #HowWeHospitalist, it is clear we work hard, we teach, we care, we have pride in our work, we advocate for others, we serve our communities, and we are talented, tireless, dedicated. Whatever comes next, we are the teams that will lead into the future.

## HELP SHORTEN TIME TO RECOVERY

## For patients hospitalized with COVID-191

## **INDICATION**

VEKLURY is indicated for the treatment of adults and pediatric patients  $\geq$ 12 years old and weighing  $\geq$ 40 kg requiring hospitalization for COVID-19. VEKLURY should only be administered in a hospital or healthcare setting capable of providing acute care comparable to inpatient hospital care.

EXIT

## **IMPORTANT SAFETY INFORMATION**

## Contraindication

• VEKLURY is contraindicated in patients with a history of clinically significant hypersensitivity reactions to VEKLURY or any of its components.

## Warnings and precautions

- Hypersensitivity, including infusion-related and anaphylactic reactions: Hypersensitivity, including infusion-related and anaphylactic reactions, has been observed during and following administration of VEKLURY. Monitor patients under close medical supervision for hypersensitivity reactions during and following administration of VEKLURY. Symptoms may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnea, wheezing, angioedema, rash, nausea, diaphoresis, and shivering. Slower infusion rates (maximum infusion time ≤120 minutes) can potentially prevent these reactions. If a severe infusion-related hypersensitivity reaction occurs, immediately discontinue VEKLURY and initiate appropriate treatment (see Contraindications).
- Increased risk of transaminase elevations: Transaminase elevations have been observed in healthy volunteers and in patients with COVID-19 who received VEKLURY; these elevations have also been reported as a clinical feature of COVID-19. Perform hepatic laboratory testing in all patients (see Dosage and administration). Consider discontinuing VEKLURY if ALT levels increase to >10x ULN. Discontinue VEKLURY if ALT elevation is accompanied by signs or symptoms of liver inflammation.
- Risk of reduced antiviral activity when coadministered with chloroquine or hydroxychloroquine: Coadministration of VEKLURY with chloroquine phosphate or hydroxychloroquine sulfate is not recommended based on data from cell culture experiments, demonstrating potential antagonism, which may lead to a decrease in the antiviral activity of VEKLURY.

## **Adverse reactions**

- The most common adverse reaction ( $\geq$ 5% all grades) was nausea.
- The most common lab abnormalities ( $\geq$ 5% all grades) were increases in ALT and AST.

## **Drug interactions**

• Drug interaction trials of VEKLURY and other concomitant medications have not been conducted in humans.







## (Median 10 days vs 15 days with placebo; recovery rate ratio: 1.29 [95% Cl, 1.12-1.49], p<0.001)

Recovery included hospital discharge for some patients with or without limitations on activities<sup>1</sup>

## Adverse reaction frequency was comparable between VEKLURY and placebo<sup>1</sup>

All adverse reactions (ARs), Grades ≥3: 41 (8%) with VEKLURY vs 46 (9%) with placebo; serious ARs: 2 (0.4%)\* vs 3 (0.6%); ARs leading to treatment discontinuation: 11 (2%)<sup>+</sup> vs 15 (3%)

ACTT-1 was a randomized, double-blind, placebo-controlled clinical trial in hospitalized patients with mild/moderate, and severe COVID-19. Patients received **VEKLURY (n=541)** or **placebo (n=521)** for up to 10 days. The primary endpoint was time to recovery within 29 days after randomization.<sup>1</sup>

\*Seizure (n=1), infusion-related reaction (n=1).

<sup>+</sup>Seizure (n=1), infusion-related reaction (n=1), transaminases increased (n=3), ALT increased and AST increased (n=1), GFR decreased (n=2), acute kidney injury (n=3).

## **IMPORTANT SAFETY INFORMATION** (cont'd)

## **Dosage and administration**

- **Dosage:** For adults and pediatric patients ≥12 years old and weighing ≥40 kg: 200 mg on Day 1, followed by once-daily maintenance doses of 100 mg from Day 2 administered only via intravenous infusion over 30 to 120 minutes.
- **Treatment duration:** For patients not requiring invasive mechanical ventilation and/or extracorporeal membrane oxygenation (ECMO): 5 days; may be extended up to 5 additional days (10 days total) if clinical improvement is not observed. For patients requiring invasive mechanical ventilation and/or ECMO: 10 days.
- **Testing prior to and during treatment:** Perform eGFR, hepatic laboratory, and prothrombin time testing prior to initiating VEKLURY and during use as clinically appropriate.
- **Renal impairment:** VEKLURY is not recommended in individuals with eGFR <30 mL/min.
- Dose preparation and administration: See full Prescribing Information.

## **Pregnancy and lactation**

- Pregnancy: There are insufficient human data on the use of VEKLURY during pregnancy. Pregnant women hospitalized with COVID-19 are at risk for serious morbidity and mortality. VEKLURY should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.
- Lactation: It is not known whether VEKLURY can pass into breast milk. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

## Please see Brief Summary of full Prescribing Information on the following page.

Reference: 1. VEKLURY. Package insert. Gilead Sciences, Inc.; 2021.



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#### **VEKLURY®** (remdesivir)

## Brief summary of full Prescribing Information. Please see full Prescribing Information. Rx Only.

#### INDICATIONS AND USAGE

VEKLURY is indicated for the treatment of adults and pediatric patients  $\geq$ 12 years old and weighing  $\geq$ 40 kg requiring hospitalization for COVID-19. VEKLURY should only be administered in a hospital or healthcare setting capable of providing acute care comparable to inpatient hospital care.

## **DOSAGE AND ADMINISTRATION** [Also see Warnings and Precautions, Adverse Reactions, and Use in Specific Populations]:

**Testing Before Initiation and During Treatment**: Perform eGFR, hepatic laboratory, and prothrombin time testing prior to initiating VEKLURY and during use as clinically appropriate.

**Recommended Dosage in Adults and Pediatric Patients**  $\geq$ **12 Years Old and Weighing**  $\geq$ **40 kg:** 200 mg on Day 1, followed by once-daily maintenance doses of 100 mg from Day 2 administered only via intravenous infusion.

- Recommended duration for patients not requiring invasive mechanical ventilation and/or extracorporeal membrane oxygenation (ECMO) is 5 days and may be extended for up to 5 additional days (10 days total), if clinical improvement is not observed.
- Recommended duration for patients requiring invasive mechanical ventilation and/or ECMO is 10 days.
- VEKLURY must be diluted prior to infusion.

**Renal Impairment:** VEKLURY is not recommended in individuals with eGFR <30 mL/min. Dose Preparation and Administration *[See Full Prescribing Information for Complete Instructions on Dose Preparation, Administration, and Storage]:* 

VEKLURY must be prepared and administered under supervision of a healthcare provider and must be administered via intravenous infusion only, over 30 to 120 minutes. Do not administer the prepared diluted solution simultaneously with any other medication. VEKLURY is available in two dosage forms:

- VEKLURY for injection (supplied as 100 mg lyophilized powder in vial) must be reconstituted with Sterile Water for Injection prior to diluting in a 100 mL or 250 mL 0.9% sodium chloride infusion bag.
- VEKLURY injection (supplied as 100 mg/20 mL [5 mg/mL] solution in vial), must be diluted in a 250 mL 0.9% sodium chloride infusion bag.
- Care should be taken during admixture to prevent inadvertent microbial contamination; there is no preservative or bacteriostatic agent present in these products.

#### CONTRAINDICATIONS [Also see Warnings and Precautions]:

VEKLURY is contraindicated in patients with a history of clinically significant hypersensitivity reactions to VEKLURY or any of its components.

## WARNINGS AND PRECAUTIONS [Also see Contraindications, Dosage and Administration, and Adverse Reactions, and Drug Interactions]:

Hypersensitivity, Including Infusion-Related and Anaphylactic Reactions: Hypersensitivity, including infusion-related and anaphylactic reactions, has been observed during and following administration of VEKLURY. Monitor patients under close medical supervision for hypersensitivity reactions during and following administration of VEKLURY. Symptoms may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnea, wheezing, angioedema, rash, nausea, diaphoresis, and shivering. Slower infusion rates (maximum infusion time ≤120 minutes) can potentially prevent these signs and symptoms. If a severe infusion-related hypersensitivity reaction occurs, immediately discontinue VEKLURY and initiate appropriate treatment.

**Increased Risk of Transaminase Elevations:** Transaminase elevations have been observed in healthy volunteers and in patients with COVID-19 who received VEKLURY; the transaminase elevations were mild to moderate (Grades 1-2) in severity and resolved upon discontinuation. Because transaminase elevations have been reported as a clinical feature of COVID-19, and the incidence was similar in patients receiving placebo versus VEKLURY in clinical trials, discerning the contribution of VEKLURY to transaminase elevations in patients with COVID-19 can be challenging. Perform hepatic laboratory testing in all patients.

• Consider discontinuing VEKLURY if ALT levels increase to >10x ULN.

• Discontinue VEKLURY if ALT elevation is accompanied by signs or symptoms of liver inflammation.

**Risk of Reduced Antiviral Activity When Coadministered With Chloroquine or Hydroxychloroquine:** Coadministration of VEKLURY with chloroquine phosphate or hydroxychloroquine sulfate is not recommended based on data from cell culture experiments, demonstrating potential antagonism which may lead to a decrease in antiviral activity of VEKLURY.

#### ADVERSE REACTIONS [Also see Warnings and Precautions]:

**Clinical Trials Experience:** The safety of VEKLURY is based on data from three Phase 3 studies in 1,313 hospitalized adult subjects with COVID-19, four Phase 1 studies in 131 healthy adults, and from patients with COVID-19 who received VEKLURY under the Emergency Use Authorization or in a compassionate use program. The NIAID ACTT-1 study was conducted in hospitalized subjects with mild, moderate, and severe COVID-19 treated with VEKLURY (n=532) for up to 10 days. Study GS-US-540-5773 (Study 5773) included subjects hospitalized with severe COVID-19 and treated with VEKLURY for 5 (n=200) or 10 days (n=197). Study GS-US-540-5774 (Study 5774) was conducted in hospitalized subjects with moderate COVID-19 and treated with VEKLURY for 5 (n=191) or 10 days (n=193).

Adverse Reactions: The most common adverse reaction ( $\geq$ 5% all grades) was nausea.

*Less Common Adverse Reactions:* Clinically significant adverse reactions reported in <2% of subjects exposed to VEKLURY in clinical trials include hypersensitivity reactions, generalized seizures, and rash.

Laboratory Abnormalities: In a Phase 1 study in healthy adults, elevations in ALT were observed in 9 of 20 subjects receiving 10 days of VEKLURY (Grade 1, n=8; Grade 2, n=1);

the elevations in ALT resolved upon discontinuation. No subjects (0 of 9) who received 5 days of VEKLURY had graded increases in ALT.

