WWW.GIHEPNEWS.COM

2007-10-Year Anniversary-2017

VOL. 11 NO. 10 OCTOBER 2017

# GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

UT Southwestern Medical Center

Dr. Amit Singal and coworkers showed that outreach for colonoscopy or FIT screening improved screening rates.

## Patient and physician outreach boost CRC screening rates

**BY KARI OAKES**
*Frontline Medical News*

Can outreach improve the globally low rates of adherence to colorectal cancer screening? Yes, according to two recent studies in JAMA; the studies found that both patient-focused and physician-focused outreach approaches can result in significantly better patient participation in colorectal cancer (CRC) screening.

The first study (JAMA. 2017;318[9]:806-15) compared a colonoscopy outreach program and a fecal immunochemical test (FIT) outreach program both with each other and with usual care. The results of the pragmatic, single-site, randomized, clinical trial showed that completed screenings were higher for both outreach groups, compared with the usual-care group.

The primary outcome measure of the study was completion of the screening process, wrote Amit Singal, MD, and his coauthors. This was defined as any adherence to colonoscopy completion, the completion of annual testing for patients who had a normal FIT test, or treatment evaluation if CRC was detected during the screening process. Screenings were considered com-

*See* **Outreach** · *page 27*

## Medicare fee schedule: Proposed pay bump falls short

*Misvalued codes didn't come through.*

**BY GREGORY TWACHTMAN**
*Frontline Medical News*

Physicians will likely see a 0.31% uptick in their Medicare payments in 2018 and not the 0.5% promised in the Medicare Access and CHIP Reauthorization Act.

Officials at the Centers for Medicare & Medicaid Services were not able to find adequate funding in so-called misvalued codes to support the larger increase, as required by law, according to the proposed Medicare physician fee schedule for 2018.

CMS also failed to hit its misvalued code target in 2016, resulting in a 0.18% across-the-board reduction to the physician fee schedule in 2017 instead of the statutorily promised 0.5% increase.

Other provisions in the proposed Medicare physician fee schedule may be more palatable than the petite pay raise.

The proposal would roll back data reporting requirements of the Physician Quality Reporting System (PQRS), to better align them with the new Quality Payment Program (QPP), and will waive half of penalties assessed for not meeting PQRS requirements in 2016.

"We are proposing these changes based on stakeholder feedback and to better align with the MIPS [Merit-based Incentive

*See* **Medicare** · *page 4*

## INSIDE



## Study findings support uncapping MELD score for liver transplant

**BY DOUG BRUNK**
*Frontline Medical News*

Uncapping the current Model for End-Stage Liver Disease score may provide a better path toward making sure that patients most in need of a liver transplant get one, results from a large, long-term analysis showed.

Established in 2002, the Model for End-Stage Liver Disease (MELD) scoring system "was arbitrarily capped at 40 based on the presumption that transplanting patients with MELD greater than

*See* **MELD** · *page 20*



GI & Hepatology News
151 Fairchild Ave.,
Suite 2,
Plainview, NY 11803-1709

CHANGE SERVICE REQUESTED

Presorted Standard
U.S. Postage
PAID
Permit No. 384
Lebanon Jct. KY

# Letter from an associate editor: Hurricane Harvey's wrath

*It seemed appropriate this month for me to step aside for the Editor's commentary and provide a forum for one of our associate editors to talk about his experience during Hurricane Harvey.*

DR. ALLEN

DR. KETWAROO

***John I. Allen, MD, MBA, AGAF***
***Editor in Chief***

**BY GYANPRAKASH A. KETWAROO, MD, MSC**

We knew that a powerful storm was coming, but very few anticipated the widespread destruction Hurricane Harvey would bring. Houston is no stranger to floods, but the amount of water that Harvey unleashed was record-breaking. Areas that had never flooded were underwater, evacuations were commonplace; the devastation was heart-breaking. In the midst of significant personal tragedy, Houston came together. Neighbors took in flooded colleagues, personal boats were used for rescues, and many braved impassable roads to donate clothes, food, labor and medical aid. Shelters across the city were assisted by volunteers; community groups collected and coordinated distribution of supplies. Medical teams were mobilized to treat chronically ill patients who evacuated without their medications or those injured while escaping the floods.

At one of the largest medical centers in the world, floodgates constructed after Tropical Storm Allison kept the waters at bay. And physicians, nurses, janitors, and other employees slept in hospitals for days to provide care to our patients during the worst of the floods. Those who relieved them worked long hours to see the many patients rescheduled in the aftermath of the storm. After-work crews of neighbors continue to go from house to house removing flooded floor boards and ripping out drywall. Houston came together.

Unfortunately, these massive storms are now all too frequent, as we show solidarity with those who recently suffered in Florida, Puerto Rico, and the Caribbean from Hurricane Irma. Lessons have been learned as with prior natural disasters, including consideration of hospital-owned boats to maintain access to care while the streets remain flooded. As we slowly return to normal operations, with areas still underwater, the outpouring of support from friends and strangers across the world has been magnificent. The magnitude of loss and the psychological toll are immense. As physicians, we are guided by a professional duty to help our patients. But that ideal of serving others is seen most vividly in those small acts of kindness, of neighbor helping neighbor, that are commonplace as we recover and rebuild. Houston Strong.

---

*Dr. Ketwaroo is an assistant professor in the division of gastroenterology and hepatology at Baylor College of Medicine, Houston, and an advanced endoscopist at the Michael E. Debakey VA Medical Center in Houston. He is an associate editor for GI & Hepatology News.*

The National Guard Malcolm McClendon/Texas Military Department/Wikimedia Commons/Public Domain

WWW.GIHEPNEWS.COM
GI & HEPATOLOGY NEWS
THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

FRONTLINE MEDICAL COMMUNICATIONS



**GI & HEPATOLOGY NEWS** is the official newspaper of the American Gastroenterological Association (AGA) Institute and provides the gastroenterologist with timely and relevant news and commentary about clinical developments and about the impact of health care policy. Content for **GI & HEPATOLOGY NEWS** is developed through a partnership of the newspaper's medical board of editors (Editor in Chief and Associate Editors), Frontline Medical Communications Inc. and the AGA Institute Staff. "News from the AGA" is provided exclusively by the AGA, AGA Institute, and AGA Research Foundation. All content is reviewed by the medical board of editors for accuracy, timeliness, and pertinence. To add clarity and context to important developments in the field, select content is reviewed by and commented on by external experts selected by the board of editors.



**POSTMASTER** Send changes of address (with old mailing label) to GI & Hepatology News, Subscription Service, 151 Fairchild Ave., Suite 2, Plainview, NY 11803-1709.

The AGA Institute headquarters is located at 4930 Del Ray Avenue, Bethesda, MD 20814, ginews@gastro.org.

**Editorial Offices** 2275 Research Blvd, Suite 400, Rockville, MD 20850, 240-221-2400, fax 240-221-2548

**GI & HEPATOLOGY NEWS** (ISSN 1934-3450) is published monthly for $230.00 per year by Frontline Medical Communications Inc., 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609. Phone 973-206-3434, fax 973-206-9378

**Scan this QR Code to visit gihepnews.com**

**FRONTLINE MEDICAL COMMUNICATIONS SOCIETY PARTNERS**
**VP/Group Publisher; Director, FMC Society Partners** Mark Branca
**Editor in Chief** Mary Jo M. Dales
**Executive Editors** Denise Fulton, Kathy Scarbeck
**Editor** Lora T. McGlade
**Creative Director** Louise A. Koenig
**Director, Production/Manufacturing** Rebecca Slebodnik
**National Account Manager** Artie Krivopal, 973-206-2326, cell 973-202-5402, akrivopal@frontlinemedcom.com
**Senior Director of Classified Sales** Tim LaPella, 484-921-5001, tlapella@frontlinemedcom.com
**Advertising Offices** 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609 973-206-3434, fax 973-206-9378

**FRONTLINE MEDICAL COMMUNICATIONS**

Chairman Stephen Stoneburn
President/CEO Alan J. Imhoff
CFO Douglas E. Grose

President, Digital Douglas E. Grose
Chief Digital Officer Lee Schweizer
Vice President, Digital Publishing Amy Pfeiffer

President, Custom Solutions JoAnn Wahl
Vice President, Custom Programs Carol Nathan
Vice President, Custom Solutions Wendy Raupers

Senior Vice President, Finance Steven J. Resnick
Vice President, Human Resources & Facility Operations Carolyn Caccavelli

Vice President, Marketing & Customer Advocacy Jim McDonough
Vice President, Operations Jim Chicca
Vice President, Sales Mike Guire
Vice President, Society Partners Mark Branca
Circulation Director Jared Sonners
Corporate Director, Research & Communications Lori Raskin
Editorial Director, Clinical Karen J. Clemments

In affiliation with Global Academy for Medical Education, LLC

Vice President, Medical Education & Conferences Sylvia H. Reitman, MBA
Vice President, Events David J. Small, MBA

***#1 MOST PRESCRIBED, BRANDED BOWEL PREP KIT[1]***


# A CLEAN SWEEP

## EFFECTIVE RESULTS IN ALL COLON SEGMENTS[2]

- SUPREP® Bowel Prep Kit has been FDA-approved as a split-dose oral regimen[3]
- >90% of patients had no residual stool in all colon segments[2*†]
  - These cleansing results for the cecum included 91% of patients[2*†]
  - SUPREP Bowel Prep Kit also achieved ≥64% no residual fluid in 4 out of 5 colon segments (ascending, transverse, descending, and sigmoid/rectum)[2*†]

*Aligned with Gastrointestinal Quality Improvement Consortium (GIQuIC) performance target of ≥85% quality cleansing for outpatient colonoscopies.[4]*

**SUPREP®**
**BOWEL PREP KIT**
(sodium sulfate, potassium sulfate and magnesium sulfate)
Oral Solution

(17.5g/3.13g/1.6g) per 6 ounces

*This clinical trial was not included in the product labeling. †Based on investigator grading.

**References: 1.** IMS Health, NPA Weekly, May 2017. **2.** Rex DK, DiPalma JA, Rodriguez R, McGowan J, Cleveland M. A randomized clinical study comparing reduced-volume oral sulfate solution with standard 4-liter sulfate-free electrolyte lavage solution as preparation for colonoscopy. *Gastrointest Endosc.* 2010;72(2):328-336. **3.** SUPREP Bowel Prep Kit [package insert]. Braintree, MA: Braintree Laboratories, Inc; 2012. **4.** Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. *Gastrointest Endosc.* 2015;81(1):31-53.



HH13276BT-U

May 2017

# Many issues, biosimilars reviewed

**Medicare** *from page 1*

Payment System track of the QPP] data submission requirements for the quality performance category," according to a CMS fact sheet on the proposed fee schedule.

"This will allow some physicians who attempted to report for the 2016 performance period to avoid penalties and better align PQRS with MIPS as physicians transition to QPP," officials from the American College of Physicians said in a statement.

Other physician organizations said they believed the proposal did not go far enough.

"While the reductions in penalties represent a move in the right direction, the [American College of Rheumatology] believes CMS should establish a value modifier adjustment of zero for 2018," ACR officials said in a statement. "This would align with the agency's policy to 'zero out' the impact of the resource use component of the Merit-based Incentive Payment System in 2019, the successor to the value modifier program. This provides additional time to continue refining the cost measures and gives physicians more time to understand the program."

The proposed fee schedule also would delay implementation of the appropriate use criteria (AUC) for imaging services, a program that would deny payments for imaging services unless the ordering physician consulted the appropriate use criteria.

The American Medical Association "appreciates CMS' decision to postpone the implementation of this requirement until 2019 and to make the first year an opportunity for testing and education where consultation would not be required as a condition of payment for imaging services," according to a statement.

"We also applaud the proposed delay in implementing AUC for diagnostic imaging studies," ACR said in its statement. "We will be gauging the readiness of our members to use clinical support systems. ... We support simplifying and phasing-in the program requirements. The ACR also strongly supports larger exemptions to the program," such as physicians in small groups and rural and underserved areas.

The proposed fee schedule also seeks feedback from physicians and organizations on how Medicare Part B pays for biosimilars. Under the 2016 fee schedule, the average sales prices (ASPs) for all biosimilar products assigned to the same reference product are included in the same CPT code, meaning the ASPs for all biosimilars of a common reference product are used to determine a single reimbursement rate.

That CMS is looking deeper at this is being seen as a plus.

Biosimilars "tied to the same reference product may not share all indications with one another or the reference product [and] a blended payment model may cause significant confusion in a multitiered biosimilars market that may include both interchangeable and noninterchangeable products," the Biosimilars Forum said in a statement.

The current situation "may lead to decreased physician confidence in how they are reimbursed and also dramatically reduce the investment in the development of biosimilars and thereby limit treatment options available to patients."

Both the Biosimilars Forum and the ACR support unique codes for each biosimilar.

"Physicians can better track and monitor their effectiveness and ensure adequate pharmacovigilance in the area of biosimilars" by employing unique codes, according to ACR officials.

"AGA agrees that there should be separate, unique codes for biosimilars; however, we have additional concerns regarding gastroenterological disorders. Specifically, inflammatory bowel disease (IBD) carries unique risks with regard to immunogenicity and currently there is a paucity of clinical data for biosimilars in people with IBD. Real-world use is often the first experience in IBD for these products."

**'AGA agrees that there should be separate, unique codes for biosimilars; however, we have additional concerns regarding gastroenterological disorders.'**

The fee schedule proposal also would expand the Medicare Diabetes Prevention Program (DPP), currently a demonstration project, taking it nationwide in 2018. The proposal outlines the payment structure and supplier enrollment requirements and compliance standards, as well as beneficiary engagement incentives.

Physicians would be paid based on performance goals being met by patients, including meeting certain numbers of service and maintenance sessions with the program as well as achieving specific weight loss goals. For beneficiaries who are able to lose at least 5% of body weight, physicians could receive up to $810. If that weight loss goal is not achieved, the most a physician could receive is $125, according to a CMS fact sheet. Currently, DPP can be employed only via office visit; however, the proposal would allow virtual make-up sessions.

"The new proposal provides more flexibility to DPP providers in supporting patient engagement and attendance and by making performance-based payments available if patients meet weight-loss targets over longer periods of time," according to the AMA.

The fee schedule also proposes more telemedicine coverage, specifically for counseling to discuss the need for lung cancer screening, including eligibility determination and shared decision making, as well psychotherapy for crisis, with codes for the first 60 minutes of intervention and a separate code for each additional 30 minutes. Four add-on codes have been proposed to supplement existing codes that cover interactive complexity, chronic care management services, and health risk assessment.

For clinicians providing behavioral health services, CMS is proposing an increased payment for providing face-to-face office-based services that better reflects overhead expenses.

The final rule is expected in early November.

gtwachtman@frontlinemedcom.com

# FLASHBACK TO 2016

2007-*10-Year Anniversary*-2017

For the final installment of this series, we "flashback" to our April 2016 issue, which featured a study examining 30-day complications among commercially insured adults undergoing colonoscopy with and without anesthesia-assisted sedation using Marketscan data (2008-2011). While the costs of utilizing anesthesia assistance for an ever-increasing proportion of routine GI procedures are significant, the effect of endoscopic sedation type on patient outcomes provides the most compelling evidence for or against this practice. In this study, use of anesthesia-assisted sedation (generally with propofol) was associated with a 13% increased risk of any 30-day complication, and specifically with an increased perforation risk in those undergoing polypectomy, hemorrhage, abdominal pain, anesthesia-associated complications, and stroke (range of odds ratios, 1.04-1.28).

However, the existence and clinical significance of this differential complication rate remains controversial. For example, a subsequent systematic review and meta-analysis (Clin Gastro Hepatol. 2017;15[12]:194-206), pooling the results of 27 studies including 2,518 patients, concluded that propofol-based sedation had a risk of cardiopulmonary adverse events similar to that of traditional agents, and a decreased risk of overall complications when used for routine GI procedures.

Several letters to the editor challenged the methods used in this systematic review/meta-analysis, such that this question remains largely unresolved. What is clear is that we continue to lack an adequate understanding of which patients are most likely to benefit from anesthesia-assisted sedation, whether due to increased risk of failing standard sedation or increased risk of complications with standard sedation. This lack of clarity, as manifested in poorly specified guidelines, has fueled likely inappropriate allocation of monitored anesthesia care to low-risk-patients (driven by a complex interplay of patient, provider, organizational, and economic factors), which has contributed to ballooning health care costs and potentially impaired access for higher-risk patients in resource-limited settings. Enhanced understanding of which patients are most likely to benefit from anesthesia-assisted sedation is an essential first step in helping to define high-value use of this resource and developing more refined clinical criteria to guide sedation decision making.

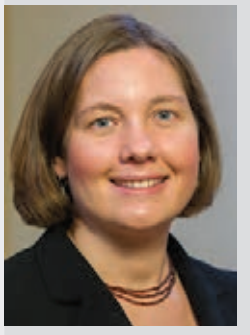

GI & HEPATOLOGY NEWS

Long-term PPI use linked to increased risk of dementia

Anesthesia service for colonoscopy ups complications

MDs, payers work on quality measures

2016 AGA TECH SUMMIT REPORT



*Megan A. Adams, MD, JD, MSc, is a clinical lecturer in the division of gastroenterology at the University of Michigan, a gastroenterologist at the Ann Arbor Mich VA, and an investigator in the VA Ann Arbor Center for Clinical Management Research. She is an associate editor of GI & Hepatology News.*

FROM THE AGA JOURNALS

# Enhanced disinfection of duodenoscopes did not reduce contamination

**BY AMY KARON**
*Frontline Medical News*

Duodenoscopes had similar rates of contamination after double high-level disinfection, standard high-level disinfection, or standard high-level disinfection followed by ethylene oxide gas sterilization, a randomized, prospective study of 516 bacterial cultures of 18 duodenoscopes showed.

