GI&Hepatology News

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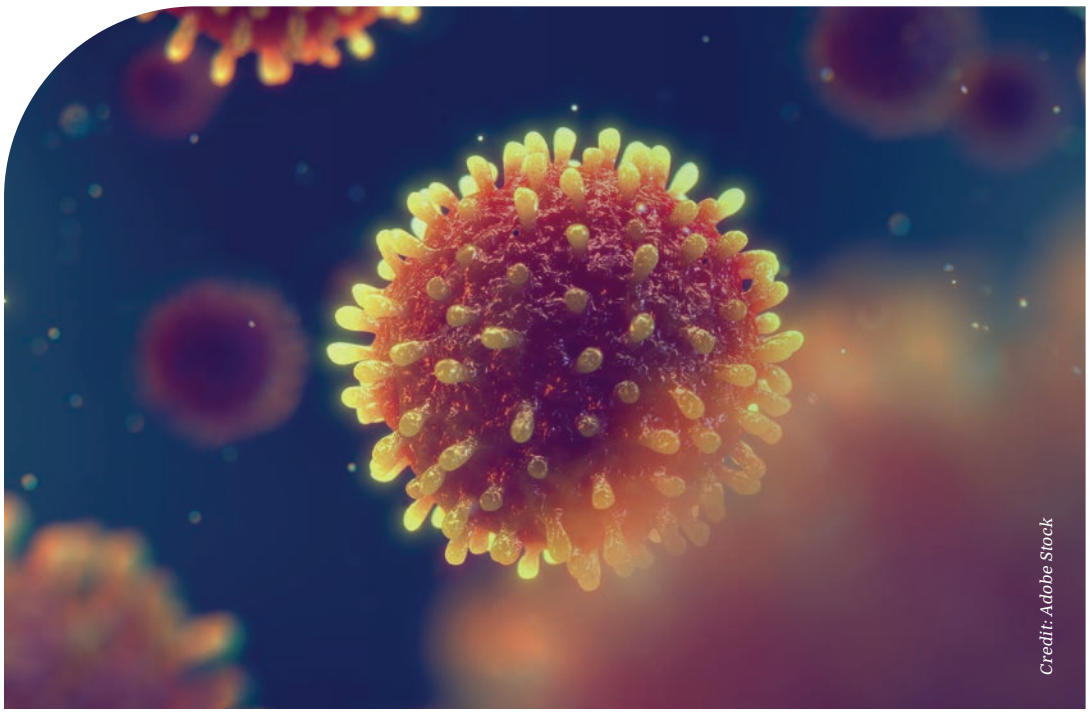

Credit: Adobe Stock

One in five reach hepatitis B functional cure with finite bepirovirsen

In two phase 3 trials, a 24-week course produced a functional cure in about 20% of patients and let many stop antiviral therapy, while none on placebo responded.

By Doug Brunk

A 24-week course of bepirovirsen enabled about one in five patients with chronic hepatitis B virus (HBV) infection to achieve a sustained functional cure after stopping long-term antiviral therapy, according to two identical phase 3 trials. No patients in the placebo group met the primary endpoint, providing phase 3 evidence that a finite treatment course can produce durable hepatitis B surface antigen (HBsAg) loss in some patients.

The findings, published in the *New England Journal of Medicine*, came from the global B-Well 1 and B-Well 2 trials, which evaluated bepirovirsen, an antisense oligonucleotide designed to block HBV messenger RNA. By reducing viral transcripts and HBsAg, the drug aims to achieve a functional cure, defined as sustained loss of HBsAg and HBV DNA levels below the lower limit of quantification for at least 24 weeks after all treatment has stopped.

Current nucleoside or nucleotide analogue therapy effectively suppresses HBV replication but rarely leads to loss of hepatitis B surface antigen, leaving most patients on lifelong treatment. A finite therapy that achieves durable viral control could offer some patients the opportunity to stop chronic antiviral therapy.

Continues • Page 11

Home calprotectin monitoring fails to reduce ulcerative colitis flares

A randomized trial of 611 patients with ulcerative colitis in remission found that bimonthly home fecal calprotectin testing did not prevent symptomatic flares when treatment decisions were left to physician discretion, pointing to a need for standardized escalation protocols.

Read More • Page 21

Coffee linked to fewer cirrhosis, liver cancer cases in large analysis

"We were able to show not only that coffee consumption is associated with lower risks of cirrhosis, hepatocellular carcinoma, and liver-related mortality, but also that it is linked to less liver fat, less fibroinflammation on MRI, and favorable biological pathways involved in fibrosis and inflammation."

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Skyrizi®
risankizumab-rzaa

For moderate to severe Crohn's disease (CD) or moderate to severe ulcerative colitis (UC) in adult patients[1]

DISCOVER HOW PATIENTS CAN FIT THE ON-BODY INJECTOR (OBI) INTO THEIR ROUTINE

FLIP TO LEARN ABOUT SKYRIZI DOSING AND THE OBI

MEET JONATHAN, A REAL SKYRIZI PATIENT

When I'm using the OBI, I sometimes answer email, scroll through social media, or even walk around the house or get the mail.

INDICATIONS[1]

Crohn's Disease: SKYRIZI is indicated for the treatment of moderately to severely active Crohn's disease in adults.
Ulcerative Colitis: SKYRIZI is indicated for the treatment of moderately to severely active ulcerative colitis in adults.

SAFETY CONSIDERATIONS[1]

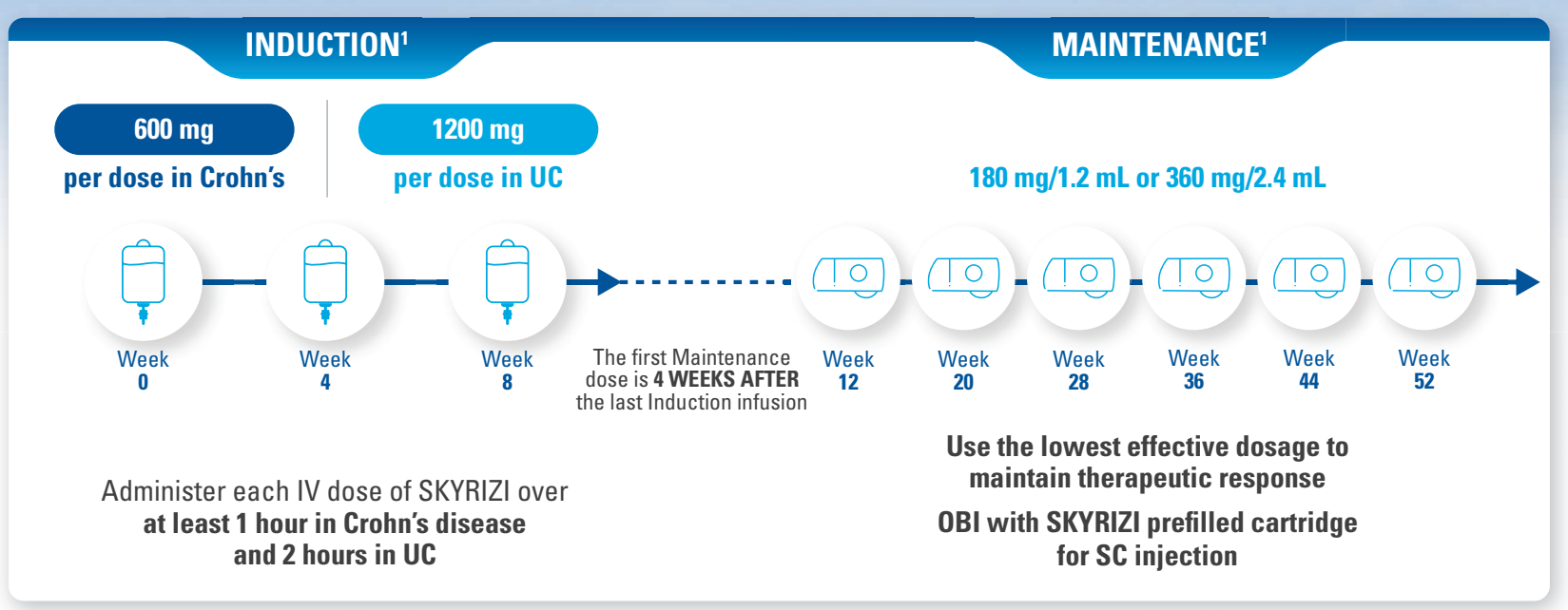
SKYRIZI is contraindicated in patients with a history of serious hypersensitivity reaction to risankizumab-rzaa or any of its excipients. Serious hypersensitivity reactions, including anaphylaxis, have been reported with use of SKYRIZI. If a serious hypersensitivity reaction occurs, discontinue SKYRIZI and initiate appropriate therapy immediately. SKYRIZI may increase the risk of infection. Instruct patients to report signs or symptoms of clinically important infection during treatment. Should such an infection occur, discontinue SKYRIZI until infection resolves. Evaluate patients for tuberculosis infection prior to initiating treatment with SKYRIZI. Drug-induced liver injury was reported in a patient with Crohn's disease during induction dosing of SKYRIZI. For the treatment of Crohn's disease and ulcerative colitis, evaluate liver enzymes and bilirubin at baseline and during induction (12 weeks). Interrupt treatment with SKYRIZI if drug-induced liver injury is suspected, until this diagnosis is excluded. Avoid use of live vaccines in SKYRIZI patients.