Laboratory abnormalities (Grades 3–4) occurring in  $\geq$ 3% of subjects receiving VEKLURY in Trials NIAID ACTT-1, Study 5773, and/or Study 5774, respectively were: ALT increased (3%,  $\leq$ 8%,  $\leq$ 3%), AST increased (6%,  $\leq$ 7%, n/a), creatinine clearance decreased, Cockcroft-Gault formula (18%,  $\leq$ 19%,  $\leq$ 5%), creatinine increased (15%,  $\leq$ 15%, n/a), eGFR decreased (18%, n/a, n/a), glucose increased (12%,  $\leq$ 11%,  $\leq$ 4%), hemoglobin decreased (15%,  $\leq$ 8%,  $\leq$ 3%), lymphocytes decreased (11%, n/a, n/a), prothrombin time increased (9%, n/a, n/a).

#### DRUG INTERACTIONS [Also see Warnings and Precautions]:

Due to potential antagonism based on data from cell culture experiments, concomitant use of VEKLURY with chloroquine phosphate or hydroxychloroquine sulfate is not recommended.

Drug-drug interaction trials of VEKLURY and other concomitant medications have not been conducted in humans. Remdesivir and its metabolites are in vitro substrates and/or inhibitors of certain drug metabolizing enzymes and transporters. The clinical relevance of these in vitro assessments has not been established.

#### **USE IN SPECIFIC POPULATIONS** [Also see **Dosage and Administration and Warnings** and **Precautions**]:

#### Pregnancy

*Risk Summary:* There are insufficient human data on the use of VEKLURY during pregnancy to inform a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

*Clinical Considerations: Disease-associated maternal and/or embryo-fetal risk:* Pregnant women hospitalized with COVID-19 are at risk for serious morbidity and mortality. VEKLURY should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and fetus.

#### Lactation

*Risk Summary:* There are no available data on the presence of remdesivir in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies, remdesivir and metabolites have been detected in the nursing pups of mothers given remdesivir, likely due to the presence of remdesivir in milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VEKLURY and any potential adverse effects on the breastfeed child from VEKLURY or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

#### **Pediatric Use**

The safety and effectiveness of VEKLURY for the treatment of COVID-19 have been established in pediatric patients  $\geq$ 12 years old and weighing  $\geq$ 40 kg. Use in this age group is based on extrapolation of pediatric efficacy from adequate and well-controlled studies in adults. The safety and effectiveness of VEKLURY have not been established in pediatric patients younger than 12 years of age or weighing less than 40 kg.

### **Geriatric Use**

Dosage adjustment is not required in patients over the age of 65 years. Appropriate caution should be exercised in the administration of VEKLURY and monitoring of elderly patients, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of potential concomitant disease or other drug therapy.

#### **Renal Impairment**

All patients must have an eGFR determined before starting VEKLURY and while receiving VEKLURY as clinically appropriate. VEKLURY is not recommended in patients with eGFR less than 30 mL/min.

#### **Hepatic Impairment**

Perform hepatic laboratory testing in all patients before starting VEKLURY and while receiving VEKLURY as clinically appropriate.

#### OVERDOSAGE

There is no human experience of acute overdosage with VEKLURY. Treatment of overdose with VEKLURY should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. There is no specific antidote for overdose with VEKLURY.

#### 214787-GS-001

For information about emergency use in hospitalized pediatric patients weighing 3.5 kg to <40 kg or <12 years old weighing  $\geq$ 3.5 kg, please see the EUA Fact Sheet and FDA Letter of Authorization available at gilead.com/remdesivir. The FDA has not approved VEKLURY for use in this population, and the safety and efficacy for this use have not been established.



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## **Maine Medical Center Research Reviews**

the Literature

By Kristen Bartlett, MD; Matthew Clark, DO; Lesley Gordon, MD, MS; Raymond Klein, MD; Adam Long, MD; Innocent Ndzana, DO; Nellie Wood, MD

Maine Medical Center

## IN THIS ISSUE

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- Apixaban plus a P2Y<sub>12</sub> inhibitor best balances bleeding and ischemic events in patients with atrial fibrillation and recent acute coronary syndrome or percutaneous coronary intervention
- 6. CPAP reduces the risk of intubation among patients with acute hypoxemic respiratory failure and COVID-19
- 7. A structured end-of-life communication strategy reduces prolonged grief in families of dying ICU patients

### By Kristen Bartlett, MD

 Negative initial CSF studies in HSV encephalitis portend worse neurologic outcomes

CLINICAL QUESTION: Does delay in diagnosis

of herpes simplex virus (HSV) encephalitis due to negative initial cerebrospinal fluid (CSF) studies affect neurologic outcomes?



Dr. Bartlett

BACKGROUND: Case

reports and series have demonstrated poor out-

comes for patients in whom diagnosis and treatment of HSV encephalitis have been delayed, though frequency and severity have not been reported.

**STUDY DESIGN:** Retrospective study

SETTING: French intensive care units (ICUs)

## **SHORT TAKES**

## Allopurinol unlikely to affect mortality in pre-existing CKD

A cohort study of patients with concurrent gout and moderate-severe chronic kidney disease (CKD) suggests that neither initiation of allopurinol nor dose adjustment per uric acid level significantly affects allcause mortality.

**CITATION:** Wei J, et al. Allopurinol initiation and all-cause mortality among patients with gout and concurrent chronic kidney disease: A population-based cohort study [published online ahead of print, 2022 Jan 25]. *Ann Intern Med*. 2022 Jan 25. doi:10.7326/M21-2347.

Kristen Bartlett, MD

SYNOPSIS: This study was a secondary analysis of a retrospective database of 273 patients with confirmed HSV encephalitis admitted to 47 ICUs. On initial lumbar puncture, 11 cases (4%) had negative HSV polymerase chain reaction (PCR) tests and 43 cases (16.5%) had normal CSF leukocyte count. All the false-negative PCR tests occurred when the lumbar puncture had been performed within four days of symptom onset. Patients with negative PCRs were more likely to have atypical presentations with focal neurologic deficits (4/11 [36.4%] versus 35/256 [13.7%]; P=0.04), as well as to have lower CSF leukocyte counts. This corresponded with delayed time to treatment with acyclovir (3 d [2–7 d] versus 0 d [0–0 d]; *P*<0.01) and higher rates of modified Rankin Score ≥4 at hospital discharge (10/11 [90.9%] versus 91/262 [34.7%]; P<0.01). This study is limited by both its retrospective nature and its small sample size.

**BOTTOM LINE:** When an alternative diagnosis is not evident in patients with a highly suspicious presentation for HSV and early negative CSF studies, clinicians should pursue a multimodal approach to diagnosis (e.g., MRI, EEG) and discontinue empiric treatment with caution, given the risks of worsened neurologic outcomes.

**CITATION:** de Montmollin E, et al. herpes simplex virus encephalitis with initial negative polymerase chain reaction in the cerebrospinal fluid: prevalence, associated factors, and clinical impact [published online ahead of print, 2022 Feb 2]. *Crit Care Med.* 2022 Feb 2. doi:10.1097/ CCM.000000000005485.

> Dr. Bartlett is a third-year internal medicine resident at Maine Medical Center, Portland, Maine, who's pursuing a career in hospital medicine.

By Matthew Clark, DO

2 Statins should be continued in hospitalized patients with COVID-19

**CLINICAL QUESTION:** Does discontinuation of

atorvastatin in those hospitalized with COVID-19 change the risk of mortality and ventilation?



BACKGROUND: Statins are ubiquitous. Statins may be beneficial in COVID-19 given their intrinsic

anti-inflammatory properties and ability to upregulate the angiotensin-converting enzyme-2 receptor. Some observational studies have linked statin use to lower mortality in COVID-19, and current guidelines recommend its continuation in those with COVID-19.

**STUDY DESIGN:** Retrospective chart analysis

**SETTING:** Electronic health records associated with HCA Healthcare (Nashville, Tenn.) facilities across 21 U.S. states

**SYNOPSIS:** Medication administration data was collected for all patients admitted with a laboratory-confirmed diagnosis of COVID-19 from 2015 to 2019. Patients (n = 146,413) were divided into three groups for analysis: continuation of statin group; discontinuation of statin group; and no statin group. Logistic regression analysis was performed to assess the associations between atorvastatin use, mortality, and mechanical ventilation.

In comparison to discontinuation of statin therapy, those who received continuous statin therapy had a reported, significant 35% reduction in odds of mortality. Compared to those with no known prior statin use, patients with continuous use had a reported, significant 28% reduction in odds of mortality. Compared to no known statin use, those with discontinuation had no change in odds of mortality (OR: 1.01). In the secondary analysis, the odds of ventilation

## **SHORT TAKES**

### White blood cell scintigraphy: a lowyield study for fever of unknown origin

A retrospective chart analysis of white blood cell scans (WBCS) in the setting of fever of unknown origin showed a low positivity rate (38%) and a high false positivity rate (62%). Among true positives, alternative studies revealed the diagnosis.

**CITATION:** Fisher RE, et al. Lack of clinical utility of labeled white blood cell scintigraphy in patients with fever of unknown origin. *Open Forum Infect Dis.* 2022;9(3):ofac015. doi: 10.1093/ofid/ofac015.

Matthew Clark, DO

### IN THE LITERATURE

were similarly decreased in the continuous group compared to the discontinuation group.

Potential confounding is a significant limitation. For example, clinical factors (such as the severity of illness) likely contributed to the discontinuation of statins on admission. A prospective, randomized, controlled trial would be helpful.

**BOTTOM LINE:** Continuation of statin therapy does not appear to be harmful, and discontinuation may be associated with poorer outcomes. Providers should follow guideline recommendations to continue statin therapy in those hospitalized with COVID-19.

**CITATION:** Andrews L, et al. Discontinuation of atorvastatin use in hospital is associated with increased risk of mortality in COVID-19 patients. *J Hosp Med.* 2022;17:169-175.

Dr. Clark is an internal medicine chief resident at Maine Medical Center, Portland, Maine who's pursuing a career in hospital medicine.

## By Lesley Gordon, MD, MS

**3** Non-gastrointestinal complications, including ischemic stroke, are more common than bleeding or perforation following screening colonoscopy in older adults

CLINICAL QUESTION: What serious non-gas-

trointestinal adverse events are due to screening colonoscopy?

BACKGROUND: Although

the gastrointestinal (GI) risks of colonoscopy have been described, the frequency and time course for non-gastrointestinal



Dr. Gordon

(non-GI) adverse events are less well understood. Prior reports of post-procedural non-GI complications are difficult to interpret, given that they did not account for the baseline rate of these events.

## **STUDY DESIGN:** Retrospective study

**SETTING:** All screening/surveillance colonoscopies in the states of California (2005-2011), Florida (2009-2015), and New York (2009-2015): a total of 4.5 million colonoscopies.