"Our results do not support the routine use of double high-level disinfection or ethylene oxide sterilization for duodenoscope reprocessing," wrote Graham M. Snyder, MD, of Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, and his associates. They stopped the study after 3 months because none of the duodenoscopes cultured multidrug-resistant organisms, the primary endpoint. "[We] found that in the nonoutbreak setting, duodenoscope contamination by multidrug-resistant organisms is extremely uncommon," they wrote in the October issue of Gastroenterology (doi: 10.1053/j.gastro.2017.06.052).

However, 16% of duodenoscopes cultured at least one colony-forming unit (CFU) after either standard high-level or double high-level disinfection, and 23% of duodenoscopes produced at least one CFU despite standard high-level disinfection followed by ethylene gas sterilization (*P* = .2), the investigators reported.

Outbreaks of carbapenem-resistant *Enterobacteriaceae* infections have been traced to duodenoscopes, even though they were reprocessed according to manufacturer instructions. In 2015, the Food and Drug Administration responded by warning that the design of duodenoscopes might preclude effective cleaning. Reasons for residual contamination remain uncertain, but biofilms, which are notoriously resistant to standard disinfection methods, might be a culprit, Dr. Snyder and his associates noted. Accordingly, some experts have suggested repeating the reprocessing cycle or adding ethylene oxide sterilization, but these measures are costly, time intensive, and not widely available. Furthermore, their efficacy "has never been systematically studied in a nonoutbreak setting," the researchers wrote.

**Multidrug-resistant organisms were cultured from 3% of rectal swabs and duodenal aspirates, but not from any of the cultures of duodenoscopes. Therefore, the study was stopped for futility. The enhanced disinfection methods failed to prevent contamination, compared with standard high-level disinfection.**

In response, they studied 516 cultures of elevator mechanisms and working channels from 18 reprocessed duodenoscopes (Olympus, model TJF-Q180). Immediately after use, each duodenoscope was manually wiped with enzymatic solution (EmPower), and then was manually reprocessed within an hour before undergoing automated reprocessing (System 83 Plus 9) with ortho-phthalaldehyde disinfectant (MetriCide OPA Plus) followed by ethanol flush. One-third of the duodenoscopes were randomly assigned to undergo double high-level disinfection with two automated reprocessing cycles, and another third underwent standard high-level disinfection followed by ethylene oxide gas sterilization (Steri-Vac sterilizer/aerator). All instruments were stored by hanging them vertically in an unventilated cabinet.

Multidrug-resistant organisms were cultured from 3% of rectal swabs and duodenal aspirates, but not from any of the cultures of duodeno-

*Continued on following page*

FROM THE AGA JOURNALS

# Study linked $H_2$-receptor antagonists, but not PPIs, to dementia

BY AMY KARON
*Frontline Medical News*

A large prospective study of middle-aged and older women found no convincing evidence that using proton pump inhibitors increased their risk of dementia, investigators reported.

However, using $H_2$-receptor antagonists for at least 9 years was associated with a slight decrease in scores of learning and working memory (mean decrease, –0.2; 95% confidence interval, –0.3 to –0.08; *P* less than .001), Paul Lochhead, MBChB, PhD, and his associates wrote in the October issue of Gastroenterology (doi: 10.1053/j.gastro.2017.06.061). "Since our primary hypothesis related to PPI [proton pump inhibitor] use, our findings for [$H_2$-receptor antagonists] should be interpreted with caution," they said.

In a recent German study of a medical claims database, use of PPIs was associated with a 44% increase in the likelihood of incident dementia (JAMA Neurol. 2016;73:410-6). "The existence of a causal mechanism linking PPI use to dementia is suggested by observations from cellular and animal models of Alzheimer's disease, where PPI exposure appears to influence amyloid-beta metabolism," Dr. Lochhead and his associates wrote. "However, other preclinical data on PPIs and Alzheimer's disease are conflicting." Noting that cognitive function predicts dementia later in life, they analyzed prospective data on medications and other potential risk factors from 13,864 participants in the Nurses' Health Study II who had completed Cogstate, a computerized, self-administered neuropsychological battery.

Study participants averaged 61 years old when they underwent cognitive testing, ranging in age from 50 to 70 years. Users of PPIs tended to be older, had more comorbidities, were less physically active, had higher body mass indexes, had less education, and ate a lower-quality diet than women who did not use PPIs. After adjustment for such confounders, using PPIs for 9-14 years was associated with a modest decrease in scores for psychomotor speed and attention (mean score difference, compared with never users, –0.06; 95% CI, –0.11 to 0.00; *P* = .03). "For comparison, in multivariable models, a 1-year increase in age was associated with mean score decreases of 0.03 for psychomotor speed and attention, 0.02 for learning and working memory, and 0.03 for overall cognition," the researchers wrote.



Next, they examined links between use of $H_2$-receptor antagonists and cognitive scores among 10,778 study participants who had used PPIs for 2 years or less. Use of $H_2$-receptor antagonists for 9-14 years predicted poorer scores on learning, working memory, and overall cognition, even after controlling for potential confounders (*P* less than or equal to .002). "The magnitudes of mean score differences were larger than those observed in the analysis of PPI use, particularly for learning and working memory," the researchers noted. Also, PPI use did not predict lower cognitive scores among individuals who had never used $H_2$-receptor antagonists.

On the other hand, using PPIs for 9-14 years was associated with the equivalent of about 2 years of age-related cognitive decline, and controlling for exposure to $H_2$-receptor antagonists weakened even this modest effect, the investigators said. Users and nonusers of PPIs tend to differ on many measures, and analyses of claims data, such as the German study above, are less able to account for these potential confounders, they noted. "Nonjudicious PPI prescribing is especially frequent among the elderly and those with cognitive impairment," they added. "Therefore, elderly individuals who have frequent contact with health providers are at increased risk of both PPI prescription and dementia diagnosis. This bias may not be completely mitigated by adjustment for comorbidities or polypharmacy."

The findings regarding $H_2$-receptor antagonists reflect those of three smaller cohort studies, and these medications are known to cause central nervous system effects in the elderly, including delirium, the researchers said. Ranitidine and cimetidine have anticholinergic effects that also could "pose a risk for adverse cognitive effects with long-term use."

Dr. Lochhead reported having no conflicts. Two coinvestigators disclosed ties to Bayer Healthcare, Pfizer, Aralez Pharmaceuticals, AbbVie, Samsung Bioepis, and Takeda.

ginews@gastro.org

Numerous possible PPI-related adverse events have been reported within the past few years; some resultant media attention has caused anxiety for patients. Dementia is a dreaded diagnosis. Therefore, initial reports that PPI treatment might be associated with an increased risk of dementia attracted considerable media attention, much of which was unbalanced and uninformed. There is no obvious biological rationale for such an association, and the risks reported initially were of small magnitude (for example, hazard ratios of approximately 1.4). However, patients cannot reliably assess levels of risk from media coverage that often veers toward sensationalism.


DR. HOWDEN

The study by Lochhead et al. is a welcome contribution to the topic of PPI safety. Using the Nurses' Health Study II database, the investigators measured cognitive function in a large group of female PPI users and nonusers. Unsurprisingly, PPI users were older and sicker than nonusers. There were quantitatively small changes in some measures of cognitive function among PPI users. However, learning and working memory scores, which are more predictive of Alzheimer's-type cognitive decline, were unaffected by PPI use.

For those prescribers with residual concerns about any association between PPIs and dementia, these prospectively collected data on cognitive function should provide further reassurance. It is appropriate that this study should have been highlighted in GI & Hepatology News, but since it lacks the potential sensationalism of studies that report a putative association, we should not expect it to be discussed on the TV evening news anytime soon!

*Colin W. Howden, MD, AGAF, is chief of gastroenterology at University of Tennessee Health Science Center, Memphis. He has been a consultant, investigator, and/or speaker for all PPI manufacturers at some time. He is currently a consultant for Takeda, Aralez, and Pfizer Consumer Health.*

*Continued from previous page*

scopes. Therefore, the study was stopped for futility. The enhanced disinfection methods failed to prevent contamination, compared with standard high-level disinfection, the researchers noted. Ten or more CFUs grew in 2% of duodenoscopes that underwent standard high-level disinfection, 4% of those that underwent double high-level disinfection, and 4% of those that underwent high-level disinfection followed by ethylene oxide sterilization (*P* = .4).

"There is no consensus on what parts of the standard high-level disinfection process should be repeated," the investigators wrote. "It is uncertain if the addition of a second cycle of manual reprocessing might have improved the effectiveness of double high-level disinfection."

Funders included the American Society for Gastrointestinal Endoscopy and Beth Israel Deaconess Medical Center. The investigators reported having no conflicts of interest.

ginews@gastro.org

FROM THE AGA JOURNALS

# Statin use cuts risks in compensated cirrhosis

BY AMY KARON
*Frontline Medical News*

For patients with compensated cirrhosis, statin therapy was associated with about a 46% decrease in the risk of hepatic decompensation and mortality and with a 27% drop in the risk of portal hypertension and variceal bleeding, according to moderate-quality evidence from a systematic review and meta-analysis of 13 studies.

Low-quality data also suggested that statins might help protect against the progression of noncirrhotic chronic liver disease, said Rebecca G. Kim of the University of California at San Diego and her associates. "Large, pragmatic randomized controlled trials in patients with compensated cirrhosis are required to confirm these observations," they wrote in the October issue of Clinical Gastroenterology and Hepatology (doi: 10.1016/j.cgh.2017.04.039).



Prior studies have reported mixed findings on how statin therapy affects chronic liver disease. For their review, Ms. Kim and her associates searched MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, Cochrane Database and Systematic Reviews, Scopus, Web of Science, and PubMed for randomized controlled trials or cohort studies published through March 25, 2017. They identified 10 cohort studies and three randomized controlled trials (of which only one looked at clinical outcomes) of adults with fibrosis without cirrhosis, compensated cirrhosis, or decompensated cirrhosis that evaluated statin exposure and reported associations between exposure and outcomes related to cirrhosis. They excluded case-control studies, cross-sectional studies, and studies that focused only on the relationship between statin use and the risk of hepatocellular carcinoma.

The resulting data set included 121,058 patients with chronic liver diseases, of whom 85% had chronic hepatitis C virus infection. A total of 46% of patients were exposed to statins, which appeared to reduce their risk of hepatic decompensation, variceal bleeding, and mortality. Among 87 such patients in five studies, statin use was associated with a 46% decrease in the risk of hepatic decompensation and death, with risk ratios of 0.54 (95% confidence intervals, 0.46-0.62 and 0.47-0.61, respectively). Statin use also was associated with a 27% lower risk of variceal bleeding or decrease in portal pressure, based on an analysis of 110 events in 236 patients from three trials (RR, 0.73; 95% CI, 0.59-0.91). Finally, statin use also was associated with a 58% lower risk of fibrosis progression or cirrhosis in patients with noncirrhotic chronic liver disease, but the 95% CIs for the risk estimate did not reach statistical significance (0.16-1.11).

Most studies lacked data on dose and duration of statin exposure, the researchers said. However, four cohort studies reported dose-dependent effects that were most pronounced after more than a year of treatment. "Similarly, several different types of statins were studied, and observed effects were assumed to be class-specific effects," the reviewers wrote. "However, it is possible that lipophilic and lipophobic statins may have differential efficacy in decreasing fibrosis progression."

Together, these findings support and add to prior studies suggesting that statin therapy is safe and can potentially reduce the risk of hepatocellular carcinoma in this patient population, they concluded. Statins "may potentially improve patient-relevant outcomes in patients with chronic liver diseases and improve survival without significant additional costs."

The reviewers acknowledged the American Gastroenterological Association Foundation, a T. Franklin Williams Scholarship Award, the National Institutes of Health, and the National Library of Medicine. They reported having no relevant conflicts of interest.

ginews@gastro.org

DR. GARCIA-TSAO

The main mechanism in the development of cirrhosis in patients with chronic liver disease (CLD) is increased hepatic fibrogenesis. The initial consequence of cirrhosis is portal hypertension, which is the main driver of decompensation (defined as the presence of ascites, variceal hemorrhage, or encephalopathy).

Portal hypertension initially results from an increase in intrahepatic resistance, which in turn results from distortion of liver vascular architecture (mostly due to fibrosis) and from intrahepatic vasoconstriction (mostly due to endothelial cell dysfunction).

Statins are widely used for reducing cholesterol levels and cardiovascular risk. However, statins ameliorate endothelial dysfunction and have additional antifibrotic, anti-inflammatory, and antithrombotic properties, all of them of potential benefit in preventing progression of CLD/cirrhosis. In fact, statins have been shown to reduce portal pressure in cirrhosis.

In a meta-analysis of 13 studies, Kim et al. demonstrated that statin use is associated with a 58% lower risk of developing cirrhosis/fibrosis progression in patients with CLD (not statistically significant), while in patients with compensated cirrhosis of any etiology, statin use was associated with a statistically significant 46% lower risk of developing decompensation and death.

Most studies in the meta-analysis were observational/retrospective. Although the authors jointly analyzed three randomized controlled trials, only one of the trials looked at clinical outcomes. This important double-blind, placebo-controlled study in patients with recent variceal hemorrhage showed a significantly lower mortality in patients randomized to simvastatin.

Therefore, although the evidence is not yet sufficient to recommend the widespread use of statins in patients with CLD/cirrhosis, providers should not avoid using statins in patients with CLD/cirrhosis who otherwise need them. In fact, they should actively look for indications that would justify their use.

*Guadalupe Garcia-Tsao, MD, is professor of medicine at Yale University, chief of digestive diseases at the VA-CT Healthcare System, and director of the clinical core of the Yale Liver Center, New Haven, Conn. She had no conflicts of interest.*

# POEM found safe, effective for achalasia after Heller myotomy

BY AMY KARON
*Frontline Medical News*

Peroral endoscopic myotomy (POEM) safely and effectively treated achalasia in patients with persistent symptoms after Heller myotomy, according to the results of a retrospective study of 180 patients treated at 13 centers worldwide.

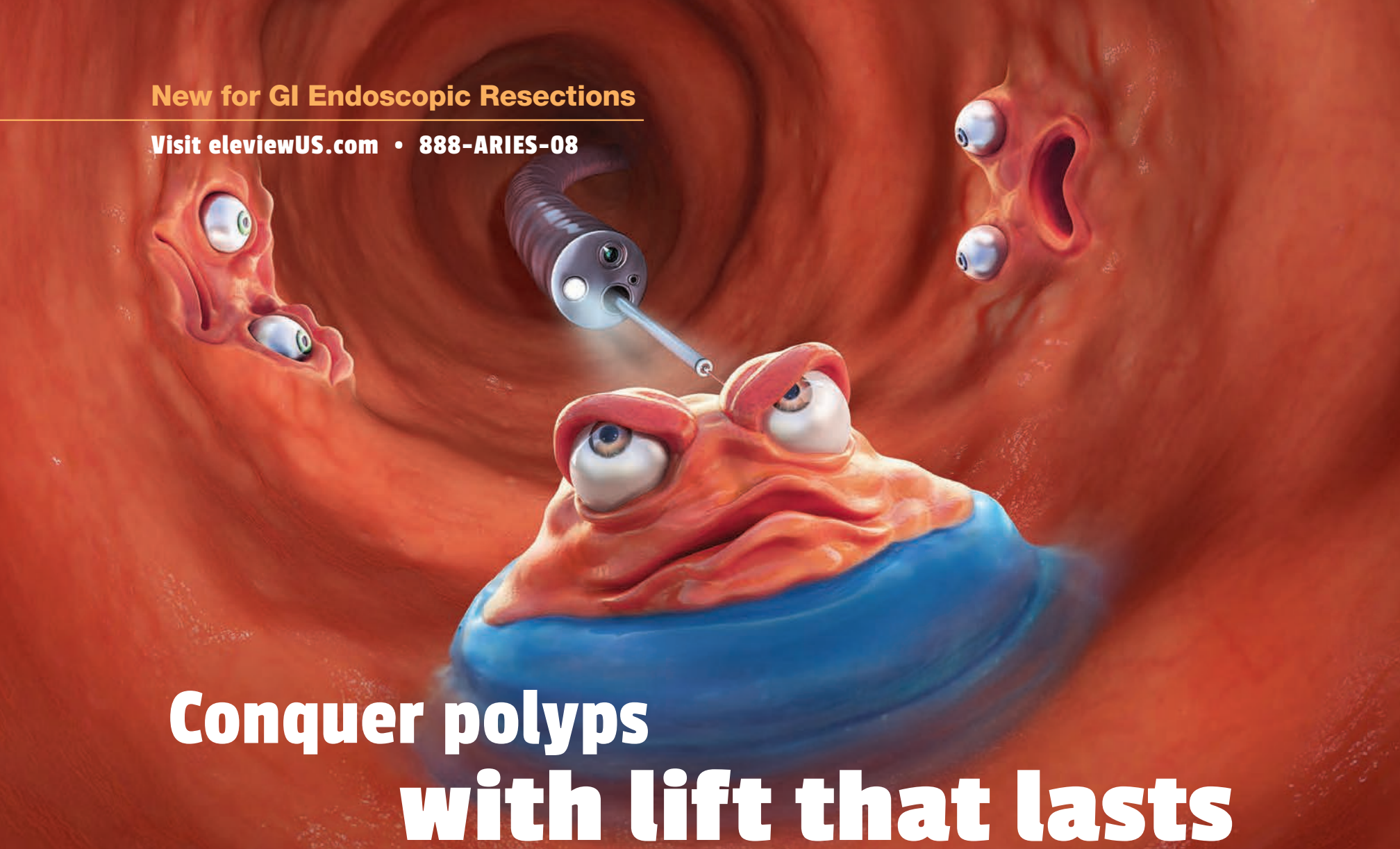
Rates of clinical success were 81% among patients who had previously undergone Heller myotomy and 94% among those who had not ($P = .01$), reported Saowanee Ngamruengphong, MD, of Johns Hopkins Medical Center, Baltimore, with her associates. The groups did not significantly differ in terms of rates of adverse events (8% and 13%, respectively), postprocedural symptomatic reflux (30% and 32%), or reflux esophagitis (44% and 52%). "Although the rate of clinical success in patients with prior Heller myotomy is lower than in those without [it], the safety profile of POEM is comparable," they wrote in the October issue of Clinical Gastroenterology and Hepatology (doi: 10.1016/j.cgh.2017.01.031).