Please see additional Important Safety Information on the last page of this advertisement.
Please see Brief Summary of full Prescribing Information on adjacent pages of this advertisement.

SKYRIZI offers

CONSISTENT DOSING YOUR PATIENTS CAN COUNT ON

With only 6 SC maintenance doses per year after 3 IV induction doses in Crohn's and UC[1]



SKYRIZI Offers the Same Maintenance Schedule and OBI Device, **Regardless of Indication or Dosage Strength[1]**

ADMINISTRATION CONSIDERATIONS

SKYRIZI is intended for use under the guidance and supervision of a healthcare professional (HCP). SKYRIZI vial for intravenous administration is intended for administration by an HCP. Prior to starting therapy, please refer to the Dosage and Administration section of the Prescribing Information for complete information on how to initiate, prepare, and administer SKYRIZI. Patients may self-inject SKYRIZI using the on-body injector with prefilled cartridge after training in subcutaneous injection technique. Provide proper training to patients and/or caregivers on the subcutaneous injection technique of SKYRIZI according to the Instructions for Use.[1]

SAFETY CONSIDERATIONS[1]

SKYRIZI is contraindicated in patients with a history of serious hypersensitivity reaction to risankizumab-rzaa or any of its excipients. Serious hypersensitivity reactions, including anaphylaxis, have been reported with use of SKYRIZI. If a serious hypersensitivity reaction occurs, discontinue SKYRIZI and initiate appropriate therapy immediately. SKYRIZI may increase the risk of infection. Instruct patients to report signs or symptoms of clinically important infection during treatment. Should such an infection occur, discontinue SKYRIZI until infection resolves. Evaluate patients for tuberculosis infection prior to initiating treatment with SKYRIZI. Drug-induced liver injury was reported in a patient with Crohn's disease during induction dosing of SKYRIZI. For the treatment of Crohn's disease and ulcerative colitis, evaluate liver enzymes and bilirubin at baseline and during induction (12 weeks). Interrupt treatment with SKYRIZI if drug-induced liver injury is suspected, until this diagnosis is excluded. Avoid use of live vaccines in SKYRIZI patients.

Please see additional Important Safety Information on the last page of this advertisement.
Please see Brief Summary of full Prescribing Information on adjacent pages of this advertisement.

Skyrizi®
risankizumab-rzaa

Get to know

THE SKYRIZI ON-BODY INJECTOR

After 3 IV induction doses, with proper training and preparation steps, your patient can administer their dose at home or in your office.[1]

COMPACT SIZE

Small enough to fit in the palm of the hand

HANDS-FREE

While adhered to the abdomen or thigh and after activation, patients can do moderate physical activities such as walking, reaching, and bending

HIDDEN NEEDLE

Discreet injection so patients don't see the needle

Please see the Instructions for Use to provide patients and/or caregivers proper training on the OBI.

"The OBI is a drug delivery system ***designed with the patient in mind.***"

– Jennifer Seminerio, MD
Director of Inflammatory Bowel Disease Center, Tampa, FL

Dr. Seminerio is a paid consultant of AbbVie.

DISCOVER WHAT PATIENTS REPORTED ABOUT THE OBI

IMPORTANT SAFETY INFORMATION[1]

Skyrizi®
risankizumab-rzaa

Hypersensitivity Reactions

SKYRIZI® (risankizumab-rzaa) is contraindicated in patients with a history of serious hypersensitivity reaction to risankizumab-rzaa or any of the excipients. Serious hypersensitivity reactions, including anaphylaxis, have been reported with the use of SKYRIZI. If a serious hypersensitivity reaction occurs, discontinue SKYRIZI and initiate appropriate therapy immediately.

Infection

SKYRIZI may increase the risk of infection. Do not initiate treatment with SKYRIZI in patients with a clinically important active infection until it resolves or is adequately treated.

In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing SKYRIZI. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If a patient develops such an infection or is not responding to standard therapy, closely monitor and discontinue SKYRIZI until the infection resolves.

Tuberculosis (TB)

Prior to initiating treatment with SKYRIZI, evaluate for TB infection and consider treatment in patients with latent or active TB for whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after SKYRIZI treatment. Do not administer SKYRIZI to patients with active TB.

Hepatotoxicity in Treatment of Inflammatory Bowel Disease

Drug-induced liver injury was reported in a patient with Crohn's disease who was hospitalized for a rash during induction dosing of SKYRIZI. For the treatment of Crohn's disease and ulcerative colitis, evaluate liver enzymes and bilirubin at baseline and during induction (12 weeks); monitor thereafter according to routine patient management. Consider an alternate treatment for patients with evidence of liver cirrhosis. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Instruct your patient to seek immediate medical attention if they experience symptoms suggestive of hepatic dysfunction.

Administration of Vaccines

Avoid use of live vaccines in patients treated with SKYRIZI. Medications that interact with the immune system may increase the risk of infection following administration of live vaccines. Prior to initiating SKYRIZI, complete all age-appropriate vaccinations according to current immunization guidelines.

Adverse Reactions

Most common (>3%) adverse reactions associated with SKYRIZI in Crohn's disease are upper respiratory infections, headache, and arthralgia in induction, and arthralgia, abdominal pain, injection site reactions, anemia, pyrexia, back pain, arthropathy, and urinary tract infection in maintenance.

Most common (≥3%) adverse reactions associated with SKYRIZI in ulcerative colitis are arthralgia in induction, and arthralgia, pyrexia, injection site reactions, and rash in maintenance.

Lipid Elevations: Increases from baseline and increases relative to placebo were observed at Week 4 and remained stable to Week 12 in patients treated with SKYRIZI in Crohn's disease. Lipid elevations observed in patients with ulcerative colitis were similar to those in Crohn's disease.

Dosage Forms and Strengths: SKYRIZI (risankizumab-rzaa) is available in a 600 mg/10 mL single-dose vial for intravenous infusion and a 180 mg/1.2 mL or 360 mg/2.4 mL single-dose prefilled cartridge with on-body injector.

Please see adjacent pages for Brief Summary of full Prescribing Information.

IBD=inflammatory bowel disease; IV=intravenous; OBI=on-body injector; Q8W=every 8 weeks; SC=subcutaneous; UC=ulcerative colitis.

Reference: 1. SKYRIZI [package insert]. North Chicago, IL: AbbVie Inc.

abbvie

SKYRIZI® (sky-RIZZ-ee) (risankizumab-rzaa) injection, for subcutaneous or intravenous use

90 mg/mL single-dose prefilled syringe
150 mg/mL single-dose pen and prefilled syringe
600 mg/10 mL single-dose vial for intravenous infusion
180 mg/1.2 mL single-dose prefilled syringe
180 mg/1.2 mL single-dose prefilled cartridge with on-body injector
360 mg/2.4 mL single-dose prefilled cartridge with on-body injector

PROFESSIONAL BRIEF SUMMARY
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

Plaque Psoriasis

SKYRIZI® is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

Psoriatic Arthritis

SKYRIZI is indicated for the treatment of active psoriatic arthritis in adults.