**SYNOPSIS:** This study reviewed databases from six months before through six months after colonoscopies and determined rates and timelines of GI (lower GI bleeding or perforation) and non-GI (acute myocardial infarction, congestive heart failure, arrhythmia, stroke/ transient ischemic attack, pneumonia, or in-hospital death) adverse events. The patients "served as their own controls," whereby the stable pre-colonoscopy event rates were used to approximate the "background rates" of these adverse events.

As expected, the elevated risk of perforation and GI bleeding after colonoscopies was much more dramatic than non-GI adverse events (e.g., observed:expected ratio of perforation the week after colonoscopy was 14 and the observed:expected ratio of transient ischemic attack was 1.58). However, when looking at the sheer number of complications, the older cohort (≥65 years old) experienced more non-GI compared to GI complications. For example, in patients ≥75 years old, colonoscopy-associated

## SHORT TAKES

## Most women with high-risk, early-stage ovarian cancer do indeed have symptoms

This retrospective chart review of 419 patients with high-risk, early-stage ovarian cancer revealed that more than 70% of patients had symptoms, most commonly abdominal/ pelvic pain (31%), increased abdominal girth or fullness (26%), abnormal vaginal bleeding (13%), and urinary symptoms (10%). This study, among others, is starting to shift the

ischemic stroke was more common than perforation (1,279 versus 912 colonoscopy-associated events).

The limitations of this study relate to its retrospective nature. Notably, we do not know whether patients had discontinued cardio- or neuroprotective medications such as anticoagulants. In addition, although the authors did a laudable job of attempting to establish background rates of adverse events, they were imperfect estimates.

**BOTTOM LINE:** This study is an important reminder that the risks of colonoscopies, especially for our older patients, extend beyond the more commonly feared GI side effects. The risk of non-GI complications must also be considered.

**CITATION:** Ladabaum U, et al. Age-specific rates and time-courses of gastrointestinal and nongastrointestinal complications associated with screening/surveillance colonoscopy. *Am J Gastroenterol*. 2021;116(12):2430-45. doi: 10.14309/ ajg.00000000001531.

### Health care systems can do more to support environmental health services employees

**CLINICAL QUESTION:** What has been the experience of environmental services (EVS) employees working during the COVID-19 pandemic?

**BACKGROUND:** EVS employees play an essential role in preventing the transmission of infectious diseases due to their work cleaning and sanitizing the hospital environment. However, they're among the lowest-remunerated health care workers and had reported feeling undervalued even prior to the onset of the pressures associated with the COVID-19 pandemic.

**STUDY DESIGN:** Semi-structured interviews, followed by qualitative thematic analysis

**SETTING:** Quaternary care academic medical center in Colorado

SYNOPSIS: 16 of 305 EVS employees were interviewed, of whom 70% identified as female, 50% as black, and 31% as Hispanic. The research team identified four core themes of the up to one-hour interviews. First, is the need for training and education, including translation and protocol refreshers. Second, is emotional strain, such as seeking meaning through their interactions with patients, the suffering they are observing in the COVID-19 patients, and the stress of exposure risk. Third, resource challenges, such as adequate personal protective equipment, staffing, turnover, and burnout. Lastly, the lack of recognition as frontline workers, both in mainstream media and in their day-to-day jobs.

narrative that ovarian cancer is a "silent disease."

**CITATION:** Chan JK, et al. Symptoms of women with high-risk early-stage ovarian cancer. *Obstet Gynecol*. 2022;139(2):157-162. doi: 10.1097/ AOG.000000000004642.

Lesley Gordon, MD

Interviewees highlighted the negative impact of hospital hierarchy, yet they also noted that acknowledgment and support from interdisciplinary colleagues played a role in mitigating the lack of recognition.

The authors take the results of these structured interviews and make recommendations for hospital systems. They recommend advocating for increasing the benefits of EVS employees to be more in line with other health care workers', enhancing native language education, and creating intentional appreciation programs.

**BOTTOM LINE:** The COVID-19 pandemic has exacerbated the stressors already facing our EVS colleagues; hospital systems must do more to provide training as well as financial and emotional support.

**CITATION:** Jordan SR, et al. Forgotten frontline workers: Environmental health service employees' perspectives on working during the COVID pandemic. *J Hosp Med*. 2022;17:158-168. doi: 10.1002/jhm.12781.

Dr. Gordon is an associate program director of the internal medicine residency at Maine Medical Center, Portland, Maine, an assistant professor at Tufts University School of Medicine, Boston, and a hospital medicine physician.

### By Raymond Klein MD



**CLINICAL QUESTION:** Can the HAS-BLED and

CHA<sub>2</sub>DS<sub>2</sub>-VASc scores be used to identify subgroups of patients with atrial fibrillation (AF) and recent acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI) who would benefit from an antithrombotic regimen other than apixaban plus a P2Y<sub>10</sub> inhibitor?



Dr. Klein

**BACKGROUND:** The combination of AF and coronary artery disease poses a clinical dilemma in choosing the optimal antithrombotic regimen. The AUGUSTUS trial, which is the basis for this post-hoc analysis, included patients with AF hospitalized for ACS and/or PCI with the planned use of a P2Y<sub>12</sub> inhibitor for at least six months. Within 14 days of the index event, patients underwent randomization to receive apixaban versus vitamin K antagonist (VKA) and to receive aspirin versus placebo.

All patients received a  $P2Y_{12}$  inhibitor (mostly clopidogrel). The antithrombotic regimen of apixaban plus a P2Y<sub>12</sub> inhibitor resulted in less bleeding and fewer hospitalizations, without significant differences in ischemic events when compared to regimens that included a VKA, aspirin, or both.

SETTING: Multiple medical centers in 33 different countries included in the AUGUSTUS trial

STUDY DESIGN: Post-hoc analysis of the AU-GUSTUS trial (open-label, two-by-two factorial, randomized, controlled trial)

SYNOPSIS: This study stratified the AUGUS-TUS patient population by baseline risks for bleeding and stroke using the HAS-BLED and CHA DS -VASc scores, respectively. A total of 4,368 patients was included in the analysis. No significant interactions were found on treatment effects of apixaban versus VKA or aspirin versus placebo across HAS-BLED and CHA, DS,-VASc scores. The data suggest an antithrombotic regimen of apixaban and a P2Y<sub>12</sub> inhibitor without aspirin is preferable across a wide range of bleeding and stroke risk in patients with AF in the first six months following ACS and/or PCI.

Notably, many guidelines recommend a short period of dual-antiplatelet therapy (often seven days) after PCI or ACS, and these findings may not apply to patients very shortly after the index event. In addition, this post-hoc analysis may be limited by the fact that the AUGUSTUS trial was not powered to detect interactions between outcomes according to these subgroups. Therefore, small but meaningful differential treatment effects in subgroups may have been obscured.

**BOTTOM LINE:** In patients with AF and recent ACS or PCI, the antithrombotic regimen of apixaban plus a P2Y<sub>12</sub> inhibitor appears best to balance bleeding risk and efficacy, irrespective of baseline HAS-BLED and CHA, DS, -VASc scores.

**CITATION:** Harskamp RE, et al. Antithrombotic therapy in patients with atrial fibrillation after acute coronary syndromes or percutaneous intervention. J Am Coll Cardiol. 2022;79(5):417-27. doi:10.1016/j.jacc.2021.11.035.

Dr. Klein is an assistant professor at Tufts University School of Medicine, Boston, and a hospital medicine physician at Maine Medical Center, Portland, Maine.

### By Innocent Ndzana, DO

**CPAP reduces the risk of intubation** among patients with acute hypoxemic respiratory failure and COVID-19

#### **CLINICAL QUESTION:** What is the role of

continuous positive airway pressure (CPAP) and high-flow nasal oxyger (HFNO) compared to conventional oxygen therapy in the management of COVID-19-related acute hypoxemic respiratory failure?



Dr. Ndzana

BACKGROUND: COVID-19 pulmonary manifestations range from pneumonitis to life-threatening acute respiratory distress syndrome (ARDS)

## Rapid antigen tests for SARS-CoV-2 have a very low false-positive rate

**SHORT TAKES** 

In a sample of 903,408 rapid antigen tests with **CITATION:** Gans JS, et al. False-positive confirmatory polymerase chain reactions (PCRs) screening asymptomatic Canadian employees during two delta-variant-driven waves of COVID-19, the false-positive rate of the rapid tests was 0.05%, most of which were due to a manufacturing defect with a single test batch.

necessitating tracheal intubation. Non-invasive oxygenation strategies are widely used in non-COVID respiratory-failure processes including congestive heart failure and chronic obstructive pulmonary disease, however, their effects on reducing mortality or preventing intubation in severe COVID-19 are not clear.

STUDY DESIGN: Parallel-group, open-label, randomized clinical trial

SETTING: Forty-eight acute care hospitals in the U.K. and Jersey.

SYNOPSIS: The 1,273 RECOVERY-RS trial enrollees were randomized to CPAP, HFNO, and conventional oxygen therapy. Inclusion criteria were known or suspected COVID-19 with acute hypoxemic respiratory failure, SPO2 of 94% or less despite a fraction of inspired oxygen of at least 0.40, and suitability for tracheal intubation if required. An initial strategy of CPAP, compared with conventional oxygen therapy, significantly reduced the composite outcome of tracheal intubation or mortality within 30 days (36% versus 44%, P=0.03). In contrast, there was no significant difference between HFNO and conventional oxygen therapy (44% versus 45%, P=0.83). This decrease in the incidence of the primary outcome was attributable to a lower need for tracheal intubation in the CPAP group. Neither HFNO nor CPAP reduced mortality as compared with conventional oxygen therapy. A major study limitation is the absence of blinding as well as the lack of standardization of the tracheal intubation threshold.

**BOTTOM LINE:** CPAP significantly reduced the need for tracheal intubation compared to conventional oxygen therapy, whereas HFNO did not. However, no significant decrease in 30-day mortality between conventional oxygen therapy and non-invasive strategies was found.

CITATION: Perkins GD, et al. Effect of noninvasive respiratory strategies on intubation or mortality among patients with acute hypoxemic respiratory failure and COVID-19: The Recovery-RS randomized clinical trial. JAMA 2022;327:546. doi: 10.1001/jama.2022.0028.

Dr. Ndzana is a hospital medicine physician at Maine Medical Center, Portland, Maine.

#### By Nellie Wood, MD



CLINICAL QUESTION: Does a proactive, threestep, support strategy decrease prolonged grief in relatives of patients who die in the intensive care unit (ICU)?

results in rapid antigen tests for SARS-CoV-2. JAMA. 2022;327(5):485-486. doi:10.1001/ jama.2021.24355.

> Adam Long, MD is a second-year internal medicine resident at Maine Medical Center, Portland, Maine.