Heller myotomy achieves a long-term symptomatic response in about 90% of patients with achalasia and has a complication rate of only about 5%, according to Dr. Ngamruengphong and her associates. When this surgery does not successfully resolve symptoms,

*Continued on page 10*

New for GI Endoscopic Resections

Visit eleviewUS.com • 888-ARIES-08



# Conquer polyps with lift that lasts

## New Eleview™ submucosal injection agent

- Provides an immediate and long-lasting cushion[1] that holds for up to 45 minutes[2]
- Increases visibility of target lesion margins[1]
- Designed to lower the risk of perforation[1]
- Appropriate for challenging polyps regardless of size, location, or type

Lasts for up to 45 minutes[2]


Eleview™ submucosal injectable composition is intended for use in gastrointestinal endoscopic procedures for submucosal lift of polyps, adenomas, early-stage cancers, or other gastrointestinal mucosal lesions, prior to excision with a snare or endoscopic device.

**Important Safety Information**

### WARNINGS AND PRECAUTIONS

- The safety of Eleview™ has not been established in pregnant or lactating women, or in children under 18 years of age.
- The endoscopist injecting Eleview™ must be experienced in the administration technique.

### CONTRAINDICATIONS

Patients with known sensitivity to any of the components contained in Eleview™.

### ADVERSE REACTIONS

Rarely, local bleeding and/or inflammatory reaction could occur which may or may not be associated with Eleview™.

**Please see Instructions for Use for complete Important Safety Information.**

**References: 1.** Eleview™ Instructions for Use, Aries Pharmaceuticals, Inc. April 2017. **2.** Data on File, Aries Pharmaceuticals, Inc.

ARIES Pharmaceuticals, Inc.
Member of Cosmo Pharmaceuticals NV Group
aries-pharma.com



Lift that lasts
Eleview™

*Continued from page 8*

patients historically have chosen between repeating it or undergoing pneumatic dilation. However, POEM posted high success rates in several small, single-center case series. Thus, the researchers analyzed data on 180 adults with achalasia whose Eckardt scores were at least 3 and who underwent POEM at 13 tertiary care centers in Australia, France, Hong Kong, India, Italy, Japan, the United Kingdom, and the United States during 2009-2015.

POEM was a technical success for 98% for the group of patients who previously had undergone Heller myotomy and for 100% for those who had not, the researchers reported. In the univariate analysis, predictors of clinical failure included prior Heller myotomy (odds ratio, 3.6; 95% confidence interval, 1.3-10.4; *P* = .02) and prior pneumatic dilation (OR, 2.9; 95% CI, 1.2-7.4; *P* = .02). In the multivariable analysis, prior Heller myotomy significantly increased the chances of clinical failure (adjusted OR, 3.0; 95% confidence interval, 1.0-8.9; *P* = .04) after accounting for prior pneumatic dilation and baseline Eckardt score. Prior pneumatic dilation reached borderline significance (adjusted OR, 2.6; 95% CI, 0.99-7.0; *P* = .05). Clinical failure was not associated with age, sex, achalasia subtypes, previous therapy, baseline Eckardt score, length of myotomy, orientation of myotomy, or extent of lower esophageal sphincter myotomy.

"Previous studies have reported that the success rates of pneumatic dilation in patients who failed prior Heller myotomy ranged between 50% and 89%," the researchers said. However, success is often short lived, with up to 45% of patients needing another procedure within 2 years, putting them at risk of "potentially serious adverse events, such as esophageal perforation or aspiration," they added.

**Success with pneumatic dilation is often short lived, with up to 45% of patients needing another procedure within 2 years, putting them at risk of 'potentially serious adverse events, such as esophageal perforation or aspiration.'**

Repeat surgical myotomy is reportedly successful in 73%-89% of cases; however, it is technically challenging because of adhesions and fibrosis from the previous surgery and is associated with a high risk of gastrointestinal perforation.

Clinicians should carefully investigate the reasons a Heller myotomy failed in order to elect a course of action, the researchers emphasized. "For instance, for patients with symptom relapse or failure to respond to surgical myotomy as a result of incomplete myotomy or myotomy fibrosis, POEM is likely to be effective," they said. "On the other hand, when the cause of persistent symptoms after surgical myotomy is tight fundoplication, a redo fundoplication should be recommended."

Dr. Ngamruengphong had no disclosures. Three coinvestigators disclosed consulting relationships with Boston Scientific, Medtronic, Sandhill Scientific, Erbe, and Cosmo Pharmaceuticals.

ginews@gastro.org

# Studies backing some accelerated approvals fall short

**BY SHARON WORCESTER**
*Frontline Medical News*

The quality of studies and data relied upon to support Food and Drug Administration accelerated drug approvals and high-risk device modifications is often lacking, two studies showed.

Between 2009 and 2013, the FDA granted accelerated approval for 22 drugs with 24 indications, which were supported by 30 preapproval studies with a median of 132 subjects. Only 12 of those studies (40%) were randomized, and only 6 (20%) were double blind. Eight (27%) included fewer than 100 subjects, and 20 (67%) included fewer than 200, reported Huseyin Naci, PhD, of the London School of Economics and Political Science, and his colleagues.

**Only 12 of those studies (40%) were randomized, and only 6 (20%) were double blind. Eight (27%) included fewer than 100 subjects, and 20 (67%) included fewer than 200.**

Further, at a minimum of 3 years after the approval, only half of the 38 confirmatory studies required by the FDA were completed, and, ultimately, only 25 of the 48 (66%) examined clinical efficacy, only 7 (18%) evaluated longer follow-up, and only 6 (16%) focused on safety, the investigators reported (JAMA. 2017 Aug 15;318[7]:626-36).

The proportion of studies that were randomized was slightly, but not significantly greater in the postapproval vs. preapproval period (56% vs. 40%), and only one was double blind. For 10 of 24 indications (42%), postapproval study requirements were completed and demonstrated efficacy based on surrogate measures, the investigators said.

Of the 14 remaining indications (58%) for which FDA study requirements had not yet been met, 2 (8%) had at least one confirmatory study that failed to demonstrate clinical benefit (without apparent action on the part of the FDA to rescind approval or impose additional requirements), 2 (8%) had a least one confirmatory study that was terminated, and 3 (13%) had at least one confirmatory study that was delayed by more than a year. The required studies for the remaining indications were progressing as planned, but for eight indications, clinical benefit had not yet been confirmed at 5 or more years after approval.

Similar concerns were seen in a review of clinical studies used to support high-risk medical device modification approvals. Such devices often undergo numerous modifications that receive FDA approval through one of six premarket approval supplement

*Continued on page 13*

WWW.GIHEPNEWS.COM

# GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

*Continued from page 11*

pathways, and a total of 83 studies that supported 78 panel-track supplements (one of the six pathways and the only one that always required clinical data) approved between April 19, 2006, and Oct. 9, 2015, were identified. Nearly all (98%) of those 78 modifications were supported by just one study; only 45% of those studies were randomized clinical trials, and only 30% were blinded, reported Sarah Y. Zheng, MD, of the University of California, San Francisco, and her colleagues (JAMA. 2017 Aug 15;318[7]:619-25).

The median number of patients in the studies was 185, and the median follow-up was 180 days. Further, of 150 primary endpoints in the studies, 121 (81%) were surrogate endpoints, 57 (38%) were compared with controls, and 6 (11%) of those involved retrospective rather than active controls.

Age and sex were not reported for all enrolled patients in 40% and 30% of the studies, respectively, and in the case of one device modification study, 91% of enrolled patients were not included in the primary analysis.

"Given the extensive modification of many PMA supplement devices and the median preapproval follow-up of 6 months, obtaining additional data via [postapproval studies] is critical. However, the FDA required [postapproval studies] for the minority (37%) of the panel-track supplements," the investigators noted, adding that only 13% of initiated postapproval studies were completed between 3 and 5 years after FDA approval, and that no warning letters, penalties, or fines were administered for noncompliance.

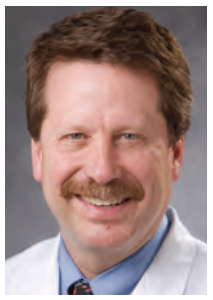
"These findings suggest that the quality of studies and data evaluated to support approval by the FDA of modifications of high-risk devices should be improved," they concluded.

Dr. Zheng and her colleagues reported having no conflicts of interest. Dr. Naci reported having no conflicts of interest. One coauthor, Aaron S. Kesselheim, MD, reported receiving unrelated grants from the FDA Office of Generic Drugs and Division of Health Communication.

sworcester@frontlinemedcom.com

**PERSPECTIVE**

## Overhaul needed to balance safety and access



The findings by Naci and colleagues and Zheng and colleagues raise concerns about whether the current regulatory system is too permissive in not requiring traditional randomized controlled trials for postmarketing evaluation of drugs that receive accelerated approval, and for high-risk medical device supplemental design modifications, Robert Califf, MD, wrote in an editorial.

However, randomization and blinding are not always feasible, and "despite the concerns raised by these two articles ... it is important to remember that decisions about postmarket requirements and monitoring of these studies are overseen by full-time FDA employees with no financial conflicts," he said, adding that "this underscores the importance of a talented workforce at the FDA with the variety of skills needed to assimilate information about manufacturing, quality systems, clinical outcomes, and the well-being and preferences of patients."

A sweeping overhaul of the overall system is also needed, and is underway, he said, noting that substantial progress in balancing safety with access to effective therapies will come from systemic changes in the ecosystem rather than from imposing more severe demands on individual products (JAMA. 2017 Aug 15;318[7]:614-6).

Indeed, it is time to seriously consider how increasingly robust data and analytic capabilities and more efficient prospective research systems can be used to address the concerns raised in these articles, he said, adding that "as technological improvements and ... connected networks of health systems make it feasible to conduct high-quality, low-cost RCTs [randomized, controlled trials] and to continuously monitor product performance, the impediments to progress are mostly those built into the culture of medicine and health care."

*Dr. Califf is with Duke Health and Duke University, Durham, N.C. He was the Commissioner of Food and Drugs, Food and Drug Administration, from February 2016 to January 2017. He currently receives consulting payments from Merck and is employed as a scientific adviser by Verily Life Sciences (Alphabet).*

# CMS releases some good news for ASCs

CMS released the Medicare Inpatient Prospective Payment System (IPPS) final rule, which affects hospital payments and includes provisions for ambulatory surgery centers (ASCs) and physician payments.

Thanks to the AGA members who submitted comments to the proposed rule, CMS withdrew plans to publicly post facility accreditation reviews and correction plans. Below is a summary of AGA's position and where CMS landed on each issue.

**1. Public display of final accreditation surveys and plans of correction.**
Summary of AGA position – AGA urged CMS to withdraw its proposal making ASC accreditation surveys open to the public. To support shared transparency objectives, AGA recommended that if CMS were to finalize its proposal, the agency should first develop standards and a framework that considers both violation severity and scope.

CMS final rule – After consideration of the public comments received, CMS will not make ASC accreditation surveys open to the public. CMS was concerned that the suggestion to have accrediting organizations post their survey reports would appear as if it was attempting to circumvent current law, which prohibits CMS from disclosing survey reports or compelling the accrediting organizations to disclose the reports themselves.

**2. EHR Incentive Program certification requirements for payment year 2018.**
Summary of AGA position – AGA supported increased flexibility for 2018 and urged CMS to allow use of EHR technology certified to the 2014 software edition OR the 2015 software edition for the 2018 EHR Incentive Program.

CMS final rule – CMS will allow health care providers to use either 2014 or 2015 CEHRT or a combination of 2014 and 2015 CEHRT for the 2018 EHR Incentive Program.

**3. Exception for ASC-based physicians under the EHR Incentive Program for payment years 2017 and 2018.**
Summary of AGA position – AGA encouraged CMS to define ASC-based as a physician or other eligible professional who provides more than 50% of Medicare billed services in an ASC. AGA was concerned that implementing a higher threshold would leave certain physicians exposed to payment penalties, because the meaningful use requirement is set at 50% or more.

CMS final rule – Unfortunately, CMS set the definition of "ASC-based" as those who provide 75% of all services in an ASC, based on previous statutory definitions.

Policy changes are effective on Oct. 1, 2017, and changes to the 2017 and 2018 EHR Incentive Program apply immediately to the 2015 and 2016 reporting period, and provide relief that will impact 2017 and 2018 payments.

ginews@gastro.org

# Help make a difference – support AGA's Research Awards program


DR. DOUGAN

Many breakthroughs have been achieved through gastroenterological and hepatological research over the past century, forming the basis of the modern medical practice.

As the charitable arm of the American Gastroenterological Association (AGA), the AGA Research Foundation contributes to this tradition of discovery by providing a key source of funding at a critical juncture in a young researcher's career.

"The Research Scholar Award will have a pivotal effect on my future career," said Michael Dougan, MD, PhD, Massachusetts General Hospital, Boston, 2017 Research Scholar

*Continued on following page*

# AGA releases new clinical guideline on therapeutic drug monitoring in IBD

AGA has issued a new clinical guideline on the role of therapeutic drug monitoring (TDM) in the management of IBD, published in the September 2017 issue of *Gastroenterology*. The guideline focuses on the application of TDM for biologic therapy, specifically anti–tumor necrosis factor-alpha (TNF) agents and thiopurines, and addresses questions about the risks and benefits of reactive TDM, routine proactive TDM, or no TDM in guiding treatment changes. See adjacent table for some of AGA's recommendations.

The guideline is accompanied by a technical review, Clinical Decision Support Tool, and patient companion, which provides key points and important information directly to patients about this approach, written at an appropriate reading level. Access the patient companion in the Patient Info Center, www.gastro.org/IBD.

ginews@gastro.org

| Statement | Strength of recommendation | Quality of evidence |
|---|---|---|
| In adults with active IBD treated with anti-TNF agents, AGA suggests reactive TDM to guide treatment changes. | Conditional recommendation | Very low quality |
| In adult patients with quiescent IBD treated with anti-TNF agents, AGA makes no recommendation regarding the use of routine proactive TDM. | No recommendation | Knowledge gap |
| In adult patients with IBD being started on thiopurines, AGA suggests routine TPMT testing (enzymatic activity or genotype) to guide thiopurine dosing. | Conditional recommendation | Low quality |
| In adult patients treated with thiopurines with active IBD or adverse effects thought to be due to thiopurine toxicity, AGA suggests reactive thiopurine metabolite monitoring to guide treatment changes. | Conditional recommendation | Very low quality |
| In adult patients with quiescent IBD treated with thiopurines, AGA suggests against routine thiopurine metabolite monitoring. | Conditional recommendation | Very low quality |

# AGA comments on Quality Payment proposed rule

AGA provided comments on a proposed rule describing potential changes to the Quality Payment Program (QPP) established under the Medicare Access and CHIP Reauthorization Act (MACRA) for the 2018 performance year. AGA thanks the many members who also submitted comments to CMS to tell the agency how proposed changes will impact you.

For year two, CMS proposed many policies that increase flexibility and incentives under the QPP. However, many proposals target solo practitioners, small practices, and other eligible clinicians with special circumstances. While we support these proposals, AGA's comments to CMS also ask for changes that are needed to make the QPP work for all gastroenterologists, such as reducing the number of points needed to avoid a payment penalty.

CMS will finalize changes to the QPP during the fall of 2017. Final changes will take effect with the performance period that begins on Jan. 1, 2018. Performance during 2018 will impact payment for services in 2020. AGA members will be notified as soon as the rule is made available by CMS.

Still unsure how to participate in year one?

Make sure your practice is prepared for the 2017 performance year. If you are eligible to participate in 2017, but choose not to, your rates will decrease by 4% in 2019. AGA's MACRA resource center provides customized advice based on your practice situation to get you on track. It's not too late to start, but if you wait until Oct. 2, 2017, the deadline to start submitting claims, it will be. Get started now, http://www.gastro.org/macra.

ginews@gastro.org

*Continued from previous page*

Award recipient. "This award enables me to establish my own research infrastructure, and lay the experimental foundations for my future work as a clinician-scientist striving to understand the complex interplay between the immune system, metabolism, and cancer."

By joining others in donating to the AGA Research Foundation, you will help to foster a new pipeline of scientists – who will be the next generation of leaders in gastroenterology.

Please make a tax-deductible donation and help us keep the best and brightest investigators working in gastroenterology and hepatology. Donate at www.gastro.org/donateonline or by mail to AGA Research Foundation, 4930 Del Ray Avenue, Bethesda, MD 20814.

ginews@gastro.org

# AGA members meet with Rep. Gene Green at Baylor College

In-district meetings with congressional representatives provide a great opportunity for AGA members to establish working relationships with legislators, and help make the voices of our profession and our patients heard.

Members of the Baylor College of Medicine gastroenterology division – Avi Ketwaroo, MD; Richa Shukla, MD; Yamini Natarajan, MD; and Jordan Shapiro, MD – had the opportunity to meet with U.S. Rep. Gene Green, a Democrat from Texas' 29th Congressional District, as part of AGA's efforts to link constituents with local representatives. The group discussed the importance of supporting increases in NIH funding to maintain similar levels based on biomedical research inflation, the importance of screening colonoscopy, and improving access to care by opposing the repeal of the Affordable Care Act.

