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The Official Voice of Emergency Medicine

NOVEMBER 2020 Volume 39 Number 11 FACEBOOK/ACEPFAN TWITTER/ACEPNOW ACEPNOW.COM

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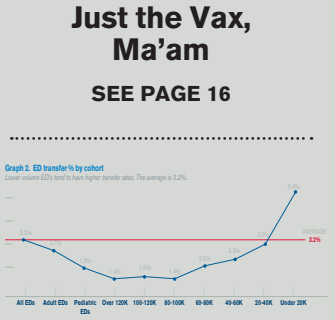


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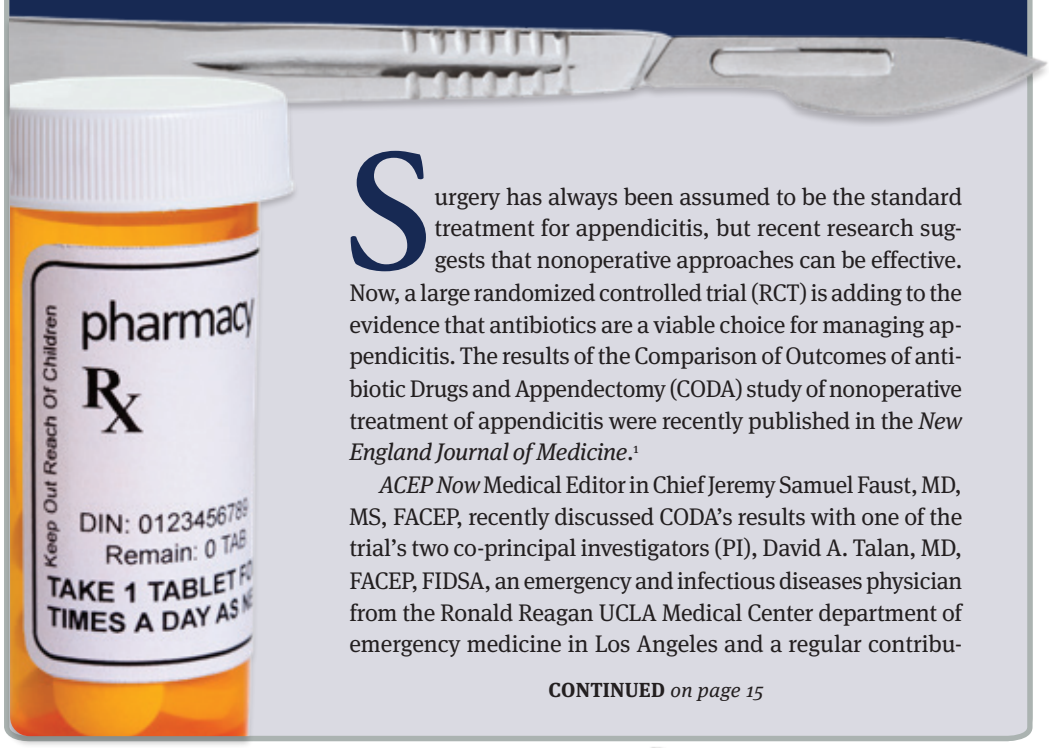
# SURGERY *or* ANTIBIOTICS for Appendicitis?

## A REVIEW OF RESULTS FROM THE CODA ANTIBIOTIC TREATMENT OF APPENDICITIS TRIAL

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Surgery has always been assumed to be the standard treatment for appendicitis, but recent research suggests that nonoperative approaches can be effective. Now, a large randomized controlled trial (RCT) is adding to the evidence that antibiotics are a viable choice for managing appendicitis. The results of the Comparison of Outcomes of antibiotic Drugs and Appendectomy (CODA) study of nonoperative treatment of appendicitis were recently published in the *New England Journal of Medicine*.[1]

*ACEP Now* Medical Editor in Chief Jeremy Samuel Faust, MD, MS, FACEP, recently discussed CODA's results with one of the trial's two co-principal investigators (PI), David A. Talan, MD, FACEP, FIDSA, an emergency and infectious diseases physician from the Ronald Reagan UCLA Medical Center department of emergency medicine in Los Angeles and a regular contribu-

**CONTINUED** *on page 15*

# For Better or Worse

## What to expect when sending patients with COVID-19 home

*by* AUSTIN KILARU, MD, MSHP; AND KATHLEEN LEE, MD

We have learned much about the novel coronavirus in the months since the start of the pandemic. But one of the major questions is one that we normally are quite comfortable with as emergency physicians: Who can be discharged, and who must be hospitalized?

While we are becoming more familiar with the risk factors for severe COVID-19 illness, including age and certain preexisting conditions, that is not the same as knowing who to admit and who to send home.

A problem noted from early in the pandemic is that some patients worsen many days after initially developing symptoms.[1] Delays in deterioration can occur with other viral illnesses but not with the characteristic pattern of COVID-19.[2] The common adage for mildly or moderately ill patients with influenza or stomach virus—"You'll start to feel better in a few days"—may not apply. Despite known risk factors, young and healthy people can still get very sick without explanation, even after "turning the corner," and others have symptoms that persist

**CONTINUED** *on page 10*

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PRO / CON

# Metal Detectors in the ED

SEE PAGE 6

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# NEWS FROM THE COLLEGE

UPDATES AND ALERTS FROM ACEP


Dr. Gillian Schmitz

## Dr. Gillian Schmitz Is Your Next ACEP President

On Sunday, Oct. 24, 2020, the ACEP Council elected Gillian Schmitz, MD, FACEP, as its President-Elect. She will assume the presidency during ACEP21. Dr. Schmitz is an associate professor at the Uniformed Services University of the Health Sciences. She is also the vice chair of education at the Brooke Army Medical Center in San Antonio, Texas. Within ACEP, Dr. Schmitz is a former chair of the Academic Affairs Committee, subcommittee chair for the Medical Legal Committee, chair for the Young Physicians Section, and former Board member for the Emergency Medicine Residents' Association (EMRA). She has been active in the Texas ACEP chapter and is a past President of the Government Services chapter. Dr. Schmitz has a medical degree from Loyola Stritch School of Medicine in Chicago and completed her residency at the University of North Carolina.

Virtual ACEP20

## ACEP20 Virtual Package Now Available

If you were unable to attend ACEP20 in late October, you can still access all of the education by purchasing Virtual ACEP20. You'll receive access to more than 250 broadcast-quality CME courses for three years after the event. Visit acep.org/virtualACEP20 to learn more.

## Virtual Grand Rounds Continue with Neurology, Cardiology Sessions

ACEP's Academic Affairs and Education Committee created the monthly Virtual Grand Rounds program in April as a way to provide free education for emergency physicians and residency programs during this time of social distancing. It allows you to track learner participation while engaging in Q&As with course faculty on different monthly topics. Once the sessions are complete, they are posted in the ACEP eCME catalog for online learning.

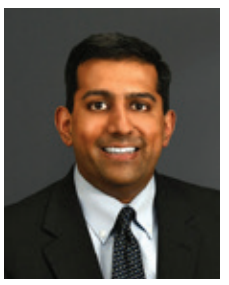
Topics previously covered include COVID-19, Physician Wellness, Airway, Ultrasound, Pediatrics, and International Perspectives on COVID-19. Register at www.acep.org/virtualgrandrounds.

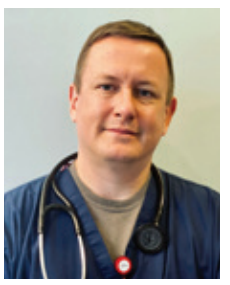
- **Nov. 18:** Neurology
- **Dec. 16:** Cardiology
- **Jan. 27:** Vulnerable Populations/Social Determinants of Health
- **Feb. 24:** Simulation: OB Emergencies with EMRA

## ACEP Council Elects New Board Members


Dr. Allison Haddock


Dr. Aisha Terry


Dr. Arvind Venkat


Dr. James Shoemaker, Jr.


Dr. Christopher S. Kang

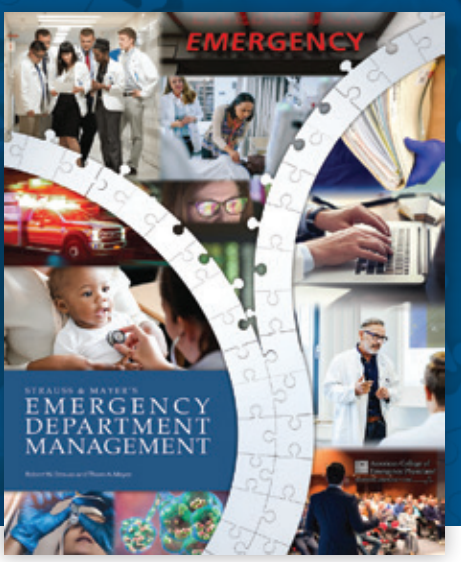
During the ACEP20 Council Meeting, the Council voted for two incumbents and two new Board members. Allison Haddock, MD, FACEP, and Aisha Terry, MD, MPH, FACEP, were re-elected to the Board, while James Shoemaker, Jr., MD, FACEP, and Arvind Venkat, MD, FACEP, were elected as new Board members.

The Board of Directors also voted on new officer roles. Christopher S. Kang, MD, FACEP, FAWM, was elected Chair of the Board, and Dr. Haddock was voted Vice President. Dr. Terry was elected Secretary-Treasurer.

## ED Directors Academy Coming Up

A virtual version of the ED Directors Academy (EDDA) Phase I kicks off Nov. 30. This first phase is designed to lay the groundwork for your success as a director, covering topics such as organizational leadership, operations, leadership and staff management, communication, inclusion, and more. The format will feature 10 modules that have to be completed before February to get credit. Learn more at www.acep.org/edda.





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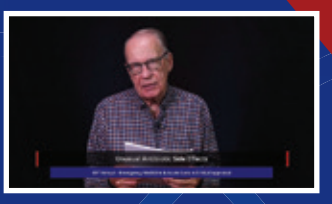
- Cardiovascular Pearls, 2019
- DKA and Hyperglycemia Update
- Sore Throat: Still Trying to Get It Right
- Sexual/Racial/Ethnic Disparities in the ED
- ACS & PE – ACEP 2019 Guidelines
- Psychiatric Patients: Medical Evaluation
- Sepsis 2019: Hot Off the Press
- Challenges of Atrial Fibrillation - Part 1
- Challenges of Atrial Fibrillation - Part 2
- Otitis Media Doesn't Cause Fever
- Pearls from *ED Leadership Monthly*
- Pearls from *Risk Management Monthly*
- Urologic Imaging Guidelines
- Pediatric Vomiting and Diarrhea
- Trauma 2019: Hot Off the Press
- Myths in Emergency Medicine
- Myths in EMS Care
- ATS/IDSA Updated Pneumonia Guidelines
- Visual Diagnosis Challenges - Part 1
- Visual Diagnosis Challenges - Part 2
- Important Recent EM Literature - Part 1*
- Important Recent EM Literature - Part 2*

*Topics listed with an asterisk (*) are 90-minute faculty panel discussions; all other topics are 30 minutes.



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- So When You Say the Word "Dizzy"... Posterior Circulation Issues
- You Called Down the Thunderclap: Subarachnoid Hemorrhage
- Cardiac Roulette: Chest Pain Risk Stratification in 2019
- An Infarct Rather Than an Accident: Stroke 2019
- Failure May Very Well Be Fatal: Acute Heart Failure
- Mostly Dead Is Still Slightly Alive: Cardiac Arrest
- Can't Catch Me: Narrow Complex Tachycardias
- Welcome to the Machine: Device Emergencies
- For the Faint of Heart: Cardiogenic Syncope
- Ripping It to Pieces: Acute Aortic Dissection
- You Can Die of a Broken Heart: Shock
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# Pro-Con: Metal Detectors in

**PRO**

## TIME TO PUT NEGATIVE PERCEPTIONS OF METAL DETECTORS TO REST

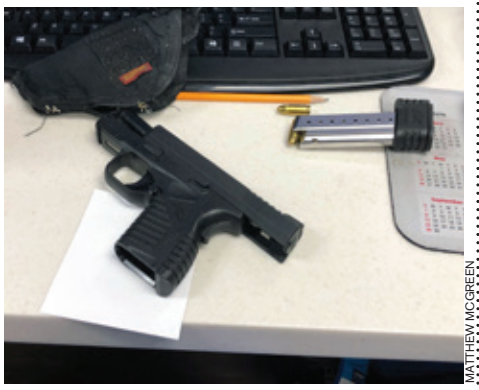
*by* DIANN M. KRYWKO, MD, FACEP

Violence in the emergency department is not a new phenomenon. Our specialty has been fighting for workplace safety for more than 25 years. ACEP issued a policy statement in 1993 titled "Protection from Physical Violence in the Emergency Department."[1] The 2016 policy revision, with the same title sans the word "physical," states that "optimal patient care can only be achieved when we are all safe and protected from violence."[2] How true. The policy calls for increased awareness and increased safety measures, including adequate security personnel, sufficient training of personnel, physical barriers, surveillance equipment, and security components.

One of the safety measures is the use of metal detectors, which include hand-held and walk-through (WT) metal detectors. It is not uncommon for ED personnel to find weapons in patient care areas that might otherwise have been confiscated prior to entry (see Figure 1). In one 26-month study, after introducing WT metal detectors in the ED entrance at one hospital, nearly 6,000 weapons, including 268 firearms and 4,842 knives, were retrieved.[3] Even with these data showing that metal detector use results in weapon retrieval, widely varying policies still exist regarding their use as screening tools to enhance safety.

There must be reasons why implementing metal detectors has barriers or else they would probably already be universal in emergency departments. Concerns for efficacy, cost with regard to staffing and equipment, and perception are a few of those barriers. The study by Malka et al addresses efficacy.[3] Cost would vary with types of equipment purchased and staffing model and would be the topic for another discussion. So let's address perceptions as a barrier to implementation of metal detectors in emergency departments.