#### **BACKGROUND:** Prolonged grief and symptoms

of anxiety, depression, and post-traumatic stress disorder (PTSD) are common among families of patients who die in the ICU. Poor communication and perceived lack of support from the ICU team are known risk factors. Prior studies have shown modest



improvement with interventions such as family meetings or bereavement pamphlets prior to death.

STUDY DESIGN: Prospective, multi-center, cluster-randomized controlled trial

SETTING: 34 ICUs in France prior to the COVID-19 pandemic

SYNOPSIS: 875 relatives of adult ICU patients for whom the decision to withdraw or withhold life-sustaining treatment had already been made were randomized to receive standard end-oflife care or a three-step support strategy. This entailed three in-person family visits with the ICU physician and nurse: first in preparation for the dying process, second in the patients' rooms when death was imminent, and third after death had occurred. The intervention clinicians received structured training in verbal and non-verbal communication followed by one month of practice. At six months, the median score on the PG-13 (a validated diagnostic scale for prolonged grief disorder) was lower in the intervention arm (19 versus 21) with fewer relatives meeting the criteria for the disorder (15% versus 21%). Symptoms of PTSD (at three months) and anxiety (at six months) were also lower. These benefits were statistically significant.

A strength of this intervention is its simplicity and low cost. However, the magnitude of the benefits was generally modest across the range of measured psychiatric outcomes. Though conducted in an ICU setting, the strategy is easily applicable to hospital medicine and addresses an important but often overlooked clinical responsibility: ongoing support of a patient's family after the decision to withdraw care has been made.

**BOTTOM LINE:** Proactive structured communication directly between the ICU team and patients' families after a decision to withhold/ withdraw care has been made improves families' symptoms of prolonged grief, anxiety, and PTSD.

CITATION: Kentish-Barnes N, et al. A three-step support strategy for relatives of patients dying in the intensive care unit: a cluster randomized trial. Lancet. 2022;399(10325):656-664.

Dr. Wood is a hospital medicine physician at Maine Medical Center, Portland, Maine.

## SHM: Advocating for You and Your Patients

By Ruth Jessen Hickman, MD

dvocacy, simply put, is the act of pleading or arguing in favor of something. It's raising the concerns and voices of a group to efficiently influence decisions and affect change within political, economic, and social institutions. This is exactly what SHM has been doing on behalf of its members and their patients for decades.

Often the process and results of advocacy go unseen and seem to move at a snail's pace. Regardless, SHM staff and volunteer clinician members of SHM's public policy committee (PPC) constantly find effective ways to combat issues that negatively impact hospitalists' ability to deliver high-quality care. Although these issues regularly impact your work lives, you might not be aware of the underlying regulatory structures and the broad, long-term efforts being made to change them.

"We've tried to be really inten-

tional about taking on just a few issues where hospitalists play a major role and where we are the content experts," said Suparna



Dr. Dutta

Dutta, MD, MPH, FHM, chief of medicine at Hartford Hospital, Hartford, Conn., and a member of SHM's public policy committee. Although SHM supports broader initiatives that affect health care in general, its primary focus is leveraging its efforts where it can make the most difference for its membership.

"I think Capitol Hill and the Centers for Medicare and Medicaid Services (CMS) generally look on SHM as a very fair impartial resource, which I think serves us well," said Dr. Dutta. "We try to make sure that the issues we get involved in are issues that are impactful not just to our membership but also to the patients that we care for and to our health care system." By building trust as an impartial resource over many years, SHM has been able to exert influence and share expertise as new policy decisions are being formed.

Ron Greeno, MD, MHM, former SHM president and PPC chairman, and the senior advisor for government affairs at SHM said many of SHM's early advocacy efforts focused on educating CMS and Congress and clarifying the goals and work of hospitalists. "Because hospitalists are new, compared to other medical specialties, things sometimes get written into policy



that unintentionally negatively impact hospitalists," he said.

As an example, as part of the original version of the Affordable Care Act, physicians were to be financially penalized if they didn't work via their own electronic medical records. However, unlike other physicians, hospitalists use only their hospital's electronic medical records by design. Dr. Greeno said, "Millions of dollars in penalties were going to be levied on hospitalists across the country—we had to do a couple of years of heavy lifting to get the law changed."

## Working with CMS

Much of SHM's work has focused on advocating with CMS for rule changes to benefit hospitalists and their patients.

For example, the 2015 Medicare Access and CHIP Reauthorization Act (MACRA) brought significant changes to the Medicare physician payment system, but some of the criteria put into place (e.g., for riskbased billing) didn't directly apply to hospitalists.

Richard J. Hilger, MD, SFHM,

current chair of the PPC and system utilization medical director at HealthPartners, Minneapolis, Minn. said, "For

providing feedback to CMS and advocating to make sure hospitalists are fairly represented in these new formulas. They have made concrete changes over time to try to more fairly capture the quality of care provided by a hospitalist.' In 2017, SHM successfully lobbied

years, SHM and the PPC have been

to get a separate billing code that hospitalists can use for Medicare. With these new alternative payment models that use outcome comparisons among physicians, this was especially critical, as hospitalists previously had to bill in a way that lumped them in with physicians (such as outpatient internal medicine physicians) caring for much less sick and less expensive patients.

One current area of discussion

with CMS is Medicare Advantage plans, especially concerning prior authoriza tions. Dahlia Rizk, DO,



Dr. Rizk MPH, FHM another PPC member and chief of

the division of hospital medicine at Mount Sinai Beth Israel Medical Center in New York, pointed out that working with such burdensome prior authorizations in this and other contexts impedes hospitalists' workflow, decreases the time they can spend with patients, and negatively impacts

staff morale.

Dr. Hilger added, "Many Medicare Advantage plans have significant delays involved when trying to get a prior authorization for a patient to go to a skilled nursing facility, which can lead to many medically unnecessary hospital days, which is both a quality and a financial issue." The heightened need for hospital beds during the pandemic has both exacerbated and highlighted the issue.

Another issue hospitalists face is problems related to observation. SHM's PPC has been working with CMS on defining appropriate uses of observation for many years. Patients placed in observation use the same hospital resources as those on inpatient service, but hospitals are reimbursed less, and patients often see huge out-ofpocket costs.

Dr. Rizk explained, "There is a big effort underway to revamp and reform the entire observation process with all of its administrative burdens and often time-consuming rules that often place physicians between patients and the insurance company. How much traction we get is yet to be seen." The PPC has advocated for these issues at the federal level and has put out two white papers to outline suggestions for reform.1

Billing issues faced by hospitals are another problem that can trickle down to physician salaries and negatively impact appropriate compensation. For the last

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Dr. Hilger

two years, SHM has been fighting against scheduled cuts to hospitalists' Medicare reimbursement. These planned cuts, resulting from a complicated series of long-term budgeting factors, would have resulted in a roughly 10% cut to Medicare reimbursement for hospitalists starting on January 1, 2022.<sup>2</sup> "These cuts were coming at exactly the wrong time considering all the work hospitalists provided during the pandemic," said Dr. Rizk.

SHM lobbied heavily for the Protecting Medicare and American Farmers from Sequester Cut Act, passed in December, which has put most of those scheduled cuts on hold for the moment. "That has been huge, but it's only temporary good news," said Dr. Dutta. "We are going to continue to advocate for a permanent solution to ensure adequate reimbursement for hospital medicine."

#### **Other issues**

Aside from educating about the specialty and working on coding and billing issues, SHM also strives for improvements in treatment options and even, for some, the ability to work in the U.S.

For example, there's positive movement on the modifications to

buprenorphine prescribing abilities with respect to the X-waiver. Before April 2021, only physicians who had completed a cumbersome eight hours of training could receive an X-waiver, allowing them to prescribe the drug to treat patients with opioid use disorder. Thanks in part to SHM, physicians are no longer required to complete such training if they treat no more than 30 patients at a time. Noted Dr. Dutta, "It is still not the robust change we need: total elimination of the waiver."

SHM and the PPC have also pushed hard for immigration adjustments for its members from other countries. One example is the Fairness for High Skilled Immigrants Act, which passed the U.S. House and Senate in 2020 but was not implemented due to congressional reconciliation issues. Presently, physician visas are allocated based on country of origin, which means that immigrants from more populous countries, like India, may have to wait decades to receive a visa, creating considerable stress.

Similarly, SHM has lobbied for the Conrad-30 Reauthorization bill, which recently lapsed and will need reauthorization this year. This bill waives the requirement that people with temporary J-1 visas leave the country for a couple of years before applying for an H1 visa if they are serving an underserved area.

### **Looking forward**

While the pandemic put the brakes on many things over the last two years, including the positive momentum SHM had gained on some of these issues, SHM and PPC members are not deterred. COVID-19 shone a spotlight on existing issues—staff burnout and shortages—and the overall flaws in our health care system. But "This is an opportunity to advocate what we've uncovered," Dr. Dutta said.

Hospitalists may be able to benefit from some of the temporary changes put in place during the pandemic, such as the 3-Midnight Rule, which has been waived by Medicare and many commercial payers for the duration of the public health emergency. Normally the rule requires that patients spend three days in the hospital on inpatient status (and not under observation) before Medicare will cover transfer to a skilled nursing facility.

PPC members and SHM staff have been working with CMS to make many such temporary changes, including new telehealth waivers, permanent. Dr. Hilger said, "It just showed how efficient the system could be without these artificial hurdles in place."

While SHM and the PPC continue to advocate on behalf of you and your patients, it's never too late to get involved. "You don't have to be on the PPC to be involved in the policy world," said Dr. Hilger. "You can start with local SHM chapters, figure out how to contact your representatives, and make your voice heard. It doesn't feel like it at the moment, but it's those phone calls, those emails, that over time chip away and can lead to major change."

Ruth Jessen Hickman, MD, is a graduate of the Indiana University School of Medicine. She is a freelance medical writer living in Bloomington, Ind.

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## Celebrating the 2021 Chapter Excellence Status Awards Recipients

he Chapter Excellence Awards are bestowed annually to recognize outstanding work conducted by chapters to carry out the SHM mission locally. They're comprised of Status Awards and Exemplary Awards. Please join *The Hospitalist* and SHM in congratulating the 2021 recipients!

