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GI&Hepatology News

October 2025

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Common Medications Do Not Raise Microscopic Colitis Risk in Seniors

BY DIANA SWIFT

MDedge News

No evidence of a causal relationship between previously suspected pharmacologic triggers and increased risk of microscopic colitis (MC) emerged from a nationwide longitudinal study of older Swedish individuals in a national database.

"Sensitivity analyses suggest that previously reported associations and persistent association with SSRI [selective serotonin reuptake inhibitor] initiation may be due to surveillance bias," wrote gastroenterologist Hamed Khalili, MD, MPH, of Massachusetts General Hospital, Boston, and colleagues in *Annals of Internal Medicine* (2025 Jul. doi: 10.7326/ANNALS-25-00268), advising clinicians to carefully balance the benefits of these medication classes against the very low likelihood of a causal relationship with MC.

While two smaller studies had challenged the belief that these medications can cause MC, Khalili told *GI & Hepatology News*, "the quality of the data that supported or refuted this hypothesis was low. Nevertheless, most in the field consider MC to be largely related to medications so we thought it was important to systematically answer this question."

While most medications thought to trigger

See **Common Medications** · *page 17*

Wegovy Approved for MASH With Fibrosis, No Cirrhosis

BY MARILYNN LARKIN

The FDA has granted accelerated approval to Novo Nordisk's Wegovy for the treatment of metabolic-associated steatohepatitis (MASH) in adults with moderate-to-advanced fibrosis but without cirrhosis.

The once-weekly 2.4-mg semaglutide subcutaneous injection is given in conjunction with a reduced-calorie diet and increased physical activity.

Among people living with overweight or obesity globally, one in three also have MASH.

The accelerated approval was based on part-one results from the ongoing two-part, phase 3 ESSENCE trial, in which Wegovy demonstrated a significant improvement in liver fibrosis with no worsening of steatohepatitis, as well as resolution of steatohepatitis with no worsening of liver fibrosis, compared with placebo at week 72. Those results were published online in April in *The New England Journal of Medicine* (2025. doi: 10.1056/NEJMoa2413258).

For the trial, 800 participants were randomly assigned to either Wegovy (534 participants) or placebo (266 participants) in addition to lifestyle changes. The mean age was 56 years and the mean BMI was 34. Most patients were White individuals (67.5%) and women (57.1%), and 55.9% of the patients had type 2 diabetes; 250 patients (31.3%) had stage II fibrosis and 550 (68.8%) had stage III fibrosis. Participants were on stable doses of lipid-lowering, glucose-management, and weight-loss medications.

At week 72, the first primary endpoint showed 63% of the 534 people treated with Wegovy achieved resolution of steatohepatitis and no worsening of liver

See **Wegovy Approved** · *page 18*

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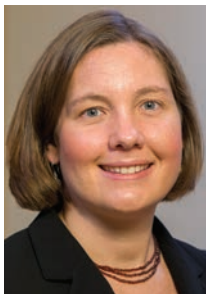
LETTER FROM THE EDITOR

Bridging the Funding Gap

Federal grants have supported cutting-edge research in scientific and biomedical fields since the mid-20th century, fueling public health breakthroughs and health innovations. This crucial support has been greatly diminished in recent months with deep cuts to federal research dollars.

As these acute policy changes continue to disrupt academic institutions and their investigators, introducing financial strain and operational uncertainty, the importance of research support from professional societies and foundations has become increasingly evident. Their targeted funding plays a critical role in sustaining biomedical research, which directly impacts clinical innovation and patient care. As one example, the AGA Research Foundation provides over $2 million annually to spur discoveries in gastroenterology and hepatology. This vital research support, awarded to 74 unique recipients (including 7 early-career Research Scholar Award recipients) in 2025, represents one of the most important investments that AGA makes in the future of gastroenterology and the patients we treat.

While foundation awards such as these cannot completely close the federal funding gap, they serve as an important lifeline in supporting the core work of early-career and established investigators in an uncertain funding environment and in funding high-risk, high-reward research that more conservative funders are often hesitant to invest in. Please consider joining me in contributing to the AGA Research Foundation to support its important work — now more than ever, the funding it provides has tremendous impact.



Dr. Adams

'The importance of research support from professional societies and foundations has become increasingly evident. Their targeted funding plays a critical role in sustaining biomedical research, which directly impacts clinical innovation and patient care.'

In this issue of *GI & Hepatology News*, we update you on the FDA's recent approval of semaglutide as a treatment for MASH with fibrosis and highlight a recent target trial emulation study that casts doubt on our traditional understanding regarding the link between common medications such as PPIs and NSAIDs and microscopic colitis in older adults. We also summarize newly released, global guidelines for pregnancy and IBD, which deserve a careful read. In this month's Member Spotlight, we feature Pascale M. White, MD, MBA, MS (Mount Sinai), a recent recipient of the AGA-Pfizer Beacon of Hope Award for Gender and Health Equity, who shares her inspirational work to improve colorectal cancer screening among underserved, high-risk patients in East Harlem. We hope you enjoy this and all the exciting content in our October issue. ■

Megan A. Adams, MD, JD, MSc
Editor in Chief

Call for Nominations

Nominate your colleagues to be featured in Member Spotlight. Email ginews@gastro.org.

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Intestinal Ultrasound Shows Promise in Predicting Prognosis of Early Crohn's Disease

BY DIANA SWIFT

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Findings on intestinal ultrasound (IUS) are useful for predicting remission in recent-onset Crohn's disease (CD), a prospective, population-based cohort of newly diagnosed patients in Denmark reported.

Adding to the growing body of evidence on the utility of this noninvasive imaging tool in monitoring disease activity in the newly diagnosed, the multicenter study published in *Clinical Gastroenterology and Hepatology* (2025 Mar. doi: 10.1016/j.cgh.2024.12.030) characterized ultrasonographic features at diagnosis and evaluated IUS's prognostic value. Existing literature has focused on patients with long-standing disease (Am J Gastroenterol. 2023 Jun. doi: 10.14309/ajg.0000000000002265).

Investigators led by first author Gorm R. Madsen, MD, PhD, of the Copenhagen Center for Inflammatory Bowel Disease in Children, Adolescents and Adults at Copenhagen University Hospital, observed continued improvement in most IUS parameters throughout the first year. "Our findings thereby emphasize the role of IUS in improving patient management, and its use in patient risk stratification already at diagnosis," the investigators wrote.

Dr. Madsen

'Ultrasonic transmural remission is achievable early in Crohn's disease and is associated with favorable outcomes, underscoring the value of intestinal ultrasound in early disease management.'

Some 38% of patients reached ultrasonic transmural remission within 3 months of diagnosis, an achievement associated with higher rates of sustained steroid-free clinical remission and reduced need for treatment escalation.

"Ultrasonic transmural remission is achievable early in Crohn's disease and is associated with favorable outcomes, underscoring the value of intestinal ultrasound in early disease management," the researchers wrote.

Study Details

While IUS is increasingly recognized for monitoring CD, little was known about its prognostic value early in the disease course. "We aimed to determine whether sonographic inflammation at diagnosis — and particularly the achievement of transmural remission after 3 months — could predict future outcomes," Madsen told *GI & Hepatology News*. "This is important, as early identification of patients at risk of surgery or treatment escalation may help guide therapy decisions more effectively."

From May 2021 to April 2023, 201 patients (mean age, 35 years; 54.2% men) with new adult-onset CD were followed by IUS and monitored with symptomatic, biochemical, and endoscopic evaluations.

After 3 months, transmural remission was achieved more often by patients with colonic disease, and no associations were found between sonographic inflammation at diagnosis and diagnostic delay.

"We were positively surprised. Nearly 40% of newly diagnosed Crohn's patients achieved transmural remission within 3 months — a higher proportion than seen in earlier studies, which mostly focused on long-standing or trial-selected populations," Madsen said. "It was also striking how strongly early IUS findings predicted the need for surgery, outperforming endoscopy and biomarkers."

In other findings, transmural remission at 3 months was significantly associated with steroid-free clinical remission at both 3 months and all subsequent follow-ups within the first year. It was also linked to a lower risk for treatment escalation during the follow-up through to 12 months: 26% vs 53% (P =.003). At 12 months, 41% had achieved transmural remission.