Crohn's Disease

SKYRIZI is indicated for the treatment of moderately to severely active Crohn's disease in adults.

Ulcerative Colitis

SKYRIZI is indicated for the treatment of moderately to severely active ulcerative colitis in adults.

CONTRAINDICATIONS

SKYRIZI is contraindicated in patients with a history of serious hypersensitivity reaction to risankizumab-rzaa or any of the excipients *[see Warnings and Precautions]*.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis, have been reported with use of SKYRIZI. If a serious hypersensitivity reaction occurs, discontinue SKYRIZI and initiate appropriate therapy immediately *[see Adverse Reactions]*.

Infections

SKYRIZI may increase the risk of infections *[see Adverse Reactions]*.

Treatment with SKYRIZI should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing SKYRIZI. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If a patient develops such an infection or is not responding to standard therapy, monitor the patient closely and do not administer SKYRIZI until the infection resolves.

Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with SKYRIZI. Across the Phase 3 psoriasis clinical studies, of the 72 subjects with latent TB who were concurrently treated with SKYRIZI and appropriate TB prophylaxis during the studies, none developed active TB during the mean follow-up of 61 weeks on SKYRIZI. Two subjects taking isoniazid for treatment of latent TB discontinued treatment due to liver injury. Of the 31 subjects from the PsO-3 study with latent TB who did not receive prophylaxis during the study, none developed active TB during the mean follow-up of 55 weeks on SKYRIZI. Consider anti-TB therapy prior to initiating SKYRIZI in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after SKYRIZI treatment. Do not administer SKYRIZI to patients with active TB.

Hepatotoxicity in Treatment of Inflammatory Bowel Disease

A serious adverse reaction of drug-induced liver injury in conjunction with a rash that required hospitalization was reported in a patient with Crohn's disease (ALT 54x ULN, AST 30x ULN, and total bilirubin 2.2x ULN) following two 600 mg intravenous doses of SKYRIZI. The liver test abnormalities resolved following administration of steroids. SKYRIZI was subsequently discontinued.

For the treatment of Crohn's disease and ulcerative colitis, evaluate liver enzymes and bilirubin at baseline, and during induction at least up to 12 weeks of treatment. Monitor thereafter according to routine patient management.

Consider other treatment options in patients with evidence of liver cirrhosis. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Instruct patients to seek immediate medical attention if they experience symptoms suggestive of hepatic dysfunction.

Administration of Vaccines

Avoid use of live vaccines in patients treated with SKYRIZI. Medications that interact with the immune system may increase the risk of infection following administration of live vaccines. Prior to initiating therapy with SKYRIZI, complete all age-appropriate vaccinations according to current immunization guidelines. No data are available on the response to live or inactive vaccines.

ADVERSE REACTIONS

The following adverse reactions are discussed in other sections of labeling:

- Hypersensitivity Reactions *[see Warnings and Precautions]*
- Infections *[see Warnings and Precautions]*
- Tuberculosis *[see Warnings and Precautions]*
- Hepatotoxicity in Treatment of Inflammatory Bowel Disease *[see Warnings and Precautions]*

Clinical Trials Experience

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

Plaque Psoriasis

A total of 2234 subjects were treated with SKYRIZI in clinical development trials in plaque psoriasis. Of these, 1208 subjects with psoriasis were exposed to SKYRIZI for at least one year.

Data from placebo- and active-controlled trials were pooled to evaluate the safety of SKYRIZI for up to 16 weeks. In total, 1306 subjects were evaluated in the SKYRIZI 150 mg group.

Table 1 summarizes the adverse drug reactions that occurred at a rate of at least 1% and at a higher rate in the SKYRIZI group than the placebo group during the 16-week controlled period of pooled clinical trials.

Table 1. Adverse Drug Reactions Occurring in ≥ 1% of Subjects with Plaque Psoriasis on SKYRIZI through Week 16

Adverse Drug Reactions	SKYRIZI N = 1306 n (%)	Placebo N = 300 n (%)
Upper respiratory infections[a]	170 (13.0)	29 (9.7)
Headache[b]	46 (3.5)	6 (2.0)
Fatigue[c]	33 (2.5)	3 (1.0)
Injection site reactions[d]	19 (1.5)	3 (1.0)
Tinea infections[e]	15 (1.1)	1 (0.3)

[a] Includes: respiratory tract infection (viral, bacterial or unspecified), sinusitis (including acute), rhinitis, nasopharyngitis, pharyngitis (including viral), tonsillitis
[b] Includes: headache, tension headache, sinus headache, cervicogenic headache
[c] Includes: fatigue, asthenia
[d] Includes: injection site bruising, erythema, extravasation, hematoma, hemorrhage, infection, inflammation, irritation, pain, pruritus, reaction, swelling, warmth
[e] Includes: tinea pedis, tinea cruris, body tinea, tinea versicolor, tinea manuum, tinea infection, onychomycosis

Adverse drug reactions that occurred in < 1% but > 0.1% of subjects in the SKYRIZI group and at a higher rate than in the placebo group through Week 16 were folliculitis and urticaria.

Specific Adverse Drug Reactions

Infections

In the first 16 weeks, infections occurred in 22.1% of the SKYRIZI group (90.8 events per 100 patient-years) compared with 14.7% of the placebo group (56.5 events per 100 patient-years) and did not lead to discontinuation of SKYRIZI. The rates of serious infections for the SKYRIZI group and the placebo group were ≤0.4%. Serious infections in the SKYRIZI group included cellulitis, osteomyelitis, sepsis, and herpes zoster. In Trials PsO-1 and PsO-2, through Week 52, the rate of infections (73.9 events per 100 patient-years) was similar to the rate observed during the first 16 weeks of treatment.

Safety Through Week 52

Through Week 52, no new adverse reactions were identified, and the rates of the adverse reactions were similar to those observed during the first 16 weeks of treatment. During this period, serious infections that led to trial discontinuation included pneumonia.

Plaque Psoriasis of the Scalp or Genital Area

The overall safety profile observed in clinical trials of subjects with moderate to severe plaque psoriasis of the scalp or genital area treated with SKYRIZI is generally consistent with the safety profile observed in previous clinical trials of subjects with moderate to severe plaque psoriasis.

Psoriatic Arthritis

The overall safety profile observed in subjects with psoriatic arthritis treated with SKYRIZI is generally consistent with the safety profile in subjects with plaque psoriasis. Additionally, in the Phase 3 placebo-controlled trials the incidence of hepatic events was higher in the SKYRIZI group (5.4%, 16.7 events per 100 patient-years) compared to the placebo group (3.9%, 12.6 events per 100 patient-years). Of these, the most common events that were reported more frequently in both the placebo group and the SKYRIZI group were ALT increased (placebo: n=12 (1.7%); SKYRIZI: n=16 (2.3%)), AST increased (placebo: n=9 (1.3%); SKYRIZI: n=13 (1.8%)), and GGT increased (placebo: n=5 (0.7%); SKYRIZI: n=8 (1.1%)). There were no serious hepatic events reported. The incidence of hypersensitivity reactions was higher in the SKYRIZI group (n=16, 2.3%) compared to the placebo group (n=9, 1.3%). In the Phase 3 placebo-controlled trials, hypersensitivity reactions reported at a higher rate in the SKYRIZI group included rash (placebo: n=4 (0.6%); SKYRIZI: n=5 (0.7%), allergic rhinitis (placebo: n=1 (0.1%); SKYRIZI: n=2 (0.3%), and facial swelling (placebo: n=0 (0.0%); SKYRIZI n=1 (0.1%). One case of anaphylaxis was reported in a subject who received SKYRIZI in the Phase 2 clinical trial.

Crohn's Disease

SKYRIZI was studied up to 12 weeks in subjects with moderately to severely active Crohn's disease in two randomized, double-blind, placebo-controlled induction trials (CD-1, CD-2) and a randomized, double-blind, placebo-controlled, dose-finding trial (CD-4; NCT02031276). Long-term safety up to 52 weeks was evaluated in subjects who responded to induction therapy in a randomized, double-blind, placebo-controlled maintenance trial (CD-3).

