WWW.GIHEPNEWS.COM

2007-10-Year Anniversary-2017

VOL. 11 NO. 11 NOVEMBER 2017

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

Doug Brunk/Frontline Medical News

Dr. John F. Kokai-Kun presented the findings on the unusual beta-lactamase treatment at IDWeek.

Ribaxamase reduced new CDI by 71%

BY DOUG BRUNK
Frontline Medical News

SAN DIEGO – Hospitalized patients who received the investigational oral agent ribaxamase had a 71% reduction in the development of new *Clostridium difficile* infection, results from a phase 2b study showed.

At an annual scientific meeting on infectious diseases, lead investigator John F. Kokai-Kun, PhD, said that the finding represents a paradigm shift in the use of intravenous beta-lactam antibiotics to prevent opportunistic infections. "We currently treat *Clostridium difficile* infection (CDI) with antibiotics, which attack the vegetative cells," said Dr. Kokai-Kun, vice president of nonclinical affairs for Rockville, Md.–based Synthetic Biologics, which is developing ribaxamase. "Since *C. diff.* is primarily a toxin-mediated disease, certain products seem to neutralize the toxin. There's also been work with probiotics and prebiotics to try to strengthen and repair the dysbiotic colon. Fecal replacement therapy has been shown to be fairly effective for treatment of recurrent *C. diff.* infection. What if we could simply block the initial insult that leads to this cascade? That's the damage

See **Ribaxamase** · *page 25*

Childhood IBD increased cancer risk in adulthood

BY BIANCA NOGRADY
Frontline Medical News

Children who had developed inflammatory bowel disease had an 18-fold greater risk of gastrointestinal cancers in later life, a new study suggests.

The cohort study found that the risk of all cancers was elevated in individuals with childhood-onset inflammatory bowel disease, but particularly in those with primary sclerosing cholangitis and ulcerative colitis.

Researchers followed 9,405 patients with childhood-onset inflammatory bowel disease to a mean age of 27 years using a Swedish national patient register (BMJ. 2017 Sep 21. doi: 10.1136/bmj.j3951).

Analysis revealed that individuals with childhood-onset inflammatory bowel disease had double the risk of any cancer, compared with the general population (hazard ratio, 2.2; 95% confidence interval, 2.0-2.5), and a 2.7-fold greater risk of developing cancer before the age of 18 years.

Primary sclerosing cholangitis was associated with a sixfold greater risk of cancer, ulcerative colitis was associated with a 2.6-fold greater risk, and patients who had had colitis for 10 years or more had a nearly fourfold greater risk of cancer (HR, 3.9).

The study also found that childhood-onset inflammatory bowel disease

See **Cancer** · *page 25*

INSIDE

MedPAC calls for MIPS repeal

BY GREGORY TWACHTMAN
Frontline Medical News

WASHINGTON – In a rare display of a near-immediate consensus, the Medicare Payment Advisory Commission agreed that the Merit-Based Incentive Payment System track of the new Quality Payment Program should be scrapped, although commission members are not yet ready to endorse a replacement plan.

MedPAC staff presented its idea of "repeal and replace" less than 10 months into the first reporting year, with staff member David V. Glass noting during an Oct. 6 meeting that "MIPS will not achieve the goal of identifying and rewarding high-value clinicians."

He cited estimates from the Centers for Medicare & Medicaid Services that compliance with MIPS will

See **MIPS** · *page 4*

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

CLINICAL CHALLENGES AND IMAGES

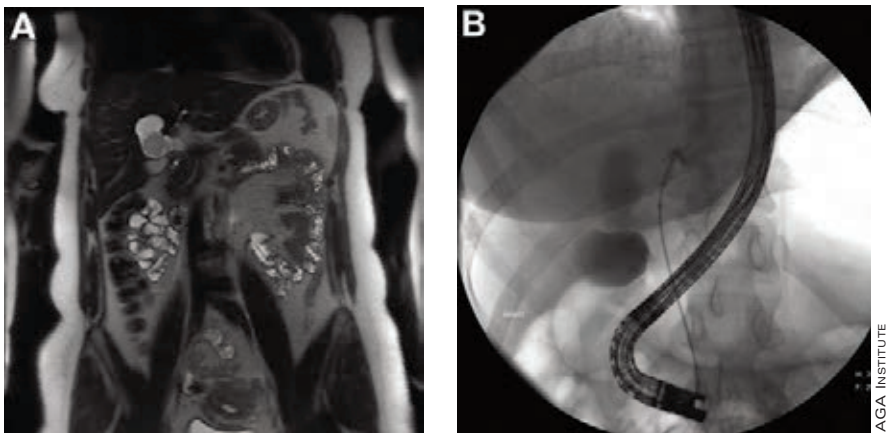
What is your diagnosis?

By Ryan Law, MD, Thomas C. Smyrk, MD, and Stephen C. Hauser, MD. Published previously in Gastroenterology (2013;144[3]:508, 658).

A 43-year-old woman presented with progressively worsening right upper-quadrant abdominal pain. The episodic pain occurred after high-fat meals and lasted from minutes to hours with accompanying nausea. Her previous medical history was notable for endometriosis. She denied other constitutional symptoms. Physical examination revealed no hepatosplenomegaly, jaundice, right upper-quadrant mass, or stigmata of chronic liver disease.

Initial laboratory evaluation yielded normal white blood cell count and liver chemistries. Ultrasonography, computed tomography, and magnetic resonance imaging of the abdomen all demonstrated a 2.0 × 4.1 × 3.9-cm, nonenhancing, elongated, cystic mass located superior to the gallbladder within the porta hepatis, with possible communication at the bile duct confluence and abutment of the right portal vein (Figure A). No definitive findings of acute cholecystitis were present.

Endoscopic retrograde cholangiopancreatography with endoscopic ultrasonography was performed to further delineate the anatomy of the lesion. On endoscopic ultrasonography, the structure in question seemed to be embedded in the hepatic parenchyma with partial extension beyond the liver edge. Adherent debris was noted within the cystic structure. No lymphadenopathy was present. Cholangiography demonstrated filling of the lesion from a central right intrahepatic duct (Figure B). Attempts at cannulation of the cyst were unsuccessful.



AGA Institute

The patient subsequently developed abnormal liver chemistries with continued right upper-quadrant pain. She was referred to an experienced hepatobiliary surgeon and underwent operative intervention.

The diagnosis is on page 29.

LETTER FROM THE EDITOR: Happy anniversary

This month marks the first-year anniversary of the Trump administration and GOP control of both Houses of Congress. With the failure of Repeal and Replace, efforts to alter the Affordable Care Act have taken a complex turn. It is more important than ever for physician leaders to understand the nuances of federal health care financing, so we can effectively advocate for our patients.

Although, only 4% of Americans purchase insurance through Marketplaces, most "Obamacare is failing" comments refer to this volatile segment. Federal support for Marketplace plans comes in two forms: premium support and cost-sharing reductions (CSR). Premium support is provided directly to individuals and families with incomes under 400% of the Federal Poverty Level (FPL) as a refundable tax credit. These funds had legislation tied to a specific budget appropriation. CSR legislation mandated insurance companies pay low-income people (less than 250% of FPL) to reduce deductibles and out-of-pocket expenses but was not tied to a specific budget appropriation. Republicans sued to stop payments since money spent must be tied to an appropriation. Although, the lawsuit is on hold, President Trump stopped payment by executive

Continued on page 6


DR. ALLEN

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

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

FIVE-STAR EFF1CACY WITH SUPREP®

Distinctive results in all colon segments

- SUPREP Bowel Prep Kit has been FDA-approved as a split-dose oral regimen[3]
- 98% of patients receiving SUPREP Bowel Prep Kit had "good" or "excellent" bowel cleansing[2*†]
- >90% of patients had no residual stool in all colon segments[2*†]
  - These cleansing results for the cecum included 91% of patients[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.

Braintree LABORATORIES, INC

HH13276AT-U May 2017

Measures not related to value?

MIPS *from page 1*

come with a $1 billion price tag, and an effort to streamline the process and make things more flexible "actually increases MIPS inherent complexity. ... Because of all this complexity, it is extremely unlikely that clinicians will understand their score or what they need to do to improve it."

"Our most basic concern is that measures used in MIPS have not been proven to be associated with high-value care," Mr. Glass said. "Many of the MIPS quality measures are process measures, assessing only the care a provider delivers within their four walls."

MedPAC staff proposed a replacement option affecting all clinicians who are not a part of an advanced Alternative Payment Model program. Under their proposal, Medicare would withhold 2% of each clinician's Medicare payments. Clinicians could earn back that 2% by joining a large reporting entity (either as part of a formal business structure or something like a virtual group); they could elect to join an advanced APM, earning back the 2% and possibly bonus payments; or they could do nothing and lose the 2%.

Measurements in the proposed value program would be similar to those employed by advanced APMs in that they would be focused on population-based measures assessing clinical quality, patient experience, and value. Potential measures would address avoidable admissions/emergency department visits, mortality, readmissions, ability to obtain care, ability to communicate with clinicians, spending per beneficiary, resource use, and rates of low-value care use. Measures would be calculated based on claims.

'Our most basic concern is that measures used in MIPS have not been proven to be associated with high-value care,' Mr. Glass said.

MedPAC commissioners were nearly unanimous in their agreement to the idea of repealing MIPS but were not ready to sign off on the proposed replacement.

"I'm really concerned about the burden on physicians, and I'm concerned about some of the outlandish potential rewards for groups under MIPS that can really dissuade them from investing and moving into APMs," commission member Paul B. Ginsburg, PhD, senior fellow in economic studies at the Brookings Institution said.

"I think we really have to get rid of MIPS and either replace it with this system, which I think has a lot of merit, or just get rid of it," said commission member Jack Hoadley, PhD, of Georgetown University in Washington, suggesting MIPS would be "even worse" than the old Sustainable Growth Rate formula over time. It is "clear to me that MIPS is not going to ... get us toward high-value care, it is not going to make clinicians' lives better, it is not going to make patients' lives better, and there is a lot of money at stake."

Commission member Dana Gelb Safran, ScD, chief performance mea-

surement and improvement officer at Blue Cross Blue Shield of Massachusetts said she did not believe that there would be any value being gained in return for the money given to clinicians who participate in MIPS.

Not everyone was on board with the proposed replacement.

"I am very much in favor of repealing MIPS, but I don't get the sense that we've gotten the replacement model quite right yet" because the proposed system does not do enough to get physicians into advanced APMs, commission member Craig Samitt, MD, chief clinical officer at Anthem, said. "So if a replacement is a voluntary model that would allow us to keep practicing health care the way we've been practicing, then that replacement is not a good replacement."

The American Medical Association declined to evaluate the proposal that was laid forth by staff.

"The AMA welcomes ideas on how to improve Medicare physician payment policies," AMA President David O. Barbe said in a statement. "We understand that MedPAC's proposals are a work in progress, so it's too early to render any judgment."

Dr. Barbe noted that the AMA recommends that physicians participate in MIPS, even if it is at the lowest level simply to avoid any penalty and continue investing in the infrastructure to participate. The AMA, AGA, and other medical societies also are asking CMS to allow those who are exempt from MIPS participation to be able to opt into the program.

The American Medical Group Association (AMGA), a trade organization representing multispecialty medical groups, however, has criticized the move by CMS to increase the number of clinicians who are exempt from MIPS.

Under the proposed expansion – which would approximately double the number of clinicians who are MIPS exempt – "MIPS no longer provides really any incentive to get to value and in fact it's a disincentive," said Chet Speed, AMGA vice president of public policy. "That is one of the realities that MedPAC was dealing with."

Mr. Speed emphasized that AMGA has not altered its policy on MIPS, which it wants to see enacted for all and has offered its own resources to help with the transition, but "if AMGA were to entertain a new position on MIPS, I think we probably would go with a more simple route, which is to just get rid of MIPS and repurpose the revenues that were in MIPS to APMs. ... We have not agreed upon that policy but that has been discussed internally."

He added that "AMGA's membership does look at MIPS as a tool that has really devolved from a value mechanism to a compliance exercise and nothing more."