Higher baseline body mass index significantly reduced the likelihood of 12-month transmural remission. For overweight, the odds ratio (OR) was 0.34 (95% CI, 0.12-0.94), while for obesity, the OR was 0.16 (95% CI, 0.04-0.73).

The International Bowel Ultrasound Segmental Activity Score in the terminal ileum at diagnosis emerged as the best predictor of ileocecal resection during the first year, with an optimal threshold of 63 (area under the curve, 0.92; sensitivity, 100%; specificity, 73%).

The use of IUS has expanded considerably in the past 3 years, and in 2024, the American Gastroenterological Association updated its clinical practice guidance on the role of this modality in inflammatory bowel disease (Clin Gastroenterol Hepatol. 2024 Jul. doi: 10.1016/j.cgh.2024.04.039).

IUS is noninvasive, radiation-free, inexpensive, and doable at the bedside with immediate results, Madsen said. "For patients, this means less anxiety and discomfort. For healthcare systems, it enables faster clinical decisions, reduced need for endoscopy or MRI, and closer disease monitoring, particularly valuable in treat-to-target strategies."

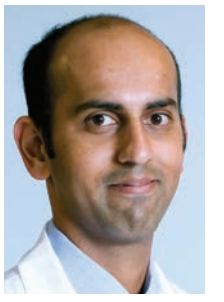
In terms of limitations, however, IUS is operator-dependent and consistent training is crucial, he added. "Certain anatomical regions, particularly the proximal small bowel, can be more challenging to evaluate. Additionally, while IUS is highly effective for assessing inflammatory activity, it becomes more difficult to accurately assess disease involvement when inflammation extends beyond approximately 20 cm of the small bowel."

Key Insights

Commenting on the Danish study from a US perspective, Anna L. Silverman, MD, a gastroenterology fellow at Icahn School of Medicine at Mount Sinai in New York City, agreed the findings in adult patients with newly diagnosed, rather than long-standing, CD contribute to the growing body of evidence supporting IUS's applicability for both treatment monitoring and prognosis.

"By focusing on early-stage CD, the study provides clearer insights into initial disease activity and response to therapy, reinforcing the value of this noninvasive, point-of-care modality," she told *GI & Hepatology News*. "These findings enhance our understanding of IUS as a tool to help guide early management decisions in CD."

Ashwin Ananthakrishnan, MBBS, MPH, AGAF, director of the Crohn's and Colitis Center at Massachusetts General Hospital and an associate professor at Harvard Medical School, both in Boston, concurred that this is an important study. "It includes newly diagnosed patients — so a very 'clean' cohort in terms of not being influenced by confounders," he told *GI & Hepatology News*.



Dr. Ananthakrishnan

"We don't fully know yet the best treatment target in CD, and this study highlights the importance of early transmural healing in determining outcomes at 1 year," he noted. In addition, the study highlighted a convenient tool that can increasingly be applied at point of care in the United States. "Colonoscopy at 3 months is not practical and has low patient acceptability, so using IUS in this circumstance would have value and impact."

Ananthakrishnan pointed to several unanswered questions, however. "Are there patients who may not have healing early but may take some extra time to achieve transmural remission, and if so, what are their outcomes? What is the best timepoint for transmural healing assessment? What is the incremental value of measuring it at 3 vs 6 months?"

In addition, he wondered, how much is the added value of IUS over clinical symptoms and/or markers such as calprotectin and C-reactive protein? "In the subset of patients with clinical and transmural remission, there was no difference in endoscopic outcomes at 1 year, so this is an unanswered question," Ananthakrishnan said.

This study was funded by an unrestricted grant from the Novo Nordisk Foundation.

Madsen reported receiving a speaker's fee from Tillotts. Multiple coauthors disclosed having various financial relationships with numerous private-sector companies, including Novo Nordisk. Silverman and Ananthakrishnan reported having no competing interests relevant to their comments. ■

Large Language Models May Reduce Time, Costs of GI Guideline Development

BY WILL PASS
MDedge News

FROM GASTROENTEROLOGY

Large language models (LLMs) may help streamline clinical guideline development by dramatically reducing the time and cost required for systematic reviews, according to a pilot study from AGA.

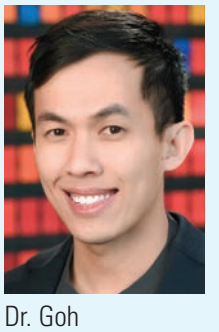

Dr. Chung

Faster, cheaper study screening could allow societies to update clinical recommendations more frequently, improving alignment with the latest evidence, lead author Sunny Chung, MD, of Yale School of Medicine, New Haven, Connecticut, and colleagues, reported.

"Each guideline typically requires 5 to 15 systematic reviews, making

Continued on following page

Ethan Goh, MD, executive director of the Stanford AI Research and Science Evaluation (ARISE) Network, described the AGA pilot as both timely and promising.


Dr. Goh

"I'm certainly bullish about the use case," he said in an interview. "Their study design and application is also robust, so I would congratulate them."

Goh, a general editor for *BMJ Digital Health & AI*, predicted "huge potential" in the strategy for both clinicians and the general population, who benefit from the most up-to-date guidelines possible.

"I believe that using AI [artificial intelligence] can represent a much faster, more cost effective, efficient way of gathering all these information sources," he said.

Still, humans will need to be involved in the process.

"[This AI-driven approach] will always need some degree of expert oversight and judgment," Goh said.

Speaking more broadly about automating study aggregation, Goh said AI may still struggle to determine which studies are most clinically relevant.

"When we use [AI models] to pull out medical references, anecdotally, I don't think they're always getting the best ones all the time, or even necessarily the right ones," he said.

And as AI models grow more impressive, these shortcomings become less apparent, potentially lulling humans into overconfidence.

"Humans are humans," Goh said. "We get lazy over time. That will be one of the challenges. As the systems get increasingly good, humans start to defer more and more of their judgment to them and say, 'All right, AI, you're doing good. Just do 100% automation.' And then [people] start fact-checking or reviewing even less."

AI could also undermine automated reviews in another way: AI-generated publications that appear genuine, but aren't, may creep into the dataset.

Despite these concerns, Goh concluded on an optimistic note.

"I think that there are huge ways to use AI tools not to replace, but to augment and support, human judgment," he said.

Dr. Goh is senior research engineer and executive director of the Stanford ARISE Network in California. He declared no conflicts of interest.

Intestinal Methanogen Overgrowth Fosters More Constipation, Less Diarrhea

BY DIANA SWIFT
MDedge News

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Patients with intestinal methanogen overgrowth (IMO) have a higher rate and severity of constipation but a lower rate and severity of diarrhea, according to a systematic review and meta-analysis published in *Clinical Gastroenterology and Hepatology* (2024 Aug. doi: 10.1016/j.cgh.2024.07.020).


Dr. Rezaie

"The distinct phenotype of patients with IMO should be incorporated in patient-reported outcome measures and further correlated with mechanistic microbiome studies," wrote investigators led by gastroenterologist Ali Rezaie, MD, MSc, medical director of the GI Motility Program at Cedars-Sinai Medical Center, Los Angeles, and director of biotechnology in the center's Medically Associated Science and Technology (MAST) Program. Recognizing specific gastrointestinal (GI) symptom profiles can improve diagnosis and treatment strategies, facilitating further clinical trials and targeted microbiome studies to optimize patient care.

Excessive luminal loads of methanogenic archaea — archaea being bacteria-like prokaryotes and one of the main three domains of the tree of life — have been implicated in the pathophysiology of various diseases, including constipation.

Study Details

To elucidate the phenotypical presentation of IMO in patients, Rezaie's group compared the prevalence and severity of GI symptoms in individuals who had IMO with those who did not have IMO. IMO was based on excess levels of this gaseous GI byproduct in exhaled breath tests.

Searching electronic databases from inception to September 2023, the researchers identified 19 eligible studies from diverse geographical regions with 1293 IMO patients and 3208 controls. Eleven studies were performed in the United States; the other studies were conducted in France (n = 2), India (n = 2), New Zealand (n = 1), South Korea (n = 1), Italy (n = 1), and the United Kingdom (n = 1). Thirteen studies were of high quality, as defined by a Newcastle-Ottawa Assessment Scale score of 6.

Patients with IMO were found to exhibit a range of GI symptoms, including bloating (78%), constipation (51%), diarrhea (33%), abdominal pain (65%), nausea (30%), and flatulence (56%).