Watch an AGA webinar, available in the AGA Community resource library for AGA members only (community.gastro.org) to learn more about how to set up congressional meetings in your district or contact Navneet Buttar, AGA government and political affairs manager, at nbuttar@gastro.org or 240-482-3221.

ginews@gastro.org

AGA Institute

Pictured from left to right: Dr. Jordan Shapiro, Rep. Gene Green, Dr. Richa Shukla, and Dr. Yamini Natarajan.

# NASH did not increase risk of poor liver transplantation

BY AMY KARON
*Frontline Medical News*

Adults with nonalcoholic steatohepatitis (NASH) fared as well on key outcome measures as other liver transplant recipients, despite having significantly more comorbidities, according to the results of a single-center retrospective cohort study.

Major morbidity, mortality, and rates of graft survival after 90 days were similar between patients who underwent transplantation for NASH and those who underwent it for another cirrhotic liver condition, wrote Eline H. van den Berg, MD, of University Medical Center Groningen (the Netherlands) with her associates. "These results are comforting, considering the expected increase of patients with NASH cirrhosis in the near future," the researchers concluded. "Future analysis regarding the recurrence of nonalcoholic fatty liver disease, development of long-term complications, long-term graft patency, and occurrence of comorbid diseases after LT [liver transplantation] is mandatory to better understand the natural history and risk profile of NASH patients and to prevent and treat its complications." The findings were published online in Digestive and Liver Disease (2017 Aug 11. doi: 10.1016/j.dld.2017.08.022).

Nonalcoholic fatty liver disease begins as steatosis and can progress to NASH, fibrosis, and cirrhosis. The global obesity epidemic is amplifying its incidence, and about 26% of patients who develop NASH ultimately develop cirrhosis. Cirrhosis itself increases the risk of in-hospital death or prolonged length of postoperative stay, but patients with NASH also have obesity and cardiovascular disease, which might "tremendously increase" the risk of poor postoperative outcomes, the researchers said. Because prior research had focused mainly on mortality and had reported conflicting results, they used the Clavien-Dindo classification system to retrospectively study rates of complications among 169 adults who underwent liver transplantation at their center from 2009 through 2015, including 34 (20%) patients with NASH cirrhosis.

**Cirrhosis itself increases the risk of in-hospital death or prolonged length of postoperative stay, but patients with NASH also have obesity and cardiovascular disease, which might 'tremendously increase' the risk of poor postoperative outcomes.**

Patients with NASH were significantly older than other transplant recipients (59 versus 55 years, $P = .01$) and had markedly higher rates of obesity (62% versus 8%; $P$ less than .01), diabetes mellitus (74% versus 20%; $P$ less than .01), metabolic syndrome (83% versus 38%; $P$ less than .01), hypertension (61% versus 30%; $P$ less than .01), and cardiovascular disease (29% versus 11%; $P$ less than .01). Despite these differences, the groups had statistically similar rates of postoperative mortality (3% in both groups), 90-day graft survival post transplantation (94% and 90%, respectively), and major postoperative complications, including biopsy-proven acute cellular rejection (3% and 7%), hepatic artery thrombosis (0% and 7%), relaparotomy (15% and 24%), primary nonfunction (0% and 1.6%), retransplantation (6% and 7%), sepsis (12% and 13%), gastrointestinal infection (24% and 36%), fever of unknown origin (18% and 14%), and renal replacement therapy (15% and 24%).

After age, sex, transplant year, and donor characteristics were accounted for, NASH patients were at significantly increased risk of grade 2 urogenital infections, compared with other patients (odds ratio, 3.4; 95% confidence interval, 1.1-10.6; $P = .03$). Grade 1 complications also were more common with NASH than otherwise (77% versus 59%), and the difference remained statistically significant in the multivariable analysis (OR, 1.6; 95% CI, 1.03-2.63; $P = .04$).

The study used a strict, internationally accepted definition of NASH – all patients either had cases confirmed by biopsy, had metabolic syndrome, or had obesity and type 2 diabetes mellitus, and, further, none had hepatitis or alcoholic liver disease. None of the patients in the study received transplants for acute liver failure or noncirrhotic liver disease, and none were 70 years or older, which is the cutoff age for liver transplantation in the Netherlands.

The investigators received no funding for the study and reported having no conflicts of interest.

ginews@gastro.org

# More transplants at higher scores

**MELD** *from page 1*

40 would be futile," researchers led by Mitra K. Nadim, MD, reported in the September 2017 issue of the Journal of Hepatology (67[3]:517-25. doi: 10.1016/j.jhep.2017.04.022). "As a result, patients with MELD greater than 40 receive the same priority as patients with MELD of 40, differentiated only by their time on the wait list."

Despite the cap at 40, they went on to note that the number of patients transplanted with a MELD score greater than 40 has increased by nearly threefold since 2002, with the greatest rates seen in Organ Procurement and Transplantation Network (OPTN) regions 5 and 7. Region 5 includes Arizona, California, Nevada, New Mexico, and Utah, while region 7 includes Illinois, Minnesota, North Dakota, South Dakota, and Wisconsin. To determine the effect of capping the MELD score, Dr. Nadim of the division of nephrology and hypertension at the University of Southern California, Los Angeles, and her associates used United Network for Organ Sharing (UNOS) data to identify 65,776 patients listed for a liver transplant from February 2002 to December 2012. They followed the patients for 30 days to analyze the wait-list mortality and posttransplant outcomes of adult patients with MELD scores greater than 40, compared with patients who had MELD scores equal to 40.

The mean age of patients was 53 years, and most were white men. The researchers reported that 3.3% of wait-listed patients had a MELD score of 40 or greater at registration, while 7.3% had MELD scores increase to 40 or greater after wait-list registration. In all, 30,369 patients (40.6%) underwent liver transplantation during the study period. Of these, 2,615 (8.6%) had a MELD score of 40 or greater at the time of their procedure. Compared with patients who had a MELD score of 40, those who had a MELD score of greater than 40 had an increased risk of death within 30 days, and the risk increased with rising scores. Specifically, the hazard ratio was 1.4 for those with a MELD score of 40-44, an HR of 2.6 for those with a MELD score of 45-49, and an HR of 5.0 for those with a MELD score of 50 or greater. There were no survival differences between the two groups at 1 and 3 years, but there was a survival benefit associated with liver transplantation as the MELD score increased above 40, the investigators reported.

"The arbitrary capping of the MELD at 40 has resulted in an unforeseen lack of objectivity for patients with MELD [score of greater than] 40 who are unjustifiably disadvantaged in a system designed to prioritize patients most in need," they concluded. "Uncapping the MELD score is another necessary step in the evolution of liver allocation and patient prioritization." They added that a significant number of patients with a MELD score of 40 or greater "likely suffer from acute-on-chronic liver failure (ACLF), a recently recognized syndrome characterized by acute liver decompensation, other organ system failures, and high short-term mortality in patients with end-stage liver disease. A capped MELD score fails to capture acute liver decompensation adequately, and data suggest that a model incorporating sudden increases in MELD predicts wait-list mortality better."

Dr. Nadim and her associates acknowledged certain limitations of the study, including its retrospective design "and that factors relating to a patient's suitability for transplantation or to a center's decision to accept or reject a liver allograft, both of which affect graft and patient survival, were not accounted for in the analysis. Despite these limitations, the study results have important implications for improving the current liver allocation policy."

The study was supported in part by the Health Resources and Services Administration. The researchers reported having no relevant financial disclosures.

dbrunk@frontlinemedcom.com

# For first-line constipation therapy, stick with the leader



## The AGA recommends PEG laxatives (like MiraLAX) as a first-line constipation treatment[1]

- ✔ 96% patient satisfaction rate*
- ✔ #1 GI-recommended laxative for over 10 years

Start with MiraLAX for proven relief of occasional constipation.

MiraLAX®
Polyethylene Glycol 3350, Powder for Solution, Osmotic Laxative

***Doctor recommended, patient approved***

*Survey of 300 consumers, 2017.

Use as directed on product labeling or as directed by your doctor.

**Reference: 1.** Clinical decision support tools. American Gastroenterological Association website. http://campaigns.gastro.org/algorithms/constipation/index.html. Accessed May 12, 2017.

# Burden of HCV cirrhosis expected to shift to women

**BY ELI ZIMMERMAN**
*Frontline Medical News*

Prevalence of hepatitis C virus (HCV) complications among women grew at a rate similar to that of men, while mortality among men was nearly double that of women, according to a study conducted through the Veterans Affairs office.

While men still have a higher prevalence of conditions such as cirrhosis, investigators expect to see a shift in the burden of care as women with HCV complications outlive men with similar diagnoses.

"The current and near-term burden in HCV-related cirrhosis was disproportionately attributed to men," according to Jennifer Kramer, PhD, investigator at the Center for Innovations in Quality, Effectiveness and Safety, Michael E. DeBakey Veterans Affairs Medical Center, Houston. "However, the trends are expected to change after 2020."

**AGA Resource**
Through the HCV Clinical Service Line, AGA offers tools to help you become more efficient, understand quality standards and improve the process of care for patients. Learn more at http://www.gastro.org/patient-care/conditions-diseases/hepatitis-c

The retrospective cohort study analyzed 264,409 HCV-infected veterans, 7,162 of whom were women, between January 2000 and December 2013.

Investigators found annual average prevalence change (AAPC) among men and women was 13.1% and 15.2%, respectively, for cirrhosis, while overall mortality was 28.7% for men, compared with 15.5% for women (J Viral Hepat. 2017 Aug 16. doi: 10.1111/jvh.12728).

Dr. Kramer and her fellow investigators also found similar rates among those with decompensated cirrhosis between 15.6% and 16.9% for women and men, respectively, and hepatocellular carcinoma, 21% and 25.3%, respectively.

Women included in the cohort were, on average, younger (48 years vs. 53 years), were less likely to use alcohol (33% vs. 45%), and were less likely to have diabetes (30% vs. 39%).

While men's prevalence growth was equal to women's, male patients are 1.7 times more likely to be infected with HCV (J Hepatol. 2012 Jun 2. doi: 10.1016/j.jhep.2012.05.018), which is reflected in overall incidence rates of complications.

**'The increasing burden of HCV complications in women is concerning,' the researchers wrote. 'Studies show that women are less likely to receive antiviral treatment than men.'**

As expected, overall incidence of cirrhosis was higher in men than in women, with incidence rates for men at 28.2% compared with 20.1% for women.

Similar differences were found in rates of decompensated cirrhosis, 18.6% in men compared with 12.4% in women, and hepatocellular carcinoma, 5.3% in men compared with 1.5% in women.

Shifting trends in burden of care toward women have investigators worried about current HCV treatment practices for female patients.

"The increasing burden of HCV complications in women is concerning," the researchers wrote. "Studies show that women are less likely to receive antiviral treatment than men."

Contrary to this claim, antiviral treatment rates among men and women in this study were almost identical: 23.6% of women and 23.3% of men. While the difference in treatment is not evident, the low rate of treatment for both men and women is another concern for Dr. Kramer and her colleagues.

"In the U.S., HCV infection remains undiagnosed in over 50% of all persons with HCV disease," the investigators wrote. "Access to highly affective yet expensive direct-acting antiviral treatment remains a challenge."

Findings from this study may not be a true representation of the U.S. HCV-infected population because patients were veterans, with differences such as a higher rate of alcohol use among women.

The researchers reported no relevant financial disclosures.

ezimmerman@frontlinemedcom.com

## DDSEPeight Digestive Diseases Self-Education Program — Quick quiz

**Q1.** A 37-year-old man presents to the clinic with a 1-week history of diarrhea. He is a poultry farmer. His symptoms started with nausea and abdominal cramps. Subsequently, he developed diarrhea, reported as 10-12 loose stools with passage of blood. He also reported high fever. Abdominal examination revealed right lower quadrant abdominal tenderness. Stool cultures were ordered and came back positive for *Campylobacter* infection.

Which of the following medications is likely to help?
A. Azithromycin
B. Amoxicillin
C. Metronidazole
D. Trimethoprim-sulfamethoxazole
E. Cefixime

**Q2.** A 38-year-old man presents for evaluation of elevated liver enzymes. His past medical history is notable for being diagnosed with emphysema when he was 32 years old. He continues to smoke ½ pack of cigarettes per day and he drinks approximately five beers per day with binge drinking on weekends. He denies a history of drug use. His laboratory data are notable for the following: aspartate aminotransferase, 139 U/L; alanine aminotransferase, 76 U/L; total bilirubin, 0.8 mg/dL; alkaline phosphatase, 104 U/L; and serum albumin, 4.1 g/dL. Additional laboratory testing showed the following: HCV Ab, negative; HBsAg, negative; HBsAb, positive; HBc Total Ab, positive; alpha-1 antitrypsin phenotype, null/null; alpha-1 antitrypsin level, undetectable; antismooth muscle antibody, negative; antinuclear antibody, negative; ferritin, 114 mcg/L; iron saturation, 37%.

Hepatic ultrasound reveals an enlarged echogenic liver with patent portal and hepatic veins.

Which of the following is the most likely cause of the underlying liver disease?
A. Nonalcoholic steatohepatitis
B Chronic hepatitis B
C. Hereditary iron overload
D. Alpha-1 antitrypsin deficiency
E. Alcohol abuse

*The answers are on page 34.*

# FDA approves faster, pangenotypic cure for hep C

**BY WHITNEY MCKNIGHT**
*Frontline Medical News*

The first pangenotypic treatment for the hepatitis C virus (HCV), which also shaves 4 weeks off current regimens, has been approved by the Food and Drug Administration.

Manufactured by AbbVie, glecaprevir/pibrentasvir (Mavyret) combines a nonstructural protein 3/4A protease inhibitor with a next-generation NS5A protein inhibitor for a once-daily, ribavirin-free treatment for adults with any of the major genotypes of chronic HCV infection.

"This approval provides a shorter treatment duration for many patients, and also a treatment option for certain patients with genotype 1 infection, the most common HCV genotype in the United States, who were not successfully treated with other direct-acting antiviral treatments in the past," Edward Cox, MD, director of the office of antimicrobial products in the FDA's Center for Drug Evaluation and Research, Silver Spring, Md., said in a statement.

The 8-week regimen is indicated in patients without cirrhosis or with compensated cirrhosis, who are new to treatment, and those with limited treatment options, such as patients with chronic kidney disease, including those on dialysis. The intervention also is indicated in adults with HCV genotype 1 who have been treated with either of the drugs in the combination, but not both.

The safety and efficacy of the treatment were evaluated in approximately 2,300 adults with genotype 1, 2, 3, 4, 5, or 6 HCV infection without or with mild cirrhosis. In the clinical trials, 92%-100% of patients treated with glecaprevir/pibrentasvir for 8, 12, or 16 weeks had no detectable serum virus levels 12 weeks after finishing treatment. The most commonly reported adverse reactions were headache, fatigue, and nausea.

The FDA directs health care professionals to test all patients for hepatitis B virus (HBV) infection before starting this direct-acting antiviral drug combination since HBV reactivation has been reported in adult patients coinfected with both viruses who were undergoing or had completed treatment with HCV direct-acting antivirals and who were not receiving HBV antiviral therapy.

wmcknight@frontlinemedcom.com

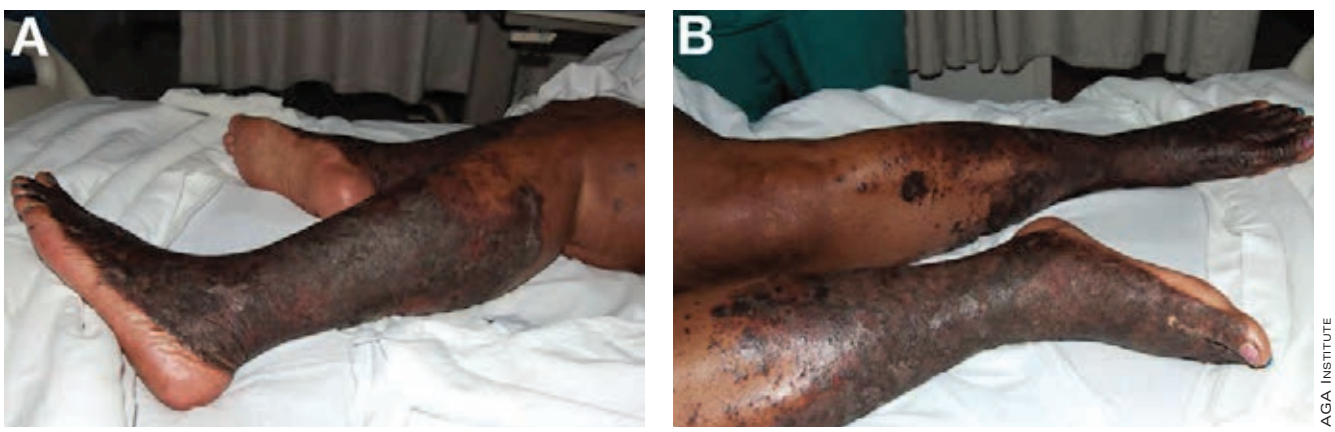
## CLINICAL CHALLENGES AND IMAGES

# What is your diagnosis?

*By Mazen Albeldawi, MD, Vivian Ebrahim, MD, and Dian Jung Chiang, MD. Published previously in Gastroenterology (2013;144[2]:275, 469).*

A 53-year-old woman with hepatitis C virus (HCV) cirrhosis was admitted to our inpatient service with several days of progressive bilateral lower extremity pruritus, accompanied by severe pain and parasthesias.