As to whether health care provider associations would come together and support the repeal of MIPS, Mr. Speed was hesitant to predict that, even though many have reservations about it, noting that it could be because the broadening of exclusions, which the AMA and most other associations support, effectively remove a lot of their membership from having to participate anyway, leaving the bigger groups such as Mayo, the Cleveland Clinic and Intermountain Healthcare to fight over a much smaller pot of bonus payments, significantly limiting the returns on investments made to be ready for the MIPS transition.

gtwachtman@frontlinemedcom.com

AGA CLINICAL PRACTICE UPDATE

Best practices for POEM in achalasia

BY SHARON WORCESTER
Frontline Medical News

Peroral endoscopic myotomy, or POEM, should be considered as primary therapy for type III achalasia and as a treatment option comparable with laparoscopic Heller myotomy (LHM) for any of the achalasia syndromes – but only when physicians with expertise are available, according to a clinical practice update from the American Gastroenterological Association.

Further, post-POEM patients should be considered at high risk of developing reflux esophagitis and should be advised of the management considerations, including potential indefinite proton pump inhibitor therapy and/or surveillance endoscopy, prior to undergoing the procedure, Peter J. Kahrilas, MD, AGAF, of Northwestern University, Chicago, and his colleagues wrote in the update, which is published in the November issue of Gastroenterology (2017. doi: 10.1053/j.gastro.2017.10.001).

In an effort to describe the place for POEM among the currently available robust treatments for achalasia, the authors conducted a literature review – their "best practice" recommendations are based on the findings from relevant publications and on expert opinion.

In determining the need for achalasia therapy, they agreed that patient-specific parameters should be considered along with published efficacy data. Important parameters include Chicago Classification subtype, comorbidities, early vs. late disease, and primary or secondary causes.

Additionally, they said POEM should be performed by experienced physicians in high-volume centers since the procedure is complex and an estimated 20-30 procedures are needed to achieve competence.


DR. KAHRILAS

The update and these proposed best practices follow the evolution of POEM over the last decade: It began as an exciting concept and is now a mainstream treatment option for achalasia, the authors said.

Concerns remain regarding post-POEM reflux, the durability of the procedure, and the learning curve for endoscopists adopting the technique," they wrote, which, when coupled with recent randomized controlled study data showing excellent and equivalent 5-year outcomes with pneumatic dilation and LHM, make the role of POEM somewhat controversial.

As part of the review, they considered the strengths and weaknesses of both POEM and LHM. The data comparing POEM with LHM or pneumatic dilation remain very limited, but based on those that do exist, the authors concluded that "POEM appears to be a safe, effective, and minimally invasive management option in achalasia in the short term."

Dr. Kahrilas received funding from the U.S. Public Health Service.

sworcester@frontlinemedcom.com

FROM THE AGA JOURNALS

Null results posted for *Helicobacter* screening, eradication

BY AMY KARON
Frontline Medical News

Compared with usual care, screening for and eradicating *Helicobacter pylori* infection did not significantly improve the risk of dyspepsia or peptic ulcer disease, use of health care services, or quality of life in a large randomized, controlled trial reported in the November issue of Clinical Gastroenterology and Hepatology (doi: 10.1016/j.cgh.2017.06.006).

After 13 years of follow-up, the prevalence of dyspepsia was 19% in both arms (adjusted odds ratio, 0.93; 95% confidence interval, 0.82-1.04), reported Maria Bomme, MD, of University of Southern Denmark in Odense, and her associates. The cumulative risk of the coprimary endpoint, peptic ulcer disease, was 3% in both groups (risk ratio, 0.93; 95% CI, 0.79-1.09). Screening and eradication also did not affect secondary endpoints such as rates of gastroesophageal reflux, endoscopy, antacid use, or health care utilization, or mental and physical quality of life.

The study "was designed to provide evidence on the effect of *H. pylori* screening at a population scale," the researchers wrote. Prior studies have suggested that eradicating *H. pylori* infection might help prevent peptic ulcers and dyspepsia and could reduce the risk of gastric cancer, the researchers noted. For this trial, they randomly assigned 20,011 adults aged 40-65 years from a single county in Denmark to receive *H. pylori* screening or usual care. Screening consisted of an outpatient blood test for *H. pylori*, which was confirmed by ^{13}C-urea breath test (UBT) if positive. Individuals with confirmed infections were offered triple eradication therapy (20 mg omeprazole, 500 mg clarithromycin, and either 1 g amoxicillin or 500 mg metronidazole) twice daily for 1 week. This regimen eradicated 95% of infections, based on UBT results from a subset of 200 individuals.

Compared with nonparticipants, the 12,530 (63%) study enrollees were significantly more likely to be female, to be 50 years or older, and married, and to have a history of peptic ulcer disease. Rates of follow-up were 92% at 1 year, 83% at 5 years, and 69% (8,658 individuals) at 13 years. Among 5,749 screened participants, 17.5% tested positive for *H. pylori*. Nearly all underwent eradication therapy. At 5 years, screening and eradication were associated with a significant reduction in the incidence of peptic ulcers and associated complications and with modest improvements in dyspepsia, health care visits for dyspepsia, and sick leave days, compared with usual care. But the prevalence of dyspepsia waned in both groups over time and did not significantly differ between groups at 13 years in either the intention-to-treat or per-protocol analysis. Likewise, annual rates of peptic ulcer disease were very similar (1.9 cases/1,000 screened individuals and 2.2 cases/1,000 controls; incidence rate ratio, 0.87; 95% CI, 0.69-1.10). Rates of gastroesophageal cancer also were similar among groups throughout the study.

Screening for and eradicating *H. pylori* also did not affect the likelihood of dyspepsia or peptic ulcer disease at 13 years among individuals who were dyspeptic at baseline, the researchers said. The relatively low prevalence of *H. pylori* infection in Denmark might have diluted the effects of screening and eradication, they added.

Funders included the Region of Southern Denmark, the department of clinical research at the University of Southern Denmark, the Odense University Hospital research board, and the Aase and Ejnar Danielsens Foundation, Beckett-Fonden, and Helsefonden. The researchers reported having no conflicts of interest.

ginews@gastro.org

Continued from page 4

order. Insurance companies responded by either pulling out of markets or raising premiums by 7%-20% *over previously requested increases*. As of now, Congress is trying to pass a compromise bill. These nuances are complex but in the end they directly affect millions of Americans. These changes will directly affect our patients (consider our IBD patients for example) with loss of coverage or plans that are priced beyond peoples' financial capacity. No legislation approaches the most fundamental question, which is the expense of United States medical care.

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

Pages 6a—6b ▸

FROM THE AGA JOURNALS

Branch duct IPMNs confer increased malignancy risk

BY AMY KARON
Frontline Medical News

Patients with branch duct intraductal papillary mucinous neoplasms (BD-IPMNs) were about 19 times more likely to develop malignancies over 5 years compared with the general population, although they lacked worrisome features of malignancy at baseline.

The overall risk of malignancy in this cohort approached 8% and persisted for 10 years or more, said Ilaria Pergolini, MD, of Massachusetts General Hospital, Boston, and her associates. The findings support surveillance of this population past 5 years, although cysts that remain 1.5 cm or smaller for more than 5 years might be regarded as unlikely to become malignant, they wrote. The report appears in the November issue of Gastroenterology (doi: 10.1053/j.gastro.2017.07.019).

The researchers defined BD-IPMNs as unilocular or multilocular pancreatic cysts with a nondilated main pancreatic duct (smaller than 5 mm). They retrospectively studied 577 patients with suspected or presumed BD-IPMNs followed at Massachusetts General Hospital. Patients underwent cross-sectional imaging 3 months or more after initial diagnosis and at least once thereafter. Standardized incidence ratios were calculated based on population-level data for the United States from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program.

Patients tended to be in their mid-60s at diagnosis (range, 21-90 years) and 59% were female, said the researchers. Median follow-up time was 82 months and ranged between 6 and 329 months, but 63% of patients were followed for at least 5 years (median, 107 months). Fully 83% of patients were asymptomatic at initial diagnosis, of which 10% subsequently became symptomatic. Most patients underwent diagnostic CT, but nearly half underwent MRI/MRCP and about a third underwent endoscopic ultrasound. At diagnosis, median cyst size was 14 mm (range, 2-54 mm) and 9% of patients had cysts measuring at least 3 cm. By the end of follow-up, 55% had larger cysts than at baseline, and cysts grew by a median of 0.9 mm per year.

At diagnosis, only 1% of patients had high-risk stigmata while 12% had worrisome features such as acute pancreatitis, cysts measuring at least 3 cm, thickened or enhancing cyst walls, nonenhancing mural nodules, main pancreatic duct size of 5-9 mm, an abrupt change in caliber of the main pancreatic duct, and lymphadenopathy. During follow-up, another 13% of patients developed new worrisome features and 9% developed high-risk stigmata, while 2% experienced regression of a nodule. In all, 36% of patients had cysts with either worrisome features, high-risk stigmata, or both at some point during the study.

Among 363 patients followed for at least 5 years, 20 (5.5%) were diagnosed with high-risk dysplasia or invasive neoplasms and 4.4% developed invasive cancer, for a standardized incidence ratio of 18.8 (95% confidence interval, 9.7-32.8; *P* less than .001). Among 108 patients who had cysts measuring 1.5 cm or less, only one individual developed a distinct ductal adenocarcinoma during 5 or more years of follow-up. Of 255 patients with larger cysts, the 5-year malignancy rate was 7.5% (*P* = .01).

"We strongly support continued surveillance after 5 years from the initial diagnosis."

The investigators did not disclose external funding sources. They reported having no conflicts of interest.

ginews@gastro.org

The appropriate surveillance strategy for branch duct IPMNs is a point of debate, and numerous guidelines have offered recommendations for managing these potentially malignant neoplasms. Among the contested topics is the appropriateness of ceasing imaging surveillance of lesions that are stable over years. In 2015, an American Gastroenterological Association guideline made conditional recommendation to cease imaging surveillance of pancreatic cysts that have remained stable after 5 years, noting that only very low-quality evidence was available.

Dr. Pergolini and colleagues shed new light on this question with this retrospective review. Their study demonstrates that a dramatically increased risk of developing pancreatic malignancy persists even when a branch duct IPMN demonstrates no worrisome features or growth after 5 years of imaging surveillance. In fact, in their cohort, not only did the risk of malignancy persist among patients with branch duct IPMNs compared to population-based controls, but in fact, the risk was even greater after 5 years. The risk persisted even after 10 years of follow-up. This study lends credibility to the opinion that branch duct-type IPMNs should undergo ongoing surveillance even after 5 years of stability on imaging. Furthermore, it invites further study on smaller (less than 1.5-cm) branch duct IPMNs that remain stable over 5 years, as they appear to be very low risk and may represent a category of IPMNs that do not require indefinite surveillance.


DR. GAMBOA

Anthony Gamboa, MD, is assistant professor of medicine, program director of advanced endoscopy fellowship, division of gastroenterology, hepatology and nutrition, Vanderbilt University, Nashville, Tenn. He has no conflicts of interest.

DDSEP eight
Digestive Diseases Self-Education Program

Quick quiz

Q1. A 50-year-old woman with no past medical history presents to the emergency department with the acute onset of severe epigastric pain and vomiting. She is afebrile with a blood pressure of 100/50 mm Hg, and pulse of 110 bpm. Physical exam shows right upper-quadrant and epigastric tenderness to palpation without rebound. Labs demonstrate a WBC count of 17,000/mm^3, hemoglobin of 16 g/dL, creatinine of 1.4 mg/dL, ALT of 215 U/L, AST of 190 U/L, a total bilirubin of 2.1 mg/dL, and triglycerides of 492 mg/dL. Right upper-quadrant ultrasound reveals gallstones and a 1.2-cm common bile duct. The following day, despite being hydrated aggressively, the patient develops a fever and becomes jaundiced with worsening abdominal pain.

What would be the next step in the patient's management?