In other findings:

- Patients with IMO had a significantly higher prevalence of constipation vs controls: 47% vs 38% (odds ratio [OR], 2.04; 95% CI, 1.48-2.83; $P < .0001$).
- They had a lower prevalence of diarrhea: 37% vs 52% (OR, 0.58; 95% CI, 0.37-0.90; $P = .01$); and nausea: 32% vs 45%; (OR, 0.75; 95% CI, 0.60-0.94; $P = .01$).
- Patients with IMO had more severe constipation: standard mean deviation [SMD], 0.77 (95% CI, 0.11-1.43; $P = .02$) and a lower severity of diarrhea: SMD, -0.71 (95% CI, -1.39 to -0.03; $P = .04$). Significant heterogeneity of effect, however, was detected.
- Constipation was more prevalent in IMO diagnosed with the lactulose breath test and the glucose breath test and constipation was particularly prevalent in Europe and the United States.

Mechanism of Action

The findings on constipation and diarrhea corroborate methane's slowing physiologic effects on motility, the authors noted. It has been consistently found to delay gut transit, both small-bowel and colonic transit.

Mechanistically, methane reduces small-intestinal peristaltic velocity while augmenting non-propagating contraction amplitude, suggesting that reduction of intestinal transit time is mediated through promotion of nonpropulsive contractions.

"This study further consolidates methane's causal role in constipation and paves the way to establish validated disease-specific patient-reported outcomes," Rezaie and associates wrote, calling for longitudinal and mechanistic studies assessing the archaeome in order to advance understanding of IMO.

This study was funded in part by Nancy Stark and Stanley Lezman in support of the MAST Program's Innovation Project at Cedars-Sinai.

Rezaie serves as a consultant/speaker for Bausch Health. Cedars-Sinai Medical Center has a licensing agreement with Gemelli Biotech, in which Rezaie and a coauthor have equity. They also hold equity in Good LIFE. The coauthor consults for and has received grant support from Bausch Health. ■

Continued from previous page

the process time-consuming (averaging more than 60 weeks) and costly (more than $140,000)," the investigators wrote in *Gastroenterology* (2025 Apr. doi: 10.1053/j.gastro.2025.03.034). "One of the most critical yet time-consuming steps in systematic reviews is title and abstract screening. LLMs have the potential to make this step more efficient."

To test this approach, the investigators developed, validated, and applied a dual-model LLM screening pipeline with human-in-the-loop oversight, focusing on randomized controlled trials in AGA guidelines.

The system was built using the 2021 guideline on moderate-to-severe Crohn's disease, targeting biologic therapies for induction and maintenance of remission.

Using chain-of-thought prompting and structured inclusion criteria based on the PICO framework, the investigators deployed GPT-4o (OpenAI) and Gemini-1.5-Pro (Google DeepMind) as independent screeners, each assessing titles and abstracts according to standardized logic encoded in JavaScript Object Notation. This approach mimicked a traditional double-reviewer system.

After initial testing, the pipeline was validated in a 2025 update of the same guideline, this time spanning six focused clinical questions on advanced therapies and immunomodulators. Results were compared against manual screening by two experienced human reviewers, with total screening time documented.

The system was then tested across four additional guideline topics: fecal microbiota transplantation (FMT) for irritable bowel syndrome and *Clostridioides difficile*, gastroparesis, and hepatocellular carcinoma. A final test applied the system to a forthcoming guideline on complications of acute pancreatitis.

Across all topics, the dual-LLM system achieved 100% sensitivity in identifying randomized controlled trials (RCTs). For the 2025 update of the AGA guideline on Crohn's disease, the models flagged 418 of 4377 abstracts for inclusion, captur-ing all 25 relevant RCTs in just 48 minutes. Manual screening of the same dataset previously took almost 13 hours. Comparable accuracy and time savings were observed for the other topics.

The pipeline correctly flagged all 13 RCTs in 4820 studies on FMT for irritable bowel syndrome, and all 16 RCTs in 5587 studies on FMT for *Clostridioides difficile*, requiring 27 and 66 minutes, respectively. Similarly, the system captured all 11 RCTs in 3919 hepatocellular carcinoma abstracts and all 18 RCTs in 1578 studies on gastroparesis, completing each task in under 65 minutes. Early testing on the upcoming guideline for pancreatitis yielded similar results.

Cost analysis underscored the efficiency of this approach. At an estimated $175-$200 per hour for expert screeners, traditional abstract screening would cost around $2500 per review, versus approximately $100 for the LLM approach — a 96% reduction.

The investigators said that human oversight is necessary to verify the relevance of studies flagged by the models. While the system's sensitivity was consistent, it also selected articles that were ultimately excluded by expert reviewers. Broader validation will be required to assess performance across non-RCT study designs, such as observational or case-control studies, they added.

"As medical literature continues to expand, the integration of artificial intelligence into evidence synthesis processes will become increasingly vital," Dr. Chung and colleagues wrote.

The investigators reported no conflicts of interest. ■

New Guidance for Challenging Overlap of Hypermobility Syndromes and GI Symptoms

BY NANCY A. MELVILLE

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

An increase of patients presenting with the complex combination of hypermobile Ehlers-Danlos syndrome (hEDS) with co-existing gastrointestinal (GI) symptoms, postural orthostatic tachycardia syndrome (POTS), and/or mast cell activation syndrome (MCAS) has prompted the issuance of clinical practice guidance from AGA to help clinicians comprehend such cases.

"Recognizing and treating GI symptoms in patients with hEDS or hypermobility spectrum disorders and comorbid POTS or MCAS present major challenges for clinicians, who often feel under equipped to address their needs," AGA reported in the update, published in *Clinical Gastroenterology and Hepatology* (2025 May. doi: 10.1016/j.cgh.2025.02.015).

Importantly, "the poor understanding of these overlapping syndromes can lead to nonstandardized approaches to diagnostic evaluation and management," the authors noted.

"Gastroenterology providers should be aware of the features of [these syndromes] to recognize the full complexity of patients presenting with multisystemic symptoms."

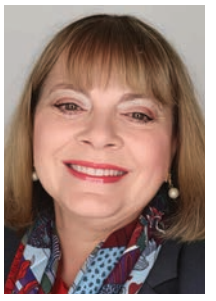
Hypermobility spectrum disorders, which include hEDS, are typically genetic, and patients experience pain along with joint hypermobility, or extreme flexibility of joints beyond the normal range of motion.

With research showing that most of those patients — up to 98% — also experience GI symptoms, gastroenterologists may be encountering them more commonly than realized, Lucinda A. Harris, MD, AGAF, of the Mayo Clinic School of Medicine, in Scottsdale, Arizona, explained to *GI & Hepatology News*.

"As our knowledge in gastroenterology has progressed, we realize that hypermobility itself predisposes individuals to disorders of brain-gut interaction," she said. "We may only be seeing the tip of the iceberg when it comes to diagnosing patients with hypermobility."

Additionally, "many of these patients have POTS, which has also been increasingly diagnosed," Harris added. "The strong overlap of these conditions prompted us to present this data."

With a lack of evidence-based understanding of the overlapping syndromes, AGA's guidance does not carry formal ratings but is drawn from a review of the published literature and expert opinion.


Dr. Harris

In addition to the key recommendation of being aware of the observed combination of syndromes, their recommendations include:

- Regarding testing for POTS/MCAS, it should be targeted to patients presenting with clinical manifestations of the disorders, but universal testing for POTS/MCAS in all patients with hEDS or hypermobility spectrum disorders is not currently supported by the evidence, the guidance advises.
- Gastroenterologists seeing patients with disorders of gut-brain interaction should inquire about joint hypermobility and strongly consider incorporating the Beighton score for assessing joint hypermobility into their practice as a screening tool; if the screen is positive, gastroenterologists may consider applying 2017 diagnostic criteria to diagnose hEDS or offer appropriate referral to a specialist where resources are available, the AGA recommends.
- Medical management of GI symptoms in hEDS or hypermobility spectrum disorders and POTS/MCAS should focus on treating the most prominent GI symptoms and abnormal GI function test results.
- In addition to general disorders of gut-brain interactions and GI motility disorder treatment, management should also include treating any symptoms attributable to POTS and/or MCAS.