Our institutional policy currently mandates activation of WT metal detectors only when EMS arrival of gunshot wound victims is identified. In meetings addressing increasing ED violence, administrators argued that the presence of a metal detectors at the entrance



MATTHEW MCGREEN

**Fig. 1:** Weapon seized in the acute resuscitation bay.

to the emergency department might convey to the public the impression of a potentially dangerous environment. In other words, utilizing our metal detectors 365-24-7 would create a bad public image. This would result in fewer visits and referrals and loss of revenue for our hospital. That got our analytical wheels turning. If we feel safer when metal detectors are used at a public place where concern exists for violence, such as the airport, why wouldn't patients, visitors, and staff feel safer in the health care arena with the same precautions? Was this negative perception concern real?

Two studies looked into metal detectors perception back in 1997. In the first, 75 percent of patients already felt safe and 68 percent were satisfied with the security. However, 11 percent felt a fear of being physically harmed in the emergency department, and two-thirds reported they would feel better with a metal detector in use. The authors concluded that the concerns over the potential for negative imaging around metal detectors was not warranted.[4] In the second study, 80 percent of patrons and 85 percent of employees liked the metal detector, with 89 percent of patrons and 73 percent of employees feeling safer with its use. Thirty-nine percent were more likely to return because of it, while just 1 percent said they were less likely to return as a result.[5]

In 2017, Dr. Russell Allinder, Dr. Steven Saef, and I set out to determine the current perception of metal detector and security officer usage in our emergency department. We realized that public perception may have changed over the course of those two decades and that negative perception might be a valid concern. The survey included more than 300 ED patients, visitors, and staff at our southeastern academic Level 1 trauma center.

Among other results, we found that surveyed participants would not perceive the emergency department as a more dangerous place if WT metal detectors were routinely utilized. In fact, a majority of participants (75 percent) stated they would feel safer if a WT metal detector was in use, with African Americans reporting greater perceived safety benefit than Caucasians in a bivariate analysis ($P<0.001$). Security officer visibility increased safety perception for 72 percent of participants. WT metal detector usage at the entrance would not adversely affect willingness to return to the emergency department for 99 percent of respondents.

Bottom line: The notion that the public perceives the emergency department as less safe and therefore avoid future ED care when metal detectors are used is simply not true, as shown in our study. This argument should not be used as an argument against their use. Emergency medicine workers are at high risk for workplace violence. We deserve to be safe while we serve populations that need us to be their safety net. Though one piece to a very large puzzle, having an active metal detector may prevent weapons in the patient care area and deter violence in the emergency department, allowing us to safely do our job.

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**DR. KRYWKO** is professor of emergency medicine at the Medical University of South Carolina.


## By the Numbers

### FIREARMS IN EDs

**EMERGENCY DEPARTMENT SHOOTERS**

**23%**

use a security officer's firearm

**27%**

of hospital-related shootings are motivated by a workplace grudge

**59.1%**

of American ED health care professionals report encountering firearms in or near the ED at least once per year

# the Emergency Department

**CON**

## ARE THE BENEFITS OF METAL DETECTORS WORTH THE COSTS?

*by* TRACY G. SANSON, MD, FACEP

When patients enter an emergency department or we begin our shifts, there is the expectation of safety. The American Society for Health Care Engineering's 2018 Hospital Security Survey found more than half of our hospitals had an increase in violence against staff from the prior year. The rise in violence in emergency departments across the country is cause for great concern. And there is movement in the right direction. In November, the House of Representatives passed the Workplace Violence Prevention for Health Care and Social Service Workers Act, requiring employers to develop and implement a workplace violence prevention plan.

Some hospitals have installed walk-through metal detectors at the main entrance to their emergency departments as part of their overall safety initiatives. Is this good policy?

Let's explore the consequences of metal detectors.

Cost is often one of the first concerns raised. The cost of the initial purchase of the metal detector is only a fraction of the total resources needed to operate it. The initial purchase is expensive, as is continued maintenance of walk-through metal detectors. Additional impacts include queuing, space, and additional staffing needs. Jon Huddy outlined the following concerns in the book *Emergency Department Design: A Practical Guide to Planning for the Future*.[1]

**Space for equipment and searches:** Adding metal detectors to your existing walk-in vestibule is not as easy as it sounds, even if you get the budget to cover the costs of the equipment and required personnel. You'll need space for the machine itself, but you'll also need space for patients and visitors to wait in line to walk through. You'll need more space immediately beyond the detection equipment to be able to search bags and people. You'll need to consider a different pathway out of the public area so that patients and visitors don't have to pass back through the detection and search area when they leave.

**Private search room:** An additional consideration is a private search room near the metal detector that can be used for more intensive searching of people who set off the metal detector even after removing items most likely to cause problems. This takes up another room in the department, but it tends to be necessary when metal detectors are used.

**X-ray equipment:** Another space hog is the X-ray machinery used to scan bags, similar to what is used in airports to check carry-on items. I've worked with a few departments that have installed X-ray equipment, and it takes up at least another 160 square feet for the machine and personnel.

**Surveying who's in line:** The largest drawback to the use of metal detectors is that it forces patients and visitors to wait in line. As a result, the queue must be staged so that clinical professionals from a reception desk, assessment area, or triage room can maintain visibility of everyone in line. At some facilities, planners have considered putting a paramedic or nurse outside the building to help with the queuing and allowing them to be close to arriving patients. This represents additional staff cost, but a risk management assessment might drive the need for it.

**Reducing queuing:** I've seen a couple of emergency departments with metal detectors come up with options to reduce the length of time people wait in the line. In one approach, a volunteer or staff member stands ahead of the metal detector, handing out bins, telling entrants to empty their pockets, and giving them instructions for passing through the metal detectors so they are ready to move through more quickly. Another option, although an expensive one, is to add a second metal detector. This doesn't necessarily mean that another security guard is needed.

**Staffing expense:** Metal detectors are a huge operational expense. One security guard has to move entrants through the detector while another security guard searches bags. At any facility, implementing metal detectors with only one security guard will result in very long lines.

**EMS patients:** More emergency departments are stationing security guards at ambulance entrances to "wand" patients as they arrive to detect weapons.[1]

But more than this, metal detectors can provide a *false sense of security*. A 1999 study found that the implementation of an ED security system increased the number and percentage of weapons confiscated before patients were placed in patient care areas but *did not* decrease the number of assaults.[2]

The American Society for Health Care Engineering's 2018 Hospital Security Survey found that 57 percent of respondents reported an increase in violent incidents against staff in the emergency department, and 52 percent saw an increase outside the emergency department. Controlling who is in the hospital is one of The Joint Commission's Environment of Care standards and is a key security tactic. Visitor-management systems, which require each visitor to sign in, provide ID or be photographed, and wear a badge, can deter unauthorized visitors.

Those of us who work in emergency medicine know that the vast majority of violence in emergency departments is verbal. And much of the physical violence that does occur does not involve the use of a weapon.

We must continue to emphasize the importance of continued training of ED personnel in the management of violent patients and potentially violent situations. The needs and demands of each emergency department vary from hospital to hospital. Proactive safety measures for emergency departments are crucial for both patients and health care professionals. Because of the limitations and practical concerns surrounding the use of metal detectors, we should instead direct funds toward durable safety plans focused on the needs of each individual emergency department.

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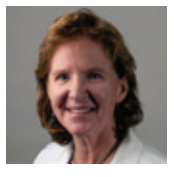


**DR. SANSON** is an emergency physician, professional speaker, and ED consultant.

**20%**
of gunshot victims in hospital-related shootings are hospital employees:

**5%** NURSES

**3%** PHYSICIANS

**HEALTH CARE-RELATED SHOOTINGS**
**67%**
have concluded before police arrival

**92%**
of health care workers felt more prepared to respond to an active shooter after completing ED-specific active shooter training

**39%** LAYPEOPLE

**27%** HEALTH CARE PROFESSIONALS

expect physicians and nurses to accept a high/very high degree of personal risk caring for patients who can't get away from an active shooter

Compiled by Kathryn Wiesendanger and Megan Ranney, MD, MPH, for AFFIRM Research (www.affirmresearch.org). Visit **ACEPNow.com** for the sources of these statistics.

# ACEP4U: Opioids & Pain Management Progress

## THE FIRST ED PAIN AND ADDICTION CARE ACCREDITATION IS AN IMPORTANT STEP IN ACEP'S EFFORTS TO COMBAT OPIOID EPIDEMIC

*by* JORDAN GRANTHAM

In early October, St. Joseph's University Medical Center Emergency Department in Paterson, New Jersey, became the first facility in the nation to earn the new ACEP Pain and Addiction Care in the Emergency Department (PACED) accreditation. This new accreditation program is another important piece of ACEP's efforts to combat the opioid crisis.

PAIN AND ADDICTION CARE IN THE ED
PACED
ACEP ACCREDITATION

### First PACED Accreditation

ACEP's PACED program launched in early 2020 and is the first of its kind to recognize emergency departments that specialize in safe and effective pain and addiction treatment while minimizing the use of opioids or prioritizing alternatives to opioids. PACED-accredited facilities will accelerate the implementation of best practices nationwide and collaborate to help ensure that emergency physicians have the resources, protocols, and training necessary to provide the highest-quality pain and addiction management.

It's fitting that the program's first accreditation was awarded to the hospital that began the landmark Alternatives to Opioids (ALTO) program back in 2016.

"Although we have made important strides in emergency department pain and addiction care, the opioid crisis continues to ravage our communities. PACED accreditation offers a structure for frontline staff and administrators to work together to ensure the safest evidence-based care is available for their entire community," said Alexis M. LaPietra, DO, FACEP, chief of pain management/addiction medicine at St. Joseph's University Medical Center.

PACED was created to benefit all three stakeholders involved: the patients, the emergency care team, and the hospitals. Importantly for emergency physicians, the program serves to accelerate the implementation of best practices while providing a structure that ensures emergency physicians have the resources and training to provide optimal pain and/or addiction management.

The program features three levels: Bronze, Silver, and Gold. The Bronze level is within reach of every hospital, and the Silver and Gold levels have higher standards that require more focused effort and resources. Learn more about this innovative new program and its accreditation requirements at www.acep.org/PACED.

ED X-Waiver
Training Corps.

### X-Waiver Training

COVID-19 has created new barriers to care, and the isolation of the pandemic has affected patients with addiction. Many clinics are reducing hours and limiting the intake of new patients. For many, the emergency department is the only source of treatment for opioid use disorder (OUD).

ACEP has been offering free, live X-waiver trainings on the Zoom platform throughout 2020. At the time this was published, ACEP had recorded 1,287 trainings through its Zoom courses this year. Though the curriculum was developed by emergency physicians, the courses are open to a broad audience. There are still opportunities for you attend a training; learn more at www.acep.org/ed-x-waiver.

### Ongoing OUD Advocacy

For years, ACEP's advocacy team has been working on legislative and regulatory issues related to the opioid crisis. In October 2018, President Donald Trump signed a sweeping legislative package of bills to address the nation's growing opioid epidemic, with former ACEP Executive Director Dean Wilkerson in attendance at the signing ceremony. Included in the package were the Alternatives to Opioids (ALTO) in the Emergency Department Act and the Preventing Overdoses While in Emergency Rooms (POWER) Act, both of which ACEP developed with the sponsoring members of Congress.

The ALTO in the Emergency Department Act (HR 5197/S 2516) established a demonstration program to implement nonopioid evidence-based pain management protocols, such as nitrous oxide, trigger-point injections, nerve blocks, and other pain management options, in hospitals across the country, based on the successful and proven ALTO program developed in New Jersey and recently implemented in several hospitals in Colorado.

The Preventing Overdoses While in Emergency Rooms (POWER) Act (HR 5176/S 2610) provides grants to establish policies and procedures for initiating medication-assisted treatment (MAT) in the emergency department. It also provides education and additional resources to help implementation of MAT in the emergency department as well as to develop best practices to provide a "warm handoff" to appropriate community resources and health care workers to keep patients engaged in treatment. MAT is a proven medical treatment that can relieve withdrawal symptoms and psychological cravings of OUD.

The first grants for these critical programs were made available in 2020, ensuring that federal resources can help support and expand emergency medicine's important efforts to address the nation's opioid crisis. Additionally, ACEP continues working with the sponsors of these laws to secure continued appropriations funding to ensure a stable funding stream for the grant programs.

As the opioid crisis continues to grow during the COVID-19 pandemic, ACEP continues working to permanently remove many of the barriers to OUD treatment, including substantial regulatory and legislative advocacy for changes that make it easier for emergency physicians to initiate MAT in the emergency department. We believe that the federal X-waiver requirement that mandates physicians take an eight-hour course and receive a Drug Enforcement Agency waiver to be able to prescribe buprenorphine outside of opioid treatment programs is a significant barrier to treatment. The presence of this X-waiver requirement has led to a misperception that buprenorphine is fundamentally different from other medications—including narcotics—that physicians are trained to prescribe. As a result, some physicians have been hesitant to pursue the waiver or engage in treatment of patients with OUD at all. We support HR 2482, the Mainstreaming Addiction Treatment Act of 2019, which would remove the X-waiver requirement.

On the regulatory side, ACEP strongly supports a modification to the current "three-day rule," which requires health care workers to administer buprenorphine one day at a time and forces patients to come back each day to receive treatment in the emergency department or other care settings. Emergency departments (even without having clinicians with X-waivers) should be able to dispense a three-day supply of buprenorphine or administer a dose that will last for at least three days. There is also legislation that would address the three-day rule. ACEP supports H.R. 2281, the "Easy Medication Access and Treatment for Opioid Addiction Act." Reimbursement of MAT has been an issue, and through ACEP's advocacy, Medicare will start reimbursing for MAT in the emergency department in 2021.