She had experienced intermittent pruritus for 2 years, but symptoms had become more severe in the 4 days before admission. Her pain was stabbing in nature and without radiation. Her pruritus has been refractory to multiple therapies including hydroxyzine, diphenhydramine, sertraline, cholestyramine, rifampin, naltrexone, topical steroids, and narrow-band ultraviolet B light therapy. She was hospitalized in March 2010 for a similar episode of intractable pruritus and pain, at which time she was diagnosed with lichen simplex chronicus. Plasmapheresis was attempted but abruptly stopped because of a blood stream infection. The patient was diagnosed with HCV cirrhosis (genotype 1A) in 2006 and was a nonresponder at 12 weeks to peginterferon-alpha and ribavirin therapy. Upon admission, her medications included sertraline 150 mg daily, hydroxyzine 25 mg 3 times daily, oxycodone-acetaminophen 5-325 mg every 4 hours, and clobetasol 0.05% ointment.



AGA Institute

On examination, hyperpigmented, lichenified plaques with erosions involving the bilateral lower extremities, extending from the calves to the dorsal aspect of both feet were noted (Figures A and B). These lesions were accompanied by desquamation, with signs of intense excoriation. Examination of a skin biopsy specimen revealed subacute psoriasiform dermatitis. Laboratory study revealed a serum HCV RNA titer of $1.4 \times 10^6$ IU/mL. What is the diagnosis and how would you treat this patient?

*The diagnosis is on page 42.*

WWW.GIHEPNEWS.COM

# GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

# Reminders are needed

**Outreach** *from page 1*

plete even if, for example, a patient in the colonoscopy arm eventually went on to have three consecutive annual FIT tests rather than a colonoscopy.

A total of 5,999 patients eligible for screening were initially randomized to one of the three study arms. Across all study arms, approximately half were lost to follow-up. These patients were excluded from the primary analysis but were included in an additional intention-to-screen analysis.

**Of the patients in the colonoscopy outreach group, 922 (38.4%) completed the screening process, compared with 671 (28.0%) in the FIT outreach group and 128 (10.7%) in the usual-care group.**

A total of 2,400 patients received a colonoscopy outreach mailing; 2,400 received FIT outreach, including a letter, the home FIT testing kit, and instructions; 1,199 received usual care. Patients in both intervention arms also received up to two phone calls if they didn't respond to the initial mailing within 2 weeks. Mailings and phone calls were conducted in English or Spanish, according to the patients' stated language preferences (those whose spoke neither language were excluded from the study).

Of the patients in the colonoscopy outreach group, 922 (38.4%) completed the screening process, compared with 671 (28.0%) in the FIT outreach group and 128 (10.7%) in the usual-care group.

Compared with the group receiving usual care, completion of the screening process was 27.7% higher in the colonoscopy outreach group and 17.3% higher in the FIT outreach group. Screening process completion was 10.4% higher for the colonoscopy outreach group, compared with the FIT outreach group (*P* less than .001 for all).

Dr. Singal, who is with the department of internal medicine at UT Southwestern Medical Center, Dallas, and his colleagues also performed several post-hoc secondary analyses. In one, they used a less-stringent definition of screening process completion in which biennial FIT testing was considered satisfactory. When this definition was applied, the colonoscopy outreach group had 0.5% lower screening process completion than the FIT outreach group. The chances of a patient receiving any screening during the study period was highest in the FIT group (65%), with 51.7% of those in the colonoscopy outreach group and 39% of those in the usual-care group receiving any screening.

"FIT has lower barriers to one-time participation but requires annual screening and diagnostic evaluation of abnormal results," wrote Dr. Singal and his colleagues.

Strengths of the study, said Dr. Singal and his colleagues, included the fact that the study took place at a "safety net" institution with a racially and socioeconomically diverse population. Also, the study design avoided volunteer bias, and offered a pragmatic head-to-head comparison of colonoscopy and FIT.

The second study took place in western France, and targeted outreach to physicians rather than patients (JAMA. 2017;318[9];816-84). When physicians were given a list of their own patients who were not up to date on CRC screening, investigators saw a small, but significant, uptick in patient participation in FIT screening.

One year after the reminders went out, FIT screening had been initiated in 24.8% of patients whose physicians had received the list, compared with 21.7% of patients of physicians who had received a more generic

*Continued on following page*

**AGA Resource**

The AGA Colorectal Cancer Clinical Service Line provides tools to help you become more efficient, understand quality standards, and improve the process of care for patients. Learn more at www.gastro.org/crc

PERSPECTIVE

## Systems change needed to increase CRC screening rates

Both studies, though they used different outreach interventions, highlight the same problem: the need to identify and execute effective colorectal cancer (CRC) screening programs. Effective screening has great lifesaving potential; if screening rates were elevated to greater than 80% in the United States, an estimated 200,000 deaths would be prevented within the next 2 decades.

The nature of CRC screening options means that a home fecal sample collection is inexpensive, and will result in an initial higher screening rate; however, complete screening via fecal occult blood testing requires annual repeats of negative tests, and patients with positive fecal occult blood tests still need colonoscopy.

Colonoscopy, although it's burdensome for patients and perhaps cost prohibitive for those without health insurance, offers a one-time test that, if negative, provides patients with a 10-year window of screening coverage.

Any effective programs to increase CRC screening rates will need to use a systems change approach, with creative interventions that take patient education, and even delivery of preventive health services, out of the context of the already too-full office visit.

Staff supports, such as the follow-up telephone calls used in the patient-targeted intervention, are key to effective interventions, especially for vulnerable populations. Additionally, institutions must ensure that they have adequate physical and staff resources to support the increased screening they are seeking to achieve.

*Michael Pignone, MD, MPH is a professor of medicine at the University of Texas at Austin. David Miller Jr., MD is a professor of internal medicine, Wake Forest University, Winston-Salem, N.C. Dr. Pignone is a medical director for Healthwise; Dr. Miller reported no relevant conflicts of interest. These remarks were drawn from an editorial accompanying the two clinical trials.*

# Less-invasive esophagectomy may mean less morbidity

**BY BRUCE JANCIN**
*Frontline Medical News*

COLORADO SPRINGS – Minimally invasive esophagectomy was associated with a significantly lower rate of postoperative major morbidity as well as a mean 1-day briefer length of stay than open esophagectomy in a propensity-matched analysis of the real-world American College of Surgeons–National Quality Improvement Program database, Mark F. Berry, MD, reported at the annual meeting of the Western Thoracic Surgical Association.

However, both of the study's discussants questioned whether the reported modest absolute reduction in major morbidity was really attributable to the minimally invasive approach or could instead have resulted from one of several potential confounders that couldn't be fully adjusted for, given inherent limitations of the ACS-NSQIP database.

"There was a statistically significant difference in morbidity," replied Dr. Berry of Stanford (Calif.) University. "It was a 4% absolute difference, which I think is probably clinically meaningful, but certainly it's not really, really dramatic."

"What I think we found is that it's safe to do a minimally invasive esophagectomy and safe for people to introduce it into their practice. But it's not necessarily something that's a game changer, unlike what's been seen with minimally invasive approaches for some other things," said Dr. Berry, who added that he didn't wish to overstate the importance of the observed difference in morbidity.

Studies from high-volume centers show that minimally invasive esophagectomy (MIE) reduces length of stay, postoperative major morbidity, and features equivalent or even slightly lower mortality than traditional open esophagectomy, the generalizability of these findings beyond such centers is questionable. That's why Dr. Berry and his coinvestigators turned to the ACS-NSQIP database, which includes all esophagectomies performed for esophageal cancer at roughly 700 U.S. hospitals, not just those done by board-certified thoracic surgeons.

Bruce Jancin/Frontline Medical News

Dr. Mark F. Berry, of Stanford University said that the results show that mininally-invasive esophagectomy is safe.

He presented a retrospective cohort study of 3,901 esophagectomy patients during 2005-2013 who met study criteria, 16.4% of whom had MIE. The use of this approach increased steadily from 6.5% of all esophagectomies in 2005 to 22.3% in 2013. A propensity-matched analysis designed to neutralize potentially confounding differences included 638 MIE and 1,914 open esophagectomy patients.

The primary outcome was the 30-day rate of composite major morbidity in the realms of various wound, respiratory, renal, and cardiovascular complications. The rate was 36.1% in the MIE group and 40.5% with open esophagectomy in the propensity-matched analysis, an absolute risk reduction of 4.4% and a relative risk reduction of 17%. Although rates were consistently slightly lower in each of the categories of major morbidity, those individual differences didn't achieve statistical significance. The difference in major morbidity became significant only when major morbidity was considered as a whole.

Mean length of stay was 9 days with MIE and 10 days with open surgery.

There was no significant difference between the two study groups in 30-day rates of readmission, reoperation, or mortality.

Discussant Donald E. Low, MD said "esophagectomy is being analysed regarding its place in all sorts of presentations, stages, and situations, so the aspect of making sure that we're delivering the services as efficiently as possible is going to become more important, not less important." That being said, he noted that there is no specific CPT code for MIE. That raises the possibility of an uncertain amount of procedural misclassification in the ACS-NSQIP database.

Also, the only significant difference in major morbidity between the two study groups was in the subcategory of intra- or postoperative bleeding requiring transfusion, which occurred in 10.8% of the MIE and 16.7% of the open esophagectomy groups, observed Dr. Low, director of the Esophageal Center of Excellence at Virginia Mason Medical Center, Seattle.

"Some of us believe that blood utilization and transfusion requirement is really a quality measure and not a complication," the surgeon said. And if that outcome is excluded from consideration, then there is no significant difference in major morbidity.

Discussant Douglas E. Wood, MD, professor and chair of the department of surgery at the University of Washington, Seattle, took the opportunity to share a self-described "pet peeve" about analyses of national surgical databases: these databases typically don't contain key details necessary to correct for provider and hospital characteristics.

"The small differences that you demonstrate could easily have been completely driven by providers who choose to do minimally invasive esophagectomy and are in higher-volume, more specialized centers," he said. "I'm not convinced of your conclusion that MIE produces less morbidity based on a 4% difference and no analysis of provider characteristics."

bjancin@frontlinemedcom.com

*Continued from previous page*

notice and 20.6% of patients whose physicians received no notification, according to first author Cedric Rat, MD, and his colleagues.

The study examined which notification approach was most effective in increasing FIT screening among the physicians' patient panels: sending general practitioners (GPs) letters that included a list of their own patients who had not undergone CRC screening, or sending them generic letters describing CRC screening adherence rates specific to their region. A usual-care group of practices received no notifications in this three-group randomized cluster design.

Patients in the patient-specific reminders group had an odds ratio of 1.27 for participation in FIT screening (*P* less than .001) compared to the usual-care group. The odds ratio for the generic-reminders group was 1.09, a nonsignificant difference.

Between-group comparison showed statistical significance for both the 3.1% difference between the patient-specific and generic-reminders groups, and for the 4.2% difference between the patient-specific and usual-care groups (*P* less than .001 for both). There was no significant difference between the generic-reminders group and the usual-care group.

Dr. Rat, professor of medicine at the Faculty of Medicine, Nantes, France, and his colleagues enrolled GPs in a total of 801 practices that included patients aged 50. Participating GPs cared for 33,044 patients who met study criteria.

Physician characteristics that were associated with higher FIT participation included younger age and an initially smaller number of unscreened patients. Patients with low socioeconomic status and those with a higher chronic disease burden were less likely to participate in FIT screening.

Dr. Rat and his colleagues noted that the busiest practices actually had higher CRC screening rates. The investigators hypothesized that a recent physician pay-for-performance grant for CRC completion might be more appealing for some busy physicians.

This was the largest study of CRC screening participation to date, according to Dr. Rat and his coauthors, and showed the small but detectable efficacy of an inexpensive intervention that, given complete patient records, is relatively easy to effect. Though the effect size was smaller than the 12% difference the investigators had anticipated seeing for the patient-specific reminders group, the study still showed that targeting physicians can be an effective public health intervention to increase CRC screening rates, said Dr. Rat and his colleagues.

None of the investigators in either study reported conflicts of interest.

koakes@frontlinemedcom.com


# The prep experience patients want. The efficacy you need.

**PREPOPIK® is an effective colonoscopy prep that is easy for patients to take –** with the lowest volume of medicine (10 oz), a choice of flavors, and a flexible hydration schedule.[1-4] **And PREPOPIK® gives you the results you want to see.**

## Demonstrated efficacy[5*]

PREPOPIK® provided excellent or good visualization of the colon

**Primary endpoint[5]:**

**84%**

**of patients taking the Split-Dose Regimen**

– vs only 74% of those taking a comparator

– In clinical trials, the most common adverse reactions associated with PREPOPIK® were nausea, headache, and vomiting

**Secondary endpoint[5]:**

**90% or more**

**of patients taking the Split-Dose Regimen achieved response in the ascending, mid, and rectosigmoid colon**

– vs only 79%, 86%, and 87%, respectively, of those taking a comparator

## Preferred by patients in a clinical trial[5*]

In the split-dose trial, patients preferred PREPOPIK® vs a Day-Before comparator[5*]

**99%**

**successfully finished their PREPOPIK® regimen**

– vs only 91% of patients who finished a comparator prep

**96%**

**would choose PREPOPIK® again**

– vs only 55% of patients who would choose the comparator prep again

*SEE CLEAR I was a phase 3, randomized, multicenter, assessor-blinded, active-controlled, noninferiority study in adult patients preparing for colonoscopy. The primary endpoint was overall colon cleansing with PREPOPIK® vs a Day-Before regimen of a comparator (2L PEG+E plus 2 x 5 mg bisacodyl tablets) using a modified Aronchick scale. The primary efficacy endpoint was the proportion of patients with successful colon cleansing, defined as bowel preparations with >90% of the mucosa seen and mostly liquid stool, assessed by blinded colonoscopists. The secondary endpoints were the quality of cleansing of the ascending, mid (transverse and descending), and rectosigmoid segments of the colon using the Ottawa scale. Patients were also required to complete a questionnaire about orange-flavored PREPOPIK®, which included the questions: "Would you ask your doctor for this preparation again if you needed another colonoscopy?" and "How easy or difficult was it to consume the prescribed bowel preparation?"

## Indication and Important Safety Information

**PREPOPIK® for oral solution is indicated for cleansing of the colon as a preparation for colonoscopy in adults.**

- PREPOPIK® is contraindicated in the following conditions: patients with severely reduced renal function, gastrointestinal obstruction or ileus, bowel perforation, toxic colitis or toxic megacolon, gastric retention, or in patients with a known allergy to any of the ingredients in PREPOPIK®.
- Patients should be advised on the importance of adequate hydration, and post-colonoscopy lab tests should be considered if a patient develops significant vomiting or signs of dehydration after taking PREPOPIK®. Patients with electrolyte abnormalities should have them corrected before treatment. Use caution when prescribing for patients who are at risk for seizures, or arrhythmias, including those patients with a history of prolonged QT, recent myocardial infarction, unstable angina, congestive heart failure, or cardiomyopathy.
- Caution should be used in patients with impaired gag reflex, regurgitation or aspiration, severe active ulcerative colitis, impaired renal function or patients taking medications that may affect renal function, electrolyte imbalance and/or water retention.
- Osmotic laxatives may produce colonic mucosal aphthous ulcerations and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Concurrent use of additional stimulant laxatives with PREPOPIK® may increase this risk.
- PREPOPIK® should not be used if gastrointestinal obstruction or perforation is suspected.
- PREPOPIK® is not for direct ingestion. Each packet must be dissolved in 5 ounces of cold water and administered at separate times, in addition to additional clear fluids, according to the dosing regimen.
- In randomized, multicenter, controlled clinical trials, nausea, headache, and vomiting were the most common treatment-emergent adverse reactions (>1%) following PREPOPIK® administration.
- Oral medication administered within one hour of the start of administration of PREPOPIK® solution may be flushed from the GI tract and the medication may not be absorbed. Prior or concomitant use of antibiotics with PREPOPIK® may reduce its efficacy. Tetracycline and fluoroquinolone antibiotics, iron, digoxin, chlorpromazine and penicillamine, should be taken at least 2 hours before and not less than 6 hours after administration of PREPOPIK® to avoid chelation with magnesium.

You are encouraged to report negative side effects of prescription drugs to FDA. Visit www.FDA.gov/medwatch, or call 800.FDA.1088

**Please see brief summary of Prescribing Information following this advertisement.**

**References: 1.** PREPOPIK® [Prescribing Information]. Parsippany, NJ: Ferring Pharmaceuticals Inc. **2.** HalfLytely® [Prescribing Information]. Braintree, MA: Braintree Laboratories, Inc. **3.** MoviPrep® [Prescribing Information]. Bridgewater, NJ: Salix Pharmaceuticals, Inc. **4.** Suprep® [Prescribing Information]. Braintree, MA: Braintree Laboratories, Inc. **5.** Rex DK, Katz PO, Bertiger G, et al. Split-dose administration of a dual-action, low-volume bowel cleanser for colonoscopy: the SEE CLEAR I study. *Gastrointest Endosc.* 2013;78(1):132-141.

FERRING PHARMACEUTICALS



**Prepopik®**
(sodium picosulfate, magnesium oxide, and anhydrous citric acid) for oral solution
10 mg/3.5 g/12 g per packet

# Prepopik®

## (sodium picosulfate, magnesium oxide, and anhydrous citric acid) for oral solution 10 mg/3.5 g/12 g per packet

**BRIEF SUMMARY: Consult the Full Prescribing Information for complete product information.**

**PREPOPIK®** (sodium picosulfate, magnesium oxide, and anhydrous citric acid) for oral solution

### INDICATIONS AND USAGE

PREPOPIK® (sodium picosulfate, magnesium oxide and anhydrous citric acid) for oral solution is indicated for cleansing of the colon as a preparation for colonoscopy in adults.