A. Abdominal CT to evaluate for pancreatic necrosis
B. Administration of heparin and insulin to decrease triglycerides
C. ERCP
D. HIDA scan
E. Initiation of antibiotics and cholecystectomy when stable

Q2. A 26-year-old woman is evaluated for assistance with weight management. She denies any significant medical or surgical history, but her BMI is 42 kg/m^2. She does not understand why she maintains this weight. She insists that she follows a careful diet of healthy foods, noting that she has several servings each day of fruits and vegetables. She does not go to a gym, but walks when she can and takes the stairs more frequently than the elevator. Upon further review, she does admit to "stress eating" episodes just once or twice each week, but dismisses this as noncontributory, since this has been normal behavior for her since high school, when she was not considered to be overweight. She describes these episodes as more typically occurring after a stressful work day, during which she may treat herself to a bag of cookies or a carton of ice cream, usually alone in her apartment in the evening after dinner. She denies nausea, vomiting, or using laxatives. She denies sleep disturbance, is usually well rested in the morning, and eats "a healthy breakfast." A routine electrolyte profile and complete blood count are unremarkable. She seeks your advice on endoscopic devices for weight loss management.

This patient would appear to have which eating disorder?

A. Nocturnal eating syndrome
B. Anorexia nervosa
C. Binge eating disorder
D. Bulimia nervosa
E. Occult purging disorder

The answers are on page 22.

FROM THE AGA JOURNALS

Alcohol showed no cardiovascular benefits in NAFLD

BY AMY KARON
Frontline Medical News

Alcohol consumption produced no apparent cardiovascular benefits among individuals with nonalcoholic fatty liver disease, according to a study of 570 white and black adults from the Coronary Artery Risk Development in Young Adults (CARDIA) longitudinal cohort published in in Gastroenterology (doi: 10.1053/j.gastro.2017.08.012).

After researchers controlled for multiple demographic and clinical confounders, alcohol use was not associated with cardiovascular risk factors such as diabetes, hypertension, or hyperlipidemia, nor with homeostatic model assessment of insulin resistance, C-reactive protein level, total cholesterol, systolic or diastolic blood pressure, coronary artery calcification, E/A ratio, or global longitudinal strain among individuals with nonalcoholic fatty liver disease (NAFLD), reported Lisa B. VanWagner, MD, of Northwestern University, Chicago, and her associates. "[A] recommendation of cardiovascular disease risk benefit of alcohol use in persons with NAFLD cannot be made based on the current findings," they wrote. They advocated for prospective, long-term studies to better understand how various types and doses of alcohol affect hard cardiovascular endpoints in patients with NAFLD.

CARDIA enrolled 5,115 black and white adults aged 18-30 years from four cities in the United States, and followed them long term. Participants were asked about alcohol consumption at study entry and again at 15, 20, and 25 years of follow-up. At year 25, participants underwent computed tomography (CT) examinations of the thorax and abdomen and tissue Doppler echocardiography with myocardial strain measured by speckle tracking.

The 570 participants with NAFLD averaged 50 years of age, 54% were black, 46% were female, and 58% consumed at least one alcoholic drink per week, said the researchers. Compared with nondrinkers, drinkers had attained significantly higher education levels, were significantly more likely to be white and male, and had a significantly lower average body mass index (34.4 kg/m^2 vs. 37.3 kg/m^2) and C-reactive protein level (4.2 vs. 6.1 mg per L), and a significantly lower prevalence of diabetes (23% vs. 37%), impaired glucose tolerance (42% vs. 49%), obesity (75% vs. 83%) and metabolic syndrome (55% vs. 66%) (P less than .05 for all comparisons). Drinkers and nondrinkers resembled each other in terms of lipid profiles, use of lipid-lowering medications, liver attenuation scores, and systolic and diastolic blood pressures, although significantly more nondrinkers used antihypertensive medications (46% vs.35%; P = .005).

Drinkers had a higher prevalence of coronary artery calcification, defined as Agatston score above 0 (42% vs. 34%), and the difference approached statistical significance (P = .05). However, after they adjusted for multiple potential confounders, the researchers found no link between alcohol consumption and risk factors for cardiovascular disease or between alcohol consumption and measures of subclinical cardiovascular disease. This finding persisted in sensitivity analyses that examined alcohol dose, binge drinking, history of cardiovascular events, and former heavy alcohol use.

Taken together, the findings "challenge the belief that alcohol use may reduce cardiovascular disease risk in persons with nonalcoholic fatty liver disease," the investigators concluded. Clinical heart failure was too rare to reliably assess, but "we failed to observe an association between alcohol use and multiple markers of subclinical changes in cardiac structure and function that may be precursors of incident heart failure in NAFLD," they wrote. More longitudinal studies would be needed to clarify how moderate alcohol use in NAFLD affects coronary artery calcification or changes in myocardial structure and function, they cautioned.

The National Institutes of Health supported the work. The investigators reported having no relevant conflicts of interest.

ginews@gastro.org

Dabigatran, rivaroxaban linked to increase in GI bleeding

BY AMY KARON
Frontline Medical News

Compared with conventional anticoagulants, both dabigatran and rivaroxaban conferred small but statistically significant increases in the risk of major gastrointestinal bleeding in a systematic review and meta-analysis of randomized trials reported in the November issue of Clinical Gastroenterology and Hepatology (doi: 10.1016/j.cgh.2017.04.031).

But other novel oral anticoagulants (NOACs) showed no such effect compared with warfarin, aspirin, or placebo, reported Corey S. Miller, MD, of McGill University, Montreal, and his associates. "The potentially increased risk of GI bleeding associated with dabigatran and rivaroxaban observed in some of our subgroup analyses merits further consideration," they wrote.

The NOACs (also known as non–vitamin K antagonist oral anticoagulants) help prevent stroke in patients with atrial fibrillation and prevent and treat venous thromboembolism. However, large AF trials have linked all except apixaban to an increased risk of major GI bleeding compared with warfarin. Dabigatran currently is the only NOAC with an approved reversal agent, "making the question of GI bleeding risk even more consequential," the authors wrote.

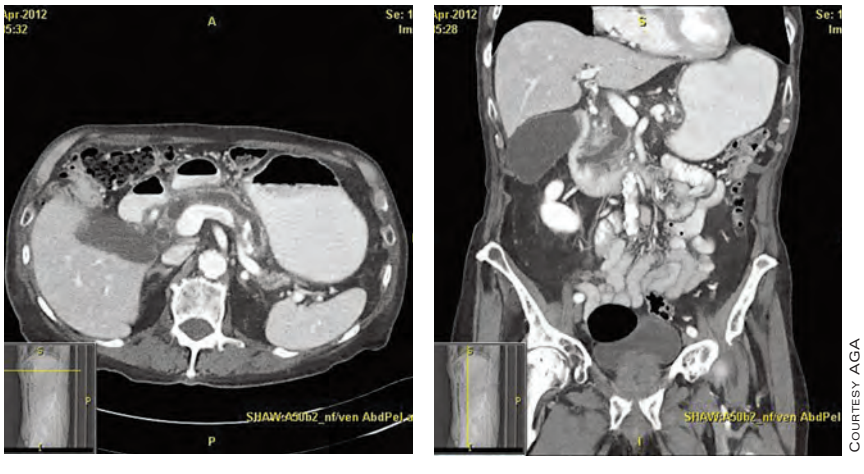
They searched the MEDLINE, EMBASE, Cochrane, and ISI Web of Knowledge databases for reports of randomized trials of NOACs for approved indications published between 1980 and January 2016, which identified 43 trials of 166,289 patients. Most used warfarin as the comparator, but one study compared apixaban with aspirin and six studies compared apixaban, rivaroxaban, or dabigatran with placebo. Fifteen trials failed to specify bleeding sources and therefore could not be evaluated for the primary endpoint, the reviewers noted.

In the remaining 28 trials, 1.5% of NOAC recipients developed major GI bleeding, compared with 1.3% of recipients of conventional anticoagulants (odds ratio, 0.98; 95% confidence interval, 0.80-1.21). Five trials of dabigatran showed a 2% risk of major GI bleeding, compared with 1.4% with conventional anticoagulation, a slight but significant increase (OR, 1.27; 95% CI, 1.04-

Continued on page 16

Correction

On page 2 of the September issue of GI & Hepatology News, the images that appeared with the second question under the DDSEP®8 Quick quiz were incorrect. The correct images are presented here:



COURTESY AGA

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

FROM THE AGA JOURNALS

Continued from page 8

1.55). Eight trials of rivaroxaban showed a similar trend (bleeding risk, 1.7% vs. 1.3%; OR, 1.40; 95% CI, 1.15-1.70). In contrast, subgroup analyses of apixaban and edoxaban found no difference in risk of major GI bleeding versus conventional treatment.

Subgroup analyses by region found no differences except in Asia, where NOACs were associated with a significantly lower odds of major GI bleeding (0.5% and 1.2%, respectively; OR, 0.45; 95% CI, 0.22-0.91).

Most studies did not report minor or nonsevere bleeds or specify bleeding location within the GI tract, the reviewers noted. Given those caveats, NOACs and conventional anticoagulants conferred similar risks of clinically relevant nonmajor bleeding (0.6% and 0.6%, respectively), upper GI bleeding (1.5% and 1.6%), and lower GI bleeding (1.0% and 1.0%).

A post hoc analysis using a random-effects model found no significant difference in risk of major GI bleeding between either rivaroxaban or dabigatran and conventional therapy, the reviewers said. In addition, the increased risk of bleeding with dabigatran was confined to the RELY and ROCKET trials of AF, both of which exposed patients to longer treatment periods. Dabigatran is coated with tartaric acid, which might have a "direct caustic effect on the intestinal lumen," they wrote. Also, NOACs are incompletely absorbed across the GI mucosa and therefore have some anticoagulant activity in the GI lumen, unlike warfarin or parenteral anticoagulants.

The reviewers disclosed no funding sources. Dr. Miller and another author reported having no conflicts of interest. One author received research grants and speaker honoraria from Boehringer Ingelheim Canada, Bayer Canada, Daiichi Sankyo, Bristol-Myers Squibb, and Pfizer Canada; another author disclosed serving as a consultant to Pendopharm, Boston Scientific, and Cook.

ginews@gastro.org

NOACs receive a lot of press now. In randomized controlled trials (RCTs) comparing NOACs to warfarin for prevention of strokes and thromboembolism in atrial fibrillation and venous thromboembolism, fewer thromboembolisms are reported, but risks of gastrointestinal bleeding vary. To expand analyses for gastrointestinal bleeding, several systematic reviews and meta-analyses are reported, including this one by C.S. Miller et al. Their goals were to delineate risks of gastrointestinal bleeding for different NOACs compared with warfarin. What can GI clinicians now recommend about gastrointestinal bleeding for patients requiring anticoagulants? While we lack RCTs to give the highest quality of evidence about GIB as a primary outcome, conclusions now depend on the weight of evidence from recent secondary data analyses, and I have some recommendations. First, although there may be differences among NOACs in risks of bleeding, all are likely to increase the risk of GI bleeding, comparable with warfarin. Some report that dabigatran and rivaroxaban have a higher risk of GI bleeding than other NOACs or warfarin, but differences are small. Second, some patients who need NOACs/warfarin have increased risks of ulcer bleeds including elderly patients and those with a history of upper GI bleeding, renal or hepatic impairment, low body weight, and concomitant antiplatelet agents. Such high-risk patients warrant treatment with a proton pump inhibitor or histamine$_2$-receptor agonists for primary prevention while on anticoagulants. Finally, for patients with severe ulcer bleeding who require anticoagulation, warfarin or NOACs should be restarted after successful endoscopic hemostasis and proton pump inhibitors, usually in 3-5 days.

Dr. Jensen is professor of medicine at the University of California, Los Angeles; associate director of the CURE Digestive Disease Research Center, staff gastroenterologist at the Ronald Reagan UCLA and West Los Angeles VA Medical Centers. He has no fincancial conflicts of interest.

Biophysical properties of HCV evolve over course of infection

BY AMY KARON

Frontline Medical News

Hepatitis C virus (HCV) particles are of lowest density and most infectious early in the course of infection, based on findings from a study of chimeric mice.

Over time, however, viral density became more heterogeneous and infectivity fell, reported Ursula Andreo, PhD, of Rockefeller University, New York, with her coinvestigators. A diet of 10% sucrose, which in rats induces hepatic secretion of very-low-density lipoprotein (VLDL), caused HCV particles to become slightly lower density and more infectious in the mice, the researchers reported. Although the shift was "minor," it "correlated with a trend toward enhanced triglyceride and cholesterol levels in the same fractions," they wrote. They recommended studying high-fat diets to determine whether altering the VLDL secretion pathway affects the biophysical properties of HCV. "A high-fat diet might have a more significant impact on the lipoprotein profile in this humanized mouse model," they wrote in Cellular and Molecular Gastroenterology and Hepatology (2017 Jul;4[3]:405-17).