Learn more about ACEP's advocacy work related to opioid use disorder at www.acep.org/opioids.

**MS. GRANTHAM** is ACEP's communications manager.

# RESIDENCY SPOTLIGHT

## WELLSPAN YORK HOSPITAL

**Twitter:** @WellSpanYHEMRes

**Location:** York, Pennsylvania

**Year founded:** 1989

**Number of residents/program length:**

12 per class/three-year program


### Secret weapons (medical)

Our community academic residency program is the best of both worlds. Our residents receive stellar clinical training in our emergency department, which sees approximately 86,000 adult and pediatric visits annually. York hospital is a tertiary care center, comprehensive stroke center, and certified chest pain center, and even performs ED extracorporeal membrane oxygenation. As a community academic program, our residents have a large amount of patient autonomy and are not just competent in procedures, but confident as well. We have a plethora of academic resources including global health, wilderness medicine, toxicology, disaster medicine, critical care, EMS, forensics, research, simulation, education, and ultrasound opportunities. We have experts in all of these specialized areas, so residents learn from the best. Our 270-plus graduates are practicing nationwide in 45 states, in a multitude of settings including fellowships and rural-, community-, and university-based emergency departments.

### Secret weapons (non-medical)

Living in York is very cost effective and comfortable. Downtown York offers many diverse dining options, and has a local baseball stadium and a theatre. There are many lakes, parks, and trails throughout York County, if you enjoy outdoor activities. York county is located in the middle of everything. By car, it is approximately four hours from Pittsburgh, three hours from New York City, 1.5–2 hours from Washington, D.C. and Philadelphia, and 45 minutes from Baltimore. Amtrak in Lancaster, Pennsylvania, is conveniently located 30 minutes away.

### Recent publication of note

Becker BA, Lahham S, Gonzales MA, et al. A prospective, multicenter evaluation of point-of-care ultrasound for small-bowel obstruction in the emergency department. *Acad Emerg Med*. 2019;26(8):921-930.

This was a multicenter, prospective, observational study examining the diagnostic accuracy of point-of-care (POC) ultrasound (US) for small bowel obstruction (SBO) in the emergency department. The study was initiated at Wellspan York Hospital, but also enrolled subjects at the University of California, Irvine, and Christiana Hospital in Wilmington, Delaware. Multiple attendings, emergency ultrasound fellows, and residents were involved in enrolling subjects and performing the ultrasounds. POC sonographer interpretation of the US for SBO, as well as blinded overread of the POC US images by the site ultrasound director, were compared to abdominal CT as the criterion standard. The results suggest that POC US for SBO is fairly sensitive in the hands of the general operator, but was considerably more specific when interpreted by individuals with more experience with US for SBO.

*—Amber Billet, MD, FACEP, program director, emergency medicine residency*

### Trivia

While in downtown York there are many signs stating that York is the first capital of the United States, it is actually the fourth. Yorkers love Pennsylvania Dutch food, including chicken corn soup, red beet eggs, scrapple, shoofly pie, apple butter, and fasnachts.

for weeks and months.[3]

While we are skilled in providing lifesaving care to patients with critical illness, a different challenge arises when we provide guidance and reassurance to patients who truly are sick, may indeed have early but serious disease, but are stable and do not require any services that hospitalization uniquely provides.

## COVID Bouncebacks

For this reason, our team studied COVID-19 patients who return to the hospital *after* an initial evaluation in the emergency department.[4] The goal was to understand how often people need hospitalization after initially appearing well enough to recover at home, as well as to identify which patients tend to worsen to the point of needing hospitalization and when that might occur. We analyzed the outcomes of 1,419 patients with COVID-19 who were evaluated and discharged from five hospital emergency departments from March through May.

The results (see Figure 1) have implications for clinicians seeking to counsel patients as well as health systems seeking to monitor the progress of patients with COVID-19. Overall, nearly 5 percent of patients returned within 72 hours and needed admission to the hospital. For context, this rate may be five times higher than that described for all ED patients.[5] An additional 3.5 percent of patients needed admission within one week. The fact that patients were hospitalized on their second visit indicates that their illness and symptoms progressed to the point where they needed a higher level of support than they could receive at home, such as oxygen, therapeutic medications, or treatments for other chronic conditions that may have been exacerbated.

We also found that certain characteristics conferred higher risk for returning to the hospital. While it was not surprising that age was a risk factor, the increase in risk was dramatic—the probability of patients older than age 60 returning for admission was 9 percent, more than three times the rate for patients ages 18–39. We found that patients with abnormal findings on chest X-ray, such as pneumonia, had double the probability of returning, as did patients who initially presented with fever or hypoxia (defined as pulse oximetry less than 95 percent on room air). Obesity, hypertension, and age (ages 41–59) were also risk factors for returning within one week.

These results do not suggest that emergency clinicians are making incorrect decisions in sending patients home, although caution is certainly warranted for patients with multiple risk factors. Rather, the data imply that our initial evaluations are a single snapshot in time for an evolving and somewhat unpredictable process.

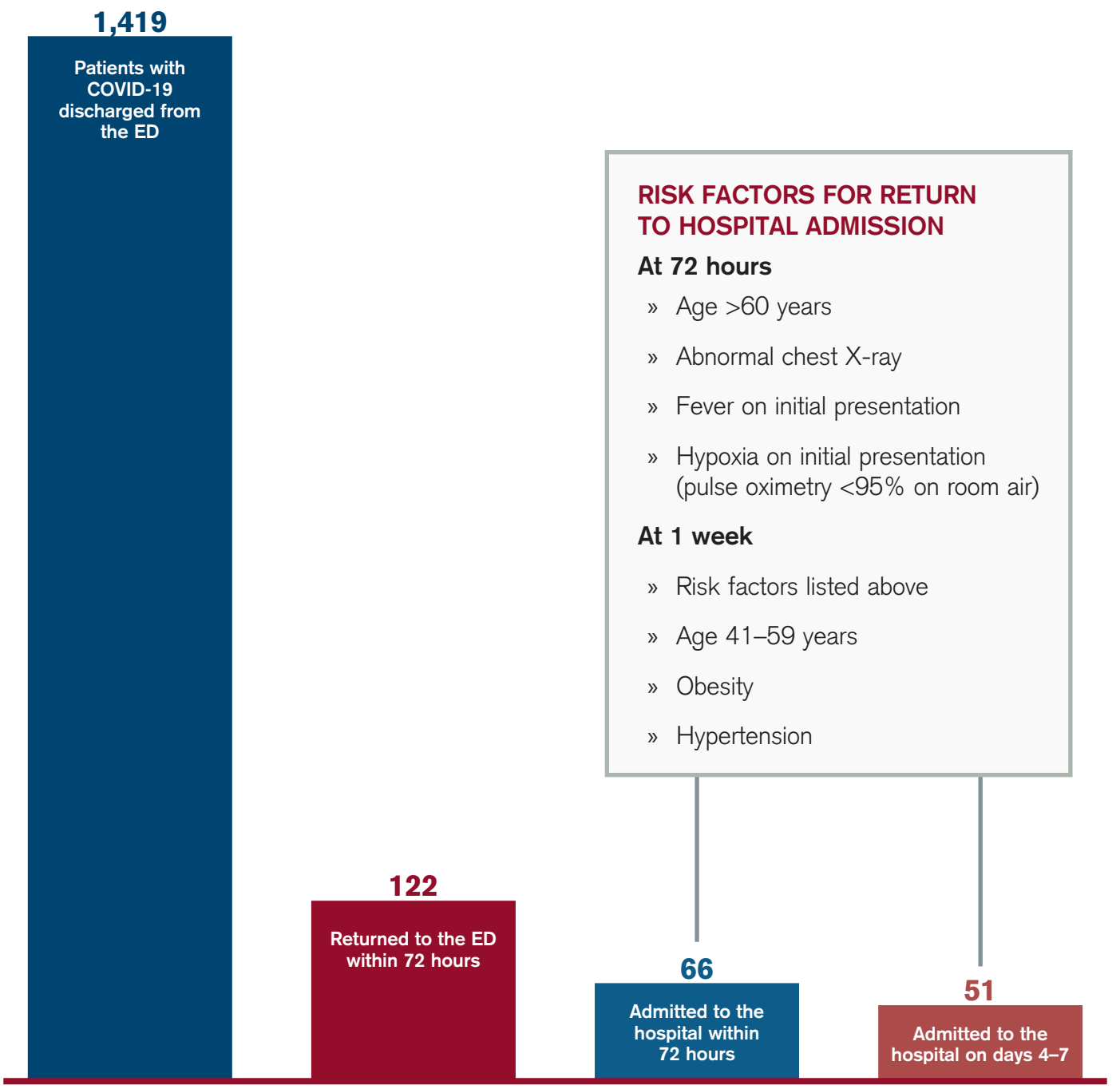
Most patients will get better. Some need more help. And for those who do not recover on their own, we need to ensure they do not delay their return so that treatments are more effective. But how can we monitor patients outside the hospital without overwhelming the outpatient care system, particularly when the transition of patients from the emergency department is already fraught with challenges?

## What Can We Do?

One type of solution has been demonstrated at our own health system through a program called COVID Watch.[6] Patients who go home from the emergency department are enrolled in a text message–based system to perform automated twice-daily check-ins, connect patients with trained clinicians if they have worsening symptoms, and advise returning to the hospital if necessary. Higher-risk patients also receive pulse oximeters to monitor oxygen levels at home.

Caring for this entirely new illness requires emergency clinicians and patients to navigate uncertainty, even beyond our normal practice. We have come a long way in the past several months. To continue to improve—and to help patients even when they are not in the hospital or clinic—we must improve our ability to communicate and coordinate care, requiring innovation and change on a population level, beyond our approach to individual patients.

**Figure 1: Outcomes for COVID-19 Patients Discharged from the ED**




CREDIT: AUSTIN KILARU

## KEY POINTS

- In this study, nearly 5 percent of patients with COVID-19 who were discharged home from the emergency department required hospital admission within 72 hours. More than 8 percent of patients required hospital admission within one week.
- Risk factors for returning to the hospital included age greater than 60, abnormal findings on chest X-ray, and fever or hypoxia upon presentation for the initial ED visit. Additional risk factors for returning within one week included obesity and hypertension.
- Emergency clinicians should discuss with patients the possibility of delayed worsening of COVID-19 illness. Patients may benefit from collaboration with outpatient clinicians or innovative monitoring systems to ensure that their symptoms can be followed while at home.

## References

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5. Cheng J, Shroff A, Khan N, et al. Emergency department return visits resulting in admission: do they reflect quality of care? *Am J Med Qual.* 2016;31(6):541-551.
6. Morgan AU, Balachandran M, Do D, et al. Remote monitoring of patients with Covid-19: cesign, implementation, and outcomes of the first 3,000 patients in COVID Watch. *NEJM Catal Innov Care Deliv.* 2020;10.1056/CAT.20.0342.

**DR. KILARU** is adjunct assistant professor of emergency medicine at Philadelphia VA Medical Center and the University of Pennsylvania in Philadelphia.

**DR. LEE** is director of innovation and assistant professor of clinical emergency medicine at the University of Pennsylvania.

IN THE EMERGENCY DEPARTMENT, FOR ADULT CHRONIC PAIN PATIENTS WITH OPIOID INDUCED CONSTIPATION (OIC)

# Take a proactive approach to OIC

## RELISTOR helps restore gut function by increasing the number of spontaneous bowel movements (SBMs)[1]

### INDICATIONS

- RELISTOR® (methylnaltrexone bromide) is an opioid antagonist. RELISTOR tablets and RELISTOR injection are indicated for the treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.
- RELISTOR injection is also indicated for the treatment of OIC in adults with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care.

### IMPORTANT SAFETY INFORMATION

- RELISTOR tablets and injection are contraindicated in patients with known or suspected mechanical gastrointestinal obstruction and patients at increased risk of recurrent obstruction, due to the potential for gastrointestinal perforation.
- Cases of gastrointestinal perforation have been reported in adult patients with opioid-induced constipation and advanced illness with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the gastrointestinal tract (e.g., peptic ulcer disease, Ogilvie's syndrome, diverticular disease, infiltrative gastrointestinal tract malignancies or peritoneal metastases). Take into account the overall risk-benefit profile when using RELISTOR in patients with these conditions or other conditions which might result in impaired integrity of the gastrointestinal tract wall (e.g., Crohn's disease). Monitor for the development of severe, persistent, or worsening abdominal pain; discontinue RELISTOR in patients who develop this symptom.
- If severe or persistent diarrhea occurs during treatment, advise patients to discontinue therapy with RELISTOR and consult their healthcare provider.
- Symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, diarrhea, abdominal pain, anxiety, and yawning have occurred in patients treated with RELISTOR. Patients having disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal and/or reduced analgesia and should be monitored for adequacy of analgesia and symptoms of opioid withdrawal.
- Avoid concomitant use of RELISTOR with other opioid antagonists because of the potential for additive effects of opioid receptor antagonism and increased risk of opioid withdrawal.