Treatment of POTS may include increase of fluid and salt intake, exercise training, and use of compression garments. Special pharmacological treatments for volume expansion, heart rate control, and vasoconstriction with integrated care from multiple specialties (eg, cardiology, neurology) should be considered in patients who do not respond to conservative lifestyle measures.

In patients presenting to gastroenterology providers, testing for mast cell disorders including MCAS should be considered in patients with hEDS or hypermobility spectrum disorders and disorders of gut-brain interaction with episodic symptoms that suggest a more generalized mast cell disorder involving two or more physiological systems. However, current data do not support the use of these tests for routine evaluation of GI symptoms in all patients with hEDS or hypermobility spectrum disorders without clinical or laboratory evidence of a primary or secondary mast cell disorder, the authors noted.

Harris explained that patients presenting with gut-brain disorders are often mistakenly classified as having irritable bowel syndrome or dyspepsia, whereas these conditions may be affecting the GI disorders they have.

"For example, a patient with Ehlers-Danlos syndrome might have problems with constipation, which is impacted by pelvic floor dysfunction," she said. "Due to their hypermobility, they may experience more pelvic floor descent than usual."

"If we do not recognize this, the patient risks developing rectal prolapse or not effectively addressing their constipation."

Regarding patient characteristics, Harris said that those with hEDS and POTS appear to more likely be women and tend to present in younger patients, aged 18-50 years. Of note, there is no genetic test for hEDS.

"The take-home point for clinicians should be to consider POTS and Ehlers-Danlos syndrome when encountering young female patients with symptoms of palpitations, hypermobility, and orthostatic intolerance," she said.

"Recognizing hypermobility is crucial, not only for GI symptoms but also to prevent joint dislocations, tendon ruptures, and other connective tissue issues."

Clinicians are further urged to "offer informed counseling, and guide patients away from unreliable sources or fragmented care to foster therapeutic relationships and evidence-based care," the authors added.

Deciphering Gut-Brain Disorder Challenges

Commenting to *GI & Hepatology News*, Clair Francomano, MD, a professor of medical and molecular genetics at the Indiana University School of Medicine, in Indianapolis, said the new guidance sheds important light on the syndromes.


Dr. Francomano

"I'm delighted to see this guidance offered through the AGA as it will encourage gastroenterologists to think of EDS, POTS and MCAS when they are evaluating patients with disorders of gut-brain interaction," Francomano said.

"This should allow patients to receive more accurate and timely diagnoses and appropriate management."

Francomano noted that the Ehlers-Danlos Society, which provides information for clinicians and patients alike on the syndromes, and where she serves on the medical scientific board, has also been active in raising awareness.

"While co-occurrence of POTS and MCAS with EDS has in fact been recognized for many years, I do think awareness is increasing, in large part due to the advocacy and educational efforts of the Ehlers-Danlos Society," she said.

The take-home message? "When clinicians see disorders of the gut-brain axis, POTS or MCAS, they should be thinking, 'Could this be related to joint hypermobility or Ehlers-Danlos syndrome?' " Francomano said.

Harris reported serving as a consultant for AbbVie, Ardelyx, Salix, and Gemelli Biotech and reported receiving research support from Takeda and Anyx. Francomano did not report any relevant disclosures. ■

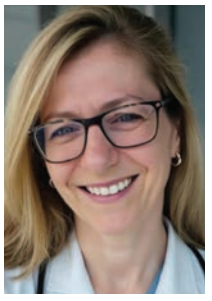
Less Invasive Screening May ID Barrett's Earlier

BY DIANA SWIFT

A new combination modality demonstrated excellent sensitivity and negative predictive value compared with endoscopy in a prospective study of at-risk veterans screened for Barrett's esophagus (BE) and esophageal adenocarcinoma (EAC), a small comparative study in US veterans found.

BE is up to three times more prevalent in veterans than in the general population.

This and other minimally invasive approaches may reduce patient anxiety and increase screening rates, according to investigators led by Katarina B. Greer, MD, MS, of the VA Northeast Ohio Healthcare System and Case Western University in Cleveland. Such screening platforms are expected to open a window on improved prognosis for EAC by offering well-tolerated, office-based testing, the authors wrote in *The American Journal of Gastroenterology* (2025 Mar. doi: 10.14309/ajg.0000000000002962).



Dr. Greer

'Available data suggest that family history is the strongest predictor of BE diagnosis. ... This points to high priority of pursuing screening in patients with family history of the condition.'

Greer and colleagues compared standard upper endoscopy with EsoCheck (EC), a nonendoscopic esophageal balloon cell-sampling device coupled with EsoGuard (EG), a DNA-based precancer screening assay, with standard upper endoscopy, an FDA-approved minimally invasive alternative.

Sensitivity and specificity of combined EC/EG for esophagogastroduodenoscopy (EGD)-detected BE/EAC were 92.9% (95% CI, 66.1-99.8) and 72.2% (95% CI, 62.1-80.8), respectively. Positive and negative predictive values were 32.5% (95% CI, 18.6-49.1) and 98.6% (95% CI, 92.4-100), respectively.

"With its strong negative predictive power, this screening modality could be a first-line tool available to a greater number of patients," Greer and associates wrote. "Data from this test support the notion that EC could be performed as a triaging test to increase the yield of diagnostic upper endoscopy 2.5-fold."

The US rates of EAC have increased more than sixfold in the past four decades and continue to rise. In 2023, 21,560 cases of EAC were diagnosed. The prognosis for EAC is still poor, with fewer than 22% of patients surviving beyond 5 years.

Current guidelines recommend sedated EGD for patients with chronic gastroesophageal reflux disease (GERD) and additional BE risk factors such as smoking, obesity, and family history. This strategy, however, often fails to detect BE when symptoms are well controlled with over-the-counter or physician-prescribed therapies, Greer and colleagues noted. It also fails to detect BE in individuals without GERD, who comprise 40% of those who develop EAC.

Fewer than 5% of EACs are diagnosed as early-stage lesions caught by surveillance of patients with previously detected BE.

Study Details

The researchers recruited veterans meeting American College of Gastroenterology criteria for endoscopic BE and EAC screening at the Louis Stokes Cleveland Veterans Affairs Medical Center.

Of 782 eligible veterans, 130 (16.6%) entered the study and 124 completed screening. Common reasons for nonparticipation included completion of upper endoscopy outside of the VA healthcare system, lack of interest in joining a research study, and no recommendation for screening from referring gastroenterology or primary care providers. Eligible candidates had gastroesophageal reflux disorder plus three additional risk factors, such as smoking, higher BMI, male sex, age 50 years or older, and family history. The mean number of risk factors was 4.1.

"Available data suggest that family history is the strongest predictor of BE diagnosis, as prevalence of BE among those with family history was 23%," Greer's group wrote. "This points to high priority of pursuing screening in patients with family history of the condition, followed by patients who share multiple risk factors."

All participants completed unsedated EC-guided distal esophageal sampling followed by a sedated EGD on the same day. The prevalence of BE/EAC was 12.9% (n = 14/2), based on standard EGD.

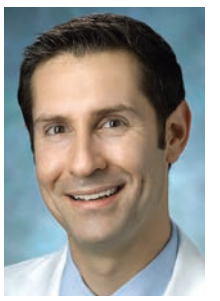
"The study was not powered to prospectively determine EC diagnostic accuracy for subgroups of nondysplastic and dysplastic BE and EAC. These data are reported for this device in development studies but not available for our study population," the authors wrote. In comparison, they noted, the Cytosponge-TFF3, another nonendoscopic screening device for EAC and BE, exhibited lower sensitivity of 79.5%-87.2%, depending on lesion length, but higher specificity of 92.4%.

LUCID DIAGNOSTICS

The EsoCheck cell collection device is designed to be coupled with EsoGuard, a DNA-based precancer screening assay.

Procedural Anxiety

Baseline scores on the short-form six-item Spielberger State-Trait Anxiety Inventory-6 (STAI-6) revealed notable levels of periprocedural anxiety. STAI-6 scores range from 20 to 80, with higher scores indicating more severe anxiety. In the VA study, scores ranged from 20 to 60, and most domains constituting the scores were the same before and after the procedure. Participants did, however, report a statistically significant decrease in sense of worry after EC and reported good tolerability for both EC and EG.



Dr. Sloan

'It will be interesting to see similar studies in the non-VA population as well. As the study notes, veterans are an enriched population with a higher prevalence of Barrett's esophagus.'