## 2021 Status Awards

SHM



## PLATINUM CHAPTER EXCELLENCE AWARD

Atlanta Connecticut Hampton Roads Houston Kentucky Los Angeles Minnesota Nashville New Mexico Wiregrass



## GOLD CHAPTER EXCELLENCE AWARD

Blue Ridge Iowa Long Island Maryland Nebraska North FL North Jersey NYC/Westchester St. Louis



## SILVER CHAPTER EXCELLENCE AWARD

Boston/Eastern MA Charlotte Metro Area Lake Erie/Northern OH Maine North Dakota San Diego Western MA



## BRONZE CHAPTER EXCELLENCE AWARD

Delaware Hawaii Indiana Knoxville Memphis Oregon/Southwest WA Rhode Island SC Lowcountry South Central PA Southwest GA Tampa Bay Area Wisconsin

## **2021 Exemplary Awards**



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CHAPTER

Rhode Island Chapter



## **RESILIENCY AWARD**

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OUTSTANDING MEMBERSHIP RECRUITMENT & RETENTION

Wisconsin Chapter



MOST ENGAGED CHAPTER LEADER

Steven Smith, MD, SFHM, Nashville Chapter

## Interpretation of the Urine Drug Screen

## By John M. Cunningham, MD; Elizabeth Gillespie, MD; Kimberly A. Indovina, MD

**Case** A 40-year-old male with depression, post-traumatic stress disorder, and chronic pain presents with somnolence and a respiratory rate of 10 breaths per minute that responded to naloxone in the field. The patient's outpatient prescriptions include sertraline, prazosin, and as-needed hydrocodone. The urine drug screen (UDS) is positive for opiates and benzodiazepines.

**Brief overview** Although UDS is commonly ordered and easy to perform, interpretation isn't straightforward and misinterpretation is common.<sup>1</sup> Toxicology literature cites significant limitations to the UDS, both diagnostic and managementrelated.<sup>2</sup> The simplicity of "positive" and "negative" can mislead clinicians into overlooking other clinical scenarios that can fall into those two categories. This has significant implications for medical diagnosis and decisions.

The UDS is frequently used in the acute care setting. Emergency department (ED) clinicians may use the UDS in the initial assessment of patients presenting with a severe overdose, acute encephalopathy, psychosis, and other toxidromes. Hospitalists safely transition patients from their early management of a suspected overdose back to the outpatient setting through careful medication reconciliation and the diagnosis of substance use disorders. Hospitalists also work collaboratively with outpatient prescribing clinicians regarding the ongoing prescription of opioids or sedative-hypnotic drugs. Therefore, it is important to understand the diagnostic characteristics and interpretation of the UDS to make the best possible clinical decisions for the patient.

**Overview** The UDS commonly used in the acute care setting is an immunoassay, which uses antibodies to detect a drug and/or its metabolites. A negative result doesn't necessarily mean the drug is absent, it means the amount present is below the cut-off level for detection. A positive result means the immunoassay has detected a substance of a similar chemical structure to the screening target. Detection time is the time since ingestion during which the drug or its metabolites will be detected by the immunoassay.1 This can vary significantly between drugs of the same class and is important to consider when interpreting a UDS. For example,



## **KEY**

- Reliably detected by opiate screening assay
- Sometimes detected by opiate screening assay



Dr. Cunningham



Dr. Indovina

Dr. Indovina is a hospitalist and palliative medicine physician at Denver Health and an assistant professor of medicine at the University of Colorado. Dr. Cunningham is a hospitalist at Denver Health and an assistant professor of medicine at the University of Colorado. Dr. Gillespie is a hospitalist at Denver Health, an assistant professor of medicine at the University of Colorado, and an MPH candidate at the Colorado School of Public Health.

long-acting benzodiazepines may be detected up to 30 days, whereas short-acting benzodiazepines may be detected for up to three days.1

Most immunoassays for opiates (non-synthetic, natural opiates) use antibodies to morphine to set the threshold for a positive versus negative screen. Both codeine and heroin are opiates that get metabolized to morphine. (Figure 1) Semisynthetic opioids (e.g., hydrocodone, hydromorphone, and oxycodone) and synthetic opioids (e.g., fentanyl, meperidine, tramadol, and methadone) may not be detected as "opiates" on the standard UDS since the antibodies for morphine may not cross-react with these substances.1 Immunoassay and gas chromatography/mass spectrometry (GC/ MS) testing for semisynthetic or synthetic opioids are available, but the Centers for Disease Control and Prevention (CDC) guidelines recommend using these costly tests only in circumstances where detec-

tion of specific opioids would alter patient management.3 An exception to this is fentanyl. Given the recent epidemic of fentanyl overdoses, it's essential to know if the sensitive and specific fentanyl immunoassay is available in one's own institution as it may be a separate test from the standard opiate screen.

Appropriate interpretation of the common opiate UDS is critical, as misinterpretation of a "negative screen" could result in a diagnostic error and may generate mistrust in a patient's opioid use, which can have consequences for the ongoing management of chronic pain and the patient-physician relationship.<sup>4</sup> As an example, a negative opiate screen would not rule out an opioid overdose if a patient is using synthetic or semisynthetic opioids. Similarly, a negative opiate screen does not imply non-adherence or diversion in a patient prescribed these types of opioids or if the patient is taking an opiate at a

## Unlikely to be detected by opiate screening assay

## Key Points

- Hospitalists must be aware of the limitations of UDS, understand what the UDS assay at one's own institution detects, and incorporate additional information such as history, clinical presentation, PDMP data, and response to antidotes when interpreting the UDS.
- A positive UDS result indicates detection above the cut-off screening level and does not necessarily mean that the detected substance is the cause of the patient's symptoms.
- Several commonly used medications can cause a false-positive UDS. Examples include sertraline causing a false-positive benzodiazepine screen and bupropion causing a false-positive amphetamine screen.
- Commonly used synthetic and semisynthetic opioids may not be detected on the standard opiate screen.
- Misinterpretation of the UDS can have a significant adverse impact on patient care in terms of both diagnosis and future management by prescribing physicians.

**IDT** 

low dose or on an as-needed basis. Additionally, false-positive opiate screens are rare but have been reported with the use of quinolones and rifampin.<sup>5</sup>

Benzodiazepine screen interpretation can be challenging due to the large number of benzodiazepines available, their complex metabolic pathways, and their variable half-lives. Further, several different immunoassays are available, and institutions may vary in which assay they use. For example, earlier-generation assays that detect the free or non-conjugated forms of oxazepam or nordiazepam would not detect commonly used benzodiazepines that are metabolized via an alternate pathway, such as lorazepam, alprazolam, and clonazepam.<sup>1</sup> Some later-generation assays have improved detection rates of alprazolam, but may only detect metabolites of clonazepam, temazepam, and lorazepam at high levels, leading to false negatives, especially with shorter-acting benzodiazepines.<sup>1,6</sup> (Figure 2) Benzodiazepine false positives can also occur with common medications such as sertraline or efavirenz.<sup>5</sup> Benzodiazepines are commonly administered in the ED and pre-hospital setting to patients with suspected stimulant intoxication, psychosis, or alcohol withdrawal. Therefore, appropriate interpretation of the benzodiazepine screen requires a review of medications administered prior to arrival, thorough medication reconciliation, and a knowledge of which immunoassay is used at one's institution.

The amphetamine immunoassay is nonspecific for amphetamine and methamphetamine because the assays cross-react with many medications of similar molecular structure. Positive amphetamine screening tests shouldn't be used in isolation for major clinical decision-making. Patients who screen positive should be questioned about the use of these other agents. The long list of agents associated with a false-positive UDS for amphetamine includes pseudoephedrine/ephedrine, bupropion, labetalol, ranitidine, and dietary supplements containing dimethylamylamine (DMAA).<sup>1</sup> If suspicion of amphetamine use remains high and if positive results would have major treatment implications, confirmatory testing could be performed with GC/MS.

Cocaine urine assays detect benzoylecgonine, the primary metabolite of cocaine.<sup>1,5</sup> Urine cocaine screens are highly specific for detecting recent cocaine ingestion, and false positives are exceedingly rare due to the lack of cross-reactivity with other substances. It's important to note that topical and ophthalmic anesthetic preparations containing cocaine are clinically available and can cause positive UDS results.<sup>1</sup>

## Figure 2: Simplified version of the metabolic pathway of commonly used benzodiazepines DRUG METABOLITES EXCRETION



www.cdc.gov/drugoverdose/pdf/prescribing/ CDC-DUIP-UrineDrugTesting\_FactSheet-508.pdf

Interpretation of the UDS in patients prescribed chronic opioids or benzodiazepines can present unique challenges. Misinterpretation of UDS results may lead hospitalists to believe a patient is misusing a prescribed drug. The suspicion of misuse may negatively affect how the patient's symptoms are managed by clinicians.45 Abnormal UDS results should prompt further discussion and evaluation. It may not be reasonable to make significant changes to a chronic treatment plan based on a single result. Seek more information to guide management decisions including the patient's self-report of use, Prescription Drug Monitoring Program (PDMP) data, input from the outpatient prescribing clinician, screens for additional illicit substances, and patterns of behavior (e.g., multiple visits due to complications from medication misuse). Confirmatory testing with GC/MS can be ordered in cases where either the diagnosis is unclear or confirming the presence or absence of the drug would alter future prescribing. The turnaround time for confirmatory testing is significantly longer; in our institution, it takes two days. This may limit the utility of GC/MS in the acute care setting; however, confirmatory testing may aid the outpatient prescribing clinician in addressing concerns of misuse or in making changes to home medications.

## Application to the case

This patient's immediate clinical response to naloxone is highly suggestive of opiate or opioid intoxication. The UDS was positive epines. Hydrocodone, a semisynthetic opioid, is not detected on the UDS for opiates. Therefore, the positive opiate screen is concerning for comorbid use of another opiate such as heroin, morphine, or codeine. The positive benzodiazepine screen may be a result of the patient's sertraline therapy or benzodiazepine use. A follow-up conversation with the patient and/or family, or a review of PDMP may suggest the specific substances ingested without the need for expensive confirmatory testing. Confirmatory drug testing could be performed if the clinical scenario remains unclear or if the results will influence future prescribing.

### **Bottom line**

Hospitalists' ability to accurately interpret the UDS by understanding the scope and limitations of the assay at their individual institutions is essential both for diagnosis and for transitions of care.

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## Quiz

- 1. A 55-year-old woman with chronic pain, gastroesophageal reflux disease, and depression is admitted to the hospital after presenting with somnolence and confusion. Home medications include ranitidine, bupropion, and as-needed oxycodone. UDS obtained in the ED prior to admission was negative for opiates and positive for amphetamines. Which of the following is true?
  - a. It's almost certain she recently used methamphetamines as false positives are rare.
  - b. An overdose of oxycodone can be ruled out as the cause of somnolence.
  - c. It's still unclear whether she is using methamphetamines or taking oxycodone.
  - d. Confirmatory testing with gas chromatography or mass spectrometry must be ordered.

Explanation: Based on this UDS result, it remains unclear whether the patient has used methamphetamines or oxycodone. Clinicians must be aware of the limitations of UDS and interpret results cautiously. A positive UDS amphetamine test may indicate methamphetamine use or may indicate a false-positive result from cross-reactivity with other medications. False-positive amphetamine screens are common, and this patient takes ranitidine and bupropion, both of which are known to cause false positives. Oxycodone is a semisynthetic opioid that is not detected on the standard UDS opiate assay at many institutions. Further, the use of medication in low doses or on an as-needed basis may result in a negative UDS if the amount of drug present is below the cut-off value for detection. Therefore, this patient's negative opiate UDS does not rule out oxycodone overdose, nor does it indicate with certainty whether the medication is being used in any quantity or frequency. While confirmatory testing with gas chromatography or mass spectrometry is available, it is costly and slow and should be ordered only in cases where the results will change clinical management. In many cases, further history alone provides adequate information about which substances a patient has used.