In the two induction trials (CD-1, CD-2) and the dose finding trial (CD-4), 620 subjects received the SKYRIZI intravenous induction regimen at Weeks 0, 4 and 8. In the maintenance trial (CD-3), 297 subjects who achieved clinical response, defined as a reduction in CDAI of at least 100 points from baseline after 12 weeks of induction treatment with intravenous SKYRIZI in trials CD-1 and CD-2, received a maintenance regimen of SKYRIZI either 180 mg or 360 mg subcutaneously at Week 12 and every 8 weeks thereafter for up to an additional 52 weeks.

Adverse reactions reported in > 3% of subjects in induction trials and at a higher rate than placebo are shown in Table 2.

Table 2. Adverse Drug Reactions Reported in > 3% of Subjects with Crohn's Disease Treated with SKYRIZI in Placebo-Controlled 12-Week Induction Trials (CD-1, CD-2, and CD-4)

Adverse Drug Reactions	SKYRIZI 600 mg Intravenous Infusion[a] N = 620 n (%)	Placebo N = 432 n (%)
Upper respiratory infections[b]	66 (10.6)	40 (9.3)
Headache[c]	41 (6.6)	24 (5.6)
Arthralgia	31 (5.0)	19 (4.4)

[a] SKYRIZI 600 mg as an intravenous infusion at Week 0, Week 4, and Week 8.
[b] Includes: influenza like illness, nasopharyngitis, influenza, pharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, COVID-19, nasal congestion, respiratory tract infection viral, viral pharyngitis, tonsillitis, upper respiratory tract inflammation
[c] Includes: headache, tension headache

Adverse reactions reported in >3% of subjects in the maintenance trial and at a higher rate than placebo are shown in Table 3.

Table 3. Adverse Reactions Reported in >3% of Subjects with Crohn's Disease Treated with SKYRIZI[a] in Placebo-Controlled 52-Week Maintenance Trial (CD-3)

Adverse Drug Reactions	SKYRIZI 180 mg Subcutaneous Injection N = 155 n (%)	SKYRIZI 360 mg Subcutaneous Injection N = 142 n (%)	Placebo N = 143 n (%)
Arthralgia	13 (8.4)	13 (9.2)	12 (8.4)
Abdominal pain[b]	9 (5.8)	12 (8.5)	6 (4.2)
Injection site reactions[c,d]	7 (4.5)	8 (5.6)	4 (2.8)
Anemia	7 (4.5)	7 (4.9)	6 (4.2)
Pyrexia	4 (2.6)	7 (4.9)	4 (2.8)
Back pain	3 (1.9)	6 (4.2)	3 (2.1)
Arthropathy	1 (0.6)	5 (3.5)	2 (1.4)
Urinary tract infection	1 (0.6)	5 (3.5)	4 (2.8)

[a] SKYRIZI 180 mg or 360 mg at Week 12 and every 8 weeks thereafter for up to an additional 52 weeks
[b] Includes: abdominal pain, abdominal pain upper, abdominal pain lower
[c] Includes: injection site rash, injection site erythema, injection site swelling, injection site urticaria, injection site warmth, injection site pain, injection site hypersensitivity, injection site reaction
[d] Some subjects had multiple occurrences of injection site reactions. In this table, injection site reactions are counted only once per subject for the rate calculations.

Specific Adverse Drug Reactions

Infections

In the maintenance trial (CD-3) through Week 52, the rate of infections was 32.3% (50.2 events per 100 patient-years) in subjects who received SKYRIZI 180 mg and 36.6% (60.8 events per 100 patient-years) in subjects who received SKYRIZI 360 mg compared to 36.4% (60.3 events per 100 patient-years) in subjects who received placebo after SKYRIZI induction. The rate of serious infections was 2.6% (2.7 events per 100 patient-years) in subjects who received SKYRIZI 180 mg and 5.6% (7.4 events per 100 patient-years) in subjects who received SKYRIZI 360 mg compared to 2.1% (2.4 events per 100 patient-years) in subjects who received placebo after SKYRIZI induction.

Lipid Elevations

Elevations in lipid parameters (total cholesterol and low-density lipoprotein cholesterol [LDL-C]) were first assessed at 4 weeks following initiation of SKYRIZI in the induction trials (CD-1, CD-2). Increases from baseline and increases relative to placebo were observed at Week 4 and remained stable to Week 12. Following SKYRIZI induction, mean total cholesterol increased by 9.4 mg/dL from baseline to a mean absolute value of 175.1 mg/dL at Week 12. Similarly, mean LDL-C increased by 6.6 mg/dL from baseline to a mean absolute value of 92.6 mg/dL at Week 12. Mean LDL-C increased by 3.1 mg/dL from baseline to a mean absolute value of 99.0 mg/dL at Week 52 with SKYRIZI 180 mg maintenance treatment and by 2.3 mg/dL from baseline to a mean absolute value of 102.2 mg/dL at Week 52 with SKYRIZI 360 mg maintenance treatment (CD-3).

Ulcerative Colitis

SKYRIZI was studied up to 12 weeks in subjects with moderately to severely active ulcerative colitis in a randomized, double-blind, placebo-controlled induction trial (UC-1) and a randomized, double-blind, placebo-controlled, dose-finding trial (UC-3). Long-term safety up to 52 weeks was evaluated in subjects who responded to induction therapy in a randomized, double-blind, placebo-controlled maintenance trial (UC-2).

In the induction trials (UC-1 and UC-3), 712 subjects received the SKYRIZI 1,200 mg intravenous induction regimen at Weeks 0, 4 and 8. In the maintenance trial (UC-2), 347 subjects who achieved clinical response, defined as a decrease in mMS of ≥2 points and ≥30% from baseline and a decrease in RBS ≥1 from baseline or an absolute RBS ≤1, received a maintenance regimen of SKYRIZI either 180 mg or 360 mg subcutaneously at Week 12 and every 8 weeks thereafter for up to an additional 52 weeks.

The adverse reaction reported in ≥3% subjects treated with SKYRIZI in the ulcerative colitis induction trials (UC-1 and UC-3) and at a higher rate than placebo was arthralgia (3% SKYRIZI vs 1% placebo).

Adverse reactions reported in ≥3% of subjects treated with SKYRIZI in the maintenance trial (UC-2) and at a higher rate than placebo are shown in Table 4.

Table 4. Adverse Reactions Reported in ≥3% of Subjects with Ulcerative Colitis Treated with SKYRIZI[a] in Placebo-Controlled 52-Week Maintenance Trial (UC-2)

Adverse Drug Reactions	SKYRIZI 180 mg Subcutaneous Injection N = 170 n (%)	SKYRIZI 360 mg Subcutaneous Injection N = 177 n (%)	Placebo N = 173 n (%)
Arthralgia	9 (5.3)	17 (9.6)	8 (4.6)
Pyrexia	8 (4.7)	7 (4.0)	6 (3.5)
Injection site reactions[b,c]	5 (2.9)	5 (2.8)	2 (1.2)
Rash[d]	7 (4.1)	1 (0.6)	3 (1.7)

[a] SKYRIZI 180 mg or 360 mg at Week 12 and every 8 weeks thereafter for up to an additional 52 weeks
[b] Includes: application site pain, injection site erythema, injection site pain, injection site pruritus, injection site reaction
[c] Some subjects had multiple occurrences of injection site reactions. In this table, injection site reactions are counted only once per subject for the rate calculations.
[d] Includes: rash and rash macular

Specific Adverse Drug Reactions

The rates of infections, serious infections, and lipid elevations in subjects with UC who received SKYRIZI compared to subjects who received placebo in the induction trials (UC-1 and UC-3) and maintenance trial (UC-2) were similar to the rates in subjects with CD who received SKYRIZI compared to subjects who received placebo in the induction trials (CD-1, CD-2, and CD-4) and maintenance trial (CD-3).

Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies (ADA) in the trials described below with the incidence of ADA in other trials, including those of SKYRIZI (risankizumab).

Plaque Psoriasis

By Week 52, approximately 24% (263/1079) of subjects treated with SKYRIZI at the recommended dose developed antibodies to risankizumab-rzaa. Of the subjects who developed antibodies to risankizumab-rzaa, approximately 57% (14% of all subjects treated with SKYRIZI) had antibodies that were classified as neutralizing. Higher antibody titers in approximately 1% of subjects treated with SKYRIZI were associated with lower risankizumab-rzaa concentrations and reduced clinical response.