### CONTRAINDICATIONS

PREPOPIK® is contraindicated in the following conditions:

- Patients with severely reduced renal function (creatinine clearance less than 30 mL/minute ) which may result in accumulation of magnesium [see Warnings and Precautions)]
- Gastrointestinal obstruction or ileus [see Warnings and Precautions]
- Bowel perforation
- Toxic colitis or toxic megacolon
- Gastric retention
- An allergy to any of the ingredients in PREPOPIK®

### WARNINGS AND PRECAUTIONS

#### Serious Fluid and Serum Chemistry Abnormalities

Advise patients to hydrate adequately before, during, and after the use of PREPOPIK®. Use caution in patients with congestive heart failure when replacing fluids. If a patient develops significant vomiting or signs of dehydration including signs of orthostatic hypotension after taking PREPOPIK®, consider performing post-colonoscopy lab tests (electrolytes, creatinine, and BUN) and treat accordingly. Approximately 20% of patients in both arms (PREPOPIK®, 2L of PEG + E plus two x 5-mg bisacodyl tablets) of clinical trials of PREPOPIK® had orthostatic changes (changes in blood pressure and/or heart rate) on the day of colonoscopy. In clinical trials orthostatic changes were documented out to seven days post colonoscopy. [see Adverse Reactions]

Fluid and electrolyte disturbances can lead to serious adverse events including cardiac arrhythmias or seizures and renal impairment. Fluid and electrolyte abnormalities should be corrected before treatment with PREPOPIK®. In addition, use caution when prescribing PREPOPIK® for patients who have conditions or who are using medications that increase the risk for fluid and electrolyte disturbances or that may increase the risk of adverse events of seizure, arrhythmia, and renal impairment.

#### Seizures

There have been reports of generalized tonic-clonic seizures with the use of bowel preparation products in patients with no prior history of seizures. The seizure cases were associated with electrolyte abnormalities (e.g., hyponatremia, hypokalemia, hypocalcemia, and hypomagnesemia) and low serum osmolality. The neurologic abnormalities resolved with correction of fluid and electrolyte abnormalities.

Use caution when prescribing PREPOPIK® for patients with a history of seizures and in patients at risk of seizure, such as patients taking medications that lower the seizure threshold (e.g., tricyclic antidepressants), patients withdrawing from alcohol or benzodiazepines, patients with known or suspected hyponatremia. [see Adverse Reactions]

#### Use in Patients with Renal Impairment

As in other magnesium containing bowel preparations, use caution when prescribing PREPOPIK® for patients with impaired renal function or patients taking concomitant medications that may affect renal function (such as diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or non-steroidal anti-inflammatory drugs). These patients may be at increased risk for renal injury. Advise these patients of the importance of adequate hydration before, during and after the use of PREPOPIK®. Consider performing baseline and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients. In patients with severely reduced renal function (creatinine clearance < 30 mL/min), accumulation of magnesium in plasma may occur.

#### Cardiac Arrhythmias

There have been rare reports of serious arrhythmias associated with the use of ionic osmotic laxative products for bowel preparation. Use caution when prescribing PREPOPIK® for patients at increased risk of arrhythmias (e.g., patients with a history of prolonged QT, uncontrolled arrhythmias, recent myocardial infarction, unstable angina, congestive heart failure, or cardiomyopathy). Pre-dose and post-colonoscopy ECGs should be considered in patients at increased risk of serious cardiac arrhythmias.

#### Colonic Mucosal Ulceration, Ischemic Colitis and Ulcerative Colitis

Osmotic laxatives may produce colonic mucosal aphthous ulcerations and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Concurrent use of additional stimulant laxatives with PREPOPIK® may increase this risk. The potential for mucosal ulcerations should be considered when interpreting colonoscopy findings in patients with known or suspected inflammatory bowel disease. *[see Adverse Reactions]*

#### Use in Patients with Significant Gastrointestinal Disease

If gastrointestinal obstruction or perforation is suspected, perform appropriate diagnostic studies to rule out these conditions before administering PREPOPIK®. Use with caution in patients with severe active ulcerative colitis.

#### Aspiration

Patients with impaired gag reflex and patients prone to regurgitation or aspiration should be observed during the administration of PREPOPIK®. Use with caution in these patients.

#### Not for Direct Ingestion

Each packet must be dissolved in 5 ounces of cold water and administered at separate times according to the dosing regimen. Ingestion of additional water is important to patient tolerance. Direct ingestion of the undissolved powder may increase the risk of nausea, vomiting, dehydration, and electrolyte disturbances.

### 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 clinical trials of another drug and may not reflect the rates observed in practice.

In randomized, multicenter, controlled clinical trials, nausea, headache, and vomiting were the most common adverse reactions (>1%) following PREPOPIK® administration. The patients were not blinded to the study drug. Since abdominal bloating, distension, pain/cramping, and watery diarrhea are known to occur in response to colon cleansing preparations, these effects were documented as adverse events in the clinical trials only if they required medical intervention (such as a change in study drug or led to study discontinuation, therapeutic or diagnostic procedures, met the criteria for a serious adverse event), or showed clinically significant worsening during the study that was not in the frame of the usual clinical course, as determined by the investigator.

PREPOPIK® was compared for colon cleansing effectiveness with a preparation containing two liters (2L) of polyethylene glycol plus electrolytes solution (PEG + E) and two 5-mg bisacodyl tablets, all administered the day before the procedure. Table 1 displays the most common adverse reactions in Study 1 and Study 2 for the PREPOPIK® Split-Dose and Day-Before dosing regimens, respectively, each as compared to the comparator preparation.

**Table 1: Treatment-Emergent Adverse Reactions observed in at Least (>1%) of Patients using the Split-Dose Regimen and Day-Before Regimen ****

| Adverse Reaction | Study 1: Split-Dose Regimen | | Study 2: Day-Before Regimen | |
|---|---|---|---|---|
| | PREPOPIK® (N=305) n (% = n/N) | 2L PEG+E* with 2 x 5-mg bisacodyl tablets (N=298) n (% = n/N) | PREPOPIK® (N=296) n (% = n/N) | 2L PEG+E* with 2 x 5-mg bisacodyl tablets (N=302) n (% = n/N) |
| Nausea | 8 (2.6) | 11 (3.7) | 9 (3.0) | 13 (4.3) |
| Headache | 5 (1.6) | 5 (1.7) | 8 (2.7) | 5 (1.7) |
| Vomiting | 3 (1.0) | 10 (3.4) | 4 (1.4) | 6 (2.0) |

* 2L PEG + E = two liters polyethylene glycol plus electrolytes solution.
**abdominal bloating, distension, pain/cramping, and watery diarrhea not requiring an intervention were not collected

#### Electrolyte Abnormalities

In general, PREPOPIK® was associated with numerically higher rates of abnormal electrolyte shifts on the day of colonoscopy compared to the preparation containing 2L of PEG + E plus two x 5-mg bisacodyl tablets. These shifts were transient in nature and numerically similar between treatment arms at the Day 30 visit.

#### Postmarketing Experience

The following foreign spontaneous reports have been identified during use of formulations similar to PREPOPIK®. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

*Allergic reactions*

Cases of hypersensitivity reactions including rash, urticaria, and purpura have been reported.

*Electrolyte abnormalities*

There have been reports of hypokalemia, hyponatremia and hypermagnesemia with the use of PREPOPIK® for colon preparation prior to colonoscopy.

*Gastrointestinal:*

Abdominal pain, diarrhea, fecal incontinence, and proctalgia have been reported with the use of PREPOPIK® for colon preparation prior to colonoscopy. There have been isolated reports of reversible aphthoid ileal ulcers. Ischemic colitis has been reported with the use of PREPOPIK® for colon preparation prior to colonoscopy. However, a causal relationship between these ischemic colitis cases and the use of PREPOPIK® has not been established.

*Neurologic*

There have been reports of generalized tonic-clonic seizures associated with and without hyponatremia in epileptic patients.

### DRUG INTERACTIONS

#### Drugs That May Increase Risks of Fluid and Electrolyte Abnormalities

Use caution when prescribing PREPOPIK® for patients with conditions or who are using medications that increase the risk for fluid and electrolyte disturbances or may increase the risk of seizure, arrhythmias, and prolonged QT in the setting of fluid and electrolyte abnormalities. This includes patients receiving drugs which may be associated with hypokalemia (such as diuretics or corticosteroids, or drugs where hypokalemia is a particular risk, such as cardiac glycosides) or hyponatremia. Use caution when PREPOPIK® is used in patients on non-steroidal anti-inflammatory drugs (NSAIDS) or drugs known to induce Antidiuretic Hormone Secretion (SIADH), such as tricyclic antidepressants, selective serotonin re-uptake inhibitors, antipsychotic drugs and carbamazepine, as these drugs may increase the risk of water retention and/or electrolyte imbalance. Consider additional patient evaluations as appropriate. *[see Adverse Reactions]*

#### Potential for Altered Drug Absorption

Oral medication administered within one hour of the start of administration of PREPOPIK® solution may be flushed from the GI tract and the medication may not be absorbed.

Tetracycline and fluoroquinolone antibiotics, iron, digoxin, chlorpromazine and penicillamine, should be taken at least 2 hours before and not less than 6 hours after administration of PREPOPIK® to avoid chelation with magnesium.

#### Antibiotics

Prior or concomitant use of antibiotics with PREPOPIK® may reduce efficacy of PREPOPIK® as conversion of sodium picosulfate to its active metabolite BHPM is mediated by colonic bacteria.

### USE IN SPECIFIC POPULATIONS

#### Pregnancy

Pregnancy Category B

Reproduction studies with PREPOPIK® have been performed in pregnant rats at oral doses up to 2000 mg/kg/day (about 1.2 times the recommended human dose based on the body surface area), and did not reveal any evidence of impaired fertility or harm to the fetus due to PREPOPIK®. The reproduction study in rabbits was not adequate, as treatment-related mortalities were observed at all doses. A pre and postnatal development study in rats showed no evidence of any adverse effect on pre and postnatal development at oral doses up to 2000 mg/kg twice daily (about 1.2 times the recommended human dose based on the body surface area). There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, PREPOPIK® should be used during pregnancy only if clearly needed.

#### Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when PREPOPIK® is administered to a nursing woman.

#### Pediatric Use

The safety and effectiveness of PREPOPIK® in pediatric patients has not been established.

#### Geriatric Use

In controlled clinical trials of PREPOPIK®, 215 of 1201 (18%) patients were 65 years of age or older. The overall incidence of treatment-emergent adverse events was similar among patients ≥65 years of age (73%) and patients <65 years of age (71%). Among all patients ≥65 years of age, the proportion of patients with successful colon cleansing was greater in the PREPOPIK® group (81.1%) than in the comparator group (70.9%).

#### Renal Insufficiency

Patients with impaired renal function or patients taking concomitant medications that may affect renal function (such as diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or non-steroidal anti-inflammatory drugs) may be at increased risk for further renal injury. Advise these patients of the importance of adequate hydration before, during and after the use of PREPOPIK®. Consider performing baseline and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients. In patients with severely reduced renal function (creatinine clearance < 30 mL/min), accumulation of magnesium in plasma may occur. The signs and symptoms of hypermagnesemia may include, but are not limited to, diminished or absent deep tendon reflexes, somnolence, hypocalcemia, hypotension, bradycardia, muscle, respiratory paralysis, complete heart block, and cardiac arrest.

### OVERDOSAGE

The patient who has taken an overdose should be monitored carefully, and treated symptomatically for complications.

Toll free number for providers and patients to call with questions:
1-(888)-FERRING (1-(888)-337-7464)

Rx only

MANUFACTURED FOR:

FERRING PHARMACEUTICALS

FERRING PHARMACEUTICALS INC.
Parsippany, NJ 07054



Based on 8109000012

Rev 02/2017 PK/069/2014/US(2)

# ADRs highest among GIs, women, early-career docs

BY AMY KARON
*Frontline Medical News*

Gastroenterologists, female physicians, and physicians who were less than a decade out of residency had significantly higher adenoma detection rates (ADRs) than their counterparts in a retrospective cohort study of colonoscopists.

"Efforts to target physicians with lower-quality performance are needed," wrote Ateev Mehrotra, MD, MPH, of Harvard Medical School in Boston, with his associates. The study, one of the first to use natural language processing to compare electronic health data from geographically diverse health care systems, was published online in Gastrointestinal Endoscopy (2017 Aug 30. doi: 10.1016/j.gie.2017.08.023).

Physicians are known to have varying ADRs, but underlying reasons remain unclear. Specialty training and caseload have shown varying effects across studies, and differences in patient populations also seem to play a role, the researchers said. Because most attempts to improve ADRs have failed, they looked for predictors of better performance by using natural language–processing software to study all 104,618 outpatient colonoscopy reports and pathology reports from adults aged 40 years and older who were seen between 2013 and 2015 at Kaiser Permanente Washington in Wash. state, Central Illinois Endoscopy Center in Peoria, the University of North Carolina at Chapel Hill, and University of Pittsburgh Medical Center. Among the 201 physicians in the study, all performed at least 30 colonoscopies during this period, and the analytic software was validated in a sample of more than 2,100 colonoscopy and pathology reports that were manually cross-checked. The overall ADR was 33% (range, 6%-59%), said the investigators. Gastroenterologists had an average ADR that was 9.6 percentage points higher than the ADRs of nongastroenterologists (*P* less than .001), physicians who were no more than 9 years out of residency averaged 6 percentage points higher than physicians with 27-51 years of practice (*P* = .004), and female physicians had ADRs that averaged 3.8 percentage points higher than men (*P* = .02). After controlling for patients' age, sex, and colonoscopy indication, Dr. Mehrotra and his associates found that female endoscopists had about a 26% greater odds of detecting an adenoma than did male endoscopists, gastroenterologists had about a 71% greater odds of adenoma detection than did nongastroenterologists, and physicians with 9 or fewer years of practice had about a 45% greater odds of adenoma detection than did more experienced physicians.

These associations persisted among patients who received only screening colonoscopies, who had complete colonoscopies with adequate bowel preparation, or who were younger than 80 years, the researchers said. "A deliberate and meticulous approach to colonoscopy may facilitate achievement of a high ADR, and this method may be more common among female physicians," they wrote. "This is supported by research showing that female physicians are more likely to adhere to clinical guidelines and to provide preventive care." Studies of men in other fields have found them more likely to take risks, which contradicts the methodical approach needed for a high ADR, they emphasized. "Sex differences in color perception [also] may make it easier for female physicians to identify adenomas."

Likewise, research outside gastroenterology has linked fewer years in practice with better quality of care. Improvements in fellowship training, better access to new equipment, "or simply decay of performance with age" all could explain the findings, the researchers wrote. They also cited five prior studies in which nongastroenterologists had lower ADRs. They called for studies that would further explore the reasons why specific physician traits affect performance.

Physicians in the study tended to have practiced fewer years than gastroenterologists in general in the United States, the investigators noted. "We also could not measure some other physician factors that might explain some of the variation we observed, such as type of endoscopes used."

The National Cancer Institute provided funding. The researchers did not report having conflicts of interest.

ginews@gastro.org

AGA POSTGRADUATE COURSE

# Love the liver

BY ANNA RUTHERFORD, MD, MPH

The "Love the liver" session included talks from experts in viral hepatitis, alcoholic liver disease, autoimmune and cholestatic liver disease, nonalcoholic fatty liver disease (NAFLD), and hepatocellular carcinoma (HCC).

Robert S. Brown Jr., MD, MPH, AGAF, discussed hepatitis C as the most common cause of viral death in the United States, and up to three-fourths of patients with chronic hepatitis C are not aware they are infected. CDC guidelines now recommend everyone born between 1945 and 1965 be screened once for HCV. Interferon-free, all-oral therapy for hepatitis C is now available for all genotypes, with few side effects and cure rates greater than 95%. There have been case reports of reactivation of hepatitis B in the setting of HCV treatment with direct-acting antivirals. Anyone undergoing HCV therapy should be screened for chronic hepatitis B infection and monitored for reactivation during treatment.

Michael R. Lucey, MD, characterized alcoholic liver disease as having two entities: alcohol use disorder and alcoholic liver disease. The primary treatment involves abstinence from alcohol. Baclofen is the only pharmacotherapy that helps control drinking in alcohol-related cirrhotic patients.


DR. RUTHERFORD

Keith Lindor, MD, AGAF, spoke about autoimmune and cholestatic liver disease. Only ursodeoxycholic acid and obeticholic acid have been shown to be effective for primary biliary cholangitis. Primary sclerosing cholangitis (PSC) coexists in about 7.4% of patients with inflammatory bowel disease. There are no currently recommended treatments for PSC, although emerging treatments include altering the microbiome, vancomycin, and obeticholic acid. When comparing induction treatment for autoimmune hepatitis with prednisone 40 mg/day and taper versus budesonide 3 mg t.i.d., budesonide was more effective at normalizing aspartate aminotransferase and alanine aminotransferase within 6 months of treatment.

Rohit Loomba, MD, discussed that 20% of patients with nonalcoholic steatohepatitis (NASH) are "fast progressors," meaning they will progress to cirrhosis within 10 years from diagnosis. MR elastography is the best noninvasive test for detecting fibrosis stage and advanced fibrosis in NAFLD and also can quantify steatosis grade. Lifestyle changes are the best current treatments for NAFLD and NASH: 5%-7% weight loss can improve NASH, and 10% weight loss can resolve NASH.

The four agents in most advanced stages of clinical trials for NAFLD and NASH include obeticholic acid, elafibranor, liraglutide, and cenicriviroc.

Lewis R. Roberts, MD, ChB, PhD, AGAF, closed with a discussion of HCC. Primary etiologies of liver disease leading to HCC vary throughout the world, with hepatitis C and NAFLD being major contributors in the United States. Worldwide, the variability in screening for hepatocellular carcinoma ranges from virtually no screening in countries in Africa, to well-established screening programs in Taiwan and Japan; this geographic variability has a direct impact on stage at diagnosis and overall patient survival. Recently updated American Association for the Study of Liver Diseases guidelines support use of ultrasound with or without alpha-fetoprotein for HCC surveillance in all cirrhotic patients and in patients with chronic hepatitis B (Hepatology. 2017 Jan 28. doi: 10.1002/hep.29086).