Because HCV tends to associate with lipoproteins, it shows a range of buoyant densities in the blood of infected patients. The "entry, replication, and assembly [of the virion] are linked closely to host lipid and lipoprotein metabolism," wrote Dr. Andreo and her colleagues.

They created an in vivo model to study the buoyant density and infectivity of HCV particles, as well as their interaction with lipoproteins, by grafting human hepatocytes into the livers of immunodeficient mice that were homozygous recessive for fumarylacetoacetate hydrolase. Next, they infected 13 of these chimeric mice with J6-JFH1, an HCV strain that can establish long-term infections in mice that have human liver grafts (Proc Natl Acad Sci USA. 2006;103[10]:3805-9). The human liver xenograft reconstituted the FAH gene, restoring triglycerides to normal levels in the chimeric mice and creating a suitable "humanlike" model of lipoprotein metabolism, the investigators wrote.

Density fractionation of infectious mouse serum revealed higher infectivity in the low-density fractions soon after infection, which also has been observed in a human liver chimeric mouse model of severe combined immunodeficiency disease, they added. In the HCV model, the human liver grafts were conserved 5 weeks after infection, and the mice had a lower proportion of lighter, infectious HCV particles.

The researchers lacked sufficient material to directly study the composition of virions or detect viral proteins in the various density fractions. However, they determined that apolipoprotein C1 was the lightest fraction and that apolipoprotein E was mainly found in the five lightest fractions. Both these apolipoproteins are "essential factors of HCV infectivity," and neither redistributed over time, they said. They suggested using immunoelectron microscopy or mass spectrometry to study the nature and infectivity of viral particles further.

In humans, ingesting a high-fat milkshake increases detectable HCV RNA in the VLDL fraction, the researchers noted. In rodents, a sucrose diet also has been found to increase VLDL lipidation and secretion, so they gave five of the infected chimeric mice drinking water containing 10% sucrose. After 5 weeks, these mice had increased infectivity and higher levels of triglycerides and cholesterol, but the effect was small and disappeared after the sucrose was withdrawn.

HCV "circulates as a population of particles of light, as well as dense, buoyant densities, and both are infectious," the researchers concluded. "Changes in diet, as well as conditions such as fasting and feeding, affect the distribution of HCV buoyant density gradients."

Funders included the National Institutes of Health and the American Association for the Study of Liver Diseases. The investigators disclosed no conflicts.

ginews@gastro.org

FROM THE AGA JOURNALS

A hallmark of HCV infection is the association of virus particles with lipoproteins. The HCV virion (lipo-viro particle, LVP) is composed of nucleocapsid and envelope glycoproteins associated with very-low- and low-density lipoproteins, cholesterol, and apolipoproteins. The lipid components determine the size, density, hepatotropism, and infectivity of LVPs and play a role in cell entry, morphogenesis, release, and viral escape mechanisms. LVPs undergo dynamic changes during infection, and dietary triglycerides induce alterations in their biophysical properties and infectivity.


DR. BUDKOWSKA

HCV species and tissue specificity is limited to the human hepatocyte. Since hepatoma cells in vitro produce virus particles with incomplete lipoprotein composition, mouse models with transplanted human primary hepatocytes have been developed to investigate infection in vivo.

Dr. Andreo and colleagues used humanized Fah–/– mice to analyze the evolution of HCV particles during infection. As previously reported, two viral populations of different densities were detected in mice sera, with higher infectivity observed for the low-density population. The proportions and infectivity of these populations varied during infection, reflecting changes in biochemical features of the virus. Sucrose diet influenced the properties of virus particles; these properties' changes correlated with a redistribution of triglycerides and cholesterol among lipoproteins.

Changes in biochemical features of the virus during infection represent a fascinating aspect of the structural heterogeneity, which influences HCV infectivity and evolution of the disease. Further studies in experimental models that reproduce the lipoprotein-dependent morphogenesis and release of virus particles, maturation, and intravascular remodeling of HCV-associated lipoproteins would help to develop novel lipid-targeting inhibitors to improve existing therapies.

Agata Budkowska, PhD, is scientific adviser for the department of international affairs at the Institut Pasteur, Paris. She has no conflicts of interest.

GIs take on Capitol Hill

During AGA's annual Joint Committee weekend, 55 AGA members collectively attended 79 meetings with staff from the offices of their House representatives and senators, lobbying for the top concerns of gastroenterologists across the country, including:

- Continued coverage of patients through either the Affordable Care Act or another bill that has the patient's best interests in mind. More specifically, one that provides coverage for those with pre-existing conditions and for children under their parents' plan until 26 years of age, among many other important provisions.
- Changes in health care language that label a colonoscopy for cancer screening as "therapeutic," which renders a large copay for patients.
- Increased funding for the NIH.

Participants shared experiences from their time on Capitol Hill in the AGA Community forum, and encouraged others to get involved. Here are some of their reasons why.

- Your voice matters: You are constituents – which translates to votes in the minds of representatives and senators – and providing face-to-face conversation with their staffers shows them that you care about your patients and their needs, explains Siddharth Singh, MD.
- Being consistent gets your foot in the door: Some staffers recognized and remembered previous Advocacy Day participants, like Peter Liang, MD, MPH. Personally connecting could lead to follow-up communication and advocacy efforts, says Sarah Streett, MD, AGAF.
- You're indirectly (and sometimes directly) connecting with decision makers: Staff members from these offices work closely with the legislators who evaluate which policies to support or oppose. "So it's important to come to Washington, build relationships, and make the case for our science, our specialty, and our patients," says Kim Barrett, PhD, AGAF.
- Others could be advocating against you on the same issues: "I very strongly believe that it is important to keep letting our legislators know how we feel and what we believe in," shares Deborah Proctor, MD, AGAF.
- It's a rewarding experience: "Voice [your] concerns to your representatives who embrace the stories of how their decisions and policies affect your patients, practice, research, and institution," explains Susan Ramdhaney, MD, AGAF.
- It's a critical time to take action: With the current health care environment, gastroenterologists need to express the needs of their patients and profession, Dr. Streett explains.

View the full discussion and read updates from colleagues who visited with legislative staffers from California, New York, North Carolina, and Oregon in the forum, community.gastro.org.

Please contact agaadvocacy@gastro.org.

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

Implementing AGA's newest IBD guideline

If you treat patients with IBD, we hope you've reviewed our latest clinical practice guideline on the role of therapeutic drug monitoring (TDM) in the management of IBD, published in the September issue of *Gastroenterology*. The guideline focuses on the application of TDM for biologic therapy, specifically anti–tumor necrosis factor–α (TNF) agents, and for thiopurines, and addresses questions on the risks and benefits of reactive TDM, routine proactive TDM, or no TDM in guiding treatment changes. Proactive TDM is performed when patients are responding to therapy to maintain adequate serum drug concentrations and prevent loss of response or the development of anti-drug antibodies, whereas reactive TDM is performed at time of loss of response.

During the inaugural Crohn's & Colitis Congress™, taking place Jan. 18-20 in Las Vegas, experts will help you better understand how to use TDM to optimize the dosing regimen in individual patients. During a breakout session, Proactive Therapeutic Drug Monitoring – For Whom and How? Dr. Niels Vande Casteele plans to answer the following questions:

- Which patients are candidates for proactive TDM?
- When should proactive TDM be performed: during induction or maintenance therapy?
- What serum concentration thresholds should be used when carrying out proactive TDM?
- Should TDM be performed for all biologics?

Get up to speed on the latest professional guidelines – register today for the Crohn's & Colitis Congress, a partnership between the Crohn's & Colitis Foundation and AGA, crohnscolitiscongress.org.

ginews@gastro.org

AGA releases new clinical guidance on opioids in gastroenterology

The U.S. is facing an opioid epidemic – 91 Americans die every day from an opioid overdose. While all health care professionals should remain up to date on the risks associated with opioids, it is as important for GIs to understand how opioids can affect diverse parts of the gastrointestinal tract. Patients can experience GI symptoms and side effects related to the intake of opioids, including opioid-induced constipation (OIC), esophageal dysmotility, and delayed gastric emptying, according to a new AGA Clinical Practice Update published in the September 2017 issue of *Clinical Gastroenterology and Hepatology*.

GI symptoms and side effects related to the intake of opioids include constipation, esophageal dysmotility, and delayed gastric emptying.

Because of the common use of opioid medications to treat chronic pain, the authors recommend that physicians should first consider whether any gastrointestinal symptoms are directly related to the intake of opioids. In acute administration of opioids, symptomatic remedies should be used to counter the pharmacologic effects. For OIC, the bowel function index – a clinician assessment tool to appraise severity and responsiveness to current treatment – should be used to identify chronic OIC that is not responding to first-line therapies.

The clinical practice update also outlines:

- Pharmacologic effects of opiates in different regions of the gastrointestinal tract.
- Therapeutic uses of opioid receptor agonists and antagonists in gastroenterology.
- Prevention and treatment of OIC.

ginews@gastro.org

Roux-en-Y gastric bypass produced 12-year improvements

BY AMY KARON
Frontline Medical News

Severely obese individuals in the United States who underwent Roux-en-Y gastric bypass (RYGB) averaged a 27% weight loss 12 years later, with only a 3% incidence of type 2 diabetes mellitus and a 51% rate of diabetes remission, according to the results of a large multicenter observational prospective study.

In striking contrast, patients who did not undergo bariatric surgery averaged a 1%-2% weight loss at 12 years, a 26% incidence of diabetes, and only a 5%-10% rate of diabetes remission, said Ted D. Adams, PhD, of the University of Utah, Salt Lake City, and his associates. RYGB surgery also conferred substantial and statistically significant long-term improvements in systolic hypertension and lipid levels, the researchers reported in the New England Journal of Medicine (2017 Sep 20. doi: 10.1056/NEJMoa1700459).

Few prospective studies have tracked long-term outcomes after bariatric surgery. Among 1,156 participants in this study, 418 patients underwent RYGB, 417 individuals sought but did not undergo surgery – mainly for insurance reasons – and 321 individuals did not seek surgery. Participants were mostly females in their 40s or 50s at baseline, and typically weighed 120 kg-130 kg.


DR. ADAMS

"The follow-up rate exceeded 90% at 12 years," the researchers wrote. Two years after undergoing Roux-en-Y gastric bypass, patients had lost an average of 45 kg (95% confidence interval, 43-47 kg). By postoperative year 6, they had regained an average of 9 kg (average loss from baseline, 36 kg; 95% CI, 34-39 kg). But they typically gained only about 1.3 kg more between years 6 and 12, and they had about a 92% lower odds of developing diabetes mellitus, compared with individuals who did not undergo bariatric surgery (odds ratio, 0.08; *P* less than .001).

"Remission of type 2 diabetes was much more likely if the Roux-en-Y gastric bypass occurred before [patients began] treatment with insulin, presumably owing to the ability of partially viable beta cells to improve their function," the researchers noted.

Funders included the National Institute of Diabetes and Digestive and Kidney Diseases, the National Center for Research Resources, Weill Cornell Medicine, and Intermountain Healthcare. Dr. Adams reported having no relevant conflicts of interest. One coinvestigator disclosed royalties from licensing a questionnaire on weight loss and quality of life, and another coinvestigator disclosed fees for services rendered during a trial of an intragastric balloon. The remaining researchers had no relevant disclosures.

ginews@gastro.org

AGA Resource

Gastroenterologists are uniquely positioned to lead a care team to help patients with obesity achieve a healthy weight. The AGA Obesity Practice Guide was created to provide a comprehensive, multidisciplinary process to personalize innovative obesity care for safe and effective weight management. Learn more at www.gastro.org/obesity

Microbiome predicted response to high-fiber diet

BY AMY KARON
Frontline Medical News

Overweight individuals whose stool samples were abundant in *Prevotella* species lost about 2.3 kg more body fat on a 6-month high-fiber diet than individuals with a low ratio of *Prevotella* to *Bacteroides*, according to a randomized trial of 62 Danish adults.