**Please see Brief Summary of full Prescribing Information on the last page.**

# You have the power to intervene early in the ED to help address the underlying cause of OIC

## THE FIRST AND ONLY PAMORA OFFERING TWO ROUTES OF ADMINISTRATION FOR CHRONIC NON-CANCER PAIN (CNCP) PATIENTS

**In 2 clinical trials of adult patients with OIC and CNCP**

**59% of patients** (n= 150) **taking RELISTOR injection 12 mg experienced at least3 SBMs* per week vs. 38% of patients** (n=162) taking placebo (*P*<0.001) for each of the 4 weeks in the double-blind period (Study 2)^

**52% of patients** (n=200) **taking RELISTOR tablets experienced at least 3 SBMs* per week vs. 38% of patients** (n=201) taking placebo (*P*=.005) (Study 1)[1,9,†,‡]

*SBM is defined as bowel movement without the use of any laxative in previous 24 hours.[1,9]

†Responder is defined as a patient with 3 or more SBMs per week, with an increase of 1 or more SBM(s) per week over baseline, for 3 or more out of the first 4 weeks of the treatment period.[1]

‡**Study Design:** Study 1 was a 4-week, randomized, multicenter, double-blind, placebo-controlled, phase 3 study, the efficacy of RELISTOR tablets was evaluated in 401 patients (200 RELISTOR tablets, 201 placebo) with CNCP for which they were taking opioids. All patients had OIC, defined as <3 SBMs per week and at least one additional symptom of constipation.[1,9]

^Study 2 was a 4-week, multicenter, double-blind, randomized, placebo-controlled, phase 3 study. The efficacy of RELISTOR injection was evaluated in 312 patients with CNCP for which they were taking opioids. All patients had OIC, defined as <3 SBMs per week and at least one additional symptom of constipation.

**RELISTOR INJECTION IS THE ONLY PAMORA ALSO INDICATED FOR THE TREATMENT OF OIC IN ADULTS WITH ADVANCED ILLNESS OR ACTIVE CANCER PAIN WHO REQUIRE OPIOID DOSAGE ESCALATION FOR PALLIATIVE CARE**

**LEARN MORE AT RELISTORHCP.COM**

## IMPORTANT SAFETY INFORMATION *(Continued)*

- The use of RELISTOR during pregnancy may precipitate opioid withdrawal in a fetus due to the immature fetal blood-brain barrier and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Because of the potential for serious adverse reactions, including opioid withdrawal, in breastfed infants, advise women that breastfeeding is not recommended during treatment with RELISTOR. In nursing mothers, a decision should be made to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.
- A dosage reduction of RELISTOR tablets and RELISTOR injection is recommended in patients with moderate and severe renal impairment (creatinine clearance less than 60 mL/minute as estimated by Cockcroft-Gault). No dosage adjustment of RELISTOR tablets or RELISTOR injection is needed in patients with mild renal impairment.
- A dosage reduction of RELISTOR tablets is recommended in patients with moderate (Child-Pugh Class B) or severe (Child- Pugh Class C) hepatic impairment. No dosage adjustment of RELISTOR tablets is needed in patients with mild hepatic impairment (Child-Pugh Class A). No dosage adjustment of RELISTOR injection is needed for patients with mild or moderate hepatic impairment. In patients with severe hepatic impairment, monitor for methylnaltrexone-related adverse reactions and dose adjust per Prescribing Information as may be indicated.
- In the clinical studies, the most common adverse reactions were:
  **OIC in adult patients with chronic non-cancer pain**
  - RELISTOR tablets (≥ 2% of RELISTOR patients and at a greater incidence than placebo): abdominal pain (14%), diarrhea (5%), headache (4%), abdominal distention (4%), vomiting (3%), hyperhidrosis (3%), anxiety (2%), muscle spasms (2%), rhinorrhea (2%), and chills (2%).
  - RELISTOR injection (≥ 1% of RELISTOR patients and at a greater incidence than placebo): abdominal pain (21%), nausea (9%), diarrhea (6%), hyperhidrosis (6%), hot flush (3%), tremor (1%), and chills (1%).
- **OIC in adult patients with advanced illness**
  - RELISTOR injection (≥ 5% of RELISTOR patients and at a greater incidence than placebo): abdominal pain (29%) flatulence (13%), nausea (12%), dizziness (7%), and diarrhea (6%).

To report SUSPECTED ADVERSE REACTIONS, contact Salix Pharmaceuticals at 1-800-321-4576 or FDA at 1-800- FDA-1088 or www.fda.gov/medwatch

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

**REFERENCES: 1.** RELISTOR [prescribing information]. Bridgewater, NJ: Salix Pharmaceuticals. **2.** Michna E, Blonsky ER, Schulman S, et al. Subcutaneous methylnaltrexone for treatment of opioid-induced constipation in patients with chronic, nonmalignant pain: a randomized controlled study. *J Pain.* 2011;12(5):554-562. **3.** Data on file. Clinical study report MNTX3201. Salix Pharmaceuticals; 2020.

www.salix.com
400 Somerset Corporate Boulevard, Bridgewater, NJ 08807
Tel 800-321-4576

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RELISTOR® methylnaltrexone bromide Subcutaneous Injection

RELISTOR® methylnaltrexone bromide Tablets

# RELISTOR®
## methylnaltrexone bromide
Subcutaneous Injection

# RELISTOR®
## methylnaltrexone bromide
Tablets

**BRIEF SUMMARY OF PRESCRIBING INFORMATION**

**This Brief Summary does not include all the information needed to use RELISTOR safely and effectively. See full prescribing information for RELISTOR.**

**RELISTOR (methylnaltrexone bromide) 150 mg tablets, for oral use.**

**RELISTOR (methylnaltrexone bromide) injection, for subcutaneous use.**
8 mg/0.4 mL methylnaltrexone bromide in single-dose pre-filled syringe.
12 mg/0.6 mL methylnaltrexone bromide in a single-dose pre-filled syringe, or single-dose vial.

**Initial U.S. Approval: 2008**

**INDICATIONS AND USAGE**

**Opioid-Induced Constipation in Adult Patients with Chronic Non-Cancer Pain**
RELISTOR tablets and RELISTOR injection are indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

**Opioid-Induced Constipation in Adult Patients with Advanced Illness or Pain Caused by Active Cancer**
RELISTOR injection is indicated for the treatment of OIC in adult patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care.

**CONTRAINDICATIONS**
RELISTOR tablets and injection are contraindicated in patients with known or suspected gastrointestinal obstruction and patients at increased risk of recurrent obstruction, due to the potential for gastrointestinal perforation.

**WARNINGS AND PRECAUTIONS**

**Gastrointestinal Perforation**
Cases of gastrointestinal perforation have been reported in adult patients with OIC and advanced illness with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the gastrointestinal tract (e.g., peptic ulcer disease, Ogilvie's syndrome, diverticular disease, infiltrative gastrointestinal tract malignancies or peritoneal metastases). Take into account the overall risk-benefit profile when using RELISTOR in patients with these conditions or other conditions which might result in impaired integrity of the gastrointestinal tract wall (e.g., Crohn's disease). Monitor for the development of severe, persistent, or worsening abdominal pain; discontinue RELISTOR in patients who develop this symptom.

**Severe or Persistent Diarrhea**
If severe or persistent diarrhea occurs during treatment, advise patients to discontinue therapy with RELISTOR and consult their healthcare provider.

**Opioid Withdrawal**
Symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, diarrhea, abdominal pain, anxiety, and yawning have occurred in patients treated with RELISTOR. Patients having disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal and/or reduced analgesia. Take into account the overall risk-benefit profile when using RELISTOR in such patients. Monitor for adequacy of analgesia and symptoms of opioid withdrawal in such patients.

**ADVERSE REACTIONS**

**Clinical Trials Experience**
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

**Opioid-Induced Constipation in Adult Patients with Chronic Non-Cancer Pain**
The safety of RELISTOR tablets was evaluated in a double-blind, placebo-controlled trial in adult patients with OIC and chronic non-cancer pain receiving opioid analgesia. This study (Study 1) included a 12-week, double-blind, placebo-controlled period in which adult patients were randomized to receive RELISTOR tablets 450 mg orally (200 patients) or placebo (201 patients). After 4 weeks of double-blind treatment administered once daily, patients continued 8 weeks of double-blind treatment on an as needed basis (but not more than once daily).
The most common adverse reactions in adult patients with OIC and chronic non-cancer pain receiving RELISTOR tablets are shown in Table 4. Adverse reactions of abdominal pain, diarrhea, hyperhidrosis, anxiety, rhinorrhea, and chills may reflect symptoms of opioid withdrawal.

**Table 4: Adverse Reactions* in 4-Week Double-Blind, Placebo-Controlled Period of Clinical Study of RELISTOR Tablets in Adult Patients with OIC and Chronic Non-Cancer Pain (Study 1)**

| Adverse Reaction | RELISTOR Tablets n = 200 | Placebo n = 201 |
|---|---|---|
| Abdominal Pain** | 14% | 10% |
| Diarrhea | 5% | 2% |
| Headache | 4% | 3% |
| Abdominal Distention | 4% | 2% |
| Vomiting | 3% | 2% |
| Hyperhidrosis | 3% | 1% |
| Anxiety | 2% | 1% |
| Muscle Spasms | 2% | 1% |
| Rhinorrhea | 2% | 1% |
| Chills | 2% | 0% |

*Adverse reactions occurring in at least 2% of patients receiving RELISTOR tablets 450 mg once daily and at an incidence greater than placebo.
**Includes: abdominal pain, upper abdominal pain, lower abdominal pain, abdominal discomfort and abdominal tenderness

The safety of RELISTOR injection was evaluated in a double-blind, placebo-controlled trial in adult patients with OIC and chronic non-cancer pain receiving opioid analgesia. This study (Study 2) included a 4-week, double-blind, placebo-controlled period in which adult patients were randomized to receive RELISTOR injection 12 mg subcutaneously once daily (150 patients) or placebo (162 patients). After 4 weeks of double-blind treatment, patients began an 8-week open-label treatment period during which RELISTOR injection 12 mg subcutaneously was administered less frequently than the recommended dosage regimen of 12 mg once daily.
The most common adverse reactions in adult patients with OIC and chronic non-cancer pain receiving RELISTOR injection are shown in Table 5. The adverse reactions in the table below may reflect symptoms of opioid withdrawal.

**Table 5: Adverse Reactions* in 4-Week Double-Blind, Placebo-Controlled Period of Clinical Study of RELISTOR Injection in Adult Patients with OIC and Chronic Non-Cancer Pain (Study 2)**

| Adverse Reaction | RELISTOR Injection n = 150 | Placebo n = 162 |
|---|---|---|
| Abdominal Pain** | 21% | 7% |
| Nausea | 9% | 6% |
| Diarrhea | 6% | 4% |
| Hyperhidrosis | 6% | 1% |
| Hot Flush | 3% | 2% |
| Tremor | 1% | <1% |
| Chills | 1% | 0% |

*Adverse reactions occurring in at least 1% of patients receiving RELISTOR injection 12 mg subcutaneously once daily and at an incidence greater than placebo.
**Includes: abdominal pain, upper abdominal pain, lower abdominal pain, abdominal discomfort and abdominal tenderness

During the 4-week double-blind period, in patients with OIC and chronic non-cancer pain that received RELISTOR every other day, there was a higher incidence of adverse reactions, including nausea (12%), diarrhea (12%), vomiting (7%), tremor (3%), feeling of body temperature change (3%), piloerection (3%), and chills (2%) as compared to daily RELISTOR dosing. Use of RELISTOR injection 12 mg subcutaneously every other day is not recommended in patients with OIC and chronic non-cancer pain. The rates of discontinuation due to adverse reactions during the double-blind period (Study 2) were higher in the RELISTOR once daily (7%) than the placebo group (3%). Abdominal pain was the most common adverse reaction resulting in discontinuation from the double-blind period in the RELISTOR once daily group (2%).
The safety of RELISTOR injection was also evaluated in a 48-week, open-label, uncontrolled trial in 1034 adult patients with OIC and chronic non-cancer pain (Study 3). Patients were allowed to administer RELISTOR injection 12 mg subcutaneously less frequently than the recommended dosage regimen of 12 mg once daily, and took a median of 6 doses per week. A total of 624 patients (60%) completed at least 24 weeks of treatment and 477 (46%) completed the 48-week study. The adverse reactions seen in this study were similar to those observed during the 4-week double-blind period of Study 2. Additionally, in Study 3, investigators reported 4 myocardial infarctions (1 fatal), 1 stroke (fatal), 1 fatal cardiac arrest and 1 sudden death. It is not possible to establish a relationship between these events and RELISTOR.

**Opioid-Induced Constipation in Adult Patients with Advanced Illness**
The safety of RELISTOR injection was evaluated in two, double-blind, placebo-controlled trials in adult patients with OIC and advanced illness receiving palliative care: Study 4 included a single-dose, double-blind, placebo-controlled period, whereas Study 5 included a 14-day multiple dose, double-blind, placebo-controlled period.
The most common adverse reactions in adult patients with OIC and advanced illness receiving RELISTOR injection are shown in Table 6 below.

**Table 6: Adverse Reactions from All Doses in Double-Blind, Placebo-Controlled Clinical Studies of RELISTOR Injection in Adult Patients with OIC and Advanced Illness* (Studies 4 and 5)**

| Adverse Reaction | RELISTOR Injection n = 165 | Placebo n = 123 |
|---|---|---|
| Abdominal Pain** | 29% | 10% |
| Flatulence | 13% | 6% |
| Nausea | 12% | 5% |
| Dizziness | 7% | 2% |
| Diarrhea | 6% | 2% |

*Adverse reactions occurring in at least 5% of patients receiving all doses of RELISTOR injection (0.075, 0.15, and 0.3 mg/kg) and at an incidence greater than placebo
**Includes: abdominal pain, upper abdominal pain, lower abdominal pain, abdominal discomfort and abdominal tenderness

The rates of discontinuation due to adverse reactions during the double-blind, placebo-controlled clinical trials (Study 4 and Study 5) were comparable between RELISTOR (1%) and placebo (2%).

**Postmarketing Experience**
The following adverse reactions have been identified during post-approval use of RELISTOR injection. Because reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship to drug exposure.

**Gastrointestinal**
Perforation, cramping, vomiting.

**General Disorders and Administration Site Disorders**
Diaphoresis, flushing, malaise, pain. Cases of opioid withdrawal have been reported.