*Dr. Rutherford is clinical director of hepatology, Brigham & Women's Hospital, assistant professor of medicine, Harvard Medical School, Boston.*

# Bringing up the rear: Disorders of the rectum and colon

BY DAVID E. COHEN, MD, PHD, AGAF

The final session of the course opened with Uri Ladabaum, MD, entertaining the question "Colon cancer screening and surveillance: who, when, and how?" Dr. Ladabaum pointed out that there is consensus that colorectal cancer screening for average-risk individuals should begin at age 50 with a choice of modalities and that surveillance depends on the findings on each colonoscopy. He reviewed the evidence for screening modalities and for surveillance and offered perspectives on the role of the gastroenterologist/colonoscopist in the quality of colonsocopy. Douglas K. Rex, MD, AGAF followed by asking "Does every big polyp need EMR?" Dr. Rex discussed the available approaches to the large colonic polyp, including endoscopic mucosal resection, endoscopic submucosal dissection, and surgery. He provided evidence for the advantages and expanded use of EMR, with the conclusion that almost every large benign polyp needs EMR.

Asyia Ahmad, MD followed with a talk entitled, "When in Rome: Update on the Rome IV criteria for functional bowel disorders." Dr. Ahmed explained that the 2016 Rome IV classification of functional GI disorders describes a spectrum of disorders instead of the distinct ones in Rome III. Additionally, the importance of culture and language is now taken into account, with descriptions of symptoms that occur in these contexts. Novel areas of research and concepts comprise biopsychosocial, clinical applications, the patient-physician relationship, and therapies aimed at brain-gut interactions. Such therapies include cognitive-behavioral therapy, hypnosis, relaxation techniques, psychodynamic therapy, biofeedback, and mindfulness.

DR. COHEN

Jennifer A. Christie, MD, then spoke on "Pelvic floor dysfunction and constipation." Dr. Christie stressed the importance of a good history and the digital rectal exam in diagnosis of pelvic floor dysfunction. When over-the-counter or prescribed medications are not effective, the work-up should include anorectal manometry, balloon expulsion, and colonic transit testing. Attempts should be made to remove all potential offending agents, such as anticholinergics, narcotics, calcium channel blockers, and beta-blockers. Biofeedback is a safe and effective treatment for pelvic floor dysfunction. Lin Chang, MD, AGAF, continued with a talk on irritable bowel syndrome, which can be considered a combination of disorders, with clusters of symptoms and subgroups. There must be recurrent abdominal pain or discomfort at least 1 day/week for the prior 3 months, associated with 2 or more of the following: a relationship to defecation, change in stool frequency, or stool form/appearance. Risk includes genetic and environmental factors, stress/abuse, and acute gastroenteritis. After a structured evaluation, a graded treatment response is undertaken, ranging from diet/lifestyle counseling to pharmacotherapy to psychological therapies.

Neil Hyman, MD, concluded the session with a talk entitled "Disorders of the anorectum," also stressing that the history is key to the diagnosis, with an emphasis on asking the right questions. Pain may be related to fissures, thrombosed hemorrhoids, abscesses, and proctalgia/levator spasm. New technologies, and pharmacological and surgical approaches were discussed.

*Dr. Cohen is the chief of the division of gastroenterology and hepatology in the Weill department of medicine, New York–Presbyterian Hospital Center, New York.*

# It's a beautiful day to discuss inflammatory bowel disease

BY EDWARD V. LOFTUS, JR., MD, AGAF

Uma Mahadevan, MD, AGAF, and I moderated this session on IBD, and we were fortunate enough to secure four of the best IBD educators in the AGA.

David Rubin, MD, AGAF, opened with "Selecting the correct therapy for your outpatients with IBD: From mesalamine to biologics." Treatment goals have evolved from symptom control to remission based on measures of inflammation (e.g., serum C-reactive protein, fecal calprotectin, or endoscopy). For ulcerative colitis (UC), high-risk markers include extensive disease, deep ulcers, younger age at diagnosis, elevated biomarkers, and early need for steroids or hospitalization. For Crohn's disease (CD), these include younger age, extensive involvement, and fistulizing disease. The 5-aminosalicylate drugs remain a backbone in mild to moderate UC. Judicious use of corticosteroids is reasonable, but we need an exit strategy. The thiopurines are decent drugs, but studies have called into question their efficacy as monotherapy, and safety issues persist. Methotrexate is underutilized. The anti–tumor necrosis factor (TNF) biologics are excellent therapies but controversies persist as to whether these drugs require combination therapy or if they can be managed as "optimized monotherapy" with therapeutic drug monitoring (TDM). There are now two infliximab biosimilars available in the U.S.. Vedolizumab is an efficacious gut-selective anti-integrin (for both CD and UC). Ustekinumab, an anti-IL-12/23 antibody, is now available for moderate to severe CD, and has a favorable safety profile.

William Sandborn, MD, AGAF, discussed "Severe ulcerative colitis in the hospitalized patient." Severe UC is characterized by at least six bowel movements daily, blood in the stool, fever, tachycardia, anemia, and elevated ESR. Other predictors of severity include colonic dilation, deep ulcers, and lack of response to 3 days of IV corticosteroids (e.g., stool frequency more than 8/day or CRP more than 45 mg/L). About 70% of patients will respond to IV steroids; for those who don't, options include IV cyclosporine or IV infliximab. These drugs are equivalent in efficacy; however, cyclosporine toxicity can include serious or fatal infections in up to 3% of patients. The challenge with infliximab is pharmacokinetics – many severely ill patients will have protein-losing colopathy, detectable fecal infliximab levels, and lower serum levels resulting in lack of response – so early dose escalation may be required. A day-by-day algorithm for managing severe UC in the hospital was reviewed (see Clin Gastroenterol Hepatol. 2012;10:1315-25).

DR. LOFTUS

Fernando Velayos, MD, AGAF, discussed "Surveillance for dysplasia: What is the standard of care in 2017?" General principles for surveillance colonoscopy in IBD include having quiescent disease, since inflammation can reduce ability to detect lesions, and good colonic preparation. The three U.S. society guidelines recommend starting surveillance after 8 years of disease. Patients with concomitant primary schlerosing cholangitis should begin surveillance immediately. Frequency of surveillance ranges every 1-3 years depending on histology. A meta-analysis showed a higher incremental dysplasia yield with chromoendoscopy compared to standard white-light colonoscopy. If visible dysplasia can be endoscopically resected, then continued surveillance rather than colectomy is recommended.

Sunanda Kane, MD, AGAF, discussed "Managing special populations: the transitioning adolescent, the gravid, and the elderly." The transition from pediatric to adult IBD care is a high-risk time because the patient may be lost to follow-up or not adhere to the medical regimen, resulting in increased risk of flare. Successful transition requires developmental maturity of the patient, a certain style of parental involvement, and care coordination of the medical team. For women with IBD considering pregnancy, active IBD at the time of conception significantly increases the risk of flare. Women with CD who have no history of perianal disease don't have an increased risk of perianal disease with vaginal delivery. A meta-analysis of the risk of congenital malformations with thiopurines found no significant association. Infliximab levels were likely to rise in the mother during the second and third trimesters (versus no increase with adalimumab), so one could consider TDM to guide dosing. In the PIANO study, anti-TNF therapy in the third trimester was neither associated with adverse pregnancy outcomes nor with infections up to 1 year for children. Patients who develop IBD later in life are more likely to have colonic inflammation. Elderly UC patients are more likely to require surgery, and postop mortality is higher for both CD and UC.

*Dr. Loftus is a professor of medicine, division of gastroenterology and hepatology, Mayo Clinic, Rochester, Minn.*

# Add the definitive treatment for hemorrhoids to your practice.

(And smiles to your patients' faces.)

---

The CRH O'Regan System® is a non-surgical solution that is simple, fast, and 99% effective.
It's also now being performed by more than 2,500 physicians at 900 practices across the country.
Join your colleagues and get started today.

For more information, call **888.599.7949 x 1023** or visit **www.crhmedicalproducts.com**

Your patients will thank you.

CRH O'Regan System®
Non-Surgical Hemorrhoid Treatment
*Fast. Painless. Proven.*

CRH Medical
CORPORATION

# Bezlotoxumab may lower risk of *C. difficile* readmissions

BY ELI ZIMMERMAN
*Frontline Medical News*

*Clostridium difficile* infection (CDI) patients treated with bezlotoxumab were less likely to be readmitted for recurring symptoms within 30 days of discharge, according to a phase 3 trial funded by Merck.

Recurrent CDI is a burden on both patients and providers, increasing health risks with each recurrence, according to Vimalanand S. Prabhu, PhD, associate principal scientist for Merck.

"Approximately 25% of patients experience recurrent CDI. … After a first recurrence of CDI, the probability of a second recurrence is approximately 38%," according to a study cited by Dr. Prabhu and colleagues (Clin Infect Dis. 2014 Aug 1;59[3]:345-54). "Recent model-based estimates place the 2014 economic cost of CDI at $5.4 billion in the United States, mostly attributable to hospitalization."

In a randomized, double-blind, placebo-controlled study of 1,050 CDI patients, a total of 27 (5%) of 530 of those given bezlotoxumab were re-hospitalized 30 days after discharge, compared with 58 (11%) of 520 patients in the placebo group (Clin Infect Dis. 2017 Aug 11. doi. 10.1093/cid/cix523). Patients were gathered from 322 sites across 30 countries between November 2011 and May 2015.

When measuring CDI-related readmissions, the investigators found use of bezlotoxumab reduced rCDI hospitalizations by 6%, and by approximately 8% in high-risk patients, such as those over 65 years old or with severe CDI.

Bezlotoxumab works by binding to CDI toxin B, a primary cause of CDI symptoms, according to Dr. Prabhu and fellow investigators.

All investigators reported some financial involvement, whether as a full-time employee or as a consultant for Merck, which funded the study. Individually, investigators reported financial ties to similar medical companies, such as Pfizer and AstraZeneca.

**AGA Resource**
AGA offers patient education materials on *C. diff* that can help your patients better understand the infection. Learn more at http://www.gastro.org/patient-care/conditions-diseases/clostridium-difficile-infection.

ezimmerman@frontlinemedcom.com
On Twitter @eaztweets

# FDA approves second adalimumab biosimilar

BY LUCAS FRANKI
*Frontline Medical News*

The Food and Drug Administration has approved Cyltezo (adalimumab-adbm) for multiple conditions.

Cyltezo is an injectable tumor necrosis factor blocker, and is a biosimilar to adalimumab (Humira). The drug is indicated to treat moderate to severe active rheumatoid arthritis, active psoriatic arthritis, active ankylosing spondylitis, moderate to severe active Crohn's disease, moderate to severe active ulcerative colitis, moderately to severely active polyarticular juvenile idiopathic arthritis in patients 4 years of age and older, and moderate to severe plaque psoriasis.

The most common side effects are injection site infections, infection, rash, and headache. There is an increased risk of serious infection and malignancies such as lymphoma, and patients with active infections should not be started on Cyltezo.

lfranki@frontlinemedcom.com

DDSEP eight
Digestive Diseases Self-Education Program

## Quick quiz answers

**Q1:** Answer: A

*Campylobacter* species are a major cause of diarrheal illness in the world. The organism inhabits the intestinal tracts of a wide range of animal hosts, notably poultry; contamination from these sources can lead to foodborne disease. Given the self-limited nature of most *Campylobacter* infections and the limited efficacy of routine antimicrobial therapy, treatment is warranted only for patients with features of severe disease or risk for severe disease.

Patients with severe disease include individuals with bloody stools, high fever, extra-intestinal infection, worsening or relapsing symptoms, or symptoms lasting longer than 1 week. Those at risk for severe disease include patients who are elderly, pregnant, or immunocompromised. First-line agents for treatment of *Campylobacter* infection include fluoroquinolones (if sensitive) or azithromycin. *Campylobacter* is inherently resistant to trimethoprim and beta-lactam antibiotics, including penicillin and most cephalosporins.

In the United States, the rate of resistance to fluoroquinolones is also increasing. The rate of ciprofloxacin resistance among *Campylobacter* isolated in the United States increased from 0% to 19% between 1989 and 2001. Inappropriate and overprescription of fluoroquinolones in humans combined with increased fluoroquinolone use in the poultry industry in particular have contributed to the increased prevalence of fluoroquinolone resistance.

The rate of macrolide-resistance among *Campylobacter* has remained stable at less than 5% in most parts of the world.

**References**

1. Dasti J.I., Tareen A.M., Lugert R., et al. *Campylobacter jejuni*: A brief overview on pathogenicity-associated factors and disease-mediating mechanisms. Int J Med Microbiol. 2010;300:205–11.

2. Gupta A., Nelson J.M., Barrett T.J., et al. Antimicrobial resistance among *Campylobacter* strains, United States, 1997-2001. Emerging infectious diseases. Jun 2004;10(6):1102-9.

**Q2:** Answer: E

This patient has elevated transaminases with normal alkaline phosphatase and total bilirubin levels. His AST is greater than his ALT. He does not meet criteria for having nonalcolholic steatohepatitis because of his history of drinking at least five drinks per day. Additionally, his AST:ALT ratio would be atypical for classic NASH presentation. This patient does not have chronic hepatitis B as his serologies reveal that he is hepatitis B immune. This patient's labs are not suggestive of iron overload with a normal serum ferritin and normal iron saturation. Although this patient has emphysema diagnosed at a young age and an undetectable alpha-1-antitrypsin level, this patient's liver enzyme elevations are not due to alpha-1-antitrypsin deficiency. Alpha-1-antitrypsin is a glycoprotein that functions as a serine protease inhibitor and is produced predominantly in hepatocytes and then secreted from the cell.

In alpha-1-antitrypsin mutations that affect the liver (most commonly the ZZ phenotype), there is an amino acid substitution that results in the production of an abnormal alpha-1-antitrypsin molecule that polymerizes within the hepatocyte preventing secretion from the cell and resulting in abnormal accumulation of the alpha-1-antitrypsin in hepatocytes with resulting hepatic damage over time. This patient, however, has the alpha-1-antitrypsin phenotype null/null, which results in the absence of alpha-1-antitrypsin production. As such, null/null individuals are at very high risk for emphysema due to the complete absence of the alpha-1-antitrypsin enzyme. However, since null/null individuals produce no alpha-1-antitrypsin at all, there is no abnormally polymerized alpha-1-antitrypsin protein build-up. Based upon the clinical history and laboratory data, this patient's liver enzyme elevations are most likely due to alcohol abuse.

**References**

1. Fairbanks K.D., Tavill A.S. Liver disease in alpha-1-antitrypsin deficiency: A review. Am J Gastro. 2008;103:2136-41.

2. Silverman E.A., Sandhaus R.A. Alpha-1 antitrypsin deficiency. N Engl J Med. 2009;360;2749-5.

ginews@gastro.org

WWW.GIHEPNEWS.COM

# GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

# Young adults lead the ranks of the uninsured

BY RICHARD FRANKI
*Frontline Medical News*

The uninsured rate for young adults fell 50% from 2010 to 2016, according to the Agency for Healthcare Research and Quality.

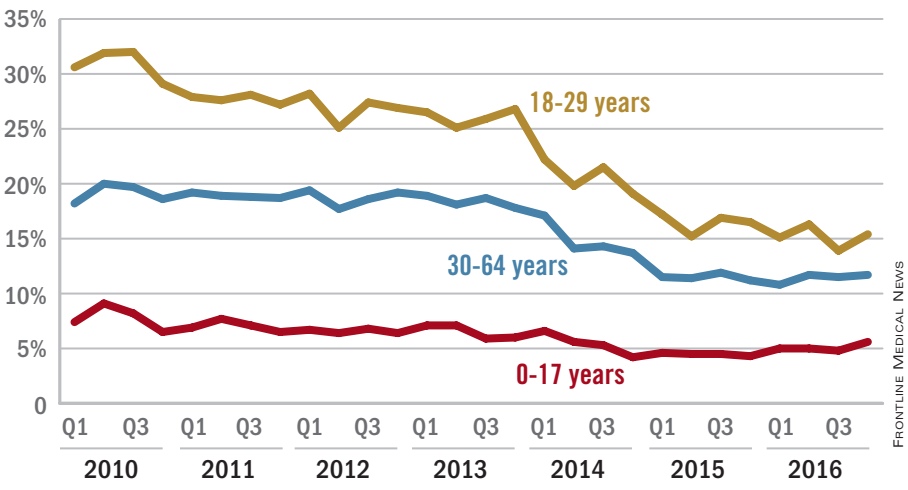
In the first quarter of 2010, 30.6% of adults aged 18-29 years did not have health insurance at the time they were interviewed for the National Health Interview Survey. By the third quarter of 2016, that figure was down to 15.4%, a drop of nearly 50%, the AHRQ said in its annual National Healthcare Quality and Disparities Report.

The reductions for Americans younger and older were robust but not as large. Among adults aged 30-64 years, the proportion who were uninsured fell almost 36%, going from 18.2% in the first quarter of 2010 to 11.7% in the third quarter of 2016. Children had the smallest reduction by age group, 24%, as their uninsured rate decreased from 7.4% to 5.6%, the AHRQ reported.

For the total population under age 65 years, the uninsured rate dropped from 17.5% in the first quarter of 2010 to 10.8% in the third quarter of 2016, the AHRQ said, for an overall reduction of 38%.

rfranki@frontlinemedcom.com

**Uninsured Americans aged 0-64 years, 2010-2016 by quarter**




**Note:** Based on data from the National Health Interview Survey.
**Source:** Agency for Healthcare Research and Quality

## PERSPECTIVE

## The benefit of the ACA on IBD patients

The annual incidence of inflammatory bowel disease has exploded in Westernized countries during the last 50 years of the 20th century resulting in a prevalence that is now hovering around 250 per 100,000 population.[1] It is estimated that there will be 2.2 million people living with IBD in the United States by 2025. Over the next decade, the prevalence and economic impact of IBD will increase, adding a greater stress to a system already struggling with unequitable variations in care and access.