## **Hospital Supply Chains**

What have we learned and where are we going?

## By Samantha C. Shapiro, MD

he supply chain. Lean manufacturing. Just-intime economy. Unless you hold a business degree or just love reading the *Wall Street Journal*, chances are these terms weren't part of your vocabulary until recently. And as health care providers, there's no real reason they should have been.

However, COVID-19 has introduced us to these terms whether we like it or not. In this article, we take a closer look at supply-chain issues and how hospitalists are keeping up. We highlight lessons learned, current challenges, and big-picture goals moving forward.

Simply defined, a supply chain is a system of producing a product from start to finish. Less simply defined, supply chains are complicated logistical networks of raw materials, suppliers, manufacturers, distributors, and retailers.<sup>1</sup> With so many moving pieces, the potential for system breakdown is high. It's sort of like the 1,000-piece train set you bought your kid for the holidays. With one piece missing, the train might not make it around the track on schedule...or at all.

The "just-in-time" or "lean manufacturing" economy is a management strategy that saves money by avoiding the costs and waste of storing surplus goods. It's the business version of pro re nata (PRN)—goods are manufactured and shipped only as needed. This sounds reasonable, until demand rapidly and unexpectedly exceeds supply, as happened during the COVID-19 pandemic.<sup>2</sup>

As we are all painfully aware, shortages of personal protective equipment (PPE) made it difficult and risky to care for patients. Hospitals were forced to compete to obtain PPE or to get creative to preserve the little they had.<sup>3</sup> Other supplies were limited too: ventilators, oxygen, hospital beds...even health care workers. But hospitalists mobilized quickly to respond. Collaboration, relationship building, and ingenuity enabled hospitals to care for patients despite unprecedented supply issues.

Kristie G. Williams, RN, MSN, vice

president, Carilion Giles and Carilion Tazewell Community Hospitals, Virginia, shared one of the countless examples of



Williams

out-of-the-box thinking during the early days of the pandemic. When missing pieces rendered some of their powered air-purifying respirators nonfunctional, a local vocational high school used their 3-D printer to manufacture new ones. "Small communities really shine when there's a crisis. We pull together. It's all about relationships," she said.

Amith Skandhan, MD, FACP, SFHM, assistant professor, internal

medicine hospitalist, and director of physician integration, Southeast Health, Dothan, Ala., echoed Ms. Williams's



Dr. Skandhan

sentiments about resourcefulness and teamwork. Dr. Skandhan co-founded the Wiregrass Chapter of SHM at his hospital. During the COVID-19 pandemic, his chapter created a weekly virtual check-in for the program directors of hospital medicine in the state of Alabama, to share information and discuss procedural challenges. This forum tackled topics such as patient flow, lab supply shortages, in-hospital PPE development, PPE autoclaving, and sharing care pathways. It particularly helped smaller institutions with limited resources caring for disadvantaged patient populations.

Dr. Skandhan said, "Over time, this forum became a channel for passing knowledge. We started building PPE in the hospital and shared data on how to do it. And now, administrators are connected with each other to address supply-chain issues."

#### Lessons learned

Unfortunately, the COVID-19 pandemic is not the first to draw attention to supply-chain issues in health care. In many ways, it simply revealed wounds that were already there. Supply-chain issues were evident as early as the 2003 Severe Acute Respiratory Syndrome (SARS) pandemic, but few articles to this effect were generated.<sup>4</sup> This time around, we're trying to respond differently.

Recent publications have identified two main lessons learned: the importance of organizational leadership, collaboration, and relationship building, both in and across organizations; and the need to diversify product resources, safeguard the supply chain, and improve technology that anticipates shortages.<sup>4,5</sup>

"This pandemic forced hospitalists to become aware that the supply chain is even an issue at all. Normally, you want an IV? You get it. You want a medication? You get it. But now the conversation has shifted to how do we get these things, how do we make these things, and how do we ensure we continue to have them. And we are connecting our hospital administrators and sharing information," Dr. Skandhan said.

Amit Vashist, MD, FACHE, senior vice president

and chief clinical officer, Ballad Health, and an actively practicing hospitalist, leads an



Dr. Vashist

integrated 21-hospital health system spanning southwest Virginia, northeast Tennessee, northwest North Carolina, and southeast Kentucky. Dr. Vashist said, "In health care, we have relied heavily on foreign-sourced products to run our hospitals, and COVID-19 exposed the limitations of this dependence. Moving forward, our group purchasing organization (GPO) is trying to have as many domestic suppliers as possible. We also created a PPE supply cache and a daily usage report that has provided more visibility to our supply chain to ensure adequate stocking levels."

## **Current challenges**

Despite significant progress in the last two years, we still have a long way to go, and current challenges are not just COVID-related.

As of January 19, 2022, the U.S. Food and Drug Administration medical-device shortages list still included PPE, as well as dialysis-related products, laboratory testing supplies and equipment, and ventilation-related products.6 Hospital bed availability remains uncertain, especially with surges caused by new virus variants.7 And most recently, we're seeing a shortage of health care workers. Some staffing issues are transient due to the temporary absence of those infected with COVID-19. During the peak of the omicron variant surge in January 2022, for example, 50% of hospitals in New Mexico reported staffing shortages.<sup>8</sup> But other shortages are more permanent.

The U.S. Bureau of Labor and Statistics estimates that nearly 300,000 health care workers have left their jobs since February 2020.<sup>9</sup> A poll of 1,000 workers from a survey research company found that 18% of health care workers have quit since





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the pandemic began.<sup>10</sup> Ms. Williams noted that at her hospital, "staffing is a huge problem now. Physicians are retiring early. Nurses are leaving the profession altogether or transitioning to travel nursing for more lucrative opportunities."

### **Big-picture goals**

With so many ongoing challenges, where should we start? For hospitalists, it comes down to one word: stability. Stability of the health care workforce, and stability of supply chains.

"Stabilizing the health care workforce needs to be a top priority," said Ms. Williams. Without medical personnel, we cannot adequately care for patients. And as workers leave health care, it puts further stress on the remaining staff due to staffing shortages. Action is needed to address the dangerous cycle that burnout has created.

Regarding stabilization of the supply chain, Dr. Vashist advocated for "ensuring U.S. ports and infrastructure become more agile so goods can be shipped to us in real-time, as well as a continued focus on domestic producers." He said "Televisions sitting in shipping containers at the Port of Los Angeles is inconvenient. But when it comes to health care supplies, it's



a matter of life and death."

Ultimately, as Dr. Skandhan candidly noted, "The goal is for physicians NOT to be discussing the supply chain at all, so we can refocus on practicing medicine."

The pandemic unveiled substantial vulnerabilities in hospital supply chains, but the lessons learned are many. We are collaborating, building relationships, and sharing information more than ever before. We are paying attention to the supply chain, and actively working to improve and safeguard it. Stability is the name of the game moving forward—stability of the supply chain and the health care workforce itself.

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## **Chapter Spotlight: Kentucky**

### By Richard Quinn

npatient beds in Kentucky run the gamut of locations. There are academic medical centers in Lexington and Louisville, a Fort Campbell field hospital along the Tennessee border, and the rural outposts of the state's southwestern counties (roughly equidistant from Louisville and Little Rock, Ark).

So it's no accident that the Kentucky chapter of SHM dedicates a lot of time, effort, and money to ensure it represents them all.

"It is important that we involve everyone, not just hospitalists from academic medical centers, to have this sense of community, because most of the hospitalists practice in the community centers, and we need

their voice," said Preetham Talari, MD, MBA, CPE, SFHM, associate chief of quality and safety in the division of



Dr. Talari

hospital medicine at UK Healthcare in Lexington. "We made a conscious effort to involve, highlight, and engage hospitalists across the state."

There are nearly 70 chapters nationally, with some states having multiple chapters to represent different regions. But Kentuckians take state pride seriously, whether it's high school basketball or hospital medicine.

The chapter, formed in 2016,

earned itself a Rising Star Award from SHM just a year later, and for the past few years has integrated a chapter-sponsored Research, Innovations, and Clinical Vignette (RIV) poster competition into the Heartland Hospital Medicine Regional Conference.

The chapter uses financial support from the SHM Chapter Initiative Fund program to fund that RIV, while the chapter uses its own funds to highlight members, celebrate National Hospitalist Day, encourage fellowships via SHM, and produce a quarterly newsletter. The support has helped grow the membership rolls from 146 in 2016 to 249 at the end of last year. Plans for future investment include tackling the state's opioid crisis by presenting best practices to deal with substance-use disorders.

Dr. Talari takes pride, not in just the geographic and practice-type diversity of the chapter, but he boasts that chapter leadership also includes those medical professionals who work hand-in-glove with hospitalists. To wit, the chapter's treasurer is Jacque Young, DNP, APRN, a nurse practitioner at the University of Louisville Hospital.

In a state like Kentucky, community hospitalists are always important.

And in a time like the coronavirus pandemic, that's ever more true.

"Lots of things have highlighted the importance of community hospitalists, I think none greater, perhaps, than COVID-19," said chapter co-founder Joseph

### Sweigart, MD, SFHM, a Team

Health hospitalist at Georgetown Community Hospital in Georgetown, a northern suburb of Lexington.

"The aca-



Dr. Sweigart

demic medical centers were full, and care was being delivered on the actual front lines in the communities. Being able to connect with and empower those people to help make sure their voice is amplified at the society level, particularly when they are in the trenches taking care of patients, is an important mission for our chapter. "

Dr. Sweigart, the chapter's immediate past president, adds that supporting community hospitalists during COVID also had a clinical mission.

"Things are moving so fast now," Dr. Sweigart said. "I trained in an era when guidelines are written every 10 years, and you're recertified every 10 years. So, once you learn something, you were good for a decade. I think when you learned something with COVID-19, you were good for like 10 minutes or 10 days. SHM did a lot of things to push content out to help people stay current, even as things were changing so rapidly."

To that end, Dr. Talari is particularly proud of the poster competition at the regional conference. Last year's event was in person the year before everything was virtual—and registration was free as a way to encourage greater engagement with medical students, residents, and their hospitalist attendings.

"There is usually talk about how critical-care specialists were at the front and center of the pandemic, but we have to highlight how hospitalists were also front and center," Dr. Talari said. "We could highlight how much hospitalists contributed during this pandemic."

It also doesn't hurt that the Kentucky chapter can pick one winner to be automatically accepted into SHM's annual convention.