Psoriatic Arthritis

By Week 28, approximately 12.1% (79/652) of subjects treated with SKYRIZI at the recommended dose developed antibodies to risankizumab-rzaa. None of the subjects who developed antibodies to risankizumab-rzaa had antibodies that were classified as neutralizing. Antibodies to risankizumab-rzaa were not associated with changes in clinical response for psoriatic arthritis. A higher proportion of subjects with anti-drug antibodies experienced hypersensitivity reactions (6.3% (5/79)) and injection site reactions (2.5% (2/79)) compared to subjects without anti-drug antibodies (3.8% (22/574) with hypersensitivity reactions and 0.7% (4/574) with injection site reactions). None of these hypersensitivity and injection site reactions led to discontinuation of risankizumab-rzaa.

Crohn's Disease

By Week 64, antibodies to risankizumab-rzaa developed in approximately 3.4% (2/58) of subjects treated with SKYRIZI induction followed by 360 mg maintenance regimen. No subjects (0/57) treated with SKYRIZI induction followed by 180 mg maintenance regimen developed antibodies to risankizumab-rzaa. None of the subjects who developed antibodies to risankizumab-rzaa had antibodies that were classified as neutralizing.

Ulcerative Colitis

By Week 64, antibodies to risankizumab-rzaa developed in approximately 8.9% (8/90) or 4.4% (4/91) of subjects treated with SKYRIZI induction followed by the 180 mg or 360 mg maintenance regimen, respectively. Of the subjects who developed antibodies to risankizumab-rzaa, 75% (6.7% of all subjects treated with SKYRIZI induction followed by the 180 mg maintenance regimen) or 50% (2.2% of all subjects treated with SKYRIZI induction followed by the 360 mg maintenance regimen), respectively, had antibodies that were classified as neutralizing.

Postmarketing Experience

The following adverse reactions have been reported during post-approval of SKYRIZI. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to SKYRIZI exposure:

- *Skin and subcutaneous tissue disorders*: eczema and rash

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors outcomes in women who become pregnant while treated with SKYRIZI. Patients should be encouraged to enroll by calling 1-877-302-2161 or visiting http://glowpregnancyregistry.com.

Risk Summary

Available pharmacovigilance and clinical trial data with risankizumab use in pregnant women are insufficient to establish a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. Although there are no data on risankizumab-rzaa, monoclonal antibodies can be actively transported across the placenta, and SKYRIZI may cause immunosuppression in the in utero-exposed infant**.** There are adverse pregnancy outcomes in women with inflammatory bowel disease *(see Clinical Considerations)*.

In an enhanced pre- and post-natal developmental toxicity study, pregnant cynomolgus monkeys were administered subcutaneous doses of 5 or 50 mg/kg risankizumab-rzaa once weekly during the period of organogenesis up to parturition. Increased fetal/infant loss was noted in pregnant monkeys at the 50 mg/kg dose *(see Data)*. The 50 mg/kg dose in pregnant monkeys resulted in approximately 5 times the exposure (AUC) in humans administered the maximum recommended induction dose (1,200 mg) and 32 times the exposure (AUC) to the maximum recommended maintenance dose (360 mg). No risankizumab-rzaa-related effects on functional or immunological development were observed in infant monkeys from birth through 6 months of age. The clinical significance of these findings for humans is unknown.

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-associated maternal and embryo/fetal risk

Published data suggest that the risk of adverse pregnancy outcomes in women with inflammatory bowel disease is associated with increased disease activity. Adverse pregnancy outcomes include preterm delivery (before 37 weeks of gestation), low birth weight (less than 2,500 g) infants, and small for gestational age at birth.

Fetal/Neonatal adverse reactions

Transport of endogenous IgG antibodies across the placenta increases as pregnancy progresses, and peaks during the third trimester. Therefore, SKYRIZI may be present in infants exposed *in utero*. The potential clinical impact of risankizumab exposure in infants exposed *in utero* should be considered.

Data

Animal Data

An enhanced pre- and post-natal developmental toxicity study was conducted in cynomolgus monkeys. Pregnant cynomolgus monkeys were administered weekly subcutaneous doses of risankizumab-rzaa of 5 or 50 mg/kg from gestation day 20 to parturition, and the cynomolgus monkeys (mother and infants) were monitored for 6 months after delivery. No maternal toxicity was noted in this study. There were no treatment-related effects on growth and development, malformations, developmental immunotoxicology, or neurobehavioral development. However, a dose-dependent increase in fetal/infant loss was noted in the risankizumab-rzaa-treated groups (32% and 43% in the 5 mg/kg and 50 mg/kg groups, respectively) compared with the vehicle control group (19%). The increased fetal/infant loss in the 50 mg/kg group was considered to be related to risankizumab-rzaa treatment. The no-observed adverse effect level (NOAEL) for maternal toxicity was identified as 50 mg/kg, and the NOAEL for developmental toxicity was identified as 5 mg/kg. The 5 mg/kg dose in pregnant monkeys resulted in approximately 0.6 times the exposure (AUC) in humans administered the maximum recommended induction dose (1,200 mg) and 5 times the exposure (AUC) in humans administered the maximum recommended maintenance dose (360 mg). In the infants, mean serum concentrations increased in a dose-dependent manner and were approximately 17%-86% of the respective maternal concentrations. Following delivery, most adult female cynomolgus monkeys and all infants from the risankizumab-rzaa-treated groups had measurable serum concentrations of risankizumab-rzaa up to 91 days postpartum. Serum concentrations were below detectable levels at 180 days postpartum.

Lactation

Risk Summary

There are no data on the presence of risankizumab-rzaa in human milk, the effects on the breastfed infant, or the effects on milk production. Endogenous maternal IgG and monoclonal antibodies are transferred in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed infant to risankizumab-rzaa are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SKYRIZI and any potential adverse effects on the breastfed infant from SKYRIZI or from the underlying maternal condition.

Pediatric Use

The safety and effectiveness of SKYRIZI have not been established in pediatric patients.

Geriatric Use

Of the 6,862 subjects exposed to SKYRIZI, a total of 664 were 65 years and older (243 subjects with plaque psoriasis, 246 subjects with psoriatic arthritis, 72 subjects with Crohn's disease and 103 subjects with ulcerative colitis), and 71 subjects were 75 years and older.

Clinical studies of SKYRIZI, within each indication, did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger adult subjects.

No clinically meaningful differences in the pharmacokinetics of risankizumab-rzaa were observed based on age.

PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Hypersensitivity Reactions

Advise patients to discontinue SKYRIZI and seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions *[see Warnings and Precautions]*.

Infections

Inform patients that SKYRIZI may lower the ability of their immune system to fight infections. Instruct patients of the importance of communicating any history of infections to the healthcare provider and contacting their healthcare provider if they develop any symptoms of an infection *[see Warnings and Precautions]*.

Hepatotoxicity in Treatment of Inflammatory Bowel Disease

Inform patients that SKYRIZI may cause liver injury, especially during the initial 12 weeks of treatment. Instruct patients to seek immediate medical attention if they experience symptoms suggestive of liver dysfunction (e.g., unexplained rash, nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine) *[see Warnings and Precautions]*.

Administration of Vaccines

Advise patients that vaccination with live vaccines is not recommended during SKYRIZI treatment and immediately prior to or after SKYRIZI treatment. Medications that interact with the immune system may increase the risk of infection following administration of live vaccines. Instruct patients to inform the healthcare practitioner that they are taking SKYRIZI prior to a potential vaccination *[see Warnings and Precautions]*.

Administration Instruction

Instruct patients or caregivers to perform the first self-injected dose under the supervision and guidance of a qualified healthcare professional for training in preparation and administration of SKYRIZI, including choosing anatomical sites for administration, and proper subcutaneous injection technique.

If using SKYRIZI 90 mg/mL, instruct patients or caregivers to administer two 90 mg single-dose syringes to achieve the full 180 mg maintenance dose or four 90 mg single-dose syringes to achieve the full 360 mg maintenance dose of SKYRIZI for Crohn's disease or ulcerative colitis.

If using SKYRIZI 180 mg/1.2 mL, instruct patients or caregivers to administer one 180 mg single-dose syringe to achieve the full 180 mg maintenance dose or two 180 mg single-dose syringes to achieve the full 360 mg maintenance dose of SKYRIZI for Crohn's disease or ulcerative colitis.