Offering an outsider's perspective on the study, Joshua Sloan, DO, an esophageal gastroenterologist at University of Minnesota Medical Center in Minneapolis, said that with the acceleration of US rates of EAC, developing a nonendoscopic screening tool to improve identification of Barrett's and perhaps early EAC is important. "The study by Greer et al helps support the use of nonendoscopic screening with EsoCheck and EsoGuard to identify these conditions," he told *GI & Hepatology News*. "It will be interesting to see similar studies in the non-VA population as well. As the study notes, veterans are an enriched population with a higher prevalence of Barrett's esophagus."

Ultimately, Sloan added, "the hope is to increase our ability to identify and manage BE before it becomes EAC. Nonendoscopic screening tools have the potential to increase diagnosis and funnel the appropriate patients for endoscopic surveillance."

The Bottom Line

"Calculations regarding effectiveness of the two-step screening strategy afforded by EC indicate that the burden of screening would be reduced by at least half (53%)," the authors wrote. Since the estimated size of the US screen-eligible population ranges from 19.7 million to 120.1 million, noninvasive tools could significantly decrease EGD procedures. A formal cost-effectiveness analysis is being conducted and will be published separately.

This study was funded by a Department of Defense award.

A coauthor reported device patents assigned to Case Western Reserve University and licensed to Lucid Diagnostics. The other authors had no competing interests to declare. Sloan disclosed speaking and/or advisory work for Sanofi-Regeneron, Phathom Pharmaceuticals, and Takeda Pharmaceuticals unrelated to his comments. ■

Reassurance for Physicians

Common Medications *from page 1*

MC were found not to be causally linked, he added, "we did observe a marginal association with SSRIs but could not rule out the possibility that the association is related to residual bias."

The authors noted that the incidence of MC in older persons is rising rapidly and is thought to account for more than 30% of chronic diarrhea cases in this group.

Despite weak evidence in the literature, the treatment guidelines of several societies, including the American Gastroenterological Association, recommend discontinuing potential pharmacologic triggers as first-line prevention or as an adjunct therapy, particularly in recurrent or refractory MC (Gastroenterology. 2015 Nov. doi: 10.1053/j.gastro.2015.11.008). But this approach may be ineffective in patients with established disease and could lead to inappropriate discontinuation of medication such as antihypertensives, the authors argued.

As to proposed mechanisms of action, said Khalili, "for PPIs [proton-pump inhibitors], people thought it was related to changes in the gut microbiome. For NSAIDs [nonsteroidal anti-inflammatory drugs], people thought it could be related to changes in the gut barrier function. But overall, not a single mechanism would have explained all the prior associations that were observed."

While medications such as PPIs and SSRIs can cause diarrhea in a small subset of users, Khalili added, "most patients generally catch these side effects very quickly and realize that stopping these medications will improve their diarrhea. This is very different than most patients we as gastroenterologists see with a new diagnosis of MC. Many of them may have been on these medications for a long time. We believe that stopping medications in these patients is unnecessary."

Study Details

The investigators looked at eligible residents in Sweden age 65 years or older in the years 2006-2017 (n = 191,482-2,634,777). Participants had no history of inflammatory bowel disease and different cohorts were examined for various common medications from calcium channel blockers to statins.

With a primary outcome of biopsy-verified MC, dates of diagnosis were obtained from Sweden's national histopathology cohort ESPRESSO (Epidemiology Strengthened by Histopathology Reports in Sweden). Among the findings:

- The 12- and 24-month cumulative incidences of MC were less than 0.05% under all treatment strategies.
- Estimated 12-month risk differences were close to null under angiotensin-converting enzyme vs calcium-channel blocker (CCB) initiation, angiotensin-receptor blocker vs CCB initiation, NSAID initiation vs noninitiation, PPI inhibitor initiation vs noninitiation, and statin initiation vs noninitiation.
- The estimated 12-month risk difference was 0.04% (95% CI, 0.03%-0.05%) for SSRIs vs mirtazapine.
- Results were similar for 24-month risk differences. Several medications such as SSRIs were also associated with increased risk for undergoing colonoscopy with a normal colorectal mucosa biopsy result.

"We think it's unlikely that stopping these medications will improve symptoms of MC," Khalili said.

Commenting on the paper but not involved in it, Jordan E. Axelrad, MD, MPH, codirector of the Inflammatory Bowel Disease Center at NYU Langone Health in New York City, said, "This study strengthens the argument that MC is an immune-mediated disease, not primarily driven by drug exposures. But future studies in diverse cohorts are required to validate these findings." He said the study nevertheless provides reassurance that previously reported associations may have been overstated or confounded by factors such as reverse causation and increased healthcare utilization preceding the MC diagnosis.

In the meantime, Axelrad added, the findings "may reduce the inclination to promptly discontinue medications historically associated with MC in newly diagnosed cases. Also, these data help shift the clinical focus away from medication cessation alone and toward a needed and broader MC management strategy. US-based validation would likely highlight these changes in our patients."

Despite concerns about the study's unmeasured confounding because of differential healthcare utilization or surveillance, the modest association observed between SSRI and MC is supported by literature linking catecholamine and serotonin to gut innate immunity and microbiota, Khalili's group wrote. "However, this finding may also be confounded by other factors including persisting surveillance and protopathic bias, especially since an association was also seen for risk for receipt of a colonoscopy with normal mucosa."

Khalili believes the Swedish results are applicable even to the more diverse US population. He noted that lack of primary care data limited measurement of and adjustment for symptoms and medical diagnoses that increase risk. But according to Axelrad, MC is more prevalent in White, older patients, who are well-represented in Swedish cohorts but to a lesser extent in US populations. "Additionally, environmental factors and medication use patterns differ between Sweden and the US, particularly in regard to over-the-counter medication access."

The findings have implications for future research in pharmacoepidemiologic studies of gastrointestinal-related outcomes. Since many routinely prescribed medications such as SSRIs were associated with an apparent increased risk for colonoscopies with normal colorectal biopsy results, future studies that examine gastrointestinal-specific adverse events should carefully consider potential surveillance bias.

In the meantime, Khalili stressed, it's important to highlight that while some of these medications cause diarrhea in a small subset of patients, stopping medications in these patients is unnecessary.

This study was supported by the National Institutes of Health (NIH) and the Swedish Research Council. Khalili disclosed grants from the Crohn's & Coiltis Foundation, the NIH and the Helmsley CharitableTrust, as well as stock ownership in Cylinder Health. One coauthor is employed by Massachusetts General Hospital. Axelrad had no relevant competing interests.

Dr. Khalili

'Sensitivity analyses suggest that previously reported associations and persistent association with SSRI [selective serotonin reuptake inhibitor] initiation may be due to surveillance bias.'

Dr. Axelrad

'This study strengthens the argument that MC is an immune-mediated disease, not primarily driven by drug exposures. But future studies in diverse cohorts are required to validate these findings.'

ADOBE STOCK

Positive ESSENCE Trial Results

Wegovy Approved *from page 1*

fibrosis compared with 34% of 266 individuals treated with placebo — a statistically significant difference.

The second primary endpoint showed 37% of people treated with Wegovy achieved improvement in liver fibrosis and no worsening of steatohepatitis compared with 22% of those treated with placebo, also a significant difference.

A confirmatory secondary endpoint at week 72 showed 33% of patients treated with Wegovy achieved both resolution of steatohepatitis and improvement in liver fibrosis compared with 16% of those treated with placebo — a statistically significant difference in response rate of 17%.

In addition, 83.5% of the patients in the semaglutide group maintained the target dose of 2.4 mg until week 72.

Wegovy is also indicated, along with diet and physical activity, to reduce the risk for major cardiovascular events in adults with known heart disease and with either obesity or overweight. It is also indicated for adults and children aged 12 years or older with obesity, and some adults with overweight who also have weight-related medical problems, to help them lose excess body weight and keep the weight off.

What's Next for Wegovy?

In February 2025, Novo Nordisk filed for regulatory approval in the European Union, followed by regulatory submission in Japan in May 2025. Also in May, the FDA accepted a filing application for oral semaglutide 25 mg.