**DRUG INTERACTIONS**

**Other Opioid Antagonists**
Avoid concomitant use of RELISTOR with other opioid antagonists because of the potential for additive effects of opioid receptor antagonism and increased risk of opioid withdrawal.

**Drugs Metabolized by Cytochrome P450 Isozymes**
In healthy subjects, a subcutaneous dose of 0.3 mg/kg of RELISTOR did not significantly affect the metabolism of dextromethorphan, a CYP2D6 substrate.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**
The use of RELISTOR during pregnancy may precipitate opioid withdrawal in a fetus due to the immature fetal blood-brain barrier and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Advise pregnant women of the potential risk to a fetus.

**Lactation**
Because of the potential for serious adverse reactions, including opioid withdrawal, in breastfed infants, advise women that breastfeeding is not recommended during treatment with RELISTOR. In nursing mothers, a decision should be made to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric Use**
Safety and effectiveness of RELISTOR tablets and injection have not been established in pediatric patients.

**Geriatric Use**
In clinical studies of RELISTOR tablets, no overall differences in effectiveness were observed. Adverse reactions were similar; however, there was a higher incidence of diarrhea in elderly patients.
In clinical studies of RELISTOR injection, no overall differences in safety or effectiveness were observed between elderly patients and younger patients.
Based on pharmacokinetic data, and safety and efficacy data from controlled clinical trials, no dosage adjustment based on age is recommended. Monitor elderly patients for adverse reactions.

**Renal Impairment**
In a study of subjects with varying degrees of renal impairment receiving RELISTOR injection subcutaneously, there was a significant increase in the exposure to methylnaltrexone in subjects with moderate and severe renal impairment (creatinine clearance less than 60 mL/minute as estimated by Cockcroft-Gault) compared to healthy subjects.
Therefore, a dosage reduction of RELISTOR tablets and RELISTOR injection is recommended in patients with moderate and severe renal impairment. No dosage adjustment of RELISTOR tablets or RELISTOR injection is needed in patients with mild renal impairment (creatinine clearance greater than 60 mL/minute as estimated by Cockcroft-Gault).

**Hepatic Impairment**
**Tablets**
In a study of subjects with varying degrees of hepatic impairment receiving a 450 mg dose of RELISTOR tablets, there was a significant increase in systemic exposure of methylnaltrexone for subjects with moderate (Child-Pugh Class B) and severe (Child-Pugh Class C) hepatic impairment compared to healthy subjects with normal hepatic function. Therefore, a dosage reduction of RELISTOR tablets is recommended in patients with moderate or severe hepatic impairment. No dosage adjustment of RELISTOR tablets is needed in patients with mild hepatic impairment (Child-Pugh Class A).

**Injection**
There was no clinically meaningful change in systemic exposure of methylnaltrexone compared to healthy subjects with normal hepatic function. No dosage adjustment of RELISTOR injection is needed for patients with mild or moderate hepatic impairment. In patients with severe hepatic impairment, monitor for methylnaltrexone-related adverse reactions.

**OVERDOSAGE**
A study of healthy subjects noted orthostatic hypotension associated with a dose of 0.64 mg/kg administered as an intravenous bolus. Monitor for signs or symptoms of orthostatic hypotension and initiate treatment as appropriate.
If a patient on opioid therapy receives an overdose of RELISTOR, the patient should be monitored closely for potential evidence of opioid withdrawal symptoms such as chills, rhinorrhea, diaphoresis or reversal of central analgesic effect.

**NONCLINICAL TOXICOLOGY**

**Carcinogenesis**
Oral administration of methylnaltrexone bromide at doses up to 200 mg/kg/day (about 81 times the subcutaneous maximum recommended human dose (MRHD) of 12 mg/day based on body surface area) in males and 400 mg/kg/day (about 162 times the subcutaneous MRHD of 12 mg/day) in females and in Sprague Dawley rats at oral doses up to 300 mg/kg/day (about 243 times the subcutaneous MRHD of 12 mg/day) for 104 weeks did not produce tumors in mice and rats.

**Mutagenesis**
Methylnaltrexone bromide was negative in the Ames test, chromosome aberration tests in Chinese hamster ovary cells and human lymphocytes, in the mouse lymphoma cell forward mutation tests and in the *in vivo* mouse micronucleus test.

**Impairment of Fertility**
Methylnaltrexone bromide at subcutaneous doses up to 150 mg/kg/day (about 122 times the subcutaneous MRHD of 12 mg/day; about 3.3 times the oral MRHD of 450 mg/day) was found to have no adverse effect on fertility and reproductive performance of male and female rats.

**Animal Toxicology and/or Pharmacology**
In an *in vitro* human cardiac potassium ion channel (hERG) assay, methylnaltrexone caused concentration-dependent inhibition of hERG current.

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## APPENDICITIS | CONTINUED FROM PAGE 1

tor to *ACEP Now*. (David R. Flum, MD, MPH, in the department of surgery at the University of Washington in Seattle, is the other co-PI.)

**JF: There have been previous studies of nonoperative treatment of appendicitis. What's different about the CODA trial?**

**DT:** It's the largest RCT of adults, 1,552 versus 530 participants for the Finnish Appendicitis Acuta (APPAC) trial.[2] In the APPAC trial, surgeries were generally open whereas in CODA they were laparoscopic. It's the first large U.S. study. CODA enrolled all patients with localized appendicitis who would typically go for appendectomy, including those with appendicolith on imaging (about 25 percent) who were excluded in the APPAC trial. CODA's primary outcome was a 30-day general health measure called EQ-5D. Also, there was EM involvement with an EM site PI at each of the 25 hospitals. CODA's results were released early because of their potential importance during the COVID-19 pandemic.

**JF: Can you summarize CODA's findings?**

**DT:** CODA found nonoperative treatment of appendicitis to be noninferior to appendectomy in terms of 30-day EQ-5D, which reflects comfort, self-care, mobility, activity, and happiness. Like studies before it, CODA found that most patients treated with antibiotics avoided surgery. Antibiotic treatment was safe, with no more serious adverse events, which were rare. Despite the fear of appendiceal rupture and death if the appendix was not removed as soon as possible, no fatalities occurred. Appendectomy rates through 90 days were more than in past trials—25 percent in those without appendicolith (versus 19 percent for the APPAC trial) and 41 percent in those with appendicolith. This was only through 90 days; studies have found recurrence occurs through two years but then seems to level off.[3] The appendicolith subgroup also had more complications, like abscess requiring percutaneous drainage in 7 percent versus 1 percent in the surgery group. Antibiotic-treated patients returned to work more than three days sooner and, not surprisingly with occasional appendicitis recurrence, had more subsequent outpatient visits and admits.

**JF: What are the most important findings for emergency physicians?**

**DT:** A unique aspect of CODA was that if antibiotic-treated patients met the usual discharge criteria following administration of long-acting parenteral antibiotic regimen, they could be discharged home from the emergency department and have outpatient management with completion of oral antibiotics over the next nine days (not unlike how many cases of acute uncomplicated diverticulitis are now managed). This was based on a pilot study experience we described in 2017 in which over 90 percent of antibiotic-treated patients had ED discharge and all patients resolved their acute episode of appendicitis.[4] In the CODA trial, about 50 percent had ED discharge. Sites varied a lot with regard to the rate of ED discharge, never reaching more than 80 percent going home from some emergency departments. This may have reflected physician comfort and experience with antibiotic treatment.

Dr. David A. Talan

**JF: What types of antibiotic regimens did you use in the emergency department?**

**DT:** Either IV ertapenem alone (1 gram) or ceftriaxone (1 gram) and a daily-dosed metronidazole (1,500 mg). For oral treatment, we used either a fluoroquinolone (eg, levofloxacin 750 QD) and metronidazole (500 mg TID) or an advanced-generation cephalosporin (eg, cefdinir 300 mg BID) and metronidazole. We avoided amoxicillin/clavulanate because of high *E. coli* resistance rates.

**JF: How might CODA's results be helpful with the COVID-19 pandemic and upcoming flu season?**

**DT:** We forget that back in December, like every year, our hospitals were full and emergency departments were packed beyond capacity. If COVID-19 remains uncontrolled in places or resurges with schools opening, it will be critically important to have new strategies to manage patients without hospital admission. CODA showed that antibiotics remain a safe option and ED discharge is a reasonable disposition in selected patients. The expansion of telemedicine should facilitate follow-up care and minimize subsequent ED and office visits.

**JF: These RCTs were all nonblinded. How do we know that biases did not unduly influence CODA's results?**

**DT:** This was an open trial, and surgeons who managed participants may have brought their biases in caring for these patients. As is acknowledged in the paper, for example, while CODA recommended giving antibiotics at least 48 hours to work, in 11 percent of cases, patients were taken for appendectomy before this time. Whether conditions viewed as high-risk, like appendicolith, might have led to a lower threshold for appendectomy than necessary among antibiotic-treated patients is unclear. Also, the protocol did not specify how to manage patients' appendix-related concerns. Some, after full recovery, were given appendectomy when there was no evidence of acute appendicitis to, for example, address anxiety about a future recurrence or nonspecific abdominal complaints. The strength of this approach is that it provides a more real-world picture of how nonoperative treatment of appendicitis is used in the United States, but a limitation is that we may not know how effective antibiotics could be. A blinded trial with a sham operation is unlikely.

**JF: How do you think doctors and patients will process these results?**

**DT:** I think people generally will find what they want in CODA, either way. If one is comfortable with surgery, then appendectomy is a simple, safe, and permanent solution, and CODA's 90-day antibiotic-appendectomy rate of about three in 10 overall, somewhat higher than past trials, may seem too high. Also, some may worry that with antibiotic treatment, there is an extremely rare chance (about 1 percent) that a coincident appendiceal cancer will be missed, at least initially; this is of greater risk in older adults where the risk of surgical mortality, albeit low to begin with, is greater.[5] On the other hand, if one's aim is to avoid surgery and hospitalization, and return patients to work sooner, then one sees this instead as a seven in 10 chance to not get general anesthesia and your rectus muscles cut. I expect more hesitancy to recommend nonoperative treatment of appendicitis in patients with appendicolith on imaging, although surgery rates with antibiotics were still much lower overall in this subgroup. It will also take some time for many patients (and physicians) to unlearn what we have taught them for decades—"without emergency surgery, your appendix will explode and kill you"—so that they feel comfortable with the idea of nonoperative treatment. Even among those who respond, many experience anxiety about any mild abdominal pain being a recurrence. I suppose health economists and insurers could push for initial treatment with antibiotics, with ED discharge in most and appendectomy only if no response or for recurrence. Recurrences could even be re-treated with antibiotics, which has been done successfully.

**JF: Is there anything on which those in favor of nonoperative treatment of appendicitis and those against it can agree?**

**DT:** Yes. After ED evaluation establishes the diagnosis of acute, localized appendicitis, in the vast majority of patients who are stable and without signs of sepsis, we can abandon calling this an abdominal "emergency"—or even urgency. All patients should be started on antibiotics early and have their pain controlled. They should be offered both treatment options and informed of the advantages and disadvantages of appendectomy and antibiotic-only treatment. Emergency physicians can engage their patients in these discussions once the diagnosis is established. Some patients will choose surgery and be admitted as usual. Some will choose antibiotics, and of these, many can be discharged from the emergency department with close follow-up. And some will not be sure and can be started on antibiotics and followed before a decision is made. Regardless, our surgeon colleagues can get a good night's rest and see the patient in the morning or, in many cases, later in their office.

***Editor's Note:*** *Visit ACEPNow.com for the references to this article.*

# JUST THE VAX, MA'AM

## Overview of COVID-19 vaccine research

*by* JOSHUA NIFORATOS, MD, MTS

*With thousands of articles published weekly on COVID-19, navigating the literature can be daunting. To help health care professionals and the general public keep up and to fight medical misinformation, a group of emergency physicians started the website Brief19.com, which publishes analysis of COVID-19 research and policy five days a week, all for free. Here are highlights from recent Briefs. (Note:* ACEP Now*'s medical Editor in Chief, Jeremy Samuel Faust, MD, MS, MA, FACEP, is also Editor in Chief of Brief19.)*

**Table 1: Overview of Candidate COVID-19 Vaccine Categories**

| VACCINE TYPE | # OF DOSES | "SPEED"* | SCALABILITY | SAFETY | OTHER COMMENTS |
|---|---|---|---|---|---|
| Nucleic-acid | Multiple | Fast | Low to medium | Safe | Fastest to develop |
| Viral vector | Single | Medium | High | Safe | Requires booster |
| Virus | Live-attenuated: single<br>Inactivated: single | Live-attenuated: slow<br>Inactive: fast | Live-attenuated: high<br>Inactive: medium to high | Live-attenuated: slightly higher risk<br>Inactive: safer | Live-attenuated: most potent immunogenic vaccines |
| Protein-based | Multiple | Medium to fast | High | Safe | Induce elevated levels of neutralizing antibodies |

*How quickly the vaccine can become available under emergency conditions.
*Adapted from Calina et al and Jeyanathan et al.*

Face masks, face shields, and social distancing are likely our new normal for the foreseeable future. The prospects of achieving herd immunity in the United States without a vaccine appears grim.[1] The literature on SARS-CoV-2 vaccine development is growing, with approximately 248 candidate vaccines at the time of this writing.[2] Nevertheless, there are several fundamental concepts regarding vaccine development for SARS-CoV-2 that are broadly applicable and important to understand.