Instruct patients or caregivers in the technique of pen or syringe disposal.

Pregnancy

Advise patients that there is a pregnancy registry that monitors pregnancy outcomes in women exposed to SKYRIZI during pregnancy *[see Use in Specific Populations]*.

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With gratitude

Reflections on five years leading *GI & Hepatology News* — and gratitude for the team and readers who made it possible.

This September issue marks my final Letter from the Editor after five years as editor in chief of *GI & Hepatology News*. I have served on the editorial board for nearly a decade, first as an associate editor under John Allen's leadership and then in this role. Over that time, gastroenterology has changed in remarkable ways. New therapies have reshaped care for IBD, eosinophilic esophagitis, and metabolic liver disease. Telehealth and artificial intelligence have moved from novelty to routine discussion. Issues of workforce sustainability, access, equity, reimbursement, and administrative burden have become central to how we think about clinical care. Through each of these shifts, *GI & Hepatology News* has offered a place to highlight timely developments, translate evidence into practice, and reflect on the broader forces shaping our field.

GI & Hepatology News occupies an important place in AGA's publication portfolio. With a readership broader than any of AGA's scientific journals, it serves a distinct and complementary role: curating timely clinical, policy, and professional developments in an accessible format for busy clinicians. As editor in chief, I have appreciated the opportunity to highlight important clinical topics, explore cross-cutting issues affecting gastroenterologists and hepatologists, and showcase the extraordinary talent within our membership — particularly through the Member Spotlight column.

This work depends on collaboration. I am deeply grateful to the AGA team, the Conexiant team, and our associate editors, whose judgment, creativity, and commitment have shaped every issue. Their efforts — often behind the scenes — have kept *GI & Hepatology News* timely, practical, and relevant to the GI community.

Most of all, thank you to our readers. Your engagement gives *GI & Hepatology News* its purpose. Whether you read for clinical updates, policy perspectives, member stories, or practical insights for your practice, I am grateful for the time and attention you have given us each month.

I am pleased to welcome Berkeley Limketkai, MD, PhD, as the next *GI & Hepatology News* editor in chief, along with a talented team of associate editors. The publication is in excellent hands, and I look forward to seeing how they shape its next chapter.

Thank you for the privilege of serving in this role.

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

Call for nominations

Know an inspiring AGA member? Nominate them to be featured in a Member Spotlight.

Do you know an AGA member with a unique, inspiring, or particularly interesting career path? Nominate them for our Member Spotlight! We would love to share their story with the AGA community. Our members are doing remarkable work in clinical care, research, education, advocacy, and innovation, and highlighting these journeys helps celebrate the diverse experiences that shape the field of gastroenterology.

To submit a nomination or suggestion, please email the member's name and a brief note about why they would be a great feature to ginews@gastro.org. We look forward to hearing about the inspiring members in your network!

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"The distinction between 'GI care' and 'metabolic and lifestyle care' is going to collapse over the next decade...The practices that build the team and the framework now [will] be positioned for what GI is becoming."

Vivian Asamoah, MD • See page 22

Coffee linked to fewer cirrhosis, liver cancer cases in large analysis

Large UK Biobank analysis ties higher coffee intake to lower risks of cirrhosis, liver cancer, and liver-related death while identifying imaging and proteomic changes that may explain the association.

By Doug Brunk

Higher coffee consumption was associated with lower risks of cirrhosis, liver cancer, and liver-related death in a large prospective study of more than 354,000 adults followed for more than a decade. Magnetic resonance imaging (MRI) and blood protein analyses conducted in subgroups of participants also pointed to possible biologic mechanisms behind the association.

The observational analysis, published in *Clinical Gastroenterology and Hepatology*, included 354,957 UK Biobank participants who were free of cirrhosis or hepatocellular carcinoma at enrollment and who were followed for a median of 13 years. The researchers assessed self-reported coffee consumption, including the type of coffee and whether participants added sugar or artificial sweeteners. They then examined how those habits were associated with new cases of liver disease, MRI measures of liver health in a subgroup of 28,961 patients, and blood protein profiles in 44,633 patients. The analyses accounted for factors including age, sex, smoking, alcohol use, metabolic conditions, socioeconomic status, body mass index, and PNPLA3 genotype.

Compared with patients who did not drink coffee at all, those who drank at least five cups a day were 32% less likely to develop cirrhosis, 47% less likely to develop hepatocellular carcinoma, and 42% less likely to die from liver disease during follow-up. The association followed a dose-response pattern, with lower risks seen starting at as little as one to two cups a day. The findings were similar for caffeinated and decaffeinated coffee.

The investigators also examined whether adding sugar or artificial sweeteners changed the association between coffee and liver health. Overall, patients who added sweeteners had similar reductions in the risk of cirrhosis, hepatocellular carcinoma, and liver-related death as those who drank unsweetened coffee. However, they had 1.36 times the odds of elevated iron-corrected T1, an MRI marker of liver inflammation and fibrosis, compared with patients who did not add sweeteners.

MRI findings also suggested that higher coffee intake was associated with better liver health before liver disease became clinically apparent. Patients who drank at least five cups a day had less liver fat, lower liver iron levels, and lower odds of liver fibroinflammation than non-coffee drinkers. The findings were similar for caffeinated and decaffeinated coffee, suggesting that components other than caffeine may play a role.

Proteomic analyses identified 74 circulating proteins that were associated with both coffee intake and cirrhosis risk, suggesting biologic pathways related to liver function, inflammation, fibrosis, and immune regulation that may help explain coffee's observed associations with better liver health.

The authors noted several limitations of the analysis, including the reliance on self-reported coffee intake, the possibility of unmeasured confounding and reverse causation, a generally healthier MRI subgroup, and the predominantly European ancestry of the study population, which may limit the generalizability of the findings to other groups. They also said the blood protein findings require experimental studies to confirm the underlying biologic mechanisms.

"Higher coffee intake was associated with lower risks of cirrhosis, HCC, and liver-related mortality, as well as favorable MRI-based and proteomic profiles," the authors concluded. They added that the combined clinical, imaging, and molecular findings support coffee as "a simple, scalable strategy for liver disease prevention."

The study received no external funding. Ju Dong Yang, MD, reported consulting relationships with several companies; the remaining authors reported no relevant conflicts.

GI & Hepatology News invited study author Hyunseok Kim, MD, MPH, PhD, of the Karsh Division of Gastroenterology and Hepatology at Cedars-Sinai Medical Center, to comment on the implications of this work.

Why does this study matter?

Dr. Kim: Coffee has long been associated with better liver health, but most previous studies focused only on clinical outcomes such as cirrhosis or liver cancer. Our study is unique because it integrates clinical outcomes with advanced MRI biomarkers and large-scale plasma proteomics in more than 350,000 UK Biobank participants. By combining these complementary approaches, we were able to show not only that coffee consumption is associated with lower risks of cirrhosis, hepatocellular carcinoma, and liver-related mortality, but also that it is linked to less liver fat, less fibroinflammation on MRI, and favorable biological pathways involved in fibrosis and inflammation. This provides stronger biological evidence supporting coffee as a simple lifestyle factor that may promote liver health.

When you had all the data in front of you, was there a finding that surprised you?

Dr. Kim: Several findings stood out. First, we observed remarkably consistent associations across clinical outcomes, imaging biomarkers, and proteomic signatures, all pointing in the same direction. Second, both caffeinated and decaffeinated coffee showed similar associations, suggesting that compounds other than caffeine likely contribute to the liver benefits. Finally, we were intrigued that coffee drinkers had lower levels of proteins involved in fibrosis, macrophage activation, and extracellular matrix remodeling, while proteins reflecting healthier liver synthetic function were higher. These findings offer new mechanistic clues that go beyond the epidemiologic associations reported previously.

How might the findings influence clinical practice for gastroenterologists and hepatologists?

Dr. Kim: This study should not be interpreted as evidence that coffee is a treatment for chronic liver disease. However, for most patients without contraindications, moderate coffee consumption appears to be a safe, inexpensive, and potentially beneficial lifestyle habit that can complement other evidence-based interventions such as weight loss, alcohol abstinence, and management of metabolic risk factors. I hope these findings will give clinicians greater confidence when discussing dietary habits with patients and encourage further research into the biological mechanisms underlying coffee's protective effects.