The findings help explain why a high-fiber diet does not always produce meaningful weight loss, said Mads F. Hjorth, PhD, of the University of Copenhagen, and his associates. An "abundance of *Prevotella*" in the gut microbiome might underlie the "recent breakthrough in personalized nutrition," they wrote in the International Journal of Obesity.

In this study, overweight adults consumed either a high-fiber diet rich in whole grains, fruit, and vegetables, or a control diet designed to match the macronutrients of the average Danish diet. The high-fiber diet also was higher in protein (18% vs. 16.4%) and lower in fat (30.4% vs. 33.8%) than the control diet. The researchers performed genera-specific quantitative polymerase chain reaction of stool samples at baseline and tracked weight, waist circumference, and fat mass using dual-energy x-ray absorptiometry (Int J Obes [Lond]. 2017 Sep 8. doi: 10.1038/ijo.2017.220).

At the start of the study, 28 (45%) participants had a high (0.28; 95% confidence interval, 0.11-7.5) ratio of *Prevotella* to *Bacteroides* and 34 (55%) had a much lower ratio (0.00007) but did not otherwise differ significantly by age, sex, body weight, or fasting insulin levels. After 26 weeks, the high-*Prevotella* group lost an average of 3.2 kg more fat on the high-fiber diet than the control diet (*P* less than .001). In contrast, the low-*Prevotella* group lost only 0.9 kg more fat with the high-fiber diet, a statistically insignificant difference from the control diet. Changes in waistline circumference reflected the findings – the high-fiber diet produced a 4.8-cm average reduction in the high-*Prevotella* group, compared with a 0.8-cm reduction in the low-*Prevotella* group.

Next, the researchers asked all 62 participants to follow the high-fiber diet, but did not provide them with food. After 1 year, the high-*Prevotella* group had maintained a 1.2-kg weight loss, compared with baseline, while the low-*Prevotella* group had regained 2.8 kg of body weight (*P* less than .001). Thus, baseline *Prevotella*-to-*Bacteroides* ratio explained a 4-kg difference in responsiveness to the high-fiber diet, the researchers concluded. The difference was even more marked when they excluded eight participants with undetectable levels of *Prevotella*.


NIC_OL/THINKSTOCK

Only two individuals switched from a low to a high *Prevotella*-to-*Bacteroides* ratio during the 6-month intervention period, which reflects prior findings that the intestinal microbiome is difficult to shift without "extreme changes, such as complete removal of carbohydrates from the diet," the researchers wrote. Individual gut microbiome might affect energy absorption from different types of foods, the ability to utilize fiber, gut-brain signaling, or the secretion of hormones affecting appetite, they hypothesized. Thus, *Prevotella*-to-*Bacteroides* ratio "may serve as a biomarker to predict future weight loss success on specific diets."

Gelesis provided funding. Dr. Hjorth and two coinvestigators reported having applied for a patent on the use of biomarkers to predict response to weight loss efforts. The remaining five researchers had no conflicts.

ginews@gastro.org

CDC: Forty percent of cancers linked to overweight

BY IAN LACY
Frontline Medical News

Being overweight or obese significantly increased the risk of developing at least 13 types of cancer, according to a report by the Centers for Disease Control and Prevention.

Now that a larger proportion of the American population is overweight or obese, the rates of obesity-related cancers have increased. Between 2005 and 2014, the rate of obesity-related cancers, excluding colorectal cancer, increased by 7%. Over the same period, non–obesity-related cancers declined, according to C. Brooke Steele, DO, of the CDC's Division of Cancer Prevention and Control, and her associates (MMWR Morb Mortal Wkly Rep. 2017 Oct 3;66[39]:1052-8).

CDC NEWS

The researchers examined the United States Cancer Statistics data set, which includes data from the National Program of Cancer Registries and the Surveillance, Epidemiology, and End Results program.

They found that 631,604 people were diagnosed with an overweight- or obesity-related cancer, 40% of nearly 1.6 million of all cancer diagnoses in 2014. The effect was more pronounced in older people (age at least 50 years), compared with younger people, with two-thirds of cases occurring in the 50- to 74-year-old age range.

Women were much more likely to have overweight- and obesity-related cancers, with higher incidence rates (218.1 per 100,000 population) than those of men (115.0 per 100,000). A contributing factor for this difference between men and women was female-specific cancers such as endometrial, ovarian, and postmenopausal breast cancers, which accounted for 42% (268,091) of overweight- and obesity-related cancers.

Researchers found that, between 2005 and 2014, the overall incidence of overweight- and obesity-related cancers (including colorectal cancer) decreased by 2%, colorectal cancer decreased by 23%, and cancers unrelated to body weight decreased by 13%. A contributing factor to the decrease in colorectal cancer was most likely cancer screening tests, which can detect and lead to the removal of precancerous polyps.

"A majority of American adults weigh more than recommended – and being overweight or obese puts people at higher risk for a number of cancers – so these findings are a cause for concern," CDC Director Brenda Fitzgerald, MD, said in a statement. "By getting to and keeping a healthy weight, we all can play a role in cancer prevention."

The researchers had no conflicts of interest to report.

ilacy@frontlinemedcom.com

Reminder calls to patients improve fecal test response

BY IAN LACY
Frontline Medical News

Automated and live phone calls were shown to improve patient return of fecal test samples for both English and Spanish speakers, based on the results of a pilot study.

Colorectal cancer (CRC) is the second deadliest cancer in the United States. Screening has been shown to be a very effective tool in decreasing the mortality and incidence of CRC, but screening rates are low with 63% of adults adhering to recommended screening schedules. This problem has been addressed by direct-mail fecal immunochemical testing (FIT) kits with associated reminders, but few studies have evaluated effectiveness of follow-up techniques on FIT return rates until this pilot study.

"While many direct-mail fecal testing programs have delivered patient reminders, ours is the first study to rigorously test the effectiveness of these reminders in a community health center population, and among patients with differing language preferences," wrote Gloria Coronado, PhD, of the Center for Health Research at Kaiser Permanente and her colleagues.

The trial had two groups, one randomized and the other nonrandomized. Nonrandomized patients had active patient portals and received email reminders through the portal. The randomized group was sorted into seven intervention groups: Four of the groups used a unimodal contact method, and three groups used a multimodal contact method. The unimodal contact methods were letter reminders, automated call reminders, text reminders, and live call reminders. The multimodal contact methods were a reminder letter plus live call reminders, automated calls plus live call reminders, and text message reminders plus live call reminders. All written materials to contact patients were developed in English and later translated into Spanish and Russian. Phone call scripts were also developed in English and later translated into Spanish but not Russian because of a lack of Russian-speaking outreach workers.

After combining early-return FIT samples, those in the nonrandomized patient portal group, and the randomized samples, the overall return rate was 32.7%.

The method of contact for patients strongly influenced return rates for patients. Patients who received live phone calls were 50% more likely to return their FIT kit, compared with those who simply received a reminder email. Both English and Spanish speakers were much more likely to return their FIT kits if they were contacted with live or automated phone calls with odds ratios of 2.17 and 3.45, respectively. All other reminder techniques that did not include a phone call had similar completion rates to that of a reminder letter.

"Automated phone calls and text messages are the least costly options to implement, yet live reminders may allow staff to address or triage other patient health care needs," they wrote.

Dr. Coronado was a coinvestigator for a study funded by Epigenomics. All other authors had no conflicts of interest to report.

ilacy@frontlinemedcom.com

FDA approves pembrolizumab for gastric and GEJ cancer

BY DAN WATSON
Frontline Medical News

The Food and Drug Administration has approved pembrolizumab (Keytruda) for the treatment of patients with recurrent locally advanced or meta-static gastric or gastroesophageal junction (GEJ) adenocarcinoma, in cases where tests confirm that the tumors contain programmed death–ligand 1 and where the disease is progressing on or after two or more prior lines of therapy.

Pembrolizumab has been approved in the United States since 2014 for the treatment of melanoma, with subsequent approvals for treatment of non–small cell lung cancer, head and neck squamous cell carcinoma, Hodgkin lymphoma, and several other advanced cancers.

The drug, now approved under the FDA's accelerated approval regulations for the current indication in a 50-mg and 100-mg injection, blocks the interaction between the PD-1 protein and its ligands.

The approval comes on the basis of the nonrandomized, open-label KEYNOTE-059 trial, which enrolled 259 patients with gastric or GEJ adenocarcinoma that progressed on at least two prior systemic treatments for advanced disease. Of the enrollees, 143 patients had tumors with a PD-L1 Combined Positive Score of 1 or greater. The primary trial outcome, the objective response rate for these 143 patients, was 13.3% (95% confidence interval; 8.2-20), with a complete response rate of 1.4% and a partial response rate of 11.9%. The duration of response ranged from at least 2.8 months to at least 19.4 months.

Continued approval for the new indication will depend upon further demonstration of a clinical benefit in confirmatory trials.

dwatson@frontlinemedcom.com

DDSEP eight
Digestive Diseases Self-Education Program

Quick quiz answers

Q1. Answer: C

Rationale: The patient presents with acute gallstone pancreatitis. In patients with gallstone pancreatitis and evidence of cholangitis, ERCP with sphincterotomy and stone extraction should be performed. The patient's fever, jaundice, and right upper-quadrant pain are sufficient to make the diagnosis of cholangitis. It is too early in the course of the disease to evaluate for pancreatic necrosis. Typically, triglyceride levels above 1,000 mg/dL are required to induce pancreatitis. Finally, while the patient has cholelithiasis, there is no evidence of cholecystitis. Therefore, a HIDA scan is not warranted.

Reference

1. Behrns K.E., Ashley S.W., Hunter J.G., Carr-Locke D. Early ERCP for gallstone pancreatitis: for whom and when? J Gastrointest Surg. 2008;12(4):629-33.

Q2. Answer: C

Rationale: Binge-eating disorder (BED) is a distinct clinical entity, which gastroenterologists are likely to encounter. A substantial fraction of patients evaluated for weight loss therapy will have BED, yet it can be difficult to recognize. Similar to bulimia, BED is characterized by binge-eating episodes, which must occur an average of once a week for at least 3 months. However, there are no recurrent inappropriate behaviors such as purging with laxatives, diuretics, or emetics (e.g., syrup of ipecac) or excessive exercise. BED patients most often do not have any specific symptoms or physical exam findings other than being overweight or obese. Very subtle characteristics include very rapid eating, eating despite satiety, eating alone due to feelings of shame, and a negative emotional context after binge eating. BED will negatively impact any interventions for obesity, unless recognized and addressed.

Nocturnal eating syndrome is similar, yet distinct, in that it is also characterized by binge eating without inappropriate compensatory purging behaviors, but prominent features include morning anorexia, nocturnal hyperphagia, and sleep disturbances. The sleep disturbances are characterized by an average of 3-4 awakenings per night, during which an average of roughly 1,100 calories might be consumed during half the episodes.

Anorexia nervosa is characterized by a restriction in food intake relative to needs which results in an inappropriately low body weight (below BMI of 17.5 kg/m^2), a fear of gaining weight or being fat despite being underweight, and inappropriate perception/experience of body image. Roughly half of patient with anorexia nervosa may also engage in binge-eating behaviors or purging behaviors.

Purging disorder is a distinct variant recognized as purging behaviors in the absence of the binge-eating behavior.

ginews@gastro.org

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

IBD treatments not ruled out

Cancer *from page 1*

was associated with an 18-fold greater risk of gastrointestinal cancer, compared with the general population, matched for age, sex, birth year, and county.

The risk was particularly high in patients with ulcerative colitis, who showed a 33-fold higher risk of colorectal cancer, while patients with Crohn's disease had a nearly 6-fold higher risk.

"Colorectal cancer is a major cause of cancer mortality in the population, and even a moderately increased incidence is likely to have a large effect on patients with inflammatory bowel disease," wrote Ola Olén, MD, of Karolinska Institutet, Stockholm, and coauthors.

When the researchers looked in more detail at the type of cancers, they saw the greatest increases in risk were for colorectal cancer (HR, 19.5) and small intestinal cancer (HR, 12.8), while the risk of liver cancer was 134 times higher (95% CI, 59.6-382).