### The Ideal Vaccine

An ideal vaccine should be effective in preventing symptomatic disease (eg, measles, mumps, and rubella vaccine), significantly reducing illness severity (eg, seasonal influenza vaccine), or preventing seroconversion to prevent infection altogether.[3,4] The ideal vaccine is multivalent and provides long-lasting immunity. The World Health Organization (WHO) recommends that effective vaccines should show a risk reduction of at least 30 percent.[5]

The ideal vaccine should be safe, ranging from no side effects to relatively minor side effects, such as headache, low-grade fever, injection site reaction, and myalgias.

Finally, the ideal vaccine should be cost-effective, be easy to administer, require a minimum number of administrations, and not require special storage conditions.[4,6]

### Vaccine Development

The development of safe and effective pharmaceuticals takes, on average, 13 years from the time of discovery to Food and Drug Administration (FDA) approval.[7] The overall failure rate of pharmaceuticals to make it through this entire process exceeds 95 percent. In the late spring, it was estimated that a SARS-CoV-2 vaccine would be available within 12 to 18 months.[8] While such estimates were seen by many as naive idealism, there are a few reasons such a timeline now looks more likely.

To begin, let's identify important questions in the vaccine life cycle, which include:[9]

1. Which antigens produce an immune response? (preclinical studies)
2. How safe is the vaccine? (Phase I clinical trials)
3. What dose is required for immunity? (Phase II clinical trials)
4. How effective is the vaccine? (Phase II and III clinical trials)
5. What is the long-term safety and efficacy in the general (heterogenous) population? (Phase IV clinical trials)

Thankfully, SARS-CoV-2 vaccine development is not starting from scratch. Attempts to develop a vaccine for coronavirus have been ongoing for years. Numerous groups have worked on a vaccine since the MERS-CoV and SARS-CoV epidemics.[10]

Another way researchers are attempting to accelerate vaccine development is by repurposing drugs. In a recent paper published in *Nature*, researchers used an open-access drug library to identify 21 different drugs that can inhibit replication of the SARS-CoV-2 virus in mammalian cell-based assays in a dose-response manner.[8]

One way to increase the odds of winning the vaccine lottery is by testing myriad potential vaccines at the same time across the globe rather than putting all efforts into just one. At press time, there were 49 different SARS-CoV-2 vaccines in various clinical trial phases, according to the London School of Hygiene & Tropical Medicine's VaC COVID-19 vaccine tracker. Ten of those vaccines are in Phase III clinical trials. Additionally, there are 199 vaccine candidates in the preclinical phase.

The WHO Solidarity vaccine trial is a global effort that is testing multiple vaccines in geographically diverse regions with high incidence and attack rates of COVID-19 through fixed and mobile research sites. Researchers estimate that a vaccine that *halves risk* should show efficacy within three to six months of a trial in these highly endemic areas.

### Vaccine Types for COVID-19

Let's look at the landscape of the potential vaccines being investigated. The main categories of candidate vaccines include nucleic-acid vaccines (DNA versus RNA vaccines), nonreplicating viral vectors vaccines, virus vaccines (live attenuated viruses versus inactivated viruses), and protein-based vaccines (subunit vaccines with antigenic fragments).[11] Table 1 shows the advantages and disadvantages of each of these categories.

The 10 candidate vaccines in Phase III clinical trials include two nucleic-acid vaccines (mRNA), four viral vector vaccines (adenovirus-based), one protein-based (recombinant coronavirus proteins plus an adjuvant), and four virus vaccines (three inactivated virus, one live attenuated virus). The one live attenuated virus vaccine in a Phase III clinical trial is using the old Bacillus Calmette-Guérin vaccine.

### Who Should Get the Vaccine First

A few major organizations, such as the WHO and the US National Academies of Sciences, Engineering, and Medicine, recommend prioritizing health care workers and those with frontline jobs.[12] Of course, when the vast majority of health care workers in the United States are white, this promotes structural health disparities by depriving those who have been disproportionately impacted by the virus of a potentially effective vaccine.[13] Expanding this to all workers in health care facilities would be a step in the right direction.

### Until a Vaccine Is FDA Approved

Face masks, social distancing, hand washing, large crowd avoidance, and personal protective equipment are the non-vaccine vaccines. They work, and they are easy to do. Until we have a safe, effective, and available vaccine, don't let your guard down.

For descriptions and updates on the vaccines currently in Phase III clinical trials, check out *The New York Times* Coronavirus Vaccine Tracker at www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html or the VaC COVID-19 vaccine tracker at https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/.

***Editor's Note:*** *Visit ACEPNow.com for the references to this article.*

**DR. NIFORATOS** is an emergency medicine resident at the Johns Hopkins School of Medicine in Baltimore and research editor of Brief19.com. Follow him on Twitter @ReverendofDoubt and Brief19 @Brief_19.

BRINGING DATA TO THE BEDSIDE

# BENCHMARKING ALLIANCE

**Dr. Augustine** is chair of the National Clinical Governance Board of US Acute Care Solutions in Canton, Ohio; clinical professor of emergency medicine at Wright State University in Dayton, Ohio; vice president of the Emergency Department Benchmarking Alliance; and a member of the ACEP Board of Directors.

# Pre-COVID ED Trends

## Performance survey data suggest more challenges lie ahead

*by* JAMES AUGUSTINE, MD, FACEP

The role of emergency department physicians and leaders has been made dramatically more important due to the surges in demand and medical system challenges produced by the COVID-19 pandemic. However, it will be essential for those leaders to look at the trends present *prior* to the pandemic and to accurately predict how they will influence the patient populations of 2021 and beyond.

The performance of emergency departments in 2019 has been summarized for the many members of the Emergency Department Benchmarking Alliance (EDBA), who provided the data needed to characterize operations prior to the pandemic. Many trends will continue, and some will be accelerated by the pandemic. Regardless, these trends all suggest emergency departments will see higher-acuity patients with more complex medical needs and play a crucial role in determining capacity. Most communities are aware of the emergency department as the portal for critical patients and unexpected events, but now the value in public health and managing community surges is even more visible—and maybe even more appreciated!

The results of the 2019 EDBA performance measures survey say emergency departments are seeing higher-acuity patients, more adults, and more EMS patients; are making more use of diagnostic tests; are transferring more ED patients; and are absorbing the early time of patients who need inpatient services (ie, boarding). The management expertise and dedication of ED leaders are therefore ever more necessary.

Here are four results lifted from the survey:

**1) Fewer children are presenting to community emergency departments.**
ED visits by patients under age 18 have decreased from about 22 percent in the years before 2011 to about 15 percent in 2019 (see Figure 1).

**2) More patients are being transferred.**
There are significant differences in rates of transfer to another hospital based on the features of emergency departments in the United States. The transfer rate is highest in small-volume emergency departments, which now amounts to 5.4 percent of the patients seen in those facilities. It appears fewer hospitals in rural communities have the resources to keep complex patients. They are closing service lines and have been unsuccessful in recruiting doctors willing to care for complex patients. Rural facilities also may incur financial penalties related to the inability to manage patients as expeditiously as larger hospitals.

ED transfer rates by cohorts (type of facility) are reflected in Figure 2. Transfer rates prior to 2011 were about 1.6 percent, and they have now doubled to 3.2 percent.

These numbers are primarily driven by smaller hospitals, but all types of emergency departments are trending toward more patient transfers. Of note, these data do *not* include freestanding emergency departments, which can place additional burdens on the transfer resources of hospitals and hospital systems.

**Figure 1. Percent of ED patients under age 18**

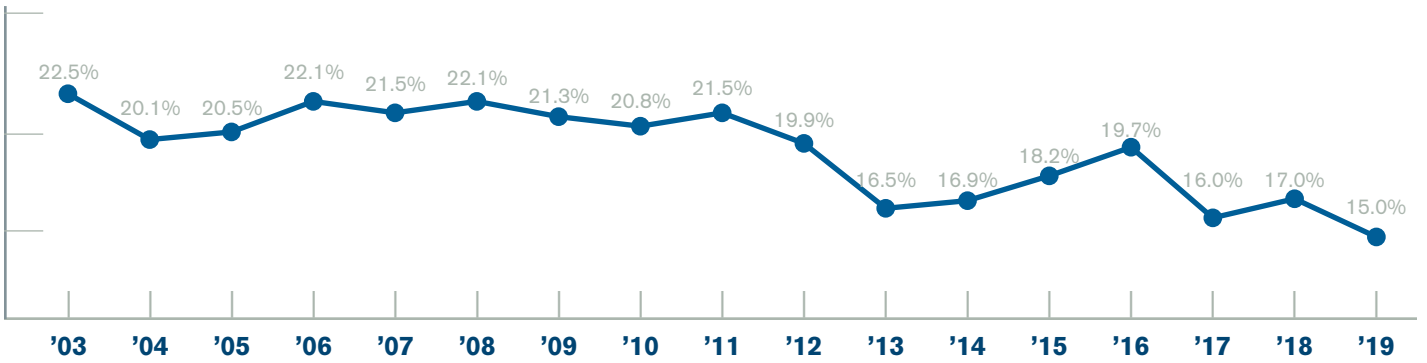



**Figure 2. ED transfer % by cohort**

*Lower volume EDs tend to have higher transfer rates. The average is 3.2%.*

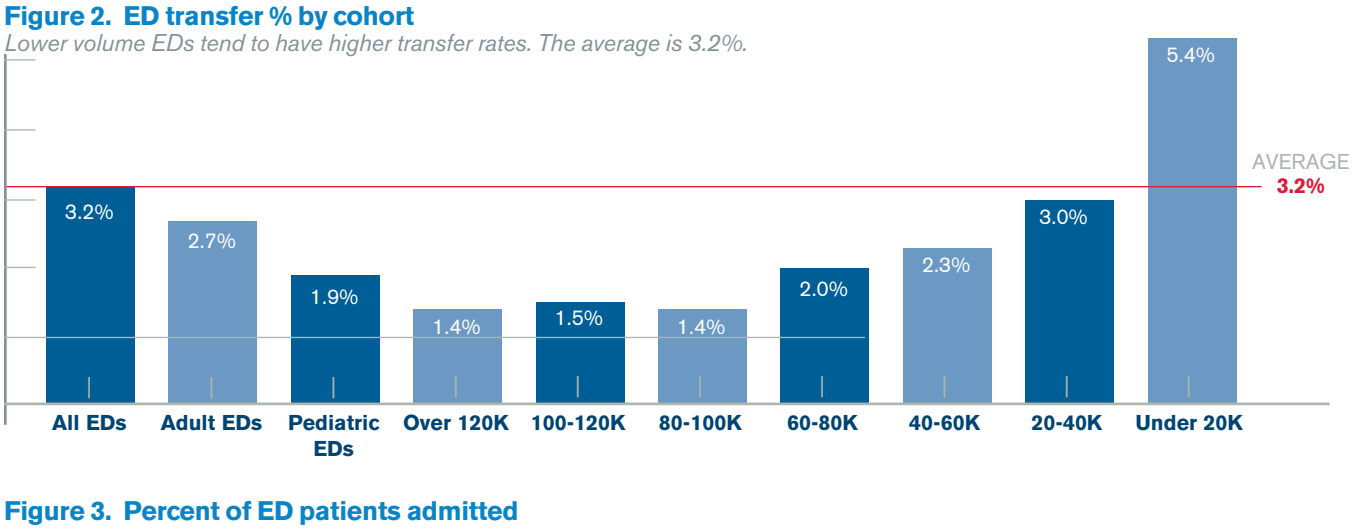
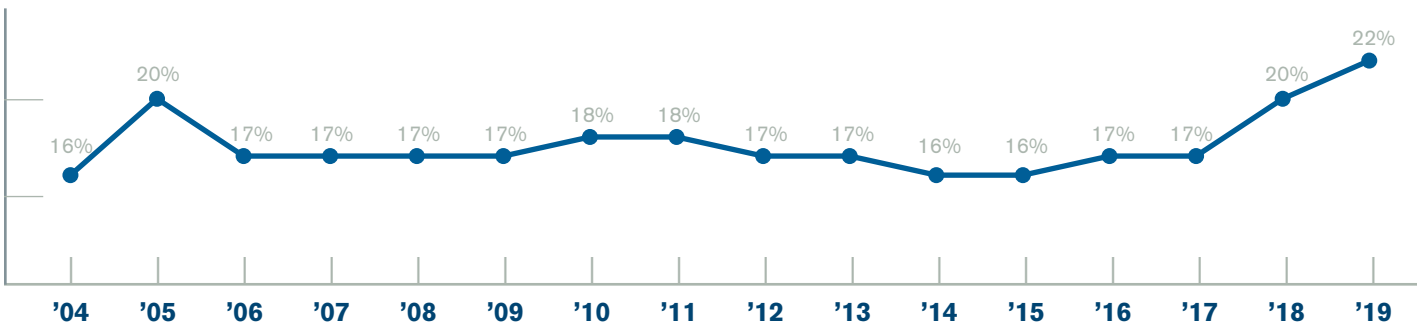



**Figure 3. Percent of ED patients admitted**




**3) The percentage of patients admitted from the emergency department to the hospital has rapidly increased.**
About 67 percent of hospital admissions are processed through the emergency department. These admissions include patients seen in the emergency department and then placed in any inpatient area of the hospital, either as "full admission" or "observation status." High-volume and adult-serving emergency departments tend to have high admission rates.

The average has increased from prior years to 22 percent (see Figure 3).

**4) Patients who require ED boarding challenge ED operations.**
Boarding time is an important contributor to overall patient processing, and it has remained stubbornly high, an annual average of about 115 minutes between 2012 and 2019.

ED boarding, time from decision-to-admit until the patient physically leaves the emergency department, remains a burden on ED performance. It accounts for about 38 percent of the time admitted patients spend in the emergency department. This time interval has been part of each hospital's required data submission to the Centers for Medicare & Medicaid Services since 2013, and results are posted on the Hospital Compare website (www.medicare.gov/hospitalcompare). It was hoped that public posting of boarding would motivate hospital administrators to improve this metric. Unfortunately, despite the work of many ED and hospital leaders to reduce boarding time, the data for 2019 list the average interval at 118 minutes.