Is there anything else you'd like to say about this work?

Dr. Kim: One of the strengths of this study is its multidimensional design. Rather than relying solely on clinical events, we incorporated MRI-derived imaging biomarkers and high-throughput proteomics to better understand the biological pathways associated with coffee consumption. This approach provides a more comprehensive picture of liver health and may help identify new therapeutic targets for preventing fibrosis and liver disease progression. While our findings are observational and do not prove causality, they provide a strong rationale for future mechanistic studies and, potentially, clinical trials evaluating dietary interventions in liver disease.

Hyunseok Kim, MD, MPH, PhD

One in five reach hepatitis B functional cure with finite bepirovirsen

Continued From Page 1

The investigators conducted two identical, randomized, double-blind, placebo-controlled trials at centers in 29 countries between December 2022 and May 2024. The studies enrolled 1,838 adults with chronic HBV infection without cirrhosis who had been taking stable nucleoside or nucleotide analogue therapy for at least six months. Eligible patients had hepatitis B surface antigen levels of 100 to 3,000 IU/mL, suppressed HBV DNA, and alanine aminotransferase (ALT) levels no more than twice the upper limit of normal. Most were hepatitis B e antigen (HBeAg)-negative at baseline.

Patients were randomly assigned in a 2:1 ratio to receive weekly subcutaneous injections of bepirovirsen 300 mg or placebo for 24 weeks while continuing their background antiviral therapy. Those who maintained HBsAg loss and undetectable HBV DNA through week 46 stopped antiviral therapy at week 48 and were evaluated 24 weeks later for the primary endpoint at week 72.

In B-Well 1, 20% of patients treated with bepirovirsen achieved a functional cure, compared with none of those who received placebo. Results were nearly identical in B-Well 2, where 19% of patients in the bepirovirsen group achieved a functional cure, while none in the placebo group did.

About one-quarter of patients treated with bepirovirsen met the criteria to stop background antiviral therapy at week 48, while none in the placebo group did. Among those who discontinued treatment, most maintained viral suppression through week 72. Overall, 23% of patients treated with bepirovirsen maintained HBV DNA levels below the lower limit of quantification after stopping antiviral therapy in both trials, compared with none who received placebo. Only 2% experienced low-level HBV DNA recurrence after treatment was discontinued, and none developed virologic or clinical relapse during follow-up.

Treatment responses were greatest among patients with lower baseline HBsAg levels. Among those with baseline HBsAg levels of 1,000 IU/mL or less, 25% in B-Well 1 and 28% in B-Well 2 achieved a functional cure. By comparison, functional cure rates were 10% and 5%, respectively, among patients with baseline HBsAg levels above 1,000 IU/mL.

Exploratory analyses also suggested recovery of immune function. Among patients who achieved a functional cure and did not have hepatitis B surface antibodies at baseline, about two-thirds developed protective antibody responses by week 72. Among the small subgroup of HBeAg-positive patients, about one-quarter lost HBeAg after treatment, although functional cure remained less common in this group.

During the 72-week study period, adverse events occurred in 91% of patients treated with bepirovirsen and 73% of those who received placebo, while serious adverse events occurred in 7% and 4%, respectively. During the 24-week treatment period, injection-site reactions were the most common adverse event, affecting 53% of patients receiving bepirovirsen vs 14% of those receiving placebo. Most reactions were mild and occurred during the first month of treatment.

During the treatment period, grade 3 or higher adverse events occurred in 16% of patients treated with bepirovirsen, compared with 3% of those who received placebo. ALT elevations were the most common severe adverse event, occurring in 6% of treated patients. Investigators noted that these temporary ALT increases occurred alongside declines in HBsAg and have previously been linked to treatment activity. Permanent discontinuation of bepirovirsen occurred in 3% of treated patients. No patients met criteria for drug-induced liver injury, and no treatment-related deaths were reported.

The investigators acknowledged several limitations. Some subgroup analyses included few patients, particularly racial and ethnic minority groups and patients who were HBeAg-positive, limiting the precision of those findings. The authors also noted that wider use of quantitative HBsAg testing will be needed to identify patients most likely to benefit from bepirovirsen in routine clinical practice.

For practicing hepatologists and gastroenterologists, the findings suggest that a 24-week course of bepirovirsen could offer selected patients with well-controlled chronic hepatitis B an opportunity to stop lifelong antiviral therapy while maintaining viral suppression. "These findings support the efficacy of bepirovirsen as a 24-week finite therapy to achieve functional cure and show added benefit over continued NA therapy as standard care in these patients," the authors concluded.

The study was funded by GSK, which designed, monitored, and analyzed the trials and provided medical writing support. Multiple authors are GSK employees.

GI & Hepatology News asked Tatyana Kushner, MD, MSCE, associate professor of medicine and director of outcomes clinical research in the division of gastroenterology & hepatology at Weill Cornell Medicine, New York, to comment on the findings.

What do you see as the main takeaway from this study?

Dr. Kushner: This is a landmark study for the hepatitis B field. Current treatments are highly effective at suppressing viral replication, but they rarely achieve loss of HBsAg, which is considered a functional cure. This is the first Phase 3 trial to demonstrate positive results in achieving functional cure in people living with chronic hepatitis B. These findings represent an important step toward a future where treatments can do more than control the virus — they may ultimately offer the possibility of curing hepatitis B.

How might the findings influence clinical practice?

Dr. Kushner: These results demonstrate that a functional cure is achievable for a subset of people living with chronic hepatitis B. If these findings lead to the approval of bepirovirsen, we could, for the first time, have a finite treatment for hepatitis B that offers the potential for functional cure, allowing some patients to discontinue lifelong antiviral therapy.

What are the next steps for this research?

Dr. Kushner: Although the Phase III B-Well trial demonstrated that functional cure is achievable in approximately 19% of patients with HBsAg levels ≤3,000 IU/mL and 28% of those with HBsAg levels ≤1,000 IU/mL, several important questions remain. First, we need a better understanding of which patients are most likely to respond to treatment and, conversely, which patients are unlikely to benefit so that therapy can be appropriately individualized and unnecessary treatment avoided. Second, longer-term follow-up is needed to determine whether functional cure is durable beyond the 96-week study period. Safety will also be an important consideration. In the trial, approximately 89% of participants experienced an adverse event, with 16% experiencing severe adverse events. The most commonly reported adverse events included elevations in liver enzymes, thrombocytopenia, and renal dysfunction. If approved for clinical use, we will need to better understand how these safety findings translate into real-world practice and what type of monitoring will be required. Finally, additional research is needed to develop effective treatment strategies for patients with baseline HBsAg levels ≥3,000 IU/mL, who were less likely to achieve functional cure with this regimen.

What message would you like to leave readers with about this work?

Dr. Kushner: This represents a very exciting advance in the treatment of chronic hepatitis B. With the anticipated approval of bepirovirsen, clinicians should begin discussing this potential future treatment option with appropriate patients. An important next step will be incorporating quantitative HBsAg testing into routine clinical practice, as this has not traditionally been performed for most patients but will likely play a key role in identifying those most likely to benefit from therapy.

Dr. Kushner disclosed that she has received research support from Gilead and Mirum and that she has served as an advisor to Gilead, Mirum, GSK and VIR.

Tatyana Kushner, MD, MSCE

Is professional coaching worth it? A practical guide for early-career gastroenterologists

Mariam Naveed, MD, FACG, and Kathryn E. Hutchins, MD, FACG

The first time many physicians seriously consider professional coaching is when something already feels off.

Burnout. An unexpected leadership conflict. A career that looks successful from the outside but feels adrift from the inside.

As program directors, we recognize this pattern. Fellows and early-career gastroenterologists are skilled at pushing through discomfort — medicine selects for it. Endurance and productivity are rewarded. Reflection rarely makes the schedule. And if we are being honest, we have been guilty of the same. We held the same assumptions about coaching. We waited longer than we should have.

This misconception is worth addressing directly: coaching is not for when things fall apart, and it is not reserved for advanced-career physician leaders. In reality, it may be most valuable before a physician reaches those inflection points. The earlier physicians develop genuine insight into their values, leadership style, and definitions of success, the more deliberately they can shape what comes next.