Furthermore, "There's an expected readout of part 2 of ESSENCE in 2029, which aims to demonstrate treatment with Wegovy lowers the risk of liver-related clinical events, compared to placebo, in patients with MASH and F2 or F3 fibrosis at week 240," a Novo Nordisk spokesperson told *GI & Hepatology News*.

"The oral form requires more active pharmaceutical ingredient. Given that we have a fixed amount of API, the injectable form enables us to treat more patients. We are currently expanding our oral and injectable production capacities globally with the aim of serving as many patients as possible."

Although the company has the technology to produce semaglutide as a pill or tablet, she said, "the US launch of oral semaglutide for obesity will be contingent on portfolio prioritization and manufacturing capacity." The company has not yet submitted the 50-mg oral semaglutide to regulatory authorities.

"The oral form requires more active pharmaceutical ingredient [API]," she noted. "Given that we have a fixed amount of API, the injectable form enables us to treat more patients. We are currently expanding our oral and injectable production capacities globally with the aim of serving as many patients as possible. It requires time to build, install, validate, and ramp up these production processes." ■

UCG/Getty Images

Sleep Changes in IBD Could Signal Inflammation

BY MARILYNN LARKIN

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Changes in sleep metrics detected with wearable technology could serve as an inflammation marker and potentially predict inflammatory bowel disease (IBD) flare-ups, regardless of whether a patient has symptoms, an observational study suggested.

Sleep data from 101 study participants over a mean duration of about 228 days revealed that altered sleep architecture was apparent only when inflammation was present — symptoms alone did not impact sleep cycles or signal inflammation.

"We thought symptoms might have an impact on sleep, but interestingly, our data showed that measurable changes like reduced rapid eye movement [REM] sleep and increased light sleep only occurred during periods of active inflammation," Robert Hirten, MD, associate professor of medicine (gastroenterology), and artificial intelligence and human health, at the Icahn School of Medicine at Mount Sinai, New York City, told *GI & Hepatology News*.

"It was also interesting to see distinct patterns in sleep metrics begin to shift over the 45 days before a flare, suggesting the potential for sleep to serve as an early indicator of disease activity," he added.

"Sleep is often overlooked in the management of IBD, but it may provide valuable insights into a patient's underlying disease state," he said. "While sleep monitoring isn't yet a standard part of IBD care, this study highlights its potential as a noninvasive window into disease activity, and a promising area for future clinical integration."

The study was published online first in *Clinical Gastroenterology and Hepatology* (2025 Jun. doi: 10.1016/j.cgh.2025.06.003).

Less REM Sleep, More Light Sleep

Researchers assessed the impact of inflammation and symptoms on sleep architecture in IBD by analyzing data from 101 individuals who answered daily disease activity surveys and wore a wearable device.

The mean age of participants was 41 years and 65.3% were women. Sixty-three participants (62.4%) had Crohn's disease (CD) and 38 (37.6%) had ulcerative colitis (UC).

Almost 40 (39.6%) participants used an Apple Watch; 50 (49.5%) used a Fitbit; and 11 (10.9%) used an Oura ring. Sleep architecture, sleep efficiency, and total hours asleep were collected from the devices. Participants were encouraged to wear their devices for at least 4 days per week and 8 hours per day and were not required to wear them at night. Participants provided data by linking their devices to ehive, Mount Sinai's custom app.

Dr. Hirten

'It was ... interesting to see distinct patterns in sleep metrics begin to shift over the 45 days before a flare, suggesting the potential for sleep to serve as an early indicator of disease activity.'

Daily clinical disease activity was assessed using the UC or CD Patient Reported Outcome-2 survey. Participants were asked to answer at least four daily surveys each week.

Associations between sleep metrics and periods of symptomatic and inflammatory flares, and combinations of symptomatic and inflammatory activity, were compared to periods of symptomatic and inflammatory remission.

Furthermore, researchers explored the rate of change in sleep metrics for 45 days before and after inflammatory and symptomatic flares.

Participants contributed a mean duration of 228.16 nights of wearable data. During active inflammation, they spent a lower percentage of sleep time in REM (20% vs 21.59%) and a greater percentage of sleep time in light sleep (62.23% vs 59.95%) than during inflammatory remission. No differences were observed in the mean percentage of time in deep sleep, sleep efficiency, or total time asleep.

During symptomatic flares, there were no differences in the percentage of sleep time in REM sleep, deep sleep, light sleep, or sleep efficiency compared with periods of inflammatory remission. However, participants slept less overall during symptomatic flares compared with during symptomatic remission.

Compared with during asymptomatic and uninflamed periods, during asymptomatic but inflamed periods, participants spent a lower percentage of time in REM sleep, and more time in light sleep; however, there were no differences in sleep efficiency or total time asleep.

Similarly, participants had more light sleep and less REM sleep during symptomatic and inflammatory flares than during asymptomatic and uninflamed periods — but there were no differences in the percentage of time spent in deep sleep, in sleep efficiency, and the total time asleep.

Symptomatic flares alone, without inflammation, did not impact sleep metrics, the researchers concluded. However, periods with active inflammation were associated with a significantly smaller percentage of sleep time in REM sleep and a greater percentage of sleep time in light sleep.

The team also performed longitudinal mapping of sleep patterns before, during, and after disease exacerbations by analyzing sleep data for 6 weeks before and 6 weeks after flare episodes.

They found that sleep disturbances significantly worsen leading up to inflammatory flares and improve afterward, suggesting that sleep changes may signal upcoming increased disease activity. As for the intersection of inflammatory and symptomatic flares, altered sleep architecture was evident only when inflammation was present.

"These findings raise important questions about whether intervening on sleep can actually impact inflammation or disease trajectory in IBD," Hirten said. "Next steps include studying whether targeted sleep interventions can improve both sleep and IBD outcomes."

While this research is still in the early stages, he said, "it suggests that sleep may have a relationship with inflammatory activity in IBD. For patients, it reinforces the value of paying attention to sleep changes."

The findings also show the potential of wearable devices to guide more personalized monitoring, he added. "More work is needed before sleep metrics can be used routinely in clinical decision-making."

Validates the Use of Wearables

Commenting on the study for *GI & Hepatology News*, Michael Mintz, MD, a gastroenterologist at Weill Cornell Medicine and New York–Presbyterian in New York City, observed that gastrointestinal symptoms often do not correlate with objective disease activity in IBD, creating a diagnostic challenge for gastroenterologists.

"Burdensome, expensive, and/or invasive testing, such as colonoscopies, stool tests, or imaging, are frequently required to monitor disease activity," he said.

"This study is a first step in objectively monitoring inflammation in a patient-centric way that does not create undue burden to our patients," Dr. Mintz added. "It also provides longitudinal data that suggests changes in sleep patterns can pre-date disease flares, which ideally can lead to earlier intervention to prevent disease complications."

Like Hirten, he noted that clinical decisions, such as changing IBD therapy, should not be based on the results of this study. "Rather this provides validation that wearable technology can provide useful objective data that correlates with disease activity."

Furthermore, he said, it is not clear whether analyzing sleep data is a cost-effective way of monitoring IBD disease activity, or whether that data should be used alone or in combination with other objective disease markers, to influence clinical decision-making.

"This study provides proof of concept that there is a relationship between sleep characteristics and objective inflammation, but further studies are needed," he said. "I am hopeful that this technology will give us another tool that we can use in clinical practice to monitor disease activity and improve outcomes in a way that is comfortable and convenient for our patients."

This study was supported by a grant to Hirten from the US National Institutes of Health. Hirten reported receiving consulting fees from Bristol Meyers Squibb and AbbVie; stock options from Salvo Health; and research support from Janssen, Intralytix, EnLiSense, and Crohn's and Colitis Foundation. Mintz declared no competing interests.

Member SPOTLIGHT

New York GI Links Health Equity, Cancer Screening

BY JENNIFER LUBELL
MDedge News

Pascale M. White, MD, MBA, MS, never tires of excising precancerous polyps.

"To know that I have removed something that could have been potentially dangerous to this patient in years to come, that wasn't causing any symptoms but silently lurking there" is a great feeling, said Dr. White, an associate professor with dual appointments in the divisions of gastroenterology and liver diseases at the Icahn School of Medicine at Mount Sinai, New York.

"When I do procedures, I always go in with the mindset that this could be a lifesaving procedure for this patient. And that definitely keeps me excited about the field," she said.

Colorectal cancer is preventable, but when it comes to screening, there are large health disparities. African Americans are 20% more likely to get diagnosed with colorectal cancer and 40% more likely to die from the disease. "Knowing that there are low screening rates among this population, there's a lot of work to be done with mitigating those disparities," said Dr. White, who has made it her life's work to expand access to care and address health inequities.

Dr. White is an inaugural director of Health Equity in Action for Liver and Digestive Diseases (HEALD) and an inaugural fellow of the United Hospital Fund's Health Equity Fellowship. In 2025, she received the AGA-Pfizer Beacon of Hope Award, which celebrates three women in the field who have played a key role in advancing gender and health equity in medicine.

Much of her work involves going directly into communities and educating patients and providers on the different choices for colorectal cancer screening. "Through the United Hospital Fund's Health Equity Fellowship, I have partnered with an East Harlem community health center to conduct seminars and tailor a one-page shared decision tool for colorectal cancer screening to jumpstart discussions on screening choices between patients and providers," said Dr. White.

In an interview, she offered more details about her mission to connect with communities to improve screening rates for colorectal cancer.

Courtesy Dr. Pascale M. White

Dr. Pascale M. White

Can you discuss your work with HEALD?

Dr. White: HEALD is a growing initiative to identify and address any access barriers to our screening programs. At this time, I'm working to identify how patients are getting referred to us in our division for colorectal cancer screening and how we can create a more streamlined and robust pathway for patients in the community, namely at Federally Qualified Health Centers in East Harlem.

You co-founded the Association of Black Gastroenterologists and Hepatologists (ABGH) in 2021. What are you hoping to accomplish with this organization?

Dr. White: ABGH was co-founded by 11 of us from across the country for the purpose of addressing healthcare disparities in GI [gastrointestinal] and liver diseases that disproportionately affect Black patients. Our mission is to promote health equity, advance science, and develop the careers of Black gastroenterologists, hepatologists, and scientists.

Our mentorship program is one way we give back to incoming residents who are interested in pursuing a career in GI. The Nurturing, Excelling, and Unifying Sisters in Medicine (NEXUS) conference centers the perspectives of Black women in medicine from all specialties. The ABGH Summit is an educational conference that features renowned experts in the health equity space.

But at the center of it all is our community outreach. When we started the organization after Chadwick Boseman's death during the height of the COVID pandemic, all our community events were held over Zoom. Now with our in-person events you can feel the energy in the room. Our main community facing event is called Bustin' A Gut. It's a genius combination of comedy and medical education. We have a panel of physicians and comedians. The physicians talk about a range of GI topics such as colorectal cancer screening choices, alarm signs or symptoms of colon cancer, nutrition, and general gut health. The community members feel comfortable asking their questions and the comedians help keep the conversation entertaining and lighthearted. It's a true laugh and learn event.

How did you become interested in health equity? Was there a specific event or circumstance you could share?

Dr. White: It was my residency training at New York University and my experiences at Bellevue Hospital that really introduced me to a place where everyone could get care. Whether you are coming from another country or right up the street, Bellevue saw everyone who walked through its doors. This is in deep contrast to the vast majority of hospitals where if you do not have insurance, you cannot be seen. Then there are people who have access to care but are overwhelmed by the complexities of the medical system.

Consider colorectal cancer, for example. It is a preventable disease, yet most people aren't getting screened because they either don't know they should, they are fearful of the process, or they don't know how to go about getting the tests done. These are namely knowledge barriers that we can address. I thought: If there's something I could do to help patients learn about colorectal cancer screening and how they can take steps to prevent this disease, then that's how I want to spend my career.

You created the Direct Access GI Clinic (DAGIC), one of the projects that led to the AGA-Pfizer Beacon of Hope Award for Gender and Health Equity. How does DAGIC reduce wait times and improve endoscopic care coordination for underserved, high-risk patients?

Dr. White: I developed and implemented a clinic workflow that identified high-risk patients who were

Continued on following page

Courtesy Dr. Pascale M. White

Dr. Pascale M. White enjoys playing golf on the weekends when she is not in the clinic at Mount Sinai.

Continued from previous page

sent for direct-access procedures but who needed office consultations prior to their procedures. These were the sickest of the sickest patients that needed to be prioritized. Working with my nurse practitioner and office ncurse, we triaged these patients and carved out dedicated time in the week where only DAGIC patients were scheduled.

Creating this direct workflow meant that these patients no longer had to wait 3 months. They were waiting at most, 2-3 weeks to be seen. I don't take for granted that one change in a system can lead to impactful outcomes in patient care and access.

You also co-authored an update to the American College of Gastroenterology's colorectal cancer screening guidelines for African Americans. Is there anything unique and important that's worth noting?

Dr. White: We updated those guidelines to include physician recommendation as a potential barrier to screening. We know that patients are more likely to be screened if they are recommended to do so by their physician. Yet, some patients are less likely to receive a physician recommendation for screening. We need to dive deeper into the reasons why this is happening. And if there are any gaps, for example in physician knowledge, that's something we should readily address.

'I'm working to identify how patients are getting referred to us in our division for colorectal cancer screening and how we can create a more streamlined and robust pathway for patients in the community, namely at Federally Qualified Health Centers in East Harlem.'

One of your interests is guiding students, residents, and fellows. What advice would you give to aspiring medical students?

Dr. White: Keep an open mind and explore all your options before committing to a specialty. If you find the field exciting and you are motivated to spend time learning more about it, seek opportunities to conduct research and find a mentor that can further guide you on your journey. ■

LIGHTNING ROUND

What's your favorite season of the year?
Fall

What's your favorite way to spend a weekend?
Playing golf

If you could have dinner with any historical figure, who would it be?
Barack Obama

What's your go-to karaoke song?
Livin' on a Prayer by Bon Jovi

What's one thing on your bucket list?
Travel to Rome

If you could instantly learn any skill, what would it be?
Speak Mandarin

What's your favorite holiday tradition?
Watching Hallmark movies with my daughter

Are you a planner or more spontaneous?
Planner

What's the best piece of advice you've ever received?
Progress, not perfection

New Global Guidelines for Pregnancy and IBD

BY MARILYNN LARKIN

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

The first-ever global guidelines for pregnancy and inflammatory bowel disease (IBD) recommend continuing biologics and low-risk medications through pregnancy and lactation in women with IBD, suggesting this approach will not harm the fetus.

The guidelines also recommend that all women with IBD receive preconception counseling and be followed as high-risk pregnancies.

"Management of chronic illness in pregnant women has always been defined by fear of harming the fetus," said Uma Mahadevan, MD, AGAF, director of the Colitis and Crohn's Disease Center at the University of California San Francisco and chair of the Global Consensus Consortium that developed the guidelines.

As a result, pregnant women are excluded from clinical trials of experimental therapies for IBD. And when a new therapy achieves regulatory approval, there are no human pregnancy safety data, only animal data. To fill this gap, the PIANO study, of which Mahadevan is principal investigator, looked at the safety of IBD medications in pregnancy and short- and long-term outcomes of the children.

Dr. Mahadevan

'With our ongoing work in pregnancy in the patient with IBD, we realized that inflammation in the mother is the leading cause of poor outcome for the infant.'

"With our ongoing work in pregnancy in the patient with IBD, we realized that inflammation in the mother is the leading cause of poor outcome for the infant," she told *GI & Hepatology News*.

"We also have a better understanding of placental transfer of biologic agents" and the lack of exposure to the fetus during the first trimester, "a key period of organogenesis," she added.

Final recommendations were published simultaneously in six international journals, namely, *Clinical Gastroenterology and Hepatology* (2025 Aug. doi: 10.1016/j.cgh.2025.04.005), *American Journal of Gastroenterology*, *GUT*, *Inflammatory Bowel Diseases*, *Journal of Crohn's and Colitis*, and *Alimentary Pharmacology and Therapeutics*.

Surprising, Novel Findings

Limited provider knowledge led to varied practices in caring for women with IBD who become pregnant, according to the consensus authors. Practices are affected by local dogma, available resources, individual interpretation of the literature, and fear of harming the fetus.

"The variations in guidelines by different societies and countries reflect this and lead to confusion for physicians and patients alike," the authors of the guidelines wrote.

Therefore, the Global Consensus Consortium — a group of 39 IBD experts, including teratologists and maternal fetal medicine specialists and seven patient advocates from six continents — convened to review and assess current data and come to an agreement on best practices. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process was used when sufficient published data were available, and the Research and Development process when expert opinion was needed to guide consistent practice.