The researchers also saw a 2.7-fold increased risk of lymphoid neoplasms associated with childhood inflammatory bowel disease, particularly in individuals with ulcerative colitis or Crohn's disease. The most common lymphoid neoplasms were non-Hodgkin lymphomas, followed by Hodgkin lymphomas.

Commenting on possible explanations for the associations seen in the study, the authors said that patients with inflammatory bowel disease may have their gastrointestinal cancers diagnosed earlier than the general population because of regular endoscopies.

They also said that thiopurines and TNF inhibitors – both used to treat inflammatory bowel disease – could not be ruled out as a possible cause of the increase in cancer risk, but their study was not powered to pick up such an effect.

"Instead, we suggest that extent and duration of chronic inflammation might be the main driving mechanisms underlying the increased risk of cancer," they wrote.

The authors noted that their study did not include data on the smoking status of individuals, which could be significant, because smoking is known to reduce the risk of ulcerative colitis and increase the risk of Crohn's disease and cancer. However, they pointed out that the majority of patients would not have been smoking at the time of their initial inflammatory bowel disease diagnosis, and would have been unlikely to take up the habit after their diagnosis.

With the observation that the risk of cancer in inflammatory bowel disease was higher in patients who were younger when diagnosed with the disease, the authors suggested that age of onset be considered when designing surveillance strategies for cancer in this group.

The Stockholm County Council and the Karolinska Institutet, the Swedish Cancer Society, the Swedish Research Council, and the Swedish Foundation for Strategic Research supported the study. One author received grants from the Swedish Medical Society, Magtarmfonden, the Jane and Dan Olsson Foundation, the Mjölkdroppen Foundation, the Bengt Ihre Research Fellowship in gastroenterology, and the Karolinska Institutet Foundations. No conflicts of interest were declared.

Thiopurines and TNF inhibitors – both used to treat inflammatory bowel disease – could not be ruled out. 'Instead, we suggest that extent and duration of chronic inflammation might be the main driving mechanisms underlying the increased risk of cancer.'

ginews@gastro.org

Degrades excess antibiotic

Ribaxamase *from page 1*

caused to the gut microbiome by the antibiotic that's excreted to the intestine."

That's where ribaxamase comes in, he said at the combined annual meetings of the Infectious Diseases Society of America, the Society for Healthcare Epidemiology of America, the HIV Medicine Association, and the Pediatric Infectious Diseases Society. Ribaxamase is an orally administered beta-lactamase designed to degrade penicillin and cephalosporins in the intestinal lumen. It's formulated for release in the proximal small intestine and is expected to be given during or a short time after administration of IV beta-lactam antibiotics such as ceftriaxone. "This is expected to degrade the excess antibiotics that are excreted into the small intestine via the bile," Dr. Kokai-Kun explained. "It's designed to prevent disruption of the gut microbiome and thus protect from opportunistic GI infections like CDI."

Early-stage clinical studies demonstrated that ribaxamase was well tolerated and that it is not systemically absorbed, while phase 2 studies showed that ribaxamase degrades ceftriaxone in the intestine to below the level of detection while not affecting the pharmacokinetics of ceftriaxone in the plasma.

Results from 16S rRNA sequencing of DNA extracted from fecal samples suggests that ribaxamase 'appears to protect the gut microbiome from the onslaught of the ceftriaxone.'

For the current study, 412 patients were enrolled at 84 multinational clinical sites. These patients were admitted to the hospital for treatment of a lower respiratory tract infection and were randomized 1:1 to receive ceftriaxone plus 150 mg ribaxamase or ceftriaxone plus placebo. Patients in both groups could also receive an oral macrolide at the discretion of the clinical investigator.

The researchers also obtained fecal samples at screening, 72 hours post antibiotic treatment, and at the end of a 4-week follow-up visit, to determine colonization by opportunistic pathogens and to examine changes in the gut microbiome.

Patients were monitored for 6 weeks for diarrhea and CDI. Diarrhea was defined as three or more loose or watery stools in a 24-hour period. "If that occurred, then we collected a sample, which was sent to the local lab to determine the presence of *C. difficile* toxins," Dr. Kokai-Kun said.

The average age of study participants was 70 years, and about one-third in each arm received oral macrolides. The number of adverse events and serious adverse events were similar between active and placebo arms, and there was no trend associated with ribaxamase use. The lower respiratory tract infection cure rate to the ceftriaxone treatment was about 99% in both arms at 72 hours post treatment and at 2 weeks post treatment.

To analyze changes in the gut microbiome, the researchers conducted 16S rRNA sequencing of DNA extracted from fecal samples. In all, 652 samples were sequenced from 229 patients. Results from that analysis suggests that ribaxamase "appears to protect the gut microbiome from the onslaught of the ceftriaxone," he said.

Ribaxamase reduced the incidence of new-onset CDI by 71%, compared with placebo ($P = .045$). "It apparently did this by protecting the integrity of the gut microbiome," Dr. Kokai-Kun said. "There was also a significant reduction of new colonization by vancomycin-resistant enterococci at 72 hours and 4 weeks ($P = .0001$ and $P = .0002$, respectively) which is an opportunistic pathogen that is known to be able to inhabit gut microbiome when there is dysbiosis."

The study was sponsored by Synthetic Biologics. Dr. Kokai-Kun is an employee of the company.

dbrunk@frontlinemedcom.com

AGA Resource

Help your patients better understand *C. difficile* by using AGA's patient education materials available at http://www.gastro.org/patient-care/conditions-diseases/clostridium-difficile-infection

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

CLINICAL CHALLENGES AND IMAGES

The diagnosis

Answer to "What's your diagnosis?" on page 2: Hepatic foregut duplication cyst and concurrent acute gangrenous cholecystitis

Our patient underwent operative intervention for cholecystitis; the surgical specimen showed acute cholecystitis with necrosis. Surgical enucleation of the unilocular cyst was also performed. No communication to the gallbladder was identified. Histologically, three distinct layers were noted (mucosa, submucosa, and muscularis propria), consistent with a foregut duplication cyst (Figure C). The muscularis propria contained a rudimentary myenteric plexus, including ganglion cells, identified on S100 staining (Figure D, upper right; higher power, Figure E). The cyst was lined by multilayered cuboidal epithelium with cilia, beneath which there were scattered, nondescript glands.

The imaging findings also raised consideration of other possible etiologies. Malignancy has reportedly arisen from all of these various lesions; therefore, surgical excision was indicated given the concern over etiology.

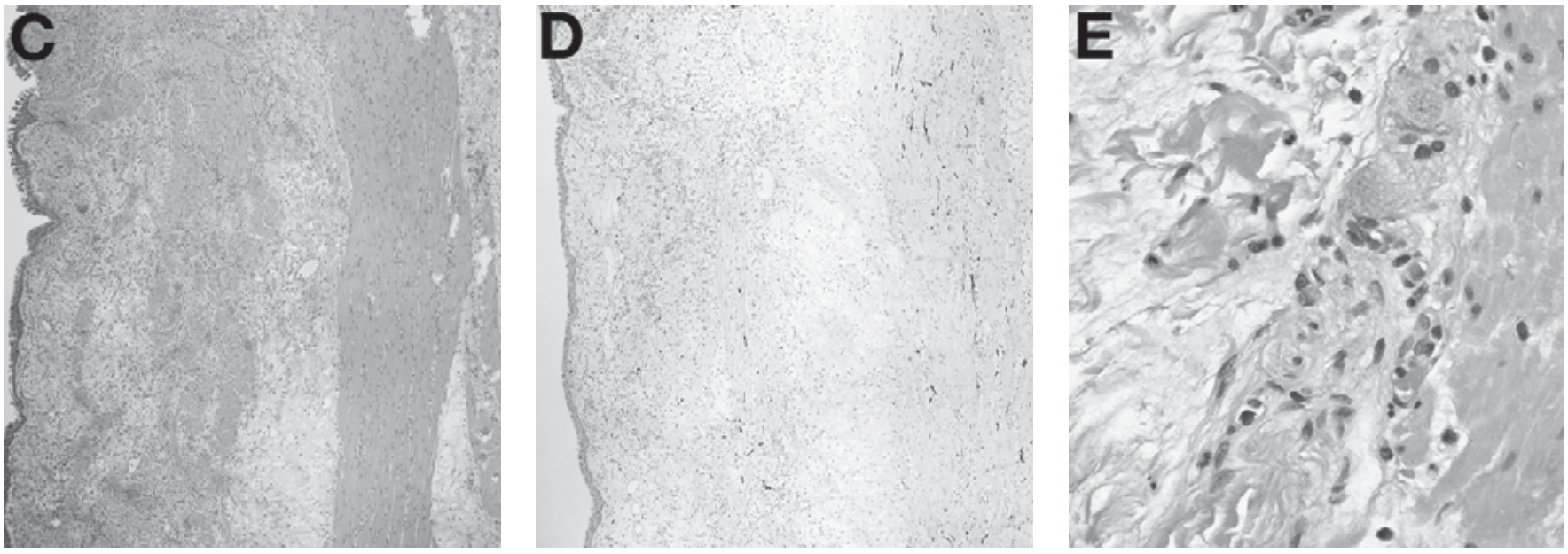
Two examples of foregut duplication cyst within the liver have been described in the literature, one representing duplicated duodenum[1] and one ileum.[2] The classic histologic features of foregut duplications include 1) well-developed smooth muscle layers, including muscularis mucosa and muscularis propria, 2) an epithelial lining that may be gastric, intestinal, or respiratory type, and 3) contiguity to the foregut segment that is duplicated.

Our differential diagnosis also included ciliated hepatic foregut cyst; however, that entity should have ciliated epithelium surrounded by disorganized bundles of smooth muscle and a dense fibrous outer capsule.[3] The imaging findings also raised consideration of other possible etiologies, including intrahepatic biliary mucinous cystadenoma, gallbladder duplication, and type II choledochal cyst. Typical findings of these lesions were not identified. Malignancy has reportedly arisen from all of these various lesions; therefore, surgical excision was indicated given the concern over etiology.

References

1. Imamoglu K.H., Walt, A.J. Duplication of the duodenum extending into liver. Am J Surg. 1977;133:628-32.
2. Seidman J.D., Yale-Loehr A.J., Beaver B., et al. Alimentary duplication presenting as an hepatic cyst in a neonate. Am J Surg Pathol. 1991;15:695-8.
3. Vick D.J., Goodman Z.D., Deavers M.T., et al. Ciliated hepatic foregut cyst: A study of six cases and review of the literature. Am J Surg Pathol. 1999;23:671-7.

ginews@gastro.org



AGA Institute

To boost HCV testing in baby boomers, offer the option

BY LUCAS FRANKI
Frontline Medical News

Rates of hepatitis C testing increased among New York adults born between 1945 and 1965 after the state passed a law mandating that health care providers offer HCV testing to people of that age, according to a report from the Centers for Disease Control and Prevention.

In 2013, the year before the new law became effective on Jan. 1, 2014, the total of specimens collected for HCV testing from the 106 clinics that reported data for both 2013 and 2014 was 538,229. In the following year after the law became effective, 813,492 samples were collected from the same clinics, an increase of 51.1% over 2013. The rate of increase for New York Medicaid recipients was similar at 52%.

CDC NEWS

The number of new HCV cases also increased significantly from 2013 to 2014: Medicaid data indicate that 13,839 people were newly diagnosed with HCV in 2013, and 18,614 people were diagnosed in 2014, an increase of 35%. Other HCV surveillance data showed an increase of 39.8% in 2014 compared to 2011-2013.

"This report highlights the potential for state laws to promote HCV testing and the utility of HCV surveillance and Medicaid claims data to monitor the quality of HCV testing and linkage to care for HCV-infected persons," the CDC investigators concluded.

Find the full report in the MMWR (doi: 10.15585/mmwr.mm6638a3).

lfranki@frontlinemedcom.com

Docs should engage employers directly on payment

BY GREGORY TWACHTMAN
Frontline Medical News

WASHINGTON – If doctors want to improve their reimbursement and at the same time be a catalyst for reducing costs to the overall health care delivery system, they need to be stronger advocates for themselves.