The EDBA Performance Measures Summits have been used to unify the definitions used across the industry, and that process has been used to accurately define boarding time and the burden on the emergency department of admitted patients. There is ongoing work to identify hospitals that have reduced boarding time by making ED patient flow more efficient.

### Prioritizing ED Management Challenges

The need for emergency physicians has dramatically increased due to patient needs and medical system challenges fueled by the COVID-19 pandemic. However, the advent of telemedicine programs has provided another ready source of care for patients with low-acuity, unscheduled care needs; those patients will largely disappear from the ED population for the foreseeable future.

Emergency physician leaders must appreciate trends present through 2019 and work collaboratively with hospital leaders to serve a changing emergency population in 2021 and beyond. The need to move admitted patients up to the inpatient units is a particularly important management priority.

The EDBA Summits have provided a dedicated group of federal, regional, and emergency leaders the opportunity to develop reasonable standards and performance measures for the industry. The definitions published after the 2018 summit have recently been published, and they provide guidance to ED leaders who are developing data management processes that improve performance.[1]

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Reimagining Emergency Medicine

# A Focus on the Patient

By Janet Young, MD

**The urgency of the coronavirus pandemic** is opening new windows of change in emergency medicine. At long last, we have an opportunity to make care more accessible, affordable, and compassionate. As emergency providers, are we ready for it? I believe so, but we all have work to do to ensure the success of this new standard of care delivery.

## IMPROVING CARE CONTINUITY

One of the most frustrating aspects of emergency medicine is the limited impact we have on a patient's health. While we can save lives, long-term outcomes depend on the accessibility of appropriate follow-up care.

Today more than ever, it's crucial for emergency medicine providers to connect to the support systems of our patients. Many ED teams already call back discharged patients who are at-risk or lack primary care access. Some providers are now going one step further and making the callback a virtual follow up visit. This provides incredible value to patients who may not have access to their pre-pandemic providers, clinics, and resources.

Other EDs are using patient care navigation, both in person and virtual, to improve care continuity. Care navigators work with patients to schedule needed follow-up appointments. They can also connect them with community resources that assist with housing, utilities, food, and other necessities.

Improving ED care continuity benefits everyone involved. Providers are more comfortable discharging patients who have reliable access to follow-up care. For the patient, this means returning to the familiar comforts of home and family. For hospitals, it creates a more efficient patient flow and builds community loyalty.

## ADOPTING NEW SKILLS

The shift to virtual care demands new skills and attitudes. Among my colleagues, technology adoption seems to cause the most anxiety. However, I believe our biggest cultural shift involves communication skills and rapport.

Emergency medicine providers have a less than stellar rep for bedside manner and customer service. In a way, it's totally understandable; the niceties may slip when you're racing to a diagnosis and treatment plan. But the truth is, we can't afford to be tone-deaf in a telehealth visit when we need to quickly win trust through a screen. Virtual care demands a warmer, more empathic approach that will require many of us to adapt.

However, our efforts will likely be rewarded in the form of improved work-life balance. As we shift to mixed virtual and in-person care, expect to see more flexible schedules and work-at-home arrangements. In addition, many virtual care platforms integrate with the hospital EHR, which eases paperwork and administrative burdens of providers.

## LEADING THE EVOLUTION OF CARE

In these challenging times, Vituity is seizing the opportunity to improve emergency medicine and define a new standard of care. We believe that better patient care starts with empowered and resilient providers. Learn more about opportunities to join our team and be part of the transformation of healthcare: **vituity.com/careers/**

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*Janet Young, MD, is Vice President of Emergency Medicine at Vituity. She lives and practices in the San Francisco Bay Area.*

HEALTH POLICY JOURNAL CLUB

# POLICY Rx

**Dr. Dark** is assistant professor of emergency medicine at Baylor College of Medicine in Houston and executive editor of PolicyRx.org.

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# Racism in Medicine

## We must be at the forefront in correcting it

*by* CEDRIC DARK, MD, MPH, FACEP

Since the spring when coronavirus first came to our shores, and throughout a tumultuous summer focused on the centuries-old mistreatments of Black and brown peoples culminating with the killing of George Floyd at the hands of a police officer in Minneapolis, the plight of Black, indigenous, and people of color has entered the minds of many people in this country. There has been a renewal of focus on addressing issues of racism and discrimination within our societal institutions and also within the house of medicine.


This summer, editorial boards and authors who penned manuscripts have come under fire for publishing overtly sexist and racist material in the medical literature—studies that have subsequently been retracted.[1,2] The indignities of 2020, a year that seems only superseded by the summer of 1968 in terms of national outrage, prompted me and my colleague Alden Landry to write, "We certainly cannot disrupt a racist culture as long as those at the top of the pecking order continue to maintain their dominance and exert their influence from behind the cloak of suits and ties."[3]

Systemic racism has been present within this country and the house of modern medicine since their inceptions. Although the fight to remedy these evils has been ongoing for ages, the current generation appears poised and willing to continue the struggle begun by generations past. Correcting inequities cannot occur only in the political arena without additionally requiring change inside ourselves, including in our everyday doctor-patient interactions.

We all know racial disparities exist in the consideration and treatment of Black, indigenous, and other people of color within emergency departments, ranging from thrombolysis treatment to restraints for psychiatric patients to pain management for renal colic, so let us work at correcting them on our next shift.[4–6]

As this current Health Policy Journal Club column describes, it is up to us to be at the forefront for promoting "egalitarianism, social justice, and compassion" for every patient who entrusts us with their life regardless of their race, color, religion, sex, national origin, disability, or sexual orientation. To do anything less would discredit the oath we took as physicians to practice our art with uprightness and honor.

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## EMRA+POLICYRx HEALTH POLICY JOURNAL CLUB

## Racism Is the Ultimate Pre-Existing Condition

*by* NIKKOLE TURGEON

Recently, leaders across states and municipalities have declared racism a public health crisis after years of tireless advocacy and evidence demonstrating this fact.[1] The COVID-19 pandemic, having captivated the world, has demonstrated our nation's unwillingness to protect communities of Black, indigenous, and people of color (BIPOC). There is ample evidence on other racial disparities prevalent throughout health care. It is no surprise that COVID-19 disproportionately affects communities of color so starkly. Racism, not race, is the ultimate pre-existing condition.

A recent article yet again noted racial disparities found in analgesic use in patients presenting to the emergency department for kidney stones.[2] This study used data from the Premier Hospital Database, an all-payer hospital discharge database that captures about 20 percent of all discharges from nearly 700 private and academic hospitals. The study's primary focus was on the quantity of analgesia, specifically opioid and IV nonopioid (ketorolac) pain medication.

The study found that Black and Hispanic patients with acute renal colic received less opioid pain medication than white patients. White patients received a median of 20 morphine milligram equivalents (MME), while Black patients received 3 MME less and Hispanic patients received 5.4 MME fewer ($P<0.0001$). Additionally, there was a difference in the administration of ketorolac, a nonsteroidal anti-inflammatory drug (NSAID), in combination or as monotherapy despite ample evidence suggesting that NSAIDs are as, if not more, effective than opioids for acute renal colic. These differences were not explained by geographic or practice setting differences, suggesting that unrecognized health care worker biases were the culprit. These data suggest we need to vigilantly evaluate the etiology of these biases on an individual and systemic scale.

Despite the dedication of emergency departments to serve "anyone, anywhere, anytime," evidence exists that unacceptable disparities in the emergency care for BIPOC persist. As the COVID-19 pandemic continues, it underscores the inextricable link between health care and racism. Woven into the fabric of emergency medicine are the principles of egalitarianism, social justice, and compassion for the poor and underserved. As such, we have a unique position to be at the forefront of addressing racism by cultivating equitable environments and implementing anti-racist policies in the delivery of high-quality health care.

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**MS. TURGEON** is a student the Robert Larner, M.D. College of Medicine at the University of Vermont.

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# SKEPTICS' GUIDE TO EMERGENCY MEDICINE

**Dr. Milne** is chief of emergency medicine and chief of staff at South Huron Hospital, Ontario, Canada. He is on the Best Evidence in Emergency Medicine faculty and is creator of the knowledge translation project the Skeptics' Guide to Emergency Medicine (www.TheSGEM.com).

# "Pink Ladies" and Pain

## Studies probe whether antacid monotherapy or GI cocktails work better for epigastric pain

*by* KEN MILNE, MD

### The Case

A 43-year-old woman arrives at the emergency department complaining of epigastric pain after eating a large lunch. She has presented to the emergency department a few times before for a similar presentation and been diagnosed with gastroesophageal reflux disease (GERD). She is usually given a "GI cocktail" to treat her symptoms while the workup is being completed. She says it works but tastes awful and asks if there is anything else she could try this time.

### Clinical Question

Is antacid plus lidocaine better than antacid alone in treating patients presenting to the emergency department with epigastric pain?

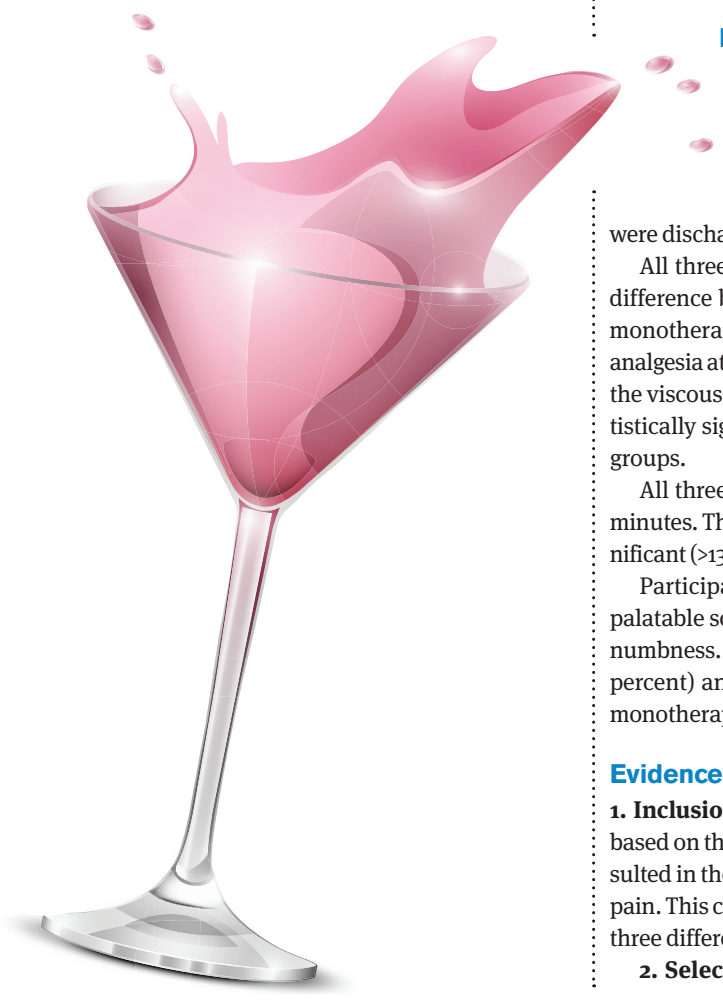
### Background

Antacid, either alone or combined with other medications, is routinely given to ED patients suffering with epigastric pain. Such medications include viscous lidocaine, an antihistamine, a proton pump inhibitor, or an anticholinergic.[1,2] In the United States, the combination treatment has been referred to as a "GI cocktail," while in Canada and Australia it is commonly called a "pink lady."

A previous randomized control trial (RCT) compared 30 mL of antacid with or without 15 mL of viscous lidocaine. It found that the addition of lidocaine significantly increased pain relief and decreased patient pain scores compared to antacid alone.[3]

Another RCT compared antacid plus either viscous lidocaine or a benzocaine solution. The result from this trial found no statistical difference between the two interventions. It should be noted that there was no antacid monotherapy group in this second trial.[4]

A third RCT compared 30 mL of antacid monotherapy, antacid with 10 mL of an anticholinergic, and antacid with anticholinergic and 10 mL of 2% viscous lidocaine. This trial demonstrated that all three treatments had clinical efficacy, with no statistical difference in pain relief between the different treatment groups. The authors' conclusion was to recommend antacid monotherapy in these patients.[5]



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**Reference:** Warren J, Cooper B, Jermakoff A, et al. Antacid monotherapy is more effective in relieving epigastric pain than in combination with lidocaine: a randomized double-blind clinical trial [published online ahead of print June 29, 2020]. *Acad Emerg Med*.

- **Population:** Adult patients 18 years and older with epigastric pain or dyspepsia presenting to the emergency department.
- **Intervention:** Viscous group received 10 mL oral lidocaine 2% viscous gel plus 10 mL antacid.
- **Comparison:**
  - » Solution group received 10 mL lidocaine 2% solution plus 10 mL antacid.
  - » Antacid group received 20 mL antacid monotherapy.
- **Outcome:**
  - » **Primary Outcome:** Change in pain scores on 100 mm visual analog scale (VAS) at 30 minutes.
  - » **Secondary Outcomes:** Medication palatability (ie, taste, bitterness, texture, and overall acceptability) using a VAS, change in pain score 60 minutes post administration, and adverse events.

### Authors' Conclusions

"A 20 mL dose of antacid alone is no different in analgesic efficacy than a 20 mL mixture of antacid and lidocaine (viscous or solution). Antacid monotherapy was more palatable and acceptable to patients. A change in practice is therefore recommended to cease adding lidocaine to antacid for management of dyspepsia and epigastric pain in the ED."

### Key Results

There were 89 participants enrolled in the trial who could be analyzed. Thirty received the viscous treatment, 31 the solution, and 28 antacid monotherapy. The mean age was early 40s, around two-thirds were female, and 80 percent were discharged with a gastrointestinal diagnosis.