It was reassuring to review recent data from the Agency for Healthcare Research and Quality that showed the uninsured rate for young adults aged 18-29 years fell 50% from 2010 to 2016. This age group is the ages at which IBD is most commonly diagnosed and is an important population for IBD treatment. We need to apply appropriate therapy for active inflammation to avoid fibrotic complications.[2] Because of the annual cost of pharmaceutical therapy in IBD averages $14,000 per patient, insurance coverage is critical.

The AGA has published a position statement on replacement of the Affordable Care Act.[3]

AGA strongly urges Congress to include the following provisions in any health care package:

- Ensure patient access to and coverage of specialty care.
- Ensure patient access to and coverage of evidence-based preventive screenings without cost-sharing.
- No discrimination because of a pre-existing condition.
- Insurers cannot discriminate based on sex.
- Parents should be allowed to keep their children on their plans until age 26.
- A ban on annual and lifetime caps.

**References**

1. Kaplan G.G., Ng S.C. Understanding and preventing the global increase of inflammatory bowel disease. Gastroenterology. 2017;152:313-21.

2. Rieder F., Fiocchi C., Rogler G. Mechanisms, management, and treatment of fibrosis in patients with inflammatory bowel disease. Gastroenterology. 2017;152:340-8.

3. http:/www.gastro.org/take-action/top-issues/patient-protections-and-access-to-care.

*Larry R. Kosinski, MD, MBA, AGAF, is a managing partner of the Illinois Gastroenterology Group and the president and chief medical officer of the technology company SonarMD.*

## CLINICAL CHALLENGES AND IMAGES

## The diagnosis

**Answer to "What's your diagnosis?" on page 23: Necrolytic acral erythema**

The patient's clinicopathologic picture is consistent with necrolytic acral erythema (NAE). Notably, her serum zinc level was 121 mcg/dL (normal is greater than 55 mcg/dL). The patient was started on oral zinc supplementation. Several days after initiation of zinc therapy, her pain and pruritus dramatically improved.

NAE is a rare condition, first described in a cohort study of seven Egyptian patients with active HCV infection in 1996, and is considered a distinctive cutaneous presentation of HCV infection.[1] Clinical presentation typically involves severe pruritus on acral surfaces accompanied by pain and a burning sensation. The skin findings include well-circumscribed, dusky, erythematous to hyperpigmented plaques with variable scaling and erosion that extend from dorsal feet to the legs. The pathogenesis of NAE remains unknown. However, it has been proposed that zinc deficiency and dysregulation secondary to hepatocellular dysfunction in HCV infection, is associated with NAE.[2]

Zinc supplementation has shown favorable outcomes in NAE patients with zinc deficiency.[3] However, the appropriate threshold of serum zinc level in patients with NAE is unclear. Herein, we have reported a patient with NAE who responded to zinc supplementation despite a normal zinc level. A plausible explanation is that clinical zinc deficiency may occur in the skin before the development of decreased serum zinc levels.

Skin pruritus is a common presentation in patients with chronic HCV infection. Increased awareness of the distinct features of NAE may result in early diagnosis and initiation of effective therapy. Zinc supplementation may be beneficial in NAE patients with and without decreased serum zinc level.

**References**

1. el Darouti, M., Abu el Ela, M. Necrolytic acral erythema: a cutaneous marker of viral hepatitis C. Int J Dermatol. 1996;35:252-6.

2. Hadziyannis, S.J. Skin diseases associated with hepatitis C virus infection. J Eur Acad Dermatol Venereol. 1998;10:12-21.

3. Abdallah, M.A., Hull, C., Horn, T.D. Necrolytic acral erythema: A patient from the United States successfully treated with oral zinc. Arch Dermatol. 2005;141:85-7.

ginews@gastro.org

# Uninsured rate falls to record low of 8.8%

**BY PHIL GALEWITZ, KAISER HEALTH NEWS**

Three years after the Affordable Care Act's coverage expansion took effect, the number of Americans without health insurance fell to 28.1 million in 2016, down from 29 million in 2015, according to a federal report released Sept. 12.

The latest numbers from the U.S. Census Bureau showed the nation's uninsured rate dropped to 8.8%. It had been 9.1% in 2015.

Both the overall number of uninsured and the percentage are record lows.

The latest figures from the Census Bureau effectively close the book on President Obama's record on lowering the number of uninsured. He made that a linchpin of his 2008 campaign, and his administration's effort to overhaul the nation's health system through the ACA focused on expanding coverage.

When Mr. Obama took office in 2009, during the worst economic recession since the Great Depression, more than 50 million Americans were uninsured, or nearly 17% of the population.

The number of uninsured has fallen from 42 million in 2013 – before the ACA in 2014 allowed states to expand Medicaid, the federal-state program that provides coverage to low-income people, and provided federal subsidies to help lower- and middle-income Americans buy coverage on the insurance marketplaces. The decline also reflected the improving economy, which has put more Americans in jobs that offer health coverage.

The dramatic drop in the uninsured over the past few years played a major role in the congressional debate over the summer about whether to replace the 2010 health law. Advocates pleaded with the Republican-controlled Congress not to take steps to reverse the gains in coverage.

The Census Bureau numbers are considered the gold standard for tracking who has insurance because the survey samples are so large.

The uninsured rate has fallen in all 50 states and the District of Columbia since 2013, although the rate has been lower among the 31 states that expanded Medicaid as part of the health law. The lowest uninsured rate last year was 2.5% in Massachusetts, and the highest was 16.6% in Texas, the Census Bureau reported. States that expanded Medicaid had an average uninsured rate of 6.5%, compared with an 11.7% average among states that did not expand.

More than half of Americans – 55.7% – get health insurance through their jobs. But government coverage is becoming more common. Medicaid now covers more than 19% of the population and Medicare, nearly 17%.

*Kaiser Health News is a national health policy news service that is part of the nonpartisan Henry J. Kaiser Family Foundation.*

# PRACTICE MANAGEMENT TOOLBOX:
# Cultivating competencies for value-based care

**BY ZIAD GELLAD, MD, MPH, AGAF**

It is my privilege this month to assume responsibility for the "Practice Management: The Road Ahead" section of Clinical Gastroenterology and Hepatology. I am honored to join an impressive board of editors led by Dr Fasiha Kanwal, and anchored by global leaders in the field of gastroenterology and hepatology. This board of editors promises to continue the high level of excellence that has propelled the journal to its preeminent position among clinical journals. I am confident that the practice management section will uphold that tradition and continue to meet the expectation of our readers. I would like to mark this transition by acknowledging the history of the practice management section of Clinical Gastroenterology and Hepatology and outlining a vision for the future.

DR. GELLAD

The section was introduced in 2010 under the leadership of Dr. Joel V. Brill. The section, titled "Practice Management: Opportunities and Challenges," aimed to help practices navigate the disparate issues facing the field. Some of these issues included use of capnography in endoscopy, the importance of registries for quality reporting, and the burdens of meaningful use on physician practices. Dr Brill introduced this section in a video in May 2010 (https://www.youtube.com/watch?v=8FMsc2Wl5E8). Dr. Brill's reference to these "interesting and challenging times" in gastroenterology resonates even more loudly today.

With the transition of the board of editors in 2012, Dr. John I. Allen assumed stewardship of the practice management section, which was subsequently named "Practice Management: The Road Ahead" to match a parallel initiative within the American Gastroenterological Association. Dr. Allen's experience as a practicing gastroenterologist and his clairvoyance on health policy issues is unparalleled. One has to look no further than his first paper as special section editor where he outlined the dominant themes of the next 5 years, namely: the importance of demonstrating value, population management, consolidation of medical practices, increasing importance of cost, and the rise of value-based payment.[1] The Road Ahead has kept focus on these topics through educational pieces on health care reform and payment policy,[2,3] case studies in alternative payment models,[4,5] primers on quality improvement methodology,[6-8] and astute commentaries on important issues facing practicing clinicians.[9-11]



WWW.GIHEPNEWS.COM
GI & HEPATOLOGY NEWS
THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

Over the next 5 years, the Road Ahead section will continue and strengthen its focus on the current and emerging issues facing gastroenterology and hepatology practices. I believe that high-value care will continue to be a high priority for patients and payers alike. Early results with payment reform around value have been mixed, in large part because of challenges in health systems and practices developing the competencies required for such reform.[12] These competencies include governance and culture, financial readiness, health information technology, patient risk assessment, care coordination, quality, and patient centeredness. I will use this conceptual framework of organizational competencies, and their application in gastroenterology and hepatology, to help curate the Road Ahead section (Table 1). Key themes will include the following:

- Governance and culture: The structure of health delivery systems, as conceptualized by Donabedian,[13] is a key determinant of quality. Structural attributes include regulatory requirements on gastrointestinal practices, such as the rules governing use of anesthesia providers in ambulatory surgical settings; role of allied health professionals in clinical settings; and the impact of financial incentives in driving provider behavior.
- Financial readiness: Value-based reimbursement, accountable care, medical homes, reference pricing, and physician tiering are some of the new terms in this era of value-based medicine. It is important for practices to assess patient costs longitudinally and manage financial risks. The Road Ahead section will continue to include papers that describe the impact of these reforms on gastroenterology and hepatology practices while providing guidance on implementation of these new models of care. Some examples include papers on the effect of payment policy on specialty practices, the development of a medical home in inflammatory bowel disease, and the physician experience with episode-based payments for colonoscopy.
- Health information technology: All of the organizational competencies required for reform rely on a robust information technology platform that collects meaningful data and harnesses that data for analytic purposes. These platforms can be enterprise systems deployed by large health delivery systems or smaller, more nimble platforms, created by innovative start-up companies. The Road Ahead will include papers that share best practices in the use of these platforms to provide high-quality and cost-efficient care. In addition, the column will continue to explore the use of health information technology to expand the reach of clinicians beyond brick and mortar clinics.
- Patient risk assessment: Tailoring interventions to high-risk patients is necessary to deploy limited resources in a cost-effective manner. Risk assessment is also needed to more accurately and effectively personalize care for patients with chronic conditions. The column will include papers that evaluate risk assessment tools and/or describe real-life implementation of these tools in different contexts.
- Care coordination: The ability to provide team-based longitudinal care across the continuum of care will be integral to providing high-value health care. The column will serve as a means to disseminate best practices and innovative methods to care for increasingly complex patients, especially those with chronic diseases, such as cirrhosis and inflammatory bowel disease. For example, papers will explore the implementation of specialty medical homes, patient navigators, community-based care services, and involvement of patients in their own care.
- Quality improvement: Providing high-value care by definition will require clinicians to accurately measure the quality of care provided to patients and use data to guide process improvement. The column will continue to serve as an educational resource for clinicians with papers that discuss challenges and opportunities in quality measurement and improvement. Similarly, this section will present data on novel or impactful quality-improvement initiatives.
- Patient centeredness: Patient experience measures and patient-reported outcomes are becoming increasingly important as meaningful indicators of quality. These measures are designed to ensure that patient perspectives are incorporated into the governance, design, and delivery of health care. The column will serve as a dissemination mechanism for sharing best practices in developing, validating, implementing, and tracking patient-re-

*Continued on following page*

TABLE 1

**Organizational competencies for reform, adapted to gastroenterology**

| Organizational competency | Examples in gastroenterology |
|---|---|
| Governance and culture | Regulatory pressures on independent gastrointestinal practices[14]<br>How to structure a gastrointestinal practice for value |
| Financial readiness | Development of new bundled payments[5]<br>Impact of Medicare revaluation on gastrointestinal practice[2]<br>How to handle risk in a specialty practice |
| Health information technology | Electronic medical record workflow to measure and report colonoscopy quality measures[15]<br>Telemedicine in gastroenterology and hepatology[16] |
| Patient risk assessment | Personalized cancer prevention program[17]<br>Predictive modeling of readmission rates |
| Care coordination | Specialty medical home for cirrhosis and transplant[4]<br>Specialty medical home for inflammatory bowel disease |
| Quality | Use of Lean principles to improve colorectal cancer screening rates[18]<br>Nonendoscopic quality measures for colorectal cancer screening[19] |
| Patient centeredness | Role of patient advisory councils in practice management<br>Integration of patient-reported outcomes into practice |

Adapted from McClellan and Leavitt.[12]

Content from this column was originally published in the "Practice Management: The Road Ahead" section of *Clinical Gastroenterology and Hepatology* (2017;15:969-71).

*Continued from previous page*

ported outcomes.

Finally, this section will also serve as an outlet for ideas and case studies in health care delivery that are provocative and innovative. I would like this section to continue the invigorating conversations that are occurring at clinical meetings while at the same time engaging the entrepreneurial environment swarming around us. These innovative ideas will span all of the previously mentioned organizational competencies and will consider such topics as telemedicine, mobile health technology, and new models of gastrointestinal practice structure.

I consider Dr. Brill and Dr. Allen as mentors who have taught me tremendously about the business of medicine and the importance of physician leadership. I had the opportunity to coauthor several papers and book chapters with them. More recently, I have had the privilege to work closely with them in my role as the Chair of the American Gastroenterological Association Quality Measures Committee. It is an honor to now join their league as the editor for the Road Ahead section of Clinical Gastroenterology and Hepatology. These are indeed big shoes to fill. The section will retain the "Road Ahead" title in an acknowledgment of the continued importance of the issues outlined by Dr Allen. We will build on this theme to focus on not just the destination, but also the bumps in the road, the unexpected curves, the rest areas, beautiful vistas, and the indulgent road food. Hopefully no accidents along the way!

## Take-away points:

1. High-value care remains a priority for patients and payers alike.
2. The section will focus on papers that address competencies for high-value health care, including governance and culture, financial readiness, health information technology, patient risk assessment, care coordination, quality, and patient centeredness.
3. Innovation and entrepreneurship also create opportunities for achieving value in GI practice.



### References

1. Allen, J.I. The road ahead. Clin Gastroenterol Hepatol. 2012;10:692-6.

2. Dorn, S.D., Vesy, C.J. Medicare's revaluation of gastrointestinal endoscopic procedures: implications for academic and community-based practices. Clin Gastroenterol Hepatol. 2017;14:924-8.

3. Dorn, S.D. The road ahead 3.0: changing payments, changing practice. Clin Gastroenterol Hepatol. 2016;14:785-9.

4. Meier, S.K., Shah, N.D., Talwalkar, J.A. Adapting the patient-centered specialty practice model for populations with cirrhosis. Clin Gastroenterol Hepatol. 2016;14:492-6.

5. Mehta, S.J. Bundled payment for gastrointestinal hemorrhage. Clin Gastroenterol Hepatol. 2016;14:1681-4.

6. Weizman, A.V., Mosko, J., Bollegala, N., et al. Quality improvement primer series: launching a quality improvement initiative. Clin Gastroenterol Hepatol. 2017;14:1067-71.

7. Bernstein, M., Hou, J.K., Weizman, A.V., et al. Quality improvement primer series: how to sustain a quality improvement effort. Clin Gastroenterol Hepatol. 2017;14:1371-5.

8. Bollegala, N., Patel, K., Mosko, J.D., et al. Quality improvement primer series: the plan-do-study-act cycle and data display. Clin Gastroenterol Hepatol.

2016;14:1230-3.

9. Adams, M.A. Covert recording by patients of encounters with gastroenterology providers: path to empowerment or breach of trust?. Clin Gastroenterol Hepatol. 2017;15:13-6.

10. Oza, V.M., El-Dika, S., and Adams, M.A. Reaching safe harbor: legal implications of clinical practice guidelines. Clin Gastroenterol Hepatol. 2016;14:172-4.

11. Lin, M., Pappas, S.C., Sellin, J., et al. Curbside consultations: the good, the bad, and the ugly. Clin Gastroenterol Hepatol. 2016;14:2-4.

12. McClellan, M.B., Leavitt, M.O. Competencies and tools to shift payments from volume to value. JAMA. 2016;316:1655-56.

13. Donabedian, A. Evaluating the quality of medical care. Milbank Q. 1966;44:166-203.

14. Rosenberg, F.B., Kim, L.S., Ketover, S.R. Challenges facing independent integrated gastroenterology. Clin Gastroenterol Hepatol. 2017;15:335-8.

15. Leiman, D.A., Metz, D.C., Ginsberg, G.G., et al. A novel electronic medical record-based workflow to measure and report colonoscopy quality measures. Clin Gastroenterol Hepatol. 2016;14:333-7.

16. Cross, R.K., Kane, S. Integration of telemedicine into clinical gastroenterology and hepatology Practice. Clin Gastroenterol Hepatol. 2017;15:175-81.

17. Llor, X. Building a cancer genetics and prevention program. Clin Gastroenterol Hepatol. 2016;14:1516-20.

18. Patel, K.K., Cummings, S., Sellin, J., et al. Applying Lean design principles to a gastrointestinal endoscopy program for uninsured patients improves health care utilization. Clin Gastroenterol Hepatol. 2015;13:1556-9.

19. Saini, S.D., Adams, M.A., Brill, J.V., et al. Colorectal cancer screening quality measures: beyond colonoscopy. Clin Gastroenterol Hepatol. 2016;14:644-7.

*Dr. Gellad is an associate professor of medicine in the division of gastroenterology at Durham VA Medical Center, Durham, N.C.; and Duke Clinical Research Institute, Durham, N.C. He reports a consulting relationship with Merck & Co. and he is also a co-founder and equity holder in Higgs Boson, LLC. He is funded by Veterans Affairs Health Services Research and Development Career Development Award (CDA 14-158 ).*

## INDEX OF ADVERTISERS

WWW.GIHEPNEWS.COM
GI & HEPATOLOGY NEWS
THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE