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GI & Hepatology News

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Less Invasive Sponge Test Stratifies Risk in Patients With Barrett's Esophagus



The Cytosponge cell collection device is a minimally invasive way to perform a preliminary esophageal cell collection in an office.

BY DIANA SWIFT

FROM THE LANCET

Capsule sponge-based surveillance could be used in lieu of endoscopy for low-risk Barrett's esophagus (BE) surveillance, a prospective multisite UK study found. The biomarker risk panel collected by the panesophageal Cytosponge-on-a-string in more than 900 UK patients helped identify those at highest risk for dysplasia or cancer and needing endoscopy. It was found safe for following low-risk patients who did not need endoscopy.

Endoscopic surveillance is the clinical

standard for BE, but its effectiveness is inconsistent, wrote Rebecca C. Fitzgerald, MD, AGAF, professor in the Early Cancer Institute at the University of Cambridge in England, and colleagues in *The Lancet* (2025 Jun. doi: 10.1016/S0140-6736[25]01021-9).

"It is often performed by nonspecialists, and recent trials show that around 10% of cases of dysplasia and cancer are missed, which means some patients re-present within a year of their surveillance procedure with a symptomatic cancer that should have been diagnosed earlier," Fitzgerald told *GI & Hepatology News*.

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Can Nonresponders to Antiobesity Medicines Be Predicted?

BY MARILYNN LARKIN

Emerging research indicates that phenotype-based testing may help identify which biologic process is driving an individual's obesity, enabling clinicians to better tailor antiobesity medication (AOM) to the patient.

Currently, patient response to AOMs varies widely, with some patients responding robustly to AOMs and others responding weakly or not at all.

For example, trials of the GLP-1 semaglutide found that 32%-39.6% of people are "super responders," achieving weight loss in excess of 20%, and a subgroup of 10.2%-16.7% of individuals are nonresponders (Front Endocrinol. 2024 Jun. doi: 10.3389/fendo.2024.1382814). Similar variability was found with other AOMs, including the GLP-1 liraglutide and tirzepatide, a dual GLP-1/glucose-dependent insulinotropic polypeptide receptor agonist.

Studies of semaglutide suggest that people with obesity and type 2 diabetes (T2D) lose less weight on the drug than those without T2D, and men tend to lose less weight than women.

However, little else is known about predictors of response rates for various AOMs, and medication selection is typically based on patient or physician preference, comorbidities, medication interactions, and insurance coverage.

Although definitions of a "nonresponder" vary, the Endocrine Society's latest guideline, which many clinicians follow, states that an AOM is considered effective if patients lose more than 5% of their body

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LETTER FROM THE EDITOR

AI and GI Education: The Next Chapter

"Medicine is a science of uncertainty and an art of probability" - Sir William Osler

Artificial intelligence (AI) may reshape how we interact with the world more profoundly than any invention in history. We find ourselves in the infancy of that shift, trying to navigate where it leads. In this journey, our north star remains: What does it mean to be a physician? That question is the heartbeat of how we must rethink education in gastroenterology.

When I round with trainees, they're often excellent at answering board-style questions. But even with modest probing, they struggle with the fundamentals of probabilistic reasoning. A 2021 study confirms this gap, as clinicians and trainees routinely misinterpret pre- and post-test

probabilities in clinical settings.¹ More concerning, many also fail to communicate numerical risk in a way patients can understand.²⁻⁴ Meanwhile, AI has advanced rapidly. Large language models (LLMs) like ChatGPT now outperform medical students on standardized testing.⁵ More surprisingly, LLMs may also appear to be more empathetic. In one study, blinded reviewers compared responses to real patient questions and preferred ChatGPT's answers over physicians' nearly 80% of the time, citing greater clarity and empathy.⁶

The Immersive Science of Uncertainty

This is no longer science fiction; it is already happening in our clinics. Immersive therapy, combining AI with virtual reality, is helping our patients with irritable bowel syndrome manage their visceral pain and anxiety.⁷ If we are using these technologies to treat our patients, it is only natural that it will transform the next chapter of GI education.

Moving away from multiple-choice board questions toward immersive training, fellows will be able to rehearse medical uncertainty in a consequence-free environment. They will be able to practice communicating cancer probabilities to anxious patients, choose between biologics for inflammatory bowel disease patients with varying risk tolerances, and practice the delicate conversations around liver transplant candidacy. In the endoscopy unit, they can simulate difficult procedural decisions and work through ambiguity without risk. Ultimately, this kind of experiential learning will expose learners to countless GI

scenarios, each sharpening their understanding of probabilistic medicine and clinical judgement.

The "Art" of Probability

Machines will undoubtedly become better at calculating probabilities, simulating empathy, and understanding patient preferences than any human ever can. But they will never carry the burden of being wrong.

When a small pancreatic cyst becomes invasive cancer during surveillance, AI may calculate the odds, but it cannot deliver the diagnosis. It cannot feel the weight of the silence at the bedside. It cannot hold their hand. That moment belongs to us.

So, while it is crucial that we teach our trainees to reason more deeply, more probabilistically, the most important lesson for the next generation is this: In the age of AI, we no longer need to be the smartest presence in the room, we need to be the most human one. ■

Marc S. Piper, MD, MSc.
Associate Editor



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Top 5 Tips for Becoming an Effective Gastroenterology Consultant

BY ALLON KAHN, MD

Gastroenterology (GI) subspecialty training is carefully designed to develop expertise in digestive diseases and gastrointestinal endoscopy, while facilitating the transition from generalist to subspecialty consultant. The concept of effective consultation extends far beyond clinical expertise and has been explored repeatedly, beginning with Goldman's "Ten Commandments" in 1983.^{1,2} How should these best practices be specifically applied to GI? More importantly, what kind of experience would you want if you were the referring provider or the patient themselves?

Below are five essential tips to guide your development as a high-impact GI consultant with a reputation for excellence.

1. Be Kind

Survey studies of medical/surgical residents and attending hospitalists have demonstrated that willingness to accept consultation requests was the single factor consistently rated as most important in determining the quality of the consultation interaction.^{3,4} Unfortunately, nearly 65% of respondents reported encountering pushback when requesting subspecialty consultation.

It is critical to recognize that when you receive a GI consult request, the requester has already decided that it is needed. Whether that request comports with our individual notion of "necessary" or "important," this is a colleague's request for help. There are myriad reasons why a request may be made, but they are unified in this principle.

Effective teamwork in healthcare settings enhances clinical performance and patient safety. Positive relationships with colleagues and healthcare team members also mitigate the emotional basis for physician burnout.⁵ Be kind and courteous to those who seek your assistance. Move beyond the notion of the "bad" or "soft" consult and seek instead to understand how you can help.

A requesting physician may phrase the consult question vaguely or may know that the patient is having a GI-related issue, but



Dr. Khan

simply lack the specific knowledge to know what is needed. In these instances, it is our role to listen and help guide them to the correct thought process to ensure the best care of the patient. These important interactions establish our reputation, create our referral bases, and directly affect our sense of personal satisfaction.

2. Be Timely

GI presents an appealing breadth of pathology, but this also corresponds to a wide variety of indications for consultation and, therefore, urgency of need. In a busy clinical practice, not all requests can be urgently prioritized. However, it is the consultant's responsibility to identify patients that require urgent evaluation and intervention to avert a potential adverse outcome.

We are well-trained in the medical triage of consultations. There are explicit guidelines for assessing urgency for GI bleeding, foreign body ingestion, choledocholithiasis, and many other indications. However, there are often special contextual circumstances that will elevate the urgency of a seemingly non-urgent consult request. Does the patient have an upcoming surgery or treatment that will depend on your input? Are they facing an imminent loss of insurance coverage? Is their non-severe GI disease leading to more severe impact on non-GI organ systems? The referring provider knows the patient better than you — seek to understand the context of the consult request.

Timeliness also applies to our communication. Communicate recommendations directly to the consulting service as soon as the patient is seen. When a colleague

reaches out with a concern about a patient, make sure to take that request seriously. If you are unable to address the concern immediately, at least provide acknowledgment and an estimated timeline for response. As the maxim states, the effectiveness of a consultant is just as dependent on availability as it is on ability.

3. Be Specific

The same survey studies indicate that the second-most critical aspect of successful subspecialty consultation is delivering clear recommendations. Accordingly, I always urge my trainees to challenge me when we leave a consult interaction if they feel that our plan is vague or imprecise.

Specificity in consult recommendations is an essential way to demonstrate your expertise and provide value. Clear and definitive recommendations enhance others' perception of your skill, reduce the need for additional clarifying communication, and lead to more efficient, higher-quality care. Avoid vague language, such as asking the requester to "consider" a test or intervention. When recommending medication, specify the dose, frequency, duration, and expected timeline of effect. Rather than recommending "cross-sectional imaging," specify what modality and protocol. Instead of recommending "adequate resuscitation," specify your target endpoints. If you engage in multidisciplinary discussion, ensure you strive for a specific group consensus plan and communicate this to all members of the team.

Specificity also applies to the quality of your documentation. Ensure that your clinical notes outline your rationale for your recommended plan, specific contingencies based on results of recommended testing, and a plan for follow-up care. When referring for open-access endoscopy, specifically outline what to look for and which specimens or endoscopic interventions are needed. Be precise in your procedure documentation — avoid vague terms such as small/medium/large and instead quantify in terms of millimeter/centimeter measurement. If you do not adopt specific classification schemes (e.g. Prague classification, Paris

classification, Eosinophilic Esophagitis Endoscopic Reference Score, etc), ensure you provide enough descriptive language to convey an adequate understanding of the findings.

4. Be Helpful

A consultant's primary directive is to be of service to the consulting provider and the patient. As an educational leader, I am often asked what attributes separate a high-performing trainee from an average one. My feeling is that the most critical attribute is a sense of ownership over patient care.

As a consultant, when others feel we are exhibiting engagement and ownership in a patient's care, they perceive that we are working together as an effective healthcare team. Interestingly, survey studies of inpatient care show that primary services do not necessarily value assistance with orders or care coordination — they consider these as core aspects of their daily work. What they did value was ongoing daily progress notes/communication, regardless of patient acuity or consulting specialty. This is a potent signal that our continued engagement (both inpatient and outpatient) is perceived as helpful.

Helpfulness is further aided by ensuring mutual understanding. While survey data indicate that sharing specific literature citations may not always be perceived positively, explaining the consultant's rationale for their recommendations is highly valued. Take the time to tactfully explain your assessment of the patient and why you arrived at your specific recommendations. If your recommendations differ from what the requester expected (eg, a procedure was expected but is not offered), ensure you explain why and answer questions they may have. This fosters mutual respect and proactively averts conflict or discontent from misunderstanding.

Multidisciplinary collaboration is another important avenue for aiding our patients and colleagues. Studies across a wide range of disease processes (including GI bleeding, IBD, etc) and medical settings have demonstrated that multidisciplinary collaboration unequivocally

Continued on following page

IBD Meds: No Link with Breast Cancer Recurrence

BY WILL PASS

MDedge News

FROM CLINICAL GASTROENTEROLOGY
AND HEPATOLOGY

Medications for inflammatory bowel disease (IBD) appear to have no impact on risk of incident malignancies among patients with a history of breast cancer, according to investigators.

These findings diminish concerns that IBD therapy could theoretically reactivate dormant micrometastases, lead author Guillaume Le Cosquer, MD, of Toulouse University Hospital, France, and colleagues, reported.

"In patients with IBD, medical management of subjects with a history of breast cancer is a frequent and unresolved problem for clinicians," the investigators wrote in *Clinical Gastroenterology and Hepatology* (2024 Nov. doi: 10.1016/j.cgh.2024.09.034).

Previous studies have reported that conventional immunosuppressants and biologics do not increase risk of incident cancer among IBD patients with a prior nondigestive malignancy; however, recent guidelines from the European Crohn's and Colitis Organisation (ECCO) suggest that data are insufficient to make associated recommendations, prompting the present study.

"The major strength of our work is that it is the first to focus on the most frequent cancer (breast cancer) in patients with IBD only, with the longest follow-up after breast cancer in patients with IBD ever published," Dr. Le Cosquer and colleagues noted.

The dataset included 207 patients with IBD and a history of breast cancer, drawn from seven tertiary centers across France.

The index date was the time of breast cancer diagnosis, and

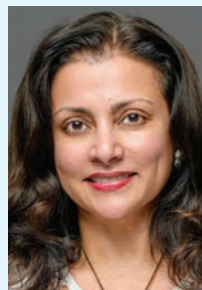
Patients with inflammatory bowel disease (IBD) are at risk for a host of other illnesses, including cancer, at rates similar to or greater than the general population. When faced with uncertainty about drug safety with a cancer diagnosis, the reflex is to avoid the therapy altogether. This may lead to significant flares which may in turn lead to difficulty in tolerating cancer therapy and a shortened and lower quality life.

Le Cosquer et al address the question of the risk of incident cancer among patients with a history of breast cancer. The authors found that the risk was related to poor prognostic factors for breast cancer and not IBD therapy. This finding should be interpreted with caution; while the analysis is the largest reported, the number of included patients is only 207. After propensity score matching, crude incidence rates per 1000 person years appeared greater in the treatment arm (28.9) vs the untreated arm (10.2) ($P = .0519$). With a greater number of patients, it is conceivable the difference is significant.

On the flip side, prior to diagnosis, the majority of IBD patients received immunosuppressant or biologic therapy; however, after the index cancer, 51.6% of patients received no treatment. The survival curves show a near 25% difference in favor of treated

patients after 300 months, albeit with very small numbers, raising the question of whether withholding IBD therapy is more harmful.

It is reassuring that the multiple papers cited in the article have not shown an increase in solid organ tumors to date. However, the practitioner needs to balance maintenance of IBD remission and overall health with the risk of complications in the patient with underlying malignancy. This complex decision making will shift over time and should involve the patient, the oncologist, and the gastroenterologist. In my practice, thiopurines are avoided and anti-integrins and interleukin-23s are preferred. However, anti-TNF agents and JAK inhibitors are used when the patients' overall benefit from disease control outweighs their (theoretical) risk for recurrence, infection, and thromboembolism.



Dr. Mahadevan

Uma Mahadevan, MD, AGAF, is the Lynne and Marc Benioff Professor of Gastroenterology and director of the Colitis and Crohn's Disease Center at the University of California, San Francisco. She declared research support from the Leona M. and Harry B. Helmsley Trust, and has served as a consultant for multiple pharmaceutical firms.

patients were followed for a median of 71 months. The median time from cancer diagnosis to initiation of IBD treatment was 28 months.

First-line post-cancer treatments included conventional immunosuppressants (19.3%), anti-TNF agents (19.8%), vedolizumab (7.2%), and ustekinumab (1.9%). Approximately half (51.6%) received no immunosuppressive therapy during follow-up.

Over the study period, 42 incident cancers were recorded (20.3%), among which 34 were breast cancer recurrences. Adjusted incidence rates per 1000 person-years were 10.2 (95% CI, 6.0-16.4) in the untreated group and 28.9 (95% CI, 11.6-59.6) in patients exposed to immunosuppressive or biologic

therapies ($P = .0519$). Incident cancer-free survival did not differ significantly between treated and untreated groups ($P = .4796$).

On multivariable analysis, independent predictors of incident cancer included T4d stage ($P = .036$), triple-negative status ($P = .016$), and follow-up duration shorter than 71 months ($P = .005$).

"Immunosuppressant and biologic use in selected patients with IBD with prior breast cancer does not seem to increase the risk of incident cancer," the investigators wrote, noting that the main predictors of cancer recurrence were known poor prognostic features of breast cancer.

Dr. Le Cosquer and colleagues acknowledged a lack of prospective safety data for biologic therapies

among patients with prior malignancy, as these individuals are often excluded from clinical trials. Still, they underscored alignment between their findings and earlier retrospective studies, including analyses from the SAPPHERE registry and Medicare data, which also found no significant increase in breast cancer recurrence with anti-TNF agents or newer biologics such as vedolizumab and ustekinumab.

"Our findings will help clinicians to make decisions in multidisciplinary meetings to start immunosuppressants or biologics in case of IBD flare-up in these patients," they concluded.

The investigators disclosed relationships with AbbVie, Janssen, Takeda, and others. ■

Continued from previous page

improves patient outcomes.⁶ The success of these collaborations relies on our willingness to fully engage in these conversations, despite the fact that they may often be logistically challenging.

We all know how difficult it can be to locate and organize multiple medical specialists with complex varying clinical schedules and busy personal lives. Choosing to do so demonstrates a dedication to providing the highest level of care and

elevates both patient and physician satisfaction. Having chosen to cultivate several ongoing multidisciplinary conferences/collaborations, I can attest to the notion that the outcome is well worth the effort.

5. Be Honest

While we always strive to provide the answers for our patients and colleagues, we must also acknowledge our limitations. Be honest with yourself when you encounter a scenario that pushes beyond the

boundaries of your knowledge and comfort. Be willing to admit when you yourself need to consult others or seek an outside referral to provide the care a patient needs. Aspiring physicians often espouse that a devotion to lifelong learning is a key driver of their desire to pursue a career in medicine. These scenarios provide a key opportunity to expand our knowledge while doing what is right for our patients.

Be equally honest about your comfort with "curbside" consultations.

Studies show that subspecialists receive on average of three to four such requests per week.⁷ The perception of these interactions is starkly discrepant between the requester and recipient. While over 80% of surveyed primary nonsurgical services felt that curbside consultations were helpful in patient care, a similar proportion of subspecialists expressed concern that insufficient clinical information was provided, even leading to a

Continued on following page

Sterile Water Bottles Unnecessary for Endoscopy

BY WILL PASS

MDedge News

FROM GASTRO HEP ADVANCES

Like diners saving on drinks, endoscopists can safely forgo sterile water in favor of tap, reducing both environmental and financial costs, according to a recent narrative review.

“No direct evidence supports the recommendation and widespread use of sterile water during gastrointestinal endoscopy procedures,” lead author Deepak Agrawal, MD, chief of gastroenterology & hepatology at the Dell Medical School, University Texas at Austin, and colleagues wrote in *Gastro Hep Advances* (2025 Jan. doi: 10.1016/j.gastha.2025.100625). “Guidelines recommending sterile water during endoscopy are based on limited evidence and mostly expert opinions.”

After reviewing the literature back to 1975, Dr. Agrawal and colleagues considered the use of sterile water in endoscopy via three frameworks: medical evidence and guidelines, environmental and broader health effects, and financial costs.

Only two studies — both from the 1990s — directly compared sterile and tap water use in endoscopy. Neither showed an increased risk of infection from tap water. In fact, some cultures from allegedly sterile water bottles grew pathogenic bacteria, while no patient complications were reported in either study.

“The recommendations for sterile water contradict observations in other medical care scenarios, for example, for the irrigation of open wounds,” Dr. Agrawal and colleagues noted. “Similarly, there is no benefit in using sterile water for enteral feeds in immunosuppressed patients, and tap water enemas are routinely acceptable for colon cleansing before sigmoidoscopies in all patients,

irrespective of immune status.”

Current guidelines, including the 2021 US multisociety guideline on reprocessing flexible GI endoscopes and accessories, recommend sterile water for procedures involving mucosal penetration but acknowledge low-quality supporting evidence (Gastrointest Endosc. 2021 Jan. doi: 10.1016/j.gie.2020.09.048). These recommendations are based on outdated studies, some unrelated to GI endoscopy, Dr. Agrawal and colleagues pointed out, and rely heavily on cross-referenced opinion statements rather than clinical data.

They went on to suggest a concerning possibility: All those plastic bottles may actually cause more health problems than prevent them. The review estimates that the production and transportation of sterile water bottles contributes over 6,000 metric tons of emissions per year from US endoscopy units alone. What’s more, as discarded bottles break down, they release greenhouse gases and microplastics, the latter of which have been linked to cardiovascular disease, inflammatory bowel disease, and endocrine disruption.

Dr. Agrawal and colleagues also underscored the financial toxicity of sterile water bottles. Considering a 1-liter bottle of sterile water costs \$3-\$10, an endoscopy unit performing 30 procedures per day spends approximately \$1000-\$3000 per month on bottled water alone. Scaled nationally, the routine use of sterile water costs tens of millions of dollars each year, not counting indirect expenses associated with stocking and waste disposal.

Considering the dubious clinical upside against the apparent environmental and financial downsides, the authors urged endoscopy units to rethink routine sterile water use.

They proposed a pragmatic model:

about how you apply it, how you communicate it, and how you make others feel in the process.

The attributes outlined above are not ancillary traits — they are essential components of high-quality consultation. When consistently applied, they enhance collaboration, improve patient outcomes, and reinforce trust within the healthcare system. By committing to them, you establish your reputation of excellence and play a role in elevating the field of gastroenterology more broadly. ■

In an editorial accompanying the study and comments to *GI & Hepatology News*, Seth A. Gross, MD, AGAF, clinical chief in the division of gastroenterology and hepatology at NYU Langone Health and professor at NYU Grossman School of Medicine, both in New York City, urged gastroenterologists to reconsider the use of sterile water in endoscopy.



Dr. Gross

While the rationale for bottled water has centered on infection prevention, Gross argued that the evidence does not hold up, noting that this practice contradicts modern values around sustainability and evidence-based care.

The two relevant clinical studies comparing sterile vs tap water in endoscopy are almost 30 years old, he said, and neither detected an increased risk of infection with tap water, leading both to conclude that tap water is “safe and practical” for routine endoscopy.

Gross also pointed out the inconsistency of sterile water use in medical practice, noting that tap water is acceptable in procedures with higher infection risk than endoscopy.

“Lastly,” he added, “most people drink tap water and not sterile water on a daily basis without outbreaks of gastroenteritis from bacterial infections.”

Gross’s comments went beyond the data to emphasize the obvious but overlooked environmental impacts of sterile water bottles. He suggested several challenging suggestions to make medicine more ecofriendly, like reducing travel to conferences, increasing the avail-

ability of telehealth, and choosing reusable devices over disposables. But “what’s hiding in plain sight,” he said, “is our use of sterile water.”

While acknowledging that some patients, like those who are immunocompromised, might still warrant sterile water, Gross supported the review’s recommendation to use tap water instead. He called on GI societies and regulatory bodies to re-examine current policy and pursue updated guidance.

“Sometimes going back to the basics,” he concluded, “could be the most innovative strategy with tremendous impact.”

Gross reported no conflicts of interest.

start the day with a new sterile or reusable bottle, refill with tap water for subsequent cases, and recycle the bottle at day’s end. Institutions should ensure their tap water meets safety standards, they added, such as those outlined in the Joint Commission’s 2022 R3 Report on standards for water management (www.joint-commission.org/en-us/standards/r3-report/r3-report-32).

Dr. Agrawal and colleagues also called on GI societies to revise existing guidance to reflect today’s clinical and environmental realities. Until strong evidence supports the need for sterile water, they wrote, the smarter, safer, and more sustainable option may be simply turning on the tap.

The investigators disclosed relationships with Guardant, Exact Sciences, Freenome, and others. ■

Continued from previous page

fear of litigation. While straightforward, informal conversations on narrow, well-defined questions can be helpful and efficient, the consultant should always feel comfortable seeking an opportunity for formal consultation when the details are unclear or the case/question is complex.

Closing Thoughts

Being an effective GI consultant isn’t just about what you know — it’s

Dr. Kahn is based in the division of gastroenterology and hepatology at Mayo Clinic, Scottsdale, Arizona. He reports no conflicts of interest in regard to this article.

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AI Algorithm Predicts Transfusion Need, Mortality Risk in Acute GI Bleeds

BY KATHLEEN DOHENY

FROM DDW 2025

SAN DIEGO — A novel generative artificial intelligence (AI) framework known as trajectory flow matching (TFM) can predict the need for red blood cell transfusion and mortality risk in ICU patients with acute gastrointestinal (GI) bleeding, researchers reported at Digestive Disease Week® (DDW) 2025.

Acute GI bleeding is the most common cause of digestive dis-



Ms. Zhang

“Probabilistic flow matching is a class of generative artificial intelligence that learns how a simple distribution becomes a more complex distribution with ordinary differential equations.”

ease-related hospitalization, with an estimated 500,000 hospital admissions annually. It’s known that predicting the need for red blood cell transfusion in the first 24 hours may improve resuscitation and decrease both morbidity and mortality.

However, an existing clinical score known as the Rockall Score does not perform well for predicting mortality, Xi (Nicole) Zhang, an MD-PhD student at McGill University, Montreal, told attendees at DDW. With an area under the curve of 0.65-0.75, better prediction is needed, said Zhang, whose coresearchers included Dennis Shung, MD, MHS, PhD, director of applied artificial intelligence at Yale University School of Medicine, New Haven, Connecticut.

“We’d like to predict multiple outcomes in addition to mortality,” said Zhang, who is also a student at the Mila-Quebec Artificial Intelligence Institute.

As a result, the researchers turned to the TFM approach, applying it to ICU patients with acute GI bleeding to predict both the need for transfusion and in-hospital mortality risk. The all-cause mortality rate is up to 11%, according to a 2020 study by James Y. W. Lau, MD, and colleagues (N Engl J Med. 2020 Apr. doi:

10.1056/NEJMoa1912484).

The rebleeding rate of non-variceal upper GI bleeds is up to 10.4% (Clin Gastroenterol Hepatol. 2017 Jun. doi: 10.1016/j.cgh.2017.06.029). Zhang said the rebleeding rate for variceal upper gastrointestinal bleeding is up to 65%.

The AI method the researchers used outperformed a standard deep-learning model at predicting the need for transfusion and estimating mortality risk.

Defining the AI Framework

“Probabilistic flow matching is a class of generative artificial intelligence that learns how a simple distribution becomes a more complex distribution

with ordinary differential equations,” Zhang told *GI & Hepatology News*.

“For example, if you had a few lines and shapes you could learn how it could become a detailed portrait of a face,” she said. “In our case, we start with a few blood pressure and heart rate measurements and learn the pattern of blood pressures and heart rates over time, particularly if they reflect clinical deterioration with hemodynamic instability.”

Another way to think about the underlying algorithm, Zhang said, is to think about a river with boats where the river flow determines where the boats end up. “We are trying to direct the boat to the correct dock by adjusting the flow of water in the canal. In this case we are mapping the distribution with the first few data points to the distribution with the entire patient trajectory.”

The information gained, she said, could be helpful in timing endoscopic evaluation or allocating red blood cell products for emergent transfusion.

Study Details

The researchers evaluated a cohort of 2602 patients admitted to the ICU, identified from the publicly available MIMIC-III database. They

divided the patients into a training set of 2342 patients and an internal validation set of 260 patients. Input variables were severe liver disease comorbidity, administration of vasopressor medications, mean arterial blood pressure, and heart rate over the first 24 hours.

Excluded was hemoglobin, since the point was to test the trajectory of hemodynamic parameters independent of hemoglobin thresholds used to guide red blood cell transfusion.

The outcome measures were ad-



Dr. Glissen Brown

“This is an exciting proof-of-concept study that shows generative AI methods may be applied to complex datasets in order to improve on our current predictive models and improve patient care.”

ministration of packed red blood cell transfusion within 24 hours and all-cause hospital mortality.

The TFM was more accurate than a standard deep-learning model in predicting red blood cell transfusion, with an accuracy of 93.6% vs 43.2% ($P \leq .001$). It was also more accurate at predicting all-cause in-hospital mortality, with an accuracy of 89.5% vs 42.5% ($P = .01$).

The researchers concluded that the TFM approach was able to predict the hemodynamic trajectories of patients with acute GI bleeding defined as deviation and outperformed the baseline from the measured mean arterial pressure and heart rate.

Expert Perspective

“This is an exciting proof-of-concept study that shows generative AI methods may be applied to complex datasets in order to improve on our current predictive models and improve patient care,” said Jeremy Glissen Brown, MD, MSc, an assistant professor of medicine and a practicing gastroenterologist at Duke University who has published research on the use of AI in clinical practice. He reviewed the study for *GI & Hepatology News* but was not involved in the research.

“Future work will likely look into the implementation of a version of this model on real-time data,” he said. “We are at an exciting inflection point in predictive models within GI and clinical medicine. Predictive models based on deep learning and generative AI hold the promise of improving how we predict and treat disease states, but the excitement being generated with studies such as this needs to be balanced with the tradeoffs inherent to the current paradigm of deep-learning and generative

models compared to more traditional regression-based models. These include many of the same ‘black box’ explainability questions that have risen in the age of convolutional

neural networks as well as some method-specific questions due to the continuous and implicit nature of TFM.”

Elaborating on that, Glissen Brown said: “TFM, like many deep-learning techniques, raises concerns about explainability that we’ve long seen with convolutional neural networks — the ‘black box’ problem, where it’s difficult to interpret exactly how and why the model arrives at a particular decision. But TFM also introduces unique challenges due to its continuous and implicit formulation. Since it often learns flows without explicitly defining intermediate representations or steps, it can be harder to trace the logic or pathways it uses to connect inputs to

outputs. This makes standard interpretability tools less effective and calls for new techniques tailored to these continuous architectures.”

“This approach could have a real clinical impact,” said Robert Hirten, MD, associate professor of medicine and artificial



Dr. Hirten

intelligence.

Continued on following page

Colonoscopy Screening Effective in 45- to 49-Year-Olds

BY ALICIA AULT

Screening colonoscopies in 45- to 49-year-olds yield similar rates of cancer and lesions as in 50- to 54-year-olds, according to a new analysis.

Researchers at Kaiser Permanente Northern California sought to compare yields between the two age groups to assess how a change in guidance in 2021 urging screening in the younger cohort was borne out in a real-world setting.

The researchers published their findings in *JAMA* (2025 Jun. doi: 10.1001/jama.2025.7494), concluding that the results supported screening colonoscopy in 45- to 49-year-olds.

The study compared 4380 individuals aged 45-49 years, with 7651 who were aged 50-54. All of them underwent their first colonoscopy during 2021 to 2024. About 35% percent of the younger group and 40% of the older group had any adenoma.

About 4% of each group had an advanced adenoma, 10% had any sessile serrated lesion, a little

under 2% had an advanced serrated lesion, and 0.1% in each group had colorectal cancer.

There were no significant differences in neoplasia prevalence between the groups by sex. The authors did note that the study



Dr. Patel



Dr. Calderwood

group included more Asian individuals (30%) than in the general population.

Swati G. Patel, MD, MS, director of the gastrointestinal hereditary cancer program at the University of Colorado Anschutz Medical Center, Denver, said the Kaiser study is important because its data was aggregated after the US Preventive Services Task Force lowered the screening age in 2021.

The Kaiser research “validates the initial studies” done to support that recommendation and the 2022 consensus statement by the US Multi-Society Task Force on Colorectal Cancer, which also advocated screening in 45- to 49-year-olds.

Even though the new *JAMA* study found a similar rate of cancers and precursor lesions as in previous trials, it provides “reinforcement of the rationale for decreasing the screening age,” Patel, the lead author on the consensus statement, told *GI & Hepatology News*.

The Kaiser research is “really powerful information,” she said.

“It certainly validates our current guidance to start screening for colorectal cancer at age 45,” said Audrey Calderwood, MD, director of the GI Cancer Risk and Prevention Clinic at the Dartmouth Geisel School of Medicine in Hanover, New Hampshire.

The Kaiser data provides granular information to share with younger patients who might think that they don’t need screening because they are healthy and don’t have symptoms, said Calderwood, who is also director of the Comprehensive Gastroenterology Center at Dartmouth Hitchcock Medical Center in Lebanon, New Hampshire.

Colon cancer rates for Americans under age 50 have been steadily rising for the past decade, hitting about 10 cases per 100,000 in 2022, according to the National Cancer Institute (NCI). In 2023, about 73% of eligible 50- to 75-year-olds received colorectal cancer screening based on the most recent guidelines, according to the NCI.

But screening rates in the under-50 age group are much lower. Researchers estimated in a study that only about 34.5% of those aged 45-49 received colorectal cancer screening, which included colonoscopy, stool-based tests, and CT colonography.

Patel said that estimate is “spot on” in terms of other estimates.

“I think there’s a perception that it’s a cancer of older adults and that young healthy people don’t need to worry about it,” she said, adding that getting the word out to younger Americans is a “public relations challenge,” in part because of squeamishness about discussing anything to do with stool and changes in how young people access information.

Calderwood agreed. Younger people “aren’t chatting to their friends about” colon cancer screening the way they might about mammography.

Both she and Patel noted that educating the public was an ongoing project, but that a physician’s recommendation was key.

Patel said she hoped that data provided in the Kaiser study might help “dismantle the systemic skepticism around decreasing the age recommendation” for screening.

Calderwood and Patel reported having no relevant financial relationships. ■

Continued from previous page

intelligence, Icahn School of Medicine at Mount Sinai, New York City, who also reviewed the study. “Accurately predicting transfusion needs and mortality risk in real time could support earlier, more targeted interventions for high-risk patients. While these findings still need to be validated in prospective studies, it could enhance ICU decision-making and resource allocation.”

“For the practicing gastroenterologist, we envision this system could help them figure out when to perform endoscopy in a patient admitted with acute gastrointestinal bleeding in the ICU at very high risk of exsanguination,” Zhang told *GI & Hepatology News*.

The approach, the researchers said, will be useful in identifying unique patient characteristics, make possible the identification of high-risk patients and lead to more personalized medicine.

Hirten, Zhang, and Shung had no disclosures to report. Glissen Brown reported consulting relationships with Medtronic, OdinVision, Doximity, and Olympus. The National Institutes of Health funded this study. ■



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Optimizing Weight Loss

Nonresponders from page 1

weight within 3 months.

Can nonresponders and lower responders be identified and helped? Yes, but it's complicated.

"Treating obesity effectively means recognizing that not all patients respond the same way to



Dr. Acosta

"If a patient's obesity isn't primarily rooted in the mechanisms targeted by a particular drug, their response will naturally be limited. ... The medication simply isn't the right match for their biology."

the same treatment, and that's not a failure; it's a signal," said Andres Acosta, MD, PhD, an obesity expert at Mayo Clinic, Rochester, Minnesota, and a cofounder of Phenomix Sciences, a biotech company in Menlo Park, California.

"Obesity is not a single disease. It's a complex, multifactorial condition driven by diverse biological pathways," he told *GI & Hepatology News*. "Semaglutide and other GLP-1s primarily act by reducing appetite and slowing gastric emptying, but not all patients have obesity that is primarily driven by appetite dysregulation."

Phenotype-Based Profiling

Figuring out what drives an individual's obesity is where a phenotype-based profiling test could possibly help.

Acosta and colleagues previously used a variety of validated studies and questionnaires to identify four phenotypes that represent distinct biologic drivers of obesity: hungry brain (abnormal satiation), emotional hunger (hedonic eating), hungry gut (abnormal satiety), and slow burn (decreased metabolic rate). In their pragmatic clinical trial, phenotype-guided AOM selection was associated with 1.75-fold greater weight loss after 12 months than the standard approach to drug selection, with mean weight loss of 15.9% and 9%, respectively (Obesity. 2021 Mar. doi:10.1002/oby.23120).

"If a patient's obesity isn't primarily rooted in the mechanisms targeted by a particular drug, their response will naturally be limited," Acosta said. "It's not that they're failing the medication; the medication simply isn't the right match for their biology."

For their new study, published online in *Cell Metabolism*, Acosta and colleagues built on their previous research by analyzing the genetic and nongenetic factors that influenced calories needed to reach satiation (CTS) in adults with obesity (2025 Jun. doi: 10.1016/j.cmet.2025.05.008). They then used machine learning techniques to develop a CTS gene risk score (CTS-GRS) that could be measured by a DNA

saliva test.

The study included 717 adults with obesity (mean age, 41 years; 75% women) with marked variability in satiation, ranging from 140 to 2166 kcals to reach satiation.

CTS was assessed through an ad libitum meal, combined with physiological and behavioral evaluations, including calorimetry, imaging, blood sampling, and gastric emptying tests. The largest contributors to CTS variability were sex and genetic factors, while other anthropometric measurements played lesser roles.

Various analyses and assessments of participants' CTS-GRS scores showed that individuals with a high CTS-GRS, or hungry brain phenotype, experienced significantly greater weight loss when treated with phentermine/topiramate than those with a low CTS-GRS, or hungry gut, phenotype. After 52 weeks of treatment, individuals with the hungry brain phenotype lost an average of 17.4% of their body weight compared with 11.2% in those with the hungry gut phenotype.

An analysis of a separate 16-week study showed that patients with the hungry gut phenotype responded better to the GLP-1 liraglutide, losing 6.4% total body weight, compared to 3.3% for those with the hungry brain phenotype.

Overall, the CTS-GRS test predicted drug response with up to 84% accuracy (area under the curve, 0.76 in men and 0.84 in women). The authors acknowledged that these results need to be replicated prospectively and in more diverse populations to validate the test's predictive ability.

"This kind of phenotype-based profiling allows us to predict which patients are more likely to respond

and who might need a different intervention," Acosta said. "It's a critical step toward eliminating trial-and-error in obesity treatment."

The test (MyPhenome test) is used at more than 80 healthcare clinics in the United States, according to Phenomix Sciences, which manufactures it. A company spokesperson said the test does not require FDA approval because it is used to predict obesity phenotypes to help inform treatment, but not to identify specific medications or other interventions. "If it were to do the latter," the spokesperson said, "it would be considered a 'companion diagnostic' and subject to the FDA clearance process."

What to Do if an AOM Isn't Working

It's one thing to predict whether an individual might do better on one drug vs another, but what should clinicians do meanwhile to optimize weight loss for their patients who may be struggling on a particular drug?

"Efforts to predict the response to GLP-1 therapy have been a hot topic," noted Sriram Machineni, MD, associate professor at Montefiore Medical Center, New York City, and founding director of the Fleischer Institute Medical Weight Center at Montefiore Einstein. Although the current study showed that genetic testing could predict responders, like Acosta, he agreed that the results need to be replicated in a prospective manner.

"In the absence of a validated tool for predicting response to specific medications, we use a prioritization process for trialing medications," Machineni told *GI & Hepatology News*. "The prioritization is based on the suitability of the side-effect profile to the specific patient, including contraindications; benefits independent of weight loss, such as cardiovascular protection for semaglutide; average efficacy; and financial accessibility for patients."

Predicting responders isn't straightforward, said Robert Kushner, MD, professor of medicine and medical education at the Feinberg School of Medicine at Northwestern University and medical director of the Wellness Institute at Northwestern Memorial Hospital, both in Chicago.



Dr. Kushner

"Despite looking at baseline demographic data such as race, ethnicity, age, weight, and BMI, we are unable to predict who will lose more or less weight," he told *GI & Hepatology News*. The one exception is that women generally lose more weight than men. "However, even among females, we cannot discern which females will lose more weight than other females," he said.

If an individual is not showing sufficient weight loss on a particular medication, "we first explore potential reasons that can be addressed, such as the patient is not taking the medication or is skipping doses," Kushner said. If need be, they discuss changing to a different drug to improve compliance. He also stresses the importance of making lifestyle changes in diet and physical activity for patients taking AOMs.

Often patients who do not lose at least 5% of their weight within 3 months are not likely to respond well to that medication even if they remain on it. "So, early response rates determine longer-term success," Kushner said.

Acosta said that if a patient isn't responding to one class of medication, he pivots to a treatment better aligned with their phenotype. "That could mean switching from a GLP-1 to a medication like [naltrexone/bupropion] or trying a new method altogether," he said. "The key is that the treatment decision is rooted in the patient's biology, not just a reaction to

Often patients who do not lose at least 5% of their weight within 3 months are not likely to respond well to that medication even if they remain on it. "So, early response rates determine longer-term success."

short-term results. We also emphasize the importance of long-term follow-up and support."

The goal isn't just weight loss but also improved health and quality of life, Acosta said. "Whether through medication, surgery, or behavior change, what matters most is tailoring the care plan to each individual's unique biology and needs."

The new study received support from the Mayo Clinic Clinical Research Trials Unit, Vivus, and Phenomix Sciences. Acosta is supported

Continued on following page

Why Is Early-Onset CRC Rising? New Study Provides a Clue

BY M. ALEXANDER OTTO, PA, MMS

The numbers don't lie: Colorectal cancer (CRC) has been on the rise in younger people in the United States for over 2 decades.

While the data show a clear trend, researchers still face a glaring unanswered question: Why is this happening?

A recent report in *Nature* may offer an important clue to start unraveling this early-onset CRC mystery (2025 Apr. doi: 10.1038/s41586-025-09025-8).

What the Study Found

The new analysis found that childhood exposure to a carcinogenic toxin known to cause DNA damage is strongly linked to the development of early-onset CRC.

The bacterial toxin, called colibactin, is produced by certain strains of *Escherichia coli* and other bacteria — more specifically, polyketide synthase (PKS)-positive strains. Previous research has found colibactin-related mutations can occur in up to 15% of CRC cases overall, but a link to early-onset disease has been less clear.

In this recent genetic analysis, investigators led by Marcos Díaz-Gay, PhD, analyzed CRC biopsies from 981 patients across 11 countries and 4 continents. The team tracked DNA damage from colibactin by identifying distinctive mutational signatures — called SBS88 and ID18 — left by the toxin.

Díaz-Gay and colleagues found that these mutational signatures were 3.3 times more common in patients diagnosed before 40 years of age than in those over 70 years.

Colibactin exposure was also linked to about a quarter of mutations that inactivate the colorectal tumor suppressor gene *APC*.

However, epidemiologic factors linked to CRC, such as body mass index, diet, and lifestyle, were not considered in the study, which the investigators noted is a key limitation.

"Our results show for the first time an association between the presence of colibactin-induced mutational signatures and early-onset colorectal cancer," Díaz-Gay, a genomic researcher at the Spanish National Cancer Research Center, Madrid, and colleagues wrote.

"Prior studies have indicated that mutagenesis due to colibactin exposure can occur within the first decade of life and then ceases," the investigators explained. But "this 'head start' could plausibly result in an increased risk of early-onset cancers."

What the Study Means

Trevor Graham, PhD, a professor of genomics and evolution at The Institute of Cancer Research, London, helped put the study findings into context.

Others have proposed that colibactin "could have a role in causing early-onset disease," Graham commented in a statement from the UK nonprofit Science Media Centre. "This work provides [the] strong[est] data yet that the hypothesis is correct."

Plus, Graham added, "This is very good-quality research. The authors have collected bowel cancers from countries around the world and performed whole genome sequencing on them."

"Most importantly," he said, the colibactin mutations were more common in people who got bowel cancer before 50 years of age, which "suggests the mutations caused by these bugs in the bowel could be a cause of early-onset bowel cancer, although further studies are needed to confirm this."

Although the study doesn't prove causation, "this is a very important finding," Alan Venook, MD, a gastrointestinal medical oncologist and CRC specialist at the University of California, San Francisco, told *GI & Hepatology News*. "This gives us a hook to understand what's going on."

However, "it's not at all likely that this single entity is entirely responsible for early-onset CRC," Venook clarified.

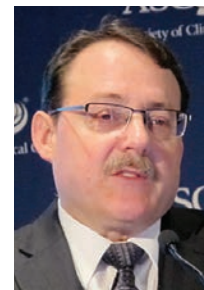
But if childhood exposure to colibactin is responsible, at least in part, for the growing incidence of early-onset CRC, it would suggest that PKS-positive bacteria have become more common in the gut microbiome of younger people over the past few decades. PKS-positive *E coli* are common, in general — found in up to 20% of healthy people and about

67% of patients with CRC.

If these bacteria are becoming more common in younger people, the reason isn't yet clear. "The working hypothesis is overuse of antibiotics in young kids," said Venook, who is collaborating with colleagues to launch an additional multi-institution investigation into the issue.

There are also clinical implications if the findings pan out, Venook said. This work could lead to a diagnostic test — perhaps one looking for circulating mutational DNA in the blood — that could "give us a leg up on who's at risk for early-onset CRC," Venook said. "That's how this could really make a difference."

The work was funded by the National Institutes of Health, Cancer Research UK, and others. Several investigators disclosed ties to io9, Inocras, Hologic, Quotient Therapeutics, and Microbiotica. Venook didn't have any disclosures; disclosure information for Graham was unavailable. ■



Dr. Venook

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by a National Institutes of Health grant.

Acosta is a co-founder and inventor of intellectual property licensed to Phenomix Sciences; has served as a consultant for Rhythm Pharmaceuticals, Gila Therapeutics, Amgen, General Mills, Boehringer Ingelheim, Currax Pharmaceuticals, Nestlé, Bausch Health, and Rare

Diseases; and has received research support or had contracts with Vivus, Satiogen Pharmaceuticals, Boehringer Ingelheim, and Rhythm Pharmaceuticals. Machineni has been involved in semaglutide and tirzepatide clinical trials and has been a consultant to Novo Nordisk, Eli Lilly, and Rhythm Pharmaceuticals. Kushner is on the scientific advisory board for Novo Nordisk. ■

New Evidence and Evolving Standards of Practice: Esophageal Varices and Barrett's Esophagus

Dear colleagues,

In the dynamic field of medicine, long-held practices are being reevaluated in light of new evidence and evolving standards of practice. In this issue of Perspectives, we present two thoughtful contributions that discuss changes in the way we approach esophageal varices and Barrett's esophagus.

Dr. Anahita Rabiee discusses the importance of prioritizing non-selective beta-blockers (NSBB) over endoscopic variceal ligation (EVL) in the primary prophylaxis of variceal bleeding in patients with compensated

cirrhosis. Drawing on data from the PREDESCI trial and real-world experience, she argues that NSBB address the upstream driver — portal hypertension — more broadly and effectively than EVL. In a complementary piece, Dr. Tarek Sawas explores the nuanced landscape of screening and surveillance in Barrett's esophagus. From how to manage irregular Z-lines, to rethinking the need for 1-year follow-up endoscopies and interpreting the implications of the BOSS trial, Dr. Sawas



Dr. Ketwaroo

advocates for a more personalized, risk-based approach.

We hope these perspectives spark dialogue and reflection in your own practice. Join the conversation on X at @AGA_GIHN.

Gyanprakash A. Ketwaroo, MD, MSc, is associate professor of medicine, Yale University, New Haven, and chief of endoscopy at West Haven VA Medical Center, both in Connecticut. He is an associate editor for GI & Hepatology News.

Choose NSBBs, Not EVL, in Patients with Compensated Cirrhosis

BY ANAHITA RABIEE, MD, MHS

I strongly favor the use of non selective beta blockers (NSBBs) in patients with compensated cirrhosis, rather than endoscopy and esophageal variceal ligation (EVL) for primary prophylaxis.

Since the results of PREDESCI trial (beta-blockers to prevent decompensation of cirrhosis in patients with clinically significant portal hypertension [CSPH]) were published in 2019, there has been much debate on the role of screening endoscopy and EVL for primary prophylaxis.

While many argue that a single randomized trial should not overturn longstanding practice, several compelling reasons convince me to choose NSBBs, when possible.

Recent guidance from major liver societies now recommends NSBBs as first line therapy for CSPH. Yet, adoption in clinical practice remains inconsistent.

Here is why I believe NSBB represent a better solution.

Treating Upstream, Not Just a Local Treatment

NSBBs such as propranolol and nadolol decrease portal pressure by decreasing portal venous

inflow through beta-1 and beta-2 adrenergic blockade. Carvedilol is often preferred given its additional alpha-1 adrenergic blocking activity making it the most effective one in decreasing the portal pressure. Therefore, NSBBs address the upstream driver of decompensation by decreasing portal pressures.

EVL, in contrast, is a local fix that only prevents variceal bleeding. Ascites, not variceal bleeding, is the most common initial decompensating event and is associated with high mortality. Preventing all forms of decompensation is clearly preferable to preventing just one.

Broader Eligibility, More Patients Benefit

CSPH is defined as hepatic venous pressure gradient (HVPG) > 10 mm Hg, the threshold where increased portal venous inflow secondary to splanchnic vasodilation and hyperdynamic circulation drives the

NSBBs • Continued on following page



Dr. Rabiee

Rethinking Screening and Surveillance in Barrett's Esophagus

BY TAREK SAWAS, MD, MPH

Barrett's esophagus (BE) is a precursor to esophageal adenocarcinoma (EAC). Despite our comprehensive guidelines, many of the day-to-day decisions still rely on clinical judgment and honest conversations with patients. This article explores common scenarios in which management decisions are nuanced and the right answer remains debatable.

Irregular Z-Line/ Ultrashort Segment BE: Leave Or Watch It?

Few findings provoke more confusion than irregular Z-line or intestinal metaplasia (IM) < 1 cm at the gastroesophageal junction (GEJ). For years, we have debated whether these subtle changes represent a precursor to EAC or simply a benign variant. We have wrestled with how to handle these cases from whether we should take biopsies to how to perform surveillance.



Dr. Sawas

The American College of Gastroenterology (ACG) guideline suggests that irregular Z-lines should not be routinely biopsied or surveyed. Similarly, the upcoming American Gastroenterology Association (AGA) surveillance guideline suggests against surveillance of IM < 1 cm citing the low individual

annual risk of progression to high-grade dysplasia (HGD) and EAC of 0.23% per year which is lower than that of non-dysplastic Barrett's esophagus (NDBE). However, this is not the entire picture.

Despite the low per-patient risk, IM < 1 cm is highly prevalent with columnar mucosa observed in approximately 15% of patients undergoing upper endoscopy. This paradox is unsettling. While any one patient with IM < 1 cm is unlikely to progress to EAC, the group accounts for a meaningful share of the EAC burden. Some experts have argued that this justifies routine biopsy and surveillance in all patients with visible columnar mucosa regardless of length. However, this approach risks overwhelming our surveillance infrastructure.

A recent decision modeling analysis suggested that at the lowest progression rates, either no surveillance or one-time endoscopy

Screen • Continued on following page

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NSBBs • *Continued from previous page*
increase in portal hypertension. This threshold has been shown to strongly predict decompensation in patients with compensated disease.

NSBBs address the upstream driver of decompensation by decreasing portal pressures. EVL, in contrast, is a local fix that only prevents variceal bleeding. ... Preventing all forms of decompensation is clearly preferable to preventing just one.

While all patients with varices have CSPH, not all patients with CSPH have varices. They can be identified by other non-invasive criteria, such as cross-sectional imaging showing collaterals or liver stiffness and platelet thresholds that have been previously validated. By restricting intervention to those with large varices and offering only EVL, we miss

the opportunity to intervene earlier and to a broader group that would benefit from this treatment.

Comprehensive Protection Without Repeated Endoscopies

Once on an appropriate NSBB dose, patients are protected against variceal bleeding (at least as effectively as EVL). This eliminates the need for repeated surveillance endoscopies to identify and treat large varices in otherwise compensated patients.

Better Tolerated and — In Many Cases — Overlaps With Existing Medication List!

While overtreatment is a concern, regular endoscopies every 2 years are also burdensome. Many patients already need beta-blockers for cardiac conditions such as atrial fibrillation, ischemic heart disease or hypertension. Carvedilol, in particular, offers dual benefit for both hepatologists and cardiologists.

It is important to emphasize that these arguments apply to compensated cirrhosis. In

decompensated disease, the approach changes. After a variceal bleed, both NSBBs and EVL are required for secondary prophylaxis. In patients with prior ascites but no variceal bleed, the benefit of NSBBs is less pronounced since decompensation has already occurred. In this setting, NSBBs can still be used selectively, but only if systolic blood pressure remains above 90 mm Hg.

The evidence supporting NSBBs over EVL in compensated cirrhosis is not perfect, but few things in medicine are. Given current data, NSBBs should be the first-line therapy in compensated cirrhosis with CSPH. Once a patient is on an appropriate and tolerated NSBB dose, routine endoscopic surveillance is unnecessary. Endoscopy should be reserved for those who cannot tolerate NSBBs, in whom EVL is then indicated if large varices are present. ■

Dr. Rabiee is based at the Yale School of Medicine, New Haven, and West Haven VA Medical Center, both in Connecticut. She has no disclosures in regard to this article.

Screen • *Continued from previous page*
can be considered. Based on these data, I do not regularly biopsy ultrashort segments unless the mucosa appears suspicious. In those with IM < 1 cm detected during a high-quality endoscopic exam, no follow-up is needed. However, if the exam is suboptimal, I perform a one-time high-quality repeat exam. If there is no evidence of dysplasia then I do not pursue any further surveillance.

The 1-Year Follow-Up Endoscopy: Is It Necessary?

Another controversy is the 1-year follow-up endoscopy after an initial diagnosis of NDBE. Proponents of this approach cite the high proportion of post-endoscopy esophageal neoplasia and cancer (PEEN/PEEC) detected in the first year after diagnosis (missed HGD/EAC). In fact, PEEN account for about a quarter of all HGD/EAC cases diagnosed during surveillance.

While this approach might mitigate PEEN/PEEC risk, it may not be necessary if the index endoscopy is high quality. To ensure high quality exams, several best practices have been proposed including:

- Use of high-definition white-light endoscopy (HD-WLE) with chromoendoscopy (virtual or dye based)
- Appropriate inspection time (1 minute per cm of circumferential BE)
- Accurate documentation using the Prague criteria
- Adherence to the Seattle protocol with additional targeted biopsies If the index endoscopy meets

these quality metrics, I typically do not bring the patient back at 1 year. However, if the exam quality is in question, then I repeat it at 1 year to establish a reliable baseline and rule out prevalent neoplasia.

Surveillance In NDBE: After BOSS, Do We Rethink Everything?

The recently published BOSS trial (Barrett's Oesophagus Surveillance

A recent decision modeling analysis suggested that at the lowest progression rates, either no surveillance or one-time endoscopy can be considered. ... I do not regularly biopsy ultrashort segments unless the mucosa appears suspicious.

Study) has reignited the debate over the value of endoscopic surveillance in NDBE. In this study, 3,453 patients with NDBE across the UK were randomized to either surveillance endoscopy every 2 years or endoscopy only as clinically indicated. After a median follow-up of 12.8 years, the trial found no significant difference in all-cause mortality between the two groups.

While these findings are important, they should be interpreted with caution. First, the primary endpoint, all-cause mortality, is not optimal for evaluating surveillance for EAC. Surveillance is not intended to reduce all-cause mortality but rather to reduce EAC-related mortality.

Second, a substantial number of patients in the no surveillance group still underwent endoscopy at intervals that were not meaningfully different from those in the surveillance group. If both groups receive similar exposure to endoscopy, the comparison loses power. Lastly, the trial was underpowered because of overestimation of progression risk during its initial design. As we have since learned, the risk of progression of NDBE is lower than originally assumed.

So where do we stand now? For me, the BOSS trial does not negate the value of surveillance. It reminds us that a one-size-fits-all approach is inefficient, and our strategy must be risk based. For low-risk individuals, particularly older adults with short-segment NDBE, surveillance may offer little benefit. But in healthier, younger patients with longer segments or additional risk factors, surveillance remains an essential tool for early neoplasia detection.

When to Stop Surveillance

Perhaps the most under-discussed point is when to stop surveillance. Existing guidelines do not account for competing mortality risks unrelated to EAC or provide specific recommendations regarding cessation of surveillance. The desired benefits of surveillance likely diminish with advanced age and greater comorbidity because of lower life expectancy and ineligibility for definitive therapy for EAC.

A recent modeling study found that the optimal ages for last surveillance were 81, 80, 77, and 73

years for men with no, mild, moderate, and severe comorbidity respectively and 75, 73, 73, and 69 years for women.

In my practice, I discuss surveillance cessation in patients older than 75 based on their comorbidities. If the risk of progression is outweighed by the risk of the procedure or by the reality of limited life expectancy, we should not

For low-risk individuals ... surveillance may offer little benefit. But in healthier, younger patients with longer segments or additional risk factors, surveillance remains an essential tool for early neoplasia detection.

hesitate to consider surveillance cessation.

In summary, a high-quality endoscopic exam in appropriately selected patients remains the cornerstone of BE surveillance. A more personalized, risk-based approach is needed taking into account competing comorbidities. Emerging technology through risk stratification tools such as biomarkers and artificial intelligence may refine our approach and help address the current limitations. ■

Dr. Sawas is based at the University of Texas Southwestern Medical Center, Dallas. He is a recipient of the AGA Early Career Investigator award, and has no disclosures in regard to this article.

Improving BE Risk Stratification

Sponge from page 1

Moreover, repeated endoscopy monitoring is stressful. “A simple nonendoscopic capsule sponge test done nearer to home is less scary and could be less operator-dependent. By reducing the burden of endoscopy in patients at very low risk we can focus more on the patients at higher risk,” she said.



Dr. Fitzgerald

“The GI community is realizing that we need a better approach to managing patients with Barrett’s. ... Outside of the UK we hope this will pave the way for nonendoscopic approaches to Barrett’s surveillance.”

In 2022, her research group had reported that the capsule sponge test, coupled with a centralized lab test for p53 and atypia, can risk-stratify patients into low-, moderate-, and high-risk groups (Lancet Oncol. 2022 Jan. doi: 10.1016/S1470-2045[21]00667-7). “In the current study, we wanted to check this risk stratification capsule sponge test in the real world. Our main aim was to see if we could conform the 2022 results with the hypothesis that the low-risk patients — more than 50% of patients in surveillance — would have a risk of high-grade dysplasia or cancer that was sufficiently low — that is, less than from 3% — and could therefore have follow-up with the capsule sponge without requiring endoscopy.”

The investigators hypothesized that the 15% at high risk would have a significant chance of dysplasia warranting endoscopy in a specialist center.

“Our results showed that in the low-risk group the risk of high-grade dysplasia or cancer was 0.4%, suggesting these patients could be

offered follow-up with the capsule sponge test,” Fitzgerald said.

The high-risk group with a double biomarker positive (p53 and atypia) had an 85% risk for dysplasia or cancer. “We call this a tier 1 or ultra-high risk, and this suggests these cases merit a specialist endoscopy in a center that could treat

the dysplasia/cancer,” she said.

Study Details

Adult participants (n = 910) were recruited from August 2020 to December 2024 in two multicenter, pro-

spective, pragmatic implementation studies from 13 hospitals. Patients with nondysplastic BE on last endoscopy had a capsule sponge test.

Patient risk was assigned as low (clinical and capsule sponge biomarkers negative), moderate (negative for capsule sponge biomarkers, positive clinical biomarkers: age, sex, and segment length), or high risk (p53 abnormality, glandular atypia regardless of clinical biomarkers, or both). The primary outcome was a diagnosis of high-grade dysplasia or cancer necessitating treatment, according to the risk group.

In the cohort, 138 (15%) were classified as having high risk, 283 (31%) had moderate risk, and 489 (54%) had low risk.

The positive predictive value for any dysplasia or worse in the high-risk group was 37.7% (95% CI, 29.7%-46.4%). Patients with both atypia and aberrant p53 had the highest risk for high-grade dysplasia or cancer with a relative risk of 135.8 (95% CI, 32.7-564.0) vs the low-risk group.

The prevalence of high-grade

dysplasia or cancer in the low-risk group was, as mentioned, just 0.4% (95% CI, 0.1%-1.6%), while the negative predictive value for any dysplasia or cancer was 97.8% (95% CI, 95.9%-98.8%). Applying a machine learning algorithm reduced the proportion needing p53 pathology review to 32% without missing any positive cases.

Offering a US perspective on the study, Nicholas J. Shaheen, MD,



Dr. Shaheen

“In addition to case-finding for Barrett’s [esophagus], a nonendoscopic sponge-based technique can also help us stratify risk, finding cases that either already harbor cancer or are at high risk to do so.”

MPH, AGAF, professor of medicine and director of the NC Translational & Clinical Sciences Institute at the University of North Carolina School of Medicine in Chapel Hill, called the findings “very provocative.”

“We have known for some time that nonendoscopic techniques could be used to screen for Barrett’s esophagus and esophageal cancer, allowing us to screen larger groups of patients in a more cost-effective manner compared to traditional upper endoscopy,” he told *GI & Hepatology News*. “This study suggests that, in addition to case-finding for Barrett’s [esophagus], a nonendoscopic sponge-based technique can also help us stratify risk, finding cases that either already harbor cancer or are at high risk to do so.”

Shaheen said these cases deserve immediate attention as they are most likely to benefit from timely endoscopic intervention. “The study also suggests that a nonendoscopic result could someday be used to decide subsequent follow-up, with low-risk patients undergoing further nonendoscopic surveillance,

while higher-risk patients would move on to endoscopy. Such a paradigm could unburden our endoscopy units from low-risk patients unlikely to benefit from endoscopy as well as increase the numbers of patients who are able to be screened.”

Fitzgerald added, “The GI community is realizing that we need a better approach to managing patients with Barrett’s [esophagus].

In the UK this evidence is being considered by our guideline committee, and it would influence the upcoming guidelines in 2025 with a requirement to continue to audit the results.

Outside of the UK we hope this will pave the way for nonendoscopic approaches to Barrett’s [esophagus] surveillance.”

One ongoing goal is to optimize the biomarkers, Fitzgerald said. “For patients with longer segments we would like to add additional genomic biomarkers to refine the risk predictions,” she said. “We need a more operator-independent, consistent method for monitoring Barrett’s [esophagus]. This large real-world study is highly encouraging for a more personalized and patient-friendly approach to Barrett’s [esophagus] surveillance.”

This study was funded by Innovate UK, Cancer Research UK, National Health Service England Cancer Alliance. Cytosponge technology is licensed by the Medical Research Council to Medtronic. Fitzgerald declared holding patents related to this test. Fitzgerald reported being a shareholder in Cyted Health. Shaheen reported receiving research funding from Lucid Diagnostics and Cyted Health, both of which are manufacturers of nonendoscopic screening devices for BE. ■

► PRACTICE MANAGEMENT

Most GI Service Chiefs Support POCUS Training, But Uptake Is Slow

BY WILL PASS

MDedge News

FROM GASTRO HEP ADVANCES

Most GI service chiefs in the US Veterans Affairs (VA) healthcare system support point-of-care ultrasound (POCUS) training, but fewer than half have the technology in their facility,

according to a national survey.

Low POCUS uptake may be explained by substantial barriers to implementation, including lack of trained instructors, necessary equipment, and support staff, lead author Keerthi Thallapureddy, MD, of the University of Texas Health San Antonio, and colleagues reported.

“POCUS is being increasingly

used by gastroenterologists due to its portability and real-time diagnostic ability,” the investigators wrote in *Gastro Hep Advances* (2025 Mar. doi: 10.1016/j.gastha.2025.100658), but “there is limited understanding of how gastroenterologists use POCUS.”

To learn more, the investigators conducted a nationwide survey

of the VA healthcare system. Separate questionnaires were sent to chiefs of staff (n = 130) and GI service chiefs (n = 117), yielding response rates of 100% and 79%, respectively.

Respondents represented a wide distribution of geographic regions and institutional complexity levels,

Continued on following page

Continued from previous page

with 80% of GI groups based at high-complexity centers and 92% in urban locations. A minority (8%) reported the presence of a liver transplant program.

Data collection focused on the prevalence of POCUS use, types of clinical applications, institutional policies and training processes, and perceived or actual barriers to wider adoption. Barriers were sorted into three categories: training, equipment, and infrastructure.

Of the 93 GI service chiefs who participated in the survey, 44% reported that at least one gastroenterologist at their facility currently uses POCUS. Most common procedural uses were paracentesis (23%) and liver biopsy (13%),



Dr. Thallapureddy

while ascites assessment (19%) and biliary visualization (7%) were the most common diagnostic uses.

Among the same respondents, 69% said they would support sending clinicians to a POCUS training course, and 37% said their teams had expressed an active interest in pursuing such training. Only 17% of facilities had a formal process in place to obtain POCUS training, and an equal proportion had implemented a facility-wide policy to guide its use.

Barriers to implementation were widespread and often multifactorial.

Most challenges related to training: 48% of sites reported a lack of trained providers, 28% cited insufficient funding for training, 24% noted a lack of training opportunities, and 14% reported difficulty securing travel funds.

Equipment limitations were also common, with 41% of sites lacking ultrasound machines and 27% lacking funding to purchase them.

Institutional infrastructure posed further hurdles. Nearly a quarter of GI chiefs (23%) reported lacking a clinician champion to lead implementation, while others cited a lack of support staff, simulation space, privileging criteria, image archiving capabilities, or standardized reporting forms.

“Our findings on current POCUS use, training, barriers, and infrastructure can guide expansion of POCUS use and training among GI groups,” Dr. Thallapureddy and

Barriers to implementation were widespread and often multifactorial. Most challenges related to training: 48% of sites reported a lack of trained providers, 28% cited insufficient funding for training, 24% noted a lack of training opportunities, and 14% reported difficulty securing travel funds.

colleagues wrote, noting that early efforts to expand access to GI-specific POCUS training are already underway.

They cited growing interest from national organizations such as the

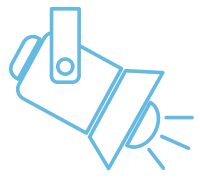
American Gastroenterological Association and the American Association for the Study of Liver Diseases, the latter of which piloted training workshops at the 2024 Liver Meeting. Similarly, the International

Bowel Ultrasound Group now offers a three-part certification program in intestinal ultrasound and is developing additional online and interactive modules to improve training accessibility.

The study was supported by the US Department of Veterans Affairs, Quality Enhancement Research Initiative Partnered Evaluation Initiative Grant, and the VA National Center for Patient Safety. The investigators reported no conflicts of interest. ■

The image shows a laptop displaying the AGA Clinical Guidance website. The website has a blue header with the AGA logo and the text "American Gastroenterological Association". Below the header, the title "Clinical Guidance" is prominently displayed in large blue letters. Underneath the title, there is a paragraph: "Check out our complete library of guidelines, clinical practice updates and patient care toolkits. With 150 resources, we have evidence-based advice to guide the care for all of your patients." At the bottom of the page, there is a search bar with the text "gastro.org/clinical-guidance". The background of the website is white with blue accents.

The image shows a hand holding a smartphone displaying the AGA GI Career Search website. The website has a white background with the AGA logo and the text "gi career search". Below the header, there is a section titled "Job Alerts" with three job listings: "Gastroenterology Physician" in San Francisco, California, "Nurse Practitioner" in Washington, D.C., and "Pediatric Gastroenterologist" in Billings, Montana. To the right of the smartphone, the text "aga gi career search" is displayed in blue. Below this, the headline "Finding the right job or candidate is at your fingertips" is written in large, bold, dark blue letters. Underneath the headline, the text "Your career hub across all disciplines and specialties in GI." is written in a smaller, blue, italicized font. At the bottom, the text "Start your search today at GICareerSearch.com." is displayed in blue.



On a Quest to Reduce Stigmas about Anal Cancer

BY JENNIFER LUBELL

MDedge News

Jessica Korman, MD, wants to erase what she says is a stigma in the gastroenterology profession surrounding anal disease.

"I think gastroenterologists are uniquely positioned to help with diagnosing anal diseases, in particular anal cancer," she said. "It is part of the digestive tract, and my mission is to help gastroenterologists remember that."

Dr. Korman is a gastroenterologist with Capital Digestive Care in Washington, DC, where she serves as chair of its Women's Committee and as a member of the board of managers. She's also the medical director of the Endoscopy Center of Washington, DC.

A recipient of the 2025 AGA Distinguished Clinician Award in Private Practice, Dr. Korman has dedicated her career to educating clinicians on anal cancer screening and anal human papillomavirus. On the research front, she participated as an investigator in the ANAL Cancer-HSIL Outcomes Research (ANCHOR) trial, which led

"Many people in the sexual and gender minority community have experienced discrimination in healthcare settings or know of someone who has ... LGBTQIA+ people may approach healthcare with the expectation of a negative encounter, or they may avoid accessing care altogether."

to international anal cancer screening guidelines (N Engl J Med. 2022 Jun. doi: 10.1056/NEJMoa2201048).

She also co-directs the International Anal Neoplasia Society (IANS) standard high-resolution anoscopy course.

When she's not serving her patients, Dr. Korman speaks in the community about anal cancer awareness and screening. In the last few years, Dr. Korman has presented grand rounds at various institutions and speaks at major medical conferences. "I just try to advocate and help gastroenterologists understand who is at risk, how to look for anal cancer, how to screen, and who



Dr. Jessica Korman

to refer. If anyone invites me to speak, I generally will do it," said Dr. Korman.

In an interview, she talked about the outcomes of the ANCHOR trial and how it may inform future research, and her work to reduce bias and stigma for LGBTQ+ patients.

You decided to become a physician after studying in Egypt and Israel and volunteering with Physicians for Human Rights. Can you talk about that journey?

Dr. Korman: I majored in Religion and Middle East studies, and I minored in Arabic. I thought I was going to become a professor of religious studies. But during my time studying abroad and volunteering for Physicians for Human Rights, I was deeply moved by how physicians connect with the core of our shared humanity. Becoming a physician allows one to meet the most fundamental of human needs — caring for another's health — in a direct and meaningful way.

My father is a physician, a gastroenterologist, but I never considered it as a career option growing up. The year after I graduated college, I accompanied my parents to my father's medical school reunion and I thought, 'Why did I never think about this?' I decided to go back to school to take the pre-med requirements. Gastroenterology seemed to combine the ability to work with my hands, do procedures, have long-term relationships with patients, and think about complex problems.

GI medicine often involves detective work. What is the most challenging case you've encountered?

Dr. Korman: Sometimes the patients who have very severe disorders of gut-brain interaction can be the most challenging because finding treatments for them or getting them to a place where they accept certain types of treatment can be really difficult. And of course, you have to put your detective hat on and make sure you have ruled out all the "zebras." It can take years to build the level of trust where patients are willing to accept the diagnosis and then pursue appropriate treatment.

I always try my best, but I don't like to give up. I will refer a patient to a colleague if they

have a problem and I can't figure out what the diagnosis is or find a treatment that works. I believe in second and third opinions. I recognize that there's a limit to what my brain can do and that we all have blind spots. Maybe someone will look at the case with fresh eyes and think of something else.

What was the most impactful outcomes of the ANAL Cancer-HSIL Outcomes Research (ANCHOR) trial?

Dr. Korman: This was a National Institutes of Health (NIH)-sponsored, randomized controlled trial with 26 clinical sites. We studied people living with HIV, as they are the most at-risk group for anal cancer.

We were looking to prove that treating high-grade squamous intraepithelial lesions (HSIL) of the anal canal would lead to a significant reduction in the rates of anal cancer. No one in the medical community would accept guidelines or recommendations about what to do with anal pre-cancers until we proved that treatment worked.

We published the findings in 2022. The study concluded when we met our endpoint earlier than expected. We were able to prove that treating high-grade anal dysplasia does indeed lead to a very significant reduction in progression to anal cancer. That ultimately led to guidelines. The International Anal Neoplasia Society came out with consensus guidelines on screening for anal cancer in January 2024 (Int J Cancer. 2024 May. doi: 10.1002/ijc.34850). In August 2024, NIH, the Centers for Disease Control and Prevention, and the Infectious Diseases Society of America came out with screening guidelines for people living with HIV.

Were there any other outcomes from this research?

Dr. Korman: One of the great things about the study is that we accumulated a bank of tissue and biologic specimens. There were about 4,500 patients randomized into the trial, but about 10,000 patients screened. So, we have a massive collection of biospecimens that we can use to ask questions about the progression of HSIL to anal cancer. We would like to understand more



COURTESY ISABELLE HYMAN

Dr. Korman and her daughters.



COURTESY DR. KORMAN

Dr. Jessica Korman, on right, and her colleagues attended the DC PRIDE festival to promote the ANCHOR study.



COURTESY DR. KORMAN

Dr. Korman and her family on vacation in Iceland.

about viral and host molecular mechanisms and hopefully find biomarkers that will identify individuals at particularly high risk of progression. It's a more precision medicine type of approach.

Education has been a cornerstone of your career. What's the most rewarding part of teaching the IANS standard high-resolution endoscopy course?

Dr. Korman: I first took the course in

2010, and that's when I started my journey of learning how to perform high-resolution endoscopy. Last year I was asked to help co-direct the course. It is now virtual and asynchronous where everything is recorded. But it was exciting to help reorganize the course, update the lectures, and make sure that everything is current.

We get to answer questions from participants from all over the world. I think there are participants from 23 countries who have taken the course, which is amazing.

Could you share your work with the LGBTQIA+ population? What specific needs/challenges does this population have with GI care?

Dr. Korman: Many people in the sexual and gender minority community have experienced discrimination in healthcare settings or know of someone who has. For these reasons, LGBTQIA+ people may approach healthcare with the expectation of a negative encounter, or they may avoid accessing care altogether. Because anal cancer disproportionately affects sexual and gender minority communities, creating a warm, inclusive environment is key to identifying who is at risk, building trust, and ensuring patients receive the care they need. When you're talking about anal

cancer, there's a lot of stigma and shame. I think people are afraid to seek care.

Gastroenterology has traditionally been an "old boys club" but that is changing. We're trying to work on educating people on how to recognize their own biases and move beyond them to provide care that's affirming and where people feel that they have a safe space to talk about their concerns. Men who have sex with men, in particular living with HIV, are at the highest risk of developing anal cancer. If you don't know that your patient is a man who has sex with men, or they don't want to disclose that they're living with HIV, you don't know to screen them, and then you're missing an opportunity to potentially prevent a cancer.

What advice would you give to aspiring medical students interested in GI?

Dr. Korman: GI is the most exciting

and interesting field. We take care of so many different organs, and we're never bored. If medical students want to get into GI, I recommend that they try to be in an office or an endoscopy center and see if it's really for them and get some hands-on experience if possible. To be truly great at this profession, you really must see it as a calling — jump in with your whole heart and not see it as just a job. If you can do that, you'll succeed.

How do you handle stress and maintain work-life balance?

Dr. Korman: Exercise. I try to work out at least five days a week. I can't live without it. That keeps me going. What do I do for fun? I spend time with my family and my friends. I enjoy going to new restaurants and being outdoors, especially near a body of water. I travel, and I love watching movies. I am also guilty of binge-watching TV on a regular basis as well. ■

Lightning Round

Coffee or tea?

Coffee, 100%

What's your favorite book?

I can't say I have just one, but I recently read *Tomorrow and Tomorrow and Tomorrow* and loved it

Beach vacation or mountain retreat?

Beach

Early bird or night owl?

Early bird

What's your go-to comfort food?

Anything with bananas

If you could travel anywhere, where would you go?

Vietnam or African safari

What's your favorite childhood memory?

Swim team when I was a kid

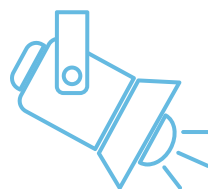
If you could instantly learn any skill, what would it be?

Playing the drums

Are you a planner or more spontaneous?

Planner, although it's not my strong suit, if I'm being honest.

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