All three treatments worked, and there was no statistical difference between groups. The solution group and antacid monotherapy group provided clinically important (>13 mm) analgesia at 30 minutes (17 mm and 20 mm, respectively), while the viscous group did not (9 mm). However, there was no statistically significant difference between the three treatments groups.

All three groups experienced additional pain relief by 60 minutes. The change in median pain scores was clinically significant (>13 mm) for all three arms (21 mm, 26 mm, and 32 mm).

Participants found antacid monotherapy to be the most palatable solution. The most frequent adverse effect was oral numbness. It was only reported in the lidocaine solution (26 percent) and viscous group (20 percent), not in the antacid monotherapy group.

### Evidence-Based Medicine Commentary

**1. Inclusion Criteria:** Patients were enrolled prospectively based on their clinician providing an antacid therapy. This resulted in the inclusion of some patients with non-GI causes of pain. This could have decreased the effect size observed in the three different treatment groups.

**2. Selection Bias:** Patients were also not enrolled overnight. Patients who present on the night shift might be different than those who present during the day shift (for example, there might be different rates of alcohol-related gastritis, or patients might present with dyspepsia more often after larger evening meals, etc.). It is unclear if this issue would have affected the results and, if so, in what direction.

**3. Blinding:** The solutions were not made to look identical. This could have unblinded the trial to the nursing staff. The patients may also have been unblinded. Lidocaine has a bitter taste and causes oral numbness. This could have introduced a placebo effect into the trial. It is been shown that bitter-tasting treatments can increase the placebo effect.[6,7] However, given the direction of this bias toward the lidocaine-containing combination therapies, this would only strengthen our confidence in the results of no statistical difference with monotherapy alone.

**4. Diagnosis:** As stated, patients were enrolled if antacid therapy was provided regardless of the diagnosis. Some patients were found to have non-GI reasons for their epigastric pain. However, there are also multiple GI causes of pain (eg, dyspepsia, GERD, gastritis, peptic ulcer disease, etc.). This trial did not have a large enough sample size to determine if antacid plus lidocaine would be more effective than antacid monotherapy in any of these subgroups.

**5. Other Comparisons:** There was no comparison to any other medications such as H2 receptor antagonists, proton pump inhibitors, and anticholinergics. We do not know from this trial whether antacid alone or in combination with lidocaine would be better, worse, or similar to these other treatment modalities, nor whether the typical GI cocktail might fare better in combination with these other treatments.

### Bottom Line

Consider using antacid monotherapy for patients presenting to the emergency department with epigastric pain rather than a lidocaine-containing combination therapy.

### Case Resolution

The workup is negative for other serious causes. You diagnose her with GERD again but give her 20 mL of an antacid without any lidocaine. Her epigastric pain resolves, and she says the medicine tasted much better than last time. You refer her to a gastroenterologist for an outpatient workup.

*Thank you to Dr. Chris Bond, an emergency medicine physician from Calgary, for his help with this review.*

**Remember to be skeptical of anything you learn, even if you heard it on the Skeptics' Guide to Emergency Medicine.**

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Q&A ABOUT OUR LITTLEST PATIENTS

# KIDS KORNER

**Dr. Jones** is assistant professor of pediatric emergency medicine at the University of Kentucky in Lexington.

**Dr. Cantor** is professor of emergency medicine and pediatrics, director of the pediatric emergency department, and medical director of the Central New York Regional Poison Control Center at Upstate Medical University in Syracuse, New York.

*by* LANDON JONES, MD, AND RICHARD M. CANTOR, MD, FAAP, FACEP

*The best questions often stem from the inquisitive learner. As educators, we love, and are always humbled by, those moments when we get to say, "I don't know." For some of these questions, you may already know the answers. For others, you may never have thought to ask the question. For all, questions, comments, concerns, and critiques are encouraged. Welcome to the Kids Korner.*

# Antibiotics for Strep

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### Question 1: In children with group A strep pharyngitis, what benefit(s) does antibiotic treatment offer?

While a potentially reasonable argument may be made about deferring antibiotic treatment of GAS-positive pharyngitis, is antibiotic treatment beneficial? To begin, an earlier RCT by Nelson evaluated 35 children ages 5–11 years with GAS confirmed by culture and randomized patients to penicillin (PCN) treatment or placebo.[1] Follow-up visits occurred at 48 hours. Patients treated with PCN had a significantly shorter duration of fever at follow-up, with 28 percent of placebo patients having persistent fever >48 hours but no treated patients having persistent fever ($P$=0.031). At 48-hour follow-up, children receiving PCN also had significantly shortened times until improved ($P$=0.008) and until well ($P$=0.022). A similar shortened duration of fever at 48 hours was seen in another RCT by Pichichero et al.[2]

A Cochrane meta-analysis by Spinks et al evaluated 27 trials with 12,835 total cases.[3] This included both adults and children and included patients with the diagnosis of sore throat, not specifically GAS. Regarding antibiotics versus placebo, the risk ratio of the incidence of developing the secondary complication of otitis media within 14 days following GAS pharyngitis antibiotic treatment was 0.30 (95 percent CI, 0.15–0.58; 11 studies), suggesting that antibiotic therapy decreased the incidence of the complication of otitis media. Similarly, the risk ratio of the incidence of developing "quinsy"—meaning peritonsillar abscess or retropharyngeal abscess—within two months following GAS antibiotic treatment was 0.15 (95 percent CI, 0.05–0.47; eight studies).

Lastly, the risk ratio of the incidence of developing acute rheumatic fever (ARF) within two months was 0.27 (95 percent CI, 0.1–0.50; 14 studies). While ARF is traditionally rare in Western countries (<1/100,000 children) when compared with developing countries (approximately 50/100,000 children) and many cases were reported before 1975, some more recent studies have demonstrated increased incidences of ARF up to 23–27/100,000.[4,5] This suggests that ARF does still exist in higher-income countries as well as developing countries.

### Conclusion

Antibiotic treatment for GAS-positive pharyngitis does demonstrate some benefits compared with placebo, and studies suggest that antibiotic treatment shortens some symptoms, including fever, and decreases the risk of developing secondary complications.

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# Steroids for Strep

### Question 2: In children with confirmed group A strep pharyngitis, do steroids shorten duration and severity of the illness?

With winter beginning, strep throat cases will start to ramp up. This month, we will look at group A strep (GAS) pharyngitis—not the broader bucket of "exudative pharyngitis" that may or may not include GAS.

We were able to find five randomized controlled trials (RCTs) that included GAS children receiving steroids.[1–5] The mean ages (in years) of patients in these five studies that included children were 26.4, 28.1, 9.7, 11.9, and 7.7, respectively—meaning the first two studies predominantly included adults. We will therefore focus on the remaining three RCTs. (This is Kids Korner, folks.)

A 2003 RCT by Bulloch et al included 184 children ages 5–16 years and evaluated adjuvant oral dexamethasone in both GAS-positive (n=85) and GAS-negative (n=99) patients.[3] Consecutive children at a single pediatric emergency department presenting with symptoms of pharyngitis were assessed and received a rapid strep test. GAS-positive and -negative patients were then randomized to receive adjuvant oral dexamethasone 0.6 mg/kg (maximum of 10 mg) or placebo. All GAS-positive patients received antibiotics. Exclusions included children who were immunocompromised, had an abscess, or had corticosteroid exposure during the preceding two months, as well as pregnant patients, patients with diabetes, or those already taking antibiotics. Follow-up was at 24 hours, 48 hours, and one month.

Pain intensity in all groups was not significantly different. Overall, there was no statistically significant change in time to complete pain relief between dexamethasone and placebo groups—independent of whether the patient was GAS positive or negative. In the GAS-positive group, though, there *was* a significantly shorter mean time to clinically significant pain relief in the dexamethasone group (6.0 hours versus 11.5 hours; $P$=0.02). This was not found in the GAS-negative group ($P$=0.32).

To summarize, GAS-positive patients receiving dexamethasone had faster initial pain relief (about six hours) but similar times to complete pain relief when compared with placebo. The authors describe this faster pain relief as "of marginal clinical importance."

The second RCT by Olympia et al evaluated a convenience sample of 125 children ages 5–18 years who presented to an urban pediatric emergency department with moderate to severe pharyngitis.[4] Exclusion criteria were similar to the study by Bulloch et al. Patients were then randomized to either receive oral dexamethasone (n=57) 0.6 mg/kg (maximum of 10 mg) or placebo (n=68), and all received a rapid strep test. If the rapid strep was positive, they received either intramuscular penicillin, oral amoxicillin, or oral azithromycin. Negative rapid strep tests were cultured. Primary endpoints were time to inception of pain relief, time to complete resolution of pain, need for further medical care, antipyretic usage, fever, and potential dexamethasone side effects.

A total of 70 children tested positive for GAS—27 in the dexamethasone group and 43 in the placebo group. Similar to the results of Bulloch et al, this study found a shorter time to initial relief of sore throat of 5.1 hours (95 percent confidence interval [CI], 0.5–10.8 hours) when comparing dexamethasone with placebo in the group that was GAS positive. The time to complete relief of sore throat, though, in this same GAS-positive group was not significantly different. For GAS-positive patients, the number was statistically significant but of uncertain clinical significance. Interestingly, the GAS-negative group had a statistically shorter time to initial relief and complete relief of sore throat of 15.3 and 32.9 hours, respectively. It is important to note, though, that the study only included patients with moderate to severe pain. No patients with mild pain were included. For children with strep throat (GAS-positive), oral dexamethasone may only mildly shorten initial pain relief.

The final RCT by Niland et al evaluated a convenience sam-

**CONTINUED** *on page 23*

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ple of 90 patients ages 4–21 years, comparing GAS-positive patients in both an urgent care and emergency department setting.[5] Patients with strep throat by positive rapid strep test were randomized to one of three arms: single oral dexamethasone 0.6 mg/kg dose (maximum of 10 mg) versus three consecutive days of once daily oral dexamethasone 0.6 mg/kg dose (maximum of 10 mg once daily) versus placebo. Primary outcomes included time to improvement/resolution of throat pain, return to general health, and return to normal activity level. All patients enrolled in the study were GAS positive; 45 children received intramuscular penicillin (n=45), and 45 children received oral amoxicillin or oral azithromycin (n=45). Six children were lost to follow-up. The results were reported as hazard ratios (HRs). Comparing one- and three-day regimens of dexamethasone showed no difference. Compared to placebo, single-dose dexamethasone demonstrated improvement of general condition (HR 1.87; 95 percent CI, 1.1–3.2; *P*=0.001) and improvement in activity level (HR 2.25; 95 percent CI, 1.2–3.93; *P*<0.001).

A systematic review by Wing et al yielded similar conclusions regarding faster pain relief in GAS-positive patients given oral dexamethasone.[6] Another review by Schams et al concluded that "for children with severe symptoms and bacterial pathogens confirmed by rapid streptococcal tests, a single dose of oral dexamethasone can be considered a safe adjunctive treatment with antibiotics."[7] Conversely, the only national guideline we are able to find on this topic is from the Italian panel on pharyngitis in children, which recommends *against* the use of steroids for pharyngitis, stating "steroids may mask signs or symptoms of underlying severe disease such as lymphomas or other malignancy, potentially leading to a delay in diagnosis."[8] They do not differentiate between GAS-positive and GAS-negative cases in their recommendations.

## Conclusion

In children who are group A strep positive by rapid strep test, a single dose of oral dexamethasone 0.6 mg/kg (maximum of 10 mg) appears to shorten initial onset of pain relief by approximately six hours. It does not appear to shorten the time to complete relief of pain.

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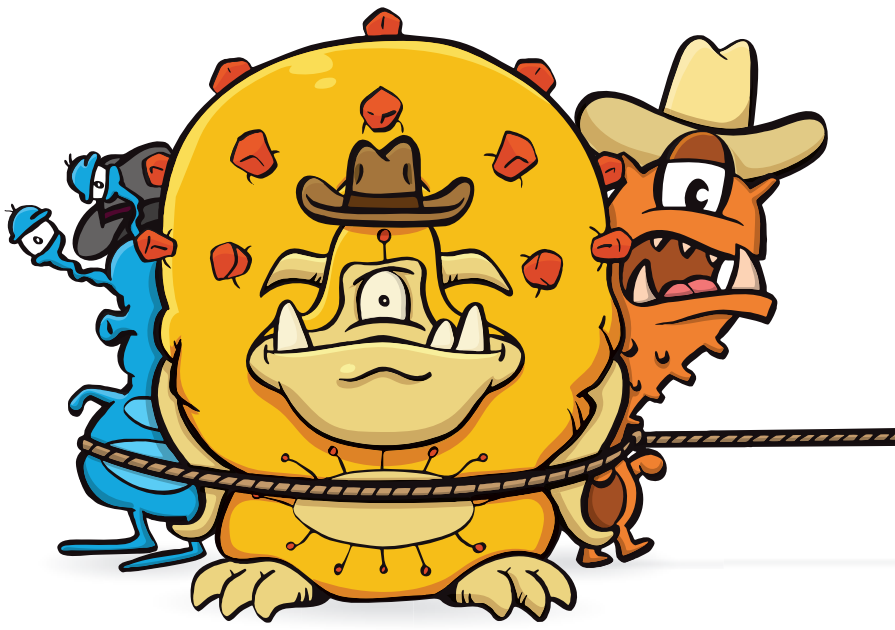

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1. Data on file, BioFire Diagnostics.
2. This test has not been FDA cleared or approved. This test has been authorized by FDA under an EUA for use by authorized laboratories. This test has been authorized only for the detection and differentiation of nucleic acid of SARS-CoV-2 from multiple respiratory viral and bacterial organisms. This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

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