This is particularly relevant in gastroenterology, where clinical productivity, procedural volume, research, teaching, leadership, national engagement, and personal responsibilities all compete for the same finite capacity, often simultaneously. The cost of operating without that clarity compounds.

One of my favorite reads on this topic (Dr. Naveed here) is Atul Gawande's 2011 New Yorker essay "Personal Best."[1] It genuinely changed how I thought about the role of coaching in a physician's life. He asks a deceptively simple question: Why do elite performers in every other field rely on coaches, while physicians rarely do? His answer has stayed with me — even highly accomplished professionals have blind spots, and an outside perspective, what he called an "outside ear," is often the only way to see them.

Setting the record straight

Coaching is not therapy, and it is not remediation. Coaching is forward-focused and goal-directed. While mentorship transfers the benefit of someone else's experience, coaching builds your own capacity to find answers. Sponsorship opens doors; coaching helps you decide which ones to walk through. As physicians and leaders, we are trained to solve problems. Coaching cultivates something different — the discipline to slow down, sit with the question, and resist reaching for an answer before you fully understand what you are dealing with. That shift is uncomfortable. It is also where the growth happens.

Why now, not later

The transition from fellow to attending is one of the highest-stakes windows in a physician's career. High-impact decisions get made quickly — practice model, subspecialty focus, leadership opportunities, work-life structure — and most of them happen under time pressure with limited protected space for reflection. Coaching protects against reactive decision-making and intentionally creates space for choices that are mission-aligned.

This matters during training, too. Working with a coach early helps answer the questions that rarely come up in case conference: What kind of practice do I actually want? What am I building my career around? That clarity guides more intentional decisions about a first job, a first leadership role, and the first real career crossroads. Waiting until you are "established" often means waiting until the habits are already set and the patterns are harder to shift.

The evidence is particularly striking for women trainees. A randomized clinical trial of group coaching in women physician trainees demonstrated significant reductions in burnout, impostor syndrome, and moral injury, alongside meaningful improvements in flourishing and self-compassion.[2] Women physicians face disproportionately higher rates of burnout, with disparities that begin during training. Group coaching, in particular, offers a structure that addresses those vulnerabilities before they compound.

What coaching looks like in practice

Not all coaching is the same. Career coaching is typically the natural entry point for early-career GIs — addressing trajectory, transitions, and the question of what you are trying to build professionally. Leadership coaching becomes relevant as physicians step into roles such as program director, section chief, or committee leader, often before formal development in communication, conflict navigation, or building institutional influence has been offered. Physician-specific coaches, many with clinical backgrounds, accelerate that work because the culture and constraints of medicine require no translation.

Where you find a coach matters too. Internal coaches are often offered as a faculty benefit and offer advantages such as lower cost, faster trust-building, and organizational familiarity. The trade-off is that confidentiality can feel uncertain and independence more limited. External coaches offer full objectivity, which is often where the most candid work happens. For anyone navigating something politically sensitive within their institution, that distinction is meaningful.

Two perspectives

We came to coaching from different places. What follows is what we found.

"I held the same misconceptions I am writing about here. I did not pursue coaching until recently, and it took navigating a challenging period at work to get there. What I found changed how I approach almost everything. The most important lesson was about curiosity: walking into a hard conversation not to prove my perspective, but to understand the other person's. The second was about culture. There is a reason people say culture eats strategy for breakfast. I had to first understand the institution's culture, its goals, and what it was actually trying to protect, before I could figure out

"I consider it a lifetime investment, because the returns are both personal and professional. Coaching gave me clarity and a strategic roadmap that is values-focused and mission-aligned. It also gave me permission to say no."

	Mentorship	Sponsorship	Coaching
Primary function	Guidance based on experience	Advocacy and opportunity creation	Facilitation of self-discovery
Key message	"Here's what I would do."	"I will open doors for you."	"What do you want, and how will you get there?"
Relationship	Directional	Influential	Reflective

Table 1. Mentorship, sponsorship, and coaching compared.

Internal: Advantages	Internal: Limitations	External: Advantages	External: Limitations
Cost often covered	Potential bias	Unbiased perspective	Higher cost
Knows organizational culture	Confidentiality risk	Full confidentiality	Unfamiliar with culture
Flexible scheduling	Role conflict risk	Deeper specialization	Scheduling challenges

Table 2. Internal vs. external coaching: key trade-offs.

how to navigate toward outcomes that worked for both of us. Coaching gave me the framework to do that. I wish I had found it sooner."

— Mariam Naveed, MD, FACG

"My first experience with coaching came through the Scrubs & Heels Matrix Mentorship program, an unexpected gift that genuinely changed my career trajectory. Coaching gave me clarity and a strategic roadmap that is values-focused and mission-aligned. It also gave me permission to say no. Before coaching, I was on more committees than I could count. Since 2022, I have continued working with a coach — both group and individual — though I have had to seek it out proactively. It has never been offered as part of my annual evaluation. I consider it a lifetime investment, because the returns are both personal and professional."

— Kathryn E. Hutchins, MD, FACG

How to start

Start with your institution. Many academic medical centers and health systems offer coaching as a faculty development benefit — ask your GME office, faculty affairs, or HR. Specialty societies are also a resource; AGA, ACG, and ASGE offer professional development programming for early-career members, and those networks often connect physicians with coaches who understand the culture of medicine. Women-focused leadership initiatives in GI are increasingly building coaching access into their programming. Organizations such as Women in Endoscopy and events such as Scrubs & Heels are among those creating this kind of structured support, alongside others doing similar work across the field. When vetting an external coach, look for International Coaching Federation credentialing as a reasonable baseline standard.[3]

Request a complimentary session before committing. Chemistry matters more than credentials — the coaching relationship is the primary vehicle for the work. If the fit is not right, that is not a failure of coaching; it is useful information. Try a different coach or a group format. Like any meaningful professional relationship, the right match sometimes takes more than one attempt.

If you are a trainee and your program does not currently offer coaching access, ask. Not because something is wrong. Because you are worth the proactive investment, and your entire career is still in front of you.

Conclusion

The culture of medicine has long treated help-seeking as a liability and deferred self-investment until it is earned. That framing is costly — for physicians, for the people they lead and train, and for the patients downstream. Coaching does not wait for the right moment. It creates one. The fellows in your program today and the early-career attendings who just left training are in the window where this matters most — while the habits are still forming, the identity is still taking shape, and the trajectory is still genuinely flexible.

Seeking guidance is not an indication of inadequacy. It is a deliberate investment in clarity, accountability, and the kind of career worth building.

We waited longer than we should have. You do not have to.

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Four-week pancreatic stent interval reduces repeat endoscopies

In a nine-center Korean randomized trial, waiting four weeks instead of two to assess prophylactic pancreatic duct stents cut endoscopic removals from 19% to 7% without raising pancreatitis risk.

By Doug Brunk

Leaving prophylactic pancreatic duct stents in place for four weeks instead of checking for removal after two weeks reduced the need for a repeat endoscopic procedure without increasing pancreatitis or other clinically important complications in patients undergoing endoscopic retrograde cholangiopancreatography (ERCP), according to a multicenter randomized trial.

"This trial provides the first prospective, multicenter randomized evidence that a four-week prophylactic pancreatic duct stent retention interval is safe and significantly reduces the need for endoscopic removal compared to a two-week interval," the study's first author, Dong Kee Jang, MD, PhD, of the division of gastroenterology in the department of medicine at Samsung Medical Center, South Korea, told *GI & Hepatology News*. "It suggests more conservative management strategy is viable without increasing the risk of post-ERCP pancreatitis."

The findings, published in *Clinical Gastroenterology and Hepatology*, may help settle a long-standing question about how long prophylactic pancreatic duct stents should remain in place after ERCP. Current guidelines disagree: The European Society of Gastrointestinal Endoscopy recommends checking for and removing retained stents within five to 10 days, while the American Society for Gastrointestinal Endoscopy recommends removal within two to four weeks.

Dr. Jang and colleagues enrolled adults undergoing ERCP at nine tertiary centers in South Korea between July 2021 and March 2024. All patients received the same 5-French, 5-cm, single-pigtail pancreatic duct stent without an internal flange after inadvertent pancreatic duct cannulation