"Some of the findings were expected, but others were novel," said Mahadevan.

Recommendations that might surprise clinicians include GRADE statement 9, which suggests that pregnant women with IBD take low-dose aspirin by 12-16 weeks' gestation to prevent preterm preeclampsia. "This is based on the ASPRE study [N Engl J Med. 2017 Aug. doi:10.1056/NEJMoa1704559], showing that women at risk of preeclampsia can lower their risk by taking low-dose aspirin," with no risk for flare, Mahadevan said.

In addition, GRADE statements 17-20 recommend/suggest that women continue their biologic throughout pregnancy without stopping. "North America has always recommended continuing during the third trimester, while Europe only recently has come to this," Mahadevan said. "However, there was always some looseness about stopping at week X, Y, or Z. Now, we do recommend continuing the dose on schedule with no holding."

Continuing medications considered low risk for use during pregnancy, such as 5-amino salicylic acids, sulfasalazine, thiopurines, and all monoclonal antibodies during preconception, pregnancy, and lactation, was also recommended.

However, small-molecule drugs such as S1P receptor molecules and JAK inhibitors should be avoided for at least 1 month, and in some cases for 3 months prior to attempting conception, unless there is no alternative for the health of the mother. They should also be avoided during lactation.

Grade statement 33, which suggests that live rotavirus vaccine may be provided in children with in utero exposure to biologics, is also new, Mahadevan noted. "All prior recommendations were that no live vaccine should be given in the first 6 months or longer if infants were exposed to biologics in utero, but based on a prospective Canadian study [Lancet Child Adolesc Health. 2023 Jun. doi: 10.1016/S2352-4642(23)00136-0], there is no harm when given to these infants."

Another novel recommendation is that women with IBD on any monoclonal antibodies, including newer interleukin-23s, may breastfeed even though there are not clinical trial data at this point. The recommendation to continue them through pregnancy and lactation is based on placental physiology, as well as on the physiology of monoclonal antibody transfer in breast milk, according to the consortium.

Furthermore, the authors noted, there was no increase in infant infections at 4 months or 12 months if they were exposed to a biologic or thiopurine (or both) during pregnancy.

Overall, the consortium recommended that all pregnancies for

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Out-of-Pocket Prep Costs Reduce Screening Colonoscopy Uptake in Vulnerable Populations

BY DIANA SWIFT

FROM GASTROENTEROLOGY

Out-of-pocket costs for bowel preparation are deterring people, especially vulnerable and underserved groups, from colonoscopy for colorectal cancer (CRC) screening, a large insurance-claims analysis in *Gastroenterology* reported (2025 Jun. doi: 10.1053/j.gastro.2025.05.025).

Moreover, this cost-sharing contravenes the preventive-care provisions for bowel preparation mandated by the Affordable Care Act (ACA).


Dr. Shah

'While some patients may be willing to pay modest out-of-pocket costs, any required payment, however small, can serve as a barrier to preventative care, particularly in underserved populations.'

Led by Gastroenterologist Eric D. Shah, MD, MBA, a clinical associate professor at the University of Michigan in Ann Arbor, the study found a significant proportion of prescribed bowel preparation claims — 53% for commercial plans and 83% for Medicare — still involve patient cost-sharing, indicating noncompliance with ACA guidelines. Although expense-sharing was less prevalent among Medicaid claims (just 27%), it was not eliminated, suggesting room for improvement in coverage enforcement across the board.

"Colon cancer is unique in that it can be prevented with colonoscopy, but where are the patients? Bowel prep is a major reason that patients defer screening," Shah told *GI & Hepatology News.* He said his group was quite surprised that the majority in the study cohort were paying something out of pocket when these costs should have been covered. "Primary care doctors may not think to ask about bowel prep costs when they order screening colonoscopies."

The findings emerged from an analysis of 2,593,079 prescription drug claims: 52.9% from commercial plans, 35% from Medicare Part D plans, and 8.3% from Medicaid plans.

"These patient costs of $30 or $50 are a real not a theoretical deterrent," said Whitney Jones, MD, a gastroenterologist, adjunct clinical professor at the University of Louisville in Kentucky, and founder of the nonprofit Colon Cancer Prevention Project. Jones was not involved in the analysis. "Some insurers require prior patient authorization for the low-dose preps, but gastroenterologists are doing so many colonoscopies they don't always have time to get a PA [prior authorization] on everyone."

With the increasing use of blood- and stool-based CRC testing, he added, "when you get a positive result, it's really important to have the procedure quickly." And appropriate bowel preparation is a small, cost-effective portion of the total costs of colonoscopy, a procedure that ultimately saves insurers significant money in treatment costs.

The authors noted that while CRC is the second-leading cause of cancer-related deaths in the US, screening rates remain low, with only 59% of adults aged 45 years or older up to date with screening. Screening rates are particularly low among racial and ethnic minority groups as compared with White individuals, a disparity that highlights the need to address existing barriers and enhance screening efforts.

In the current study, shared costs by bowel preparation volume also varied. Low-volume formulations had consistently higher out-of-pocket costs: a median of $60 for low-volume vs $10 for high-volume in commercial plans. In Medicare, 75% of high-volume claims had shared costs compared with 90% for their low-volume counterparts. The cost-sharing difference was slightly narrower with Medicaid: 27% of high-volume claims vs 30% of low-volume claims.


Dr. Jones

This is concerning, as low-volume options, which are preferred by patients for their better tolerability, can enhance uptake and adherence and improve colonoscopy outcomes. Shah advises physicians to consider prescribing low-volume preparations. "Let patients know about the potential out-of-pocket cost and about copay cards and assistance programs and use high-volume preps as an alternative rather than a go-to," he said.

As to costs across insurance types, among commercial plans, the median nonzero out-of-pocket cost was $10 for high-volume and $60 for low-volume product claims. For Medicare, the median nonzero out-of-pocket cost was $8 for high-volume and $55.99 for low-volume products.

Under the ACA, CRC screening is classified as a recommended preventive service, requiring health plans to cover it without cost-sharing. Although the Centers for Medicare & Medicaid Services previously tried to enforce this mandate in 2015 and 2016, stating that colonoscopy preparation medications should be covered at no cost, many health plans are still not compliant.

At the nonfederal level, Jones noted, Kentucky, which has a significant high-risk population, recently became the first state to pass legislation requiring health benefit plans to cover all guideline-recommended CRC exams and lab tests.

For its part, AGA has also called on payers to eliminate all cost-sharing barriers across the CRC screening continuum.

Of note, the study authors said, the higher compliance with the ACA mandate in commercial and Medicaid plans than in Medicare highlights disparities that may disproportionately affect vulnerable older adults. While nearly half of commercial patients and nearly three quarters of Medicaid patients incurred zero out-of-pocket costs, fewer than 17% of Medicare beneficiaries, or one in six, did so.

Although these costs may be low relative to the colonoscopy, they nevertheless can deter uptake of preventive screenings, potentially leading to higher CRC incidence and mortality. "While some patients may be willing to pay modest out-of-pocket costs, any required payment, however small, can serve as a barrier to preventative care, particularly in underserved populations," they wrote. "These financial barriers will continue to contribute to widening disparities and hinder progress toward equitable screening outcomes."

In the meantime, said Shah, "Physicians should advocate now to their representatives in Congress that bowel prep costs should already be covered as part of the ACA."

This study was funded by Sebela Pharmaceuticals, maker of SUFLAVE preparation. The authors had no conflicts of interest to declare. Jones is a speaker and consultant for Grail LLC. ■

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women with IBD be considered as "high risk" for complications. This is due to the fact that many parts of the world, including the US, are "resource-limited," Mahadevan explained. Since maternal fetal medicine specialists are not widely available, the consortium suggested all these patients be followed with increased monitoring and surveillance based on available resources.

In addition to the guidelines, patient videos in seven languages, a professional slide deck in English and Spanish, and a video on the global consensus are all available at https://pianostudy.org/. Clinicians can also find related patient materials created by the IBD Parenthood Project: myibdlife.gastro.org/parenthood-project.

This study was funded by The Leona B. and Harry H. Helmsley Charitable Trust. Mahadevan reported being a consultant for a variety of pharmaceutical firms. ■

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