This was the message of Harold D. Miller, president and CEO of the Center for Healthcare Quality and Payment Reform, in his presentation to the American Gastroenterological Association Partners in Value meeting on Oct. 6.

"I think the problem is that we are developing [payment models] in entirely the wrong way today," Mr. Miller said. "We are doing the top-down approach, which is where Medicare and the health plans are defining the payment system. Then physicians and hospitals have to figure out how to change care to respond to that and guess who ends up with the short end of the stick? It's the patients and the physicians."

He called specifically on doctors to exercise initiative and accept the accountability that comes with leading the charge for payment reform.

"I think there is a much better way, which is bottom up, which is to say ask the physicians and the hospitals to say what are the ways you can improve care and reduce costs," he continued. "Then get payers to provide adequate support for that but have physicians take accountability for actually achieving those results they think are possible. And then you have patients who get good care and you keep physicians and hospitals financially sustainable, which nobody in Washington is talking about how to actually do."

Getting to that point is going to require physicians to be much more proactive in who they communicate with to get the information that is necessary to build payment models from the bottom up.

"I think there are lots of potential solutions, but I think it needs to be talked about," Mr. Miller said. "If I were to leave you with one message, the problem is that employers, Congress, etc., are not hearing from physicians that you want to do something different."

He noted that part of the issue is the adversarial relationship doctors have with the payer community, noting that most "health plans demonize you all." Mr. Miller added, "They go in to employers and they tell employers that the only thing standing between the employers and certain health insurance bankruptcy is the health plan because all the doctors want to do is spend more money."

To change that, doctors need to be much more proactive in reaching out past the payer middleman to start engaging directly with employers.

"Employers do not see doctors as their partners," Mr. Miller noted. "The people who pay have to start seeing you as wanting to solve the same problem they are trying to solve." And working with employers could help physicians insofar as getting access to data that would be crucial in developing the kinds of payment models that would benefit all of the financial aspects of health care delivery while at the same time improving care.

Mr. Miller recounted how various state and local governments in Maine were trying to extract clinical information that might not be ascertained from claims data from Anthem, one of the largest health insurance companies in America. Initially, Anthem balked, prompting the state and local entities to issue requests for information and seek to replace Anthem as the main provider for its health insurance coverage.

"Anthem completely changed its attitude," he said. "All of a sudden, Anthem was back in. ... Anthem felt that impact all the way in Indianapolis. Sam Nussbaum, MD [former chief medical officer at Anthem], said to me, 'We were punished in Maine.' "

He noted that some big employers are seeking out direct contracts with health systems because they are not getting support from the health plans.

"But they need to hear from you and what it is you need and what you are going to do with it," he said. "If you say to an employer, 'I want to know how many patients are being hospitalized so that I can help you reduce hospitalizations,' do you think they are going to say nah, we are too busy for that?"

gtwachtman@frontlinemedcom.com

PRACTICE MANAGEMENT TOOLBOX: Constructing an inflammatory bowel disease patient–centered medical home

BY MIGUEL REGUEIRO, MD, AGAF, BENJAMIN CLICK, MD, DIANE HOLDER, MSW, WILLIAM SHRANK, MD, MSHS, SANDRA MCANALLEN, AND EVA SZIGETHY, MD, PHD

Inflammatory bowel diseases (IBDs) including Crohn's disease and ulcerative colitis are life-long chronic diseases with high morbidity. There has been remarkable progress in the understanding of disease pathophysiology, leading to new medical therapies and surgical approaches for the management of IBD. These trends have resulted in a marked increase in the cost of IBD care, with current estimates ranging from $14 to $31 billion in both direct and indirect costs in the United States.[1]

IBD patients have unique behavioral, preventive, and therapeutic care requirements.[2,3] Because of the complexity of care, there is a large degree of segmentation and fragmentation of IBD management across health care systems and among multiple providers. This siloed approach often falls short of seamless, efficient, high-quality, patient-centered care.

To address the increasing costs and fragmentation of chronic disease management, population-based health care has emerged as a new concept with an emphasis on reward for value, not volume. Two such examples of population-based health care include accountable care organizations and patient-centered medical homes. This concept relies on the development of new payment models and shifts the risk to the providers.[4,5] Primary care providers play a central coordinating role in these new models.[6,7] However, the role of specialists is less well defined, with limited sharing of risk for the care and costs of populations.

The IBD specialty medical home (SMH) implemented at the University of Pittsburgh Medical Center (UPMC) is an example of a new model of care. The IBD SMH is constructed to align incentives and provide up-front resources to manage a population of patients with IBD optimally – including treatment of their inflammatory disease, coexisting pain, and psychological issues.[8-10] In the case of the IBD SMH, the gastroenterologist is the principal provider for a cohort of IBD patients. The gastroenterologist is responsible for the coordination and management of health care of this population and places the IBD patient at the center of the medical universe.

In this article, we draw from our rich partnership between the UPMC Health Plan (HP) and Health System to describe the construction and deployment of the IBD SMH. Although this model is new and we still are learning, we already have seen an improvement in the overall quality of life, decreased utilization, and reduction in total cost of care for this IBD SMH population.

Constructing an IBD medical home: where to begin?

In conjunction with the UPMC HP, we designed and established an IBD patient-centered SMH, designated in July 2015 as UPMC Total Care–Inflammatory Bowel Disease.[11] The development of the medical home was facilitated by our unique integrated delivery and finance system. The UPMC HP provided important utilization data on their IBD population, which allowed for focused enrollment of the highest-utilizer patients. In addition, the UPMC HP funded positions that we hired directly as employees of our IBD SMH. These positions included the following: two nurse coordinators, two certified nurse practitioners, a dietitian, a social worker, and a psychiatrist. The UPMC HP also provided their own HP employees to work with our IBD SMH: The rare and chronic disease team included two nurses and a social worker who made house calls for a select group of patients (identified based on the frequency of their health care use). The HP also provided health coaches who worked directly with our

Continued on page 32

Giving new hope to IBD patients and more options to physicians.

BEST HOSPITALS U.S.News & WORLD REPORT HONOR ROLL 2017-18

The team at the UPMC Inflammatory Bowel Disease (IBD) Center has developed a new way to connect our leading IBD program with more than a dozen other top programs around the country. *IBD Live* is a first-of-its-kind interactive video and publication series focused exclusively on sharing information about inflammatory bowel diseases. *IBD Live* allows multiple centers to actively participate at the same time, which facilitates consistency in IBD care, the sharing of research, and an immediate exchange of treatment options for real patient cases. The conference proceedings also are published in the journal *Inflammatory Bowel Diseases* and fulfill CME accreditation. To learn more, visit **UPMCPhysicianResources.com/Gastro**.

UPMC LIFE CHANGING MEDICINE

UPMC Presbyterian Shadyside is ranked among America's Best Hospitals by *U.S. News & World Report.*

Continued from page 30

patients on lifestyle modifications, such as smoking cessation and exercise programs. Finally, the UPMC HP worked with the IBD SMH to provide support for a variety of operational functions. Examples of these important efforts included data analytics through their department of health economics, regular

Content from this column was originally published in the "Practice Management: The Road Ahead" section of *Clinical Gastroenterology and Hepatology* (2017;15:1148-53).

collaboration to assist the provider team in modifying the program, publicizing the IBD SMH to their members, and facilitating approval of IBD medications through their pharmacy department.

We acknowledge that the development and implementation of an IBD SMH will vary from region to region and depend on the relationship of payers and providers. Thus, the blueprint of our UPMC IBD Medical Home may not be replicated readily in other centers or regions. However, there are several core elements that we believe are necessary in constructing any SMH: 1) a payer willing to partner with the provider, 2) a patient population with specific characteristics, 3) a physician champion, and 4) prespecified goals and measures of success.

Payer or health plan

A SMH is based on the premise that providers and payers working together can achieve more efficient, high-quality care for patients than either party working alone. Payers have essential resources for infrastructure support, preventive services delivery, marketing and engagement expertise, large databases for risk stratification and gap closure, and care management capacity to be a valuable partner. In the short term, philanthropy, grants, and crowd-sourcing options can be used to provide initial support for components of the SMH; however, these rarely are sustainable long-term options. Thus, the most critical collaboration necessary to considering a SMH is between payer(s) (insurance company or health plan) and the specialty provider.

Ideally, the local environment should consist of a single or a few large payers to ease SMH implementation. UPMC is a large integrated delivery (25 hospitals and more than 600 clinics) and financing system (more than 3 million members and is the dominant payer in the region), with a history of leveraging payer –provider partnerships to achieve better patient care, education, and research, and thus served as an ideal collaborator in the design and launch of the IBD SMH. Most physicians in the United States do not work in an integrated payer–provider health delivery system, and partnering with a large regional payer with an interest in specialty population-based chronic care is reasonable for constructing an SMH in your medical neighborhood.

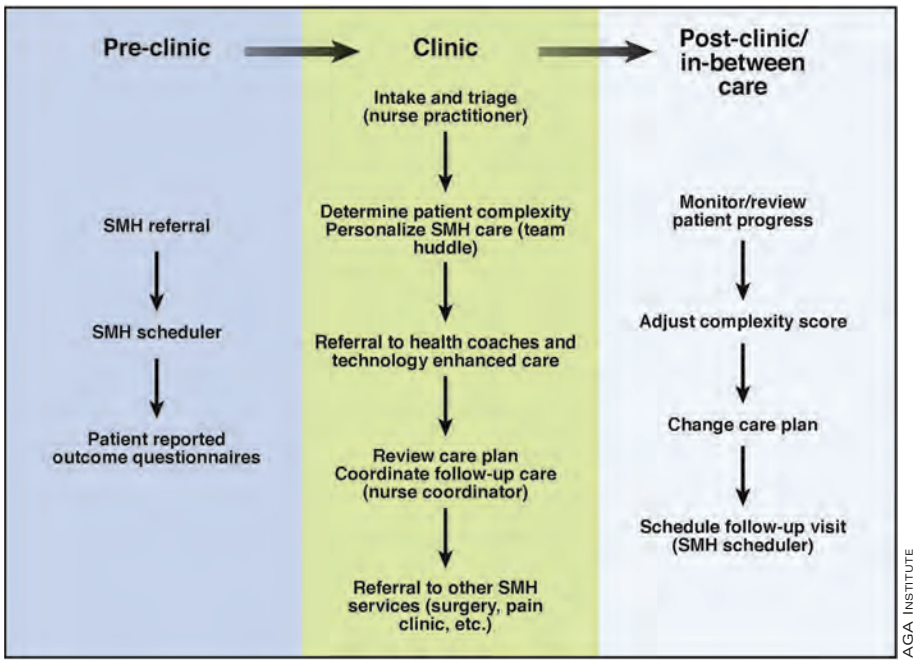


Figure 1. Patient flow through the IBD specialty medical home.

Patient population

In addition to having a collaborative health plan with large population coverage, there must exist a substantial IBD population managed by gastroenterologists. There must be a sufficient number of high-utilizer, high-cost members to justify up-front capital expenditure and return on investment. To determine the feasibility and utility of creating an IBD SMH at UPMC, we collected baseline data on the following: 1) the number of IBD patients within our IBD center and health plan, 2) a hotspotting analysis for our Pennsylvania counties, and 3) health care utilization of the IBD population of interest. At the time of the SMH inception, there were 6,319 Crohn's disease and ulcerative colitis patients (including all insurance plans) in our center, with more than 3,500 members insured by our HP. There was a 30% increase in new IBD patients to our center in the 3 years before starting the IBD SMH, and the HP had a 27% increase in overall IBD members. Based on a regional hotspotting analysis, $24.3 million of the annual total of $36.9 million was related to hospitalization costs from our IBD patients. The high-utilizer patients accounted for most of the total cost of care for our HP; 16% accounted for 48% of the per-member per-month cost and 29% accounted for 79% of the total annual cost. These baseline data supported justification for an IBD SMH.

Although there is no absolute minimum number of members (patients) required, and the SMH model can be scaled to various IBD populations, we believe that at least 1,000 patients covered by a single insurer must exist. The justification for the 1,000 patients is an estimate of the number of high-utilizer patients who would be required to justify a cost savings, and ultimately a return on investment. We calculated that at least 300 high-utilizer patients would need to be included in our IBD SMH to show a reduction in health care utilization and total cost of care. Therefore, if we assume that approximately 30% of any chronic disease population drives the majority of cost and represents the highest utilizers, we estimated that at least 1,000 patients should be covered by a single insurer.