"For many of us, myself included, the first time you go to a professional meeting, you're like, 'Oh, my gosh, I'm surrounded by my people, this is awesome," Dr. Sweigart said. "It's totally intoxicating, and it's something we hope helps bring more and more young, fresh energy and insight into the field and keep people excited about it."

But while Kentuckians are rejuvenated by the annual conference—both professionally and personally—the motivation from a once-a-year event needs support from the local chapter to last yearround.

"What's keeping the chapter running, particularly the past few years, when meetings have been limited, are our local communities," he said. "That ability to collaborate across hospitals, across institutions, and across geographic barriers is more critical than ever."

Richard Quinn is a freelance writer in New Jersey.

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## **SIG Spotlight: Hospital Medicine Administrators**

## **By Richard Quinn**

he opening minutes of the monthly online gathering for SHM's Hospital Medicine Administrators (HMA) Special Interest Group (SIG) can sound more like a support group than anything else.

"We go around checking in," said chair Elda Dede, MPA, FHM, a hospital medicine administrator with the University of Kentucky in Lexington, Ky. "How are things in your practice?' And we share all the crises and victories—and how it's going and how we're handling it. This is our time to seek solutions and exchange best practices."

Really, that's the point.

SHM has 27 SIGs that are designed to "create communities of hospitalists around topics of interest, practice areas and/or care models."

And then there's the HMA SIG, which is very much geared to mostly non-physicians. It was formed in 2017 and has several hundred members.

"We are currently offering quarterly happy-hour gatherings, with administrators from all around the country attending. It is just us administrators," Dede said. "We feel more comfortable asking questions. 'Are you facing the same challenge as me? How are you solving this? How are you doing that?""

HMA SIG vice chair Trevor Coons, who works at Mayo Clinic in Rochester, Minn. points out the group is welcoming to all SHM members, including physician leaders at any level. In fact, it can serve as the ultimate sounding board on how administrators and frontline hospitalists can work together. "At Mayo Clinic, we have

a shared leadership model," he said of decisions he makes with his clinical counterpart. "I work closely with our phy-



sician practice Dr. Coons chair. We're both leaders. He

understands the science behind the treatments and protocols. I have an MHA, so I'm accustomed to creating and administrating policies and procedures, so we complement each other."

Similarly, SIG members also have access to the expertise of professionals like Dede and Coons. And they have the expertise of others.

"We partner and help each other, certainly," Coons said. "Just because many of us work at top-tier institutions doesn't mean we think we have all the answers. That's where I always appreciate the collegiality and the ingenuity of some smaller hospitals and health systems. 'Necessity is the mother of invention' and because they may have less infrastructure in place, they have to be creative and nimble in trying new things."

He added, "Across the group, we're able to try a variety of solutions to common problems and can say, 'Hey, this worked for us. Maybe you all should try it.' That can be very helpful. The SIG partnership is symbiotic. The HMA SIG is not a group of people who pretend they have it all figured out."

One of the SIG's most successful projects is a mentorship initiative, Dede said.

"I was a mentee myself when I first started," she said. "It was really useful to me to have someone walk through my challenges with me (and say), "This is how you do this. Stay away from that. Really get involved in this.' That was truly useful advice."

Coons agrees on the value of mentorship. Sometimes it's career advice from other administrators and leaders who have already made decisions with which someone else is struggling. It's also noteworthy that mentorship isn't always just about practice management.

"We actually navigated a successful career transition for one of the mentees I worked with," Coons said. "He hadn't had to apply for a job in a while, and we just walked him through the normal things he should expect. Just having a safe person to talk to who actually makes hiring decisions was very beneficial to him. The mentee had a number of questions: 'Do I send a thank you note?' 'Yes, and here is what you say in it.' Or, 'Is it weird to ask this question?' 'Absolutely not, go ahead.' 'Can I negotiate the start date?' 'Absolutely."

Coons adds that medical training focuses—as well it should—on clinical excellence.

"Often physicians and other care practitioners are trained only in clinical care, but they weren't given a lot of tools to succeed as a manager/supervisor or as a leader," he said. "The fact that they're a really good clinician and institutional leaders have given them a vote of confidence in selecting them for leadership roles means a lot; but it still doesn't help them answer those day-to-day questions like: "This is the first time I've had to have a performance management conversation with a colleague. How do I do this?'

"Often larger institutions have an infrastructure in place to help first-time leaders like that, but especially SIG members from smaller systems or more rural communities don't always have that opportunity. So, it's nice for them to have that help and validation (from the SIG)."

Another benefit of belonging to the HMA SIG, especially over the past few years, is being able to talk about all the non-medical challenges the pandemic has shone a spotlight on, including burnout, technology, and professional development.

"Life goes on, so aside from the obvious—patient care—we also need to tend to recruitment, professional development, quality improvement, research, both within our practices and in the rest of the hospital," Dede said. "We continue to adjust the complexity of our practices to the needs of the patient population and improve leadership transparency and hospitalists' engagement, all while the pandemic goes on.

"The SIG supports us administrators in this role of bringing our practices to a level where we can continue to process promotions, hold annual awards, promote and support quality-improvement projects and the growth of our practices in general, despite the pandemic. And that contribution of the SIG to our daily lives has been priceless."

Richard Quinn is a freelance writer in New Jersey.

## **Rebuilding Trust in Health Care**

## By Ankit Mehta, MD, FACP, SFHM, and Benji K. Mathews, MD, MBA, SFHM

rust is fundamental to the practice of medicine. As the foundation of a therapeutic relationship, it's essential for effective care delivery. Trust is a fragile bond, an agreement that, in a state of vulnerability, a patient can rely on the clinician to act in their best interest with integrity and fairness. Traditionally, trust-based relationships existed solely on a patient-clinician level but in modern health care, the concept of trust operates in a complex ecosystem of health care networks, organizations, and multidisciplinary teams.1 It's the shared responsibility of all participants in the chain of care to foster trust. As hospitalists, we face an even greater challenge of building trust with patients who are facing difficult choices in states of acute vulnerability—often as virtual strangers—walking in spaces fraught with emotions. We present three elements that bolster trust: compassion, competence, and

Individual and collective acts

*credibility.* These exist on both interpersonal and organizational levels.

Trust in health care has gradually eroded in the U.S. over the last four decades. While 80% of Americans showed confidence in the medical system in 1975, only 37% expressed confidence in 2015, a dramatic fall of more than 50%.<sup>2</sup> And, the U.S. ranked 24 out of 29 in patients agreeing with the statement "all things considered, doctors in the U.S. can be trusted."<sup>3</sup> These pre-pandemic reports on public trust were an augury of signs to come.

The cause for this steep decline in trust is multifactorial. Health care in the U.S. evolved in the last few decades into a complex, byzantine system. Emerging business models have turned health care into an industry and patients into customers. And, multiple factors contribute to the fracturing of trust, including an insidious decline of trust in scientific experts, the breakdown of communities and social bonds, structural racism, existing health inequities, and an increasingly polarized media landscape. In this pandemic, the issue of public mistrust has led to our untethering, leaving us in free fall.

Trust in health care lies in relationships. Patients' trust in clinicians is dependent and intertwined with factors of the organization at large.<sup>4</sup> Therefore, elements of trust require deeper scrutiny on both interpersonal and organizational fronts. An analysis of factors that affect patients' perception of trust showed that individual/interpersonal factors (like empathy) had a relatively lower effect compared to the quality metrics of the facility (i.e., reliability, promptness, efficiency, and affordability).<sup>5</sup> In this regard, health systems bear a larger share of responsibility and ownership in steering public trust.

## Individual trust

Motivated clinicians committed to providing conscientious care to their patients are crucial in building trust. Time limitations, poor communication, unconscious biases, virtual visits, and clinician burnout can lead to the fragmentation of interpersonal relationships and contribute to the erosion of trust between patients and clinicians.

The essential elements for trust-building are compassion, competence, and credibility.<sup>5,6</sup> *Compassion* entails empathy—seeking to understand and having a genuine heart for listening. Empathetic communication is also a vital starting point to bridge inequities. *Competence* involves knowledge and thoroughness, with the ability to elicit and respond to needs efficiently. Competent clinicians exhibit humility and know when to seek help to serve patients' needs. *Credibility* is being true to one's word. It necessitates ethical actions conducted with transparency. Hospitalists should embody and model these trust-building behaviors in their practices.

### **Organizational trust**

To restore patients' trust in health care and hospital settings, person-to-person trust, while essential, cannot suffice. Simply put, organizational trust is not the sum total of interpersonal trust. Organizations must be mindful and commit to the mission of rebuilding trust. The key interpersonal factors of trust—compassion, competence, and credibility—can be extrapolated to organizations as well.

Compassion: Inequities and community partnerships—For under-resourced groups, trust has been eroded by a lack of equitable access to quality care on top of a history of biased and unethical treatment. There's an increasing awareness and acknowledgment of the inequities in communities that drive health care disparities. While health care systems strive to provide equitable care for patients within hospitals/ systems, it's imperative for health care systems to actively engage with communities to address and mitigate these disparities.

Historically, under-resourced communities have faced overt discrimination and racism from the medical community. Black and Hispanic communities still face barriers to care access.<sup>7</sup> The COVID-19 pandemic brought these inequities into sharp focus with inadequate testing, high rates of cases and deaths, and poor access to vaccines, causing attrition of trust even further.<sup>8</sup>

Health care systems and hospitals are often vested in the community as large employers and are vital to its economy. It's incumbent upon health care systems to strengthen their bonds with the communities they serve. Sincere intent and genuine effort to collaborate with populations are essential to trust-building—listening, seeking to understand, and proactively assessing community needs are important for this endeavor. In acute-care settings, the goal should be to provide the highest quality of care, focusing on the dignity of, and respect for, all patients. Additionally, developing and committing to strategies promoting health maintenance, coverage, and access for populations is paramount. Importantly, health care systems should also commit to creating equity and diversity within their own organizations. Also, advocating for broader representation of people of color and low-income groups in research and clinical trials is overdue to bridge these gaps.

Competence: Communication, quality, safety— Health care systems' commitment to providing high-quality, safe, and effective care delivered efficiently is a requisite for trust. Currently, one of the greatest challenges is to counter misinformation and relay factual information to the public cogently. According to a Pew Research Center report, Americans are divided along party lines in terms of how they view the value and



Read more about trust in the *Journal of Hospital Medicine's* trust series.

objectivity of scientists and their ability to act in the public interest.<sup>9</sup> Of note, the trust report also found that Americans tend to trust the recommendations of science practitioners involved in their direct care, more than those of researchers.<sup>9</sup> In the era when science, scientific communities, and experts are widely mistrusted while facts are politicized and come into doubt, health care systems need to make concerted efforts to actively build and maintain trust within the communities they serve. In times of uncertainty, empathetic and honest communication, both at individual and organizational levels, is crucial.