For development of an SMH, there are two approaches that may be taken: Design the medical home for the entire Health Plan's population of patients with the disease of interest, or focus only on the high-utilizing, most expensive patients. The latter will include a more complex and challenging cohort of patients, but likely will provide the opportunity to show a reduction in utilization and total cost of care than a broader all-comers population approach.

Physician champions

A successful SMH requires a physician (or health care provider) champion. IBD care within the SMH is unique and distinct from gastroenterologists' classic training and specialty care. In addition to addressing the biologic disease, the emphasis is on whole-patient care: preventive care, behavioral medicine, socioeconomic considerations of the patient, and provision of care for nongastrointestinal symptoms and diseases. In an SMH, the specialist must be willing to incorporate and address all facets of health care to improve patient outcomes.

Goals and measures of success

To ensure successful deployment of an SMH, it is important to establish shared payer–provider goals and metrics during the construction phase of the medical home. These goals should include an enrollment target number for each year, quality improvement metrics, patient experience outcomes, and metrics for a reduction in health care utilization and total cost of care. Examples of our IBD SMH year 1 and year 2 goals are outlined in Supplementary Table 1 (at http://dx.doi.org/10.1016/j.cgh.2017.05.026). In the first year of our IBD SMH, we were able to achieve our goals, and publication of our results is forthcoming. We have enrolled more than 325 patients, retained 90%, reduced emergency room visits and hospitalizations by 50%, and significantly improved quality of life. Most of our patients have been assigned an HP coach and use the electronic medical portal to communicate with the medical home. Our patient satisfaction for physician communication was 99%.

Key components of the IBD medical home

Based on our experience, we believe the following are key components of a successful IBD SMH: 1) team-based care with physician extenders, nurse coordinators, schedulers, social workers, and dietitians as essential members of the IBD SMH; 2)

Continued on following page

TABLE 1

Essential components of an inflammatory bowel disease specialty medical home

Essential components	Domain	Key elements	Iterative flexibility
Team-based care • Gastroenterologist • Psychiatrist or behavioral health specialist • Nurse practitioners • Nurse coordinators • Social worker • Dietitian • Health coaches	Transdisciplinary approach	• Gastroenterologist as principal provider • Physician extenders • Behavioral specialists • Nutritional expert • Close liaison with surgical team and pain specialist	• Start with small team and expand as demand or needs dictate • Test what is working and quickly change what is not working
Care coordination	Integration and matching resources to patient complexity in a tiered manner	A system to identify and address barriers to care, prioritize goals, and monitor patient progress toward the least-intensive care	A method to objectively rate patient complexity, development of quantifiable care plans, and criteria for escalation or de-escalation of care scope and intensity
Outcomes	Quantification of processes and outcomes	Measures of clinical processes and outcomes, quality metrics, cost - effectiveness, and staff wellness and burnout	Actionable measures with root-cause analyses to determine implementation pivots needed
Technology	Staff efficiency, care access, and scalability	Identifying clinical care gaps and using health technology to address them	Familiarity of empirically supported technologies and testing with small adaptive trials to optimize enhancement of care
Care access	• System for providing open-access scheduling and after-hours care • SMH clinic availability after emergency room visits and hospitalizations	• Schedulers or nurses devoted to care access with expertise in motivational interviewing and other clinician communication skills • Use of peer experts for patient education and moderated social support to improve care	Tracking patient preference, activation, adherence, and satisfaction for improvement opportunities

FRONTLINE MEDICAL NEWS

Continued from previous page

effective care coordination to reduce barriers to comprehensive biopsychosocial care; 3) tracking of process and outcome metrics of interest; 4) appropriate use of technology to enhance clinical care; and 5) care access (e.g., open-access appointments), after-hours care, and follow-up care after emergency room visits and hospitalizations (Table 1).

There is not a one-size-fits-all SMH model given the range of different subspecialty practices. The appropriate dose for each specific setting may vary, and we recommend an iterative deployment process starting with a few case studies and then sequentially rolling out to a larger-scale clinical sample. The goal of the initial SMH is to show feasibility and understand which components are most critical for successful implementation.

Although the eventual goal of an IBD SMH is to consolidate health care for all IBD patients, the initial launch stages are more likely to succeed if the SMH focuses on the subgroup of IBD patients who use health care excessively, often in an unplanned fashion (e.g., emergency department visits or hospitalizations). In conjunction with a payer, it is easy to identify the most costly IBD patients in a cohort. For example, for initial enrollment, the UPMC IBD SMH selected patients between the ages of 18 and 55 years, with confirmed Crohn's disease or ulcerative colitis, and evidence that IBD was a primary driver of patients' health care utilization; the latter was defined if the majority of health care expenditures in the prior year was related to IBD (as judged by International Classification of Diseases, 9th and 10th revisions, primary and secondary diagnoses).

Team-based care

A central component to our IBD SMH was the creation of an integrated team. Supplementary Table 2 (at http://dx.doi.org/10.1016/j.cgh.2017.05.026) describes various positions that are vital for a successful SMH. For a team approach to be most effective, there needs to be clear definitions or roles and role overlaps so that team members can work as a cohesive, organized, and efficient unit. Physician extenders are critical to the model's success and are trained to make routine IBD care decisions, provide basic primary care, and coordinate care with the gastroenterologist to meet patient needs. The staff-to-patient ratio requirements may vary from region to region and from SMH to SMH. The nurse coordinators and physician extenders assume the burden of day-to-day patient care, and are supervised by the gastroenterologist and psychiatrist. In our UPMC IBD SMH, the ratio of one nurse coordinator and one certified nurse practitioner per 500 patients is sufficient. In addition, one social worker, one dietitian, one scheduler, one gastroenterologist, and one psychiatrist per 1,000 patients is our current model. To date, we have enrolled more than 500 patients, and through funding from our UPMC HP, we have just hired our second nurse coordinator and second nurse practitioner in anticipation of 1,000 patients by year 4.

In an ideal team model, all staff, both behavioral and medical, are trained in basic behavioral assessment and interventions, motivational interviewing, and disease self-management techniques so that the behavioral health specialist can be considered a second-line provider or a consultant to the gastroenterologist for the most complex psychiatric patients. Figure 1 shows a typical patient's trajectory through the IBD SMH.

Care coordination and incorporation of technology

The team composition is organized to provide tiered care for optimal efficiency. For such a stepped care model to be effective and scalable, two components are essential. The first component is a care coordination system that allows for the reliable classification of the biological, psychological, social, and health systems barriers faced by patients. To this end, our SMH developed an IBD-specific complexity grid (Supplementary Table 3; at http://dx.doi.org/10.1016/j.cgh.2017.05.026) that was derived from a primary care model.[12] The second component is the use of technology-enhanced care to scale delivery of services in a population health model. Examples of technology in our SMH include the use of telemedicine/telepsychiatry by secure video, health coach virtual visits, remote monitoring, and provider-assisted behavioral interventions that patients can access on their smart phones.

New payment models for specialty medical homes

The SMH transitions away from relative value unit–based reimbursement and toward a value-based paradigm. In the SMH, the gastroenterologist serves as the principal medical provider for the IBD patient. Both pro-

viders and payers will be able to refer patients to the SMH. Data on quality metrics will be tracked and physician extenders and nurse coordinators will help ensure that goals are met. Quality improvement, preventive medicine, telemedicine, and point-of-contact mental health care will replace the volume-based relative value unit system.

Alternative payment models will be required to support the SMH. Because of the novel nature of the SMH, the optimal payment model has yet to be determined, but probably will include either a shared savings or global cap approach, with an emphasis on the total cost of care reduction. This means that the specialist in the SMH must be aware of all care, and the cost of care, that the patient receives. Biologics and other IBD therapy costs are high and will continue to increase. The sustainable model must be sufficiently supple to not disincentivize the provider to use proven and effective, albeit expensive, therapy for patients who need it most. A close working relationship between the SMH providers and the health plan chief pharmacy officer will be essential. We expect that appropriate use of medications will lead to a medical cost offset with improved IBD outcomes, a reduction in health care utilization, and optimized work and life productivity.

Conclusions

In new models of care, specialty providers partner with payers in a patient-centered system to provide principal care for patients with chronic diseases, including IBD, in an effort to reduce costs and provide efficient, high-quality care. These models will require close collaborations with payers, a sufficiently large patient population, a physician champion, and a multidisciplinary staff targeting various aspects of health care. Successful implementation of such models will help reduce costs of care while improving the patient-centered experience and outcomes.

Take-away points:

1. The IBD patient–centered medical home is a new model of care in which the specialist, i.e., gastroenetologist, serves as the principal care provider of a chronic disease population.
2. The collaboration between the payer and provider around specialty medical care advances the value-based proposition of health care reform.
3. A team-based approach that emphasizes "whole person" care is essential for specialty medical homes.
4. The IBD Specialty Medical Home has improved the quality of life of patients while reducing the unplanned care of emergency room visits and hospitalizations.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at http://dx.doi.org/10.1016/j.cgh.2017.05.026.

References

1. Mehta F. Report: economic implications of inflammatory bowel disease and its management. Am J Manag Care. 2016;22(Suppl):s51-60.
2. Mikocka-Walus A., Knowles S.R., Keefer L., et al. Controversies revisited: a systematic review of the comorbidity of depression and anxiety with inflammatory bowel diseases. Inflamm Bowel Dis. 2016;22:752-62.
3. Regueiro M., Greer J.B., Szigethy E. Etiology and treatment of pain and psychosocial issues in patients with inflammatory bowel diseases. Gastroenterology. 2017;152:430-9.e4.
4. Silow-Carroll S., Edwards J.N., Rodin D. How Colorado, Minnesota, and Vermont are reforming care delivery and payment to improve health and lower costs. Issue Brief. (Commonw Fund) 2013;10:1-9.
5. Fogelman C., Gates T. A primary care perspective on U.S. health care: part 2: thinking globally, acting locally. J Lancaster Gen Hospital. 2013;8:101-5.
6. Rosenthal M.B., Sinaiko A.D., Eastman D., et al. Impact of the Rochester medical home initiative on primary care practices, quality, utilization, and costs. Med Care. 2015;53:967-73.
7. Friedberg M.W., Rosenthal M.B., Werner R.M., et al. Effects of a medical home and shared savings intervention on quality and utilization of care. JAMA Intern Med. 2015;175:1362-8.
8. Fernandes S.M., Sanders L.M. Patient-centered medical home for patients with complex congenital heart disease. Curr Opin Pediatr. 2015;27:581-6.
9. Mikocka-Walus A.A., Andrews J.M., Bernstein C.N., et al. Integrated models of care in managing inflammatory bowel disease: a discussion. Inflamm Bowel Dis. 2012;18:1582-7.
10. Kessler R., Miller B.F., Kelly M., et al. Mental health, substance abuse, and health behavior services in patient-centered medical homes. J Am Board Fam Med. 2014;27:637-44.
11. Regueiro M.D., McAnallen S.E., Greer J.B., et al. The inflammatory bowel disease specialty medical home: a new model of patient centered care. Inflamm Bowel Dis. 2016;22:1971-80.
12. Lobo E., Ventura T., Navio M., et al. Identification of components of health complexity on internal medicine units by means of the INTERMED method. Int J Clin Pract. 2015;69:1377-86.

Dr. Regueiro and Dr. Click are in the division of gastroenterology, hepatology and nutrition, University of Pittsburgh Medical Center; Ms. Holder, Dr. Shrank, and Ms. McAnAllen are in the Insurance Services Division, University of Pittsburgh Medical Center, and Dr. Szigethy is in the Department of Psychiatry, University of Pittsburgh School of Medicine. Dr. Regueiro serves as a consultant for, on advisory boards for, and receives research support from Abbvie, Janssen, and Takeda; and Dr. Szigethy serves as a consultant for Abbvie. The remaining authors disclose no conflicts.

INDEX OF ADVERTISERS

For GI Endoscopic Resections

Visit eleviewUS.com • 888-ARIES-08

Contains Methylene Blue

Conquer polyps with lift that lasts

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

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™