Credibility: Integrity, transparency, and affordability—With extraordinary progress and expanded capabilities in medicine, modern health care has evolved into an exorbitant and complex web of systems. Health care systems are often viewed as efficient operations, driven by market forces with the central goal of maximizing profits. A cross-national data analysis of 23 countries revealed that commodification or commercialization of health care may play a significant role in the deterioration of public trust in individual physicians.

Nations that consider health care as a basic human right had higher levels of trust in physicians.<sup>3</sup> This underscores the point that interpersonal trust and organizational trust do not operate in silos but are intertwined. Patients and communities feel disconnected from the hazy interplay of insurance plans, pharmaceuticals, organizations' financial ties, and payment models within health care systems. Increasing commercialization, in which patients assume the role of customers or clients, buying services in exchange for money, makes health care transactional and less trustworthy.

Patients (and often clinicians) find billing and health care pricing processes opaque. Unexplainable price variability and expensive surprise medical bills further erode the trust of patients. Lack of standardized costs of services and medications is common. Patients' trust also varies based on health care system configurations (public/private), insurance coverages, hospital experiences, and autonomy/choice, as these contexts drive how patients manage their vulnerabilities.<sup>10</sup> It's incumbent on organizations to be transparent regarding their business models, financial ties, and billing processes. Therefore, the core tenet of restored trust should be a commitment to transparency and the creation of affordable care by health care systems.

### Steps toward restoring trust

Rebuilding public trust in health care is the need of the hour. Concerted efforts by health care systems toward building trust and a willingness to fundamentally change operations, keeping trust as a focus, is essential. Creating a culture geared toward compassion, competence,



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and credibility-on interpersonal and organizational levels—can be instrumental in fostering trust. As hospitalists, we're stakeholders and integrally involved in the operations, decision making, and functioning of hospitals. Hospitalists lead key missions in hospitals, including safety and quality. Health care systems should consider creating space and resources for "trust officers", "trust trustees", or teams with the intent to commit to restoring and maintaining trust with the communities they serve. Hospitalists are well-positioned to contribute meaningfully to this cause and to become custodians of trust and ambassadors of their organizations. Trust metrics should be devised and tracked. Trust officers should have a seat at the table in operational decisions, weighing these through the lens of trust. Trust teams can engage in transparency, advocate for equity, and improve access to care. These teams may also act as community liaisons, creating partnerships and strengthening bonds. In cases of breaches of trust, organizations should be transparent and hold parties accountable.

In this era of uncertainty, tumult, and widening chasms between patients and clinicians, building bridges of trust is a key way out of precarity.

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## **Key Cinical Question**

## What Medications Prevent Delirium in Elderly Medical Inpatients?

## By Kristen Fletcher, MD; Joseph Sweigart, MD

#### Case

79-year-old man with a history of ischemic stroke five months ago presents with fever and shortness of breath. He is admitted for hypoxia secondary to suspected aspiration pneumonia and initiated on supplemental oxygen and intravenous antibiotics. His wife reports that, during his past admission for stroke, he developed confusion and agitation while in the hospital. She asks you what can be done to prevent this.

#### Background

Delirium is a common, costly, and morbid complication of hospitalization in the elderly. Characterized by an altered sensorium with acute cognitive decline and fluctuating levels of attention, delirium is diagnosed in up to 30% of general-medical-ward patients. Intensive care unit (ICU) and surgical patients are at even higher risk for delirium. with rates as high as 50%.<sup>1</sup> Delirium results in increased in-hospital and one-year mortality rates and causes significant morbidity, including increased length of stay, postoperative complications, and the likelihood of discharge to a skilled nursing facility. Daily costs for patients with delirium are estimated to be 2.5 times higher than for those without.<sup>2</sup> Given the deleterious effects of delirium, hospitalists are searching for the best ways to prevent it. Delirium-prevention strategies are a robust area of geriatric research. Despite its high prevalence, the basic mechanism of delirium is unknown but postulated to be multifactorial. Evidence supports central neurotransmitter

imbalances playing a role in the development and maintenance of delirium.<sup>3</sup> This is further supported by typical delirium features of alteration in circadian rhythms and rapid fluctuation in cognition. As a result, sleep-pathway medications are of interest for delirium prevention via stabilization of sleep-wake cycles and neuropsychiatric function. The evidence supporting these interventions for delirium prevention is weak and variable.

## **Delirium prevention strategies**

Pharmacologic delirium prevention has been studied in three large groups: surgical, medical ICU, and medical non-ICU. The main challenge to date rests in the inherent differences of each patient population and corresponding nuances of delirium triggers; data demonstrating successful pharmacologic prevention in one group should not be extrapolated to other groups. For example, perioperative delirium is precipitated by the acute, easily identified event of operative anesthesia and recovery, which makes extrapolating surgical data on delirium to medical patients complicated and suboptimal. Several antipsychotic medications have been studied for delirium prevention in surgical patients,<sup>4</sup> but no such evidence exists for medical inpatients. Further, studies of surgical patients are limited by methodological weaknesses (i.e., comparison to no-treatment rather than to standard of care, and/or initiating prophylactic medication immediately upon waking from anesthesia, which has no corollary for medical patients).⁵

For non-ICU medical patients, melatonin and melatonin receptor agonists have been a focus of research. The available data supporting both melatonin and ramelteon come only from small, single-center studies; these studies cite a favorable tolerability profile with few adverse effects reported during the study periods.<sup>36,78</sup>

Al-Aama et al provide the most compelling study supporting low-dose melatonin3; 145 patients enrolled aged 65 years or older were randomized to receive either placebo or 0.5 mg of melatonin each night for 14 days or until hospital discharge. This study demonstrated lower rates of delirium in the melatonin arm, with an impressive number needed to treat (NNT) below six patients; mortality and length of hospital stay were unaffected.<sup>3</sup> A delirium-prevention effect of melatonin has not been reproduced in other studies, notably Jaiswal et al, which randomized patients to a placebo



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or 3 mg of melatonin and found no difference in rates of delirium prevention.<sup>7</sup>

The melatonin receptor agonist ramelteon also has small but favorable evidence for preventing non-ICU hospitalized delirium. This comes from a study of 67 patients aged 65 years or older who were randomized to receive either placebo or ramelteon 8 mg each night for seven days.<sup>6</sup> This study also showed a reduction in delirium with an NNT below four patients. Like melatonin, though, ramelteon use has not been shown to reduce hospital length of stay or mortality.

Routine recommendations for pharmacologic intervention cannot be made secondary to the paucity of compelling, consistent data. If pharmacologic prevention

INTERVENTION	PATIENT TYPE	DOSE	DELIRIUM OUTCOME	NNT/NNH
Melatonin	Medical	0.5mg PO at bedtime	Incidence Length of stay	5.2 NS
Ramelteon	Medical	8mg PO at bedtime	Incidence Length of stay	3.4 Not reported
Haloperidol	Hip fracture surgery Noncardiac surgery	0.5mg PO TID 0.5mg IV then 0.1mg/hr x12 hrs	Incidence Length of stay Incidence Length of stay	NS 5.5 days shorter (if delirium developed) 12.7 NS
Risperidone	Cardiac surgery	1mg PO upon waking from surgery	Incidence Length of stay	4.9 NS
Olanzapine	Orthopedic surgery	5mg just before and just after surgery	Incidence Length of stay	3.9 Not reported

is pursued, the dosage should be consistent with the limited available evidence. Specifically, it is important to note that the study demonstrating the benefit of melatonin uses a dose (0.5 mg) that is a fraction of the dose typically used to treat insomnia.3 This suggests that melatonin may be most effective for delirium prevention at doses much lower than those typically initiated, although further research is needed to validate those findings. Furthermore, if medication is initiated for delirium prophylaxis during hospitalization, no evidence exists to guide how long patients should continue those interventions during hospitalization, rehabilitation stays, or upon their return home.

Currently, the evidence supporting non-pharmacologic strategies for delirium prevention is much stronger than the evidence suggesting a benefit from medication treatment. A popular example of a non-pharmacologic bundle, the Hospital Elder Life Program (HELP) or a modification program thereof, consists of key components<sup>2,9</sup> including early mobilization, re-orientation strategies, sensory input, and sleep enhancement. Programs like these non-pharmacologic bundles have

## **Key Points**

- Although several antipsychotic medications have been studied for delirium prevention in surgical patients, no such evidence exists for medical inpatients.
- Melatonin receptor agonist ramelteon has small but favorable data for delirium prevention, while melatonin has conflicting outcomes.
- Strong evidence supports non-pharmacologic strategies for prevention.

shown a significant decrease in delirium incidence with no evidence of harm.<sup>2</sup> While these interventions are expensive, cost analyses have demonstrated a favorable impact because of the massive savings that may be realized with each case of delirium prevented.<sup>9</sup>

### Back to the case

You inform the wife that medications are not routinely given to prevent delirium. However, you review key components of non-medication strategies with her. Secondary to your counseling, she brings

## Quiz: What meds prevent delirium in elderly patients

- 1. The delirium-prevention strategy with the most robust body of evidence is:
  - a. Melatonin 0.5 mg at bedtime
  - b. Melatonin 3 mg at bedtime
  - c. Nonpharmacologic bundles
  - d. Ramelteon 8 mg at bedtime

*Correct option:* C. Nonpharmacologic bundles have been shown to be clinically useful and cost-effective. Such bundles most often use nonpharmacologic strategies to maintain sensory input, cognitive engagement, and sleep-wake cycles. Although limited and sometimes conflicted evidence may support some pharmacologic interventions, the most robust evidence is for nonpharmacologic bundles.

### 2. The dose of melatonin shown to reduce the incidence of delirium is:

- a.9 mg at bedtime
- b.6 mg at bedtime
- c. 3 mg at bedtime
- d.0.5 mg at bedtime

*Correct option:* D. In a single study of elderly patients, a prophylactic dose of 0.5 mg of melatonin was shown to reduce the incidence of delirium. Higher doses, though common, have not been studied in the geriatric inpatient population.

#### 3. Melatonin and ramelteon both work via:

- a. Benzodiazepine-receptor agonism
- b. Histamine receptor blockade
- c. Melatonin receptor agonism
- d. Dopamine receptor agonism

*Correct option:* C. Both melatonin and ramelteon have hypnotic properties that result from the activation of the melatonin receptor.

his glasses and hearing aids to the bedside. During his hospitalization, she tirelessly advocates for encouraging his mobility during the day and she is at his bedside each afternoon facilitating conversation and normal wake periods. He is weaned from oxygen and transitioned to oral antibiotics. His cognition remains intact, and he is discharged home with his wife.

#### **Bottom line**

Insufficient evidence exists to support the routine use of pharmacologic agents to prevent delirium in elderly medical inpatients. Several ongoing studies are underway to advance our understanding of pharmacologic delirium prevention. Non-pharmacologic bundles remain the cornerstone of preventing inpatient delirium and have been shown to be safe, effective, and reasonably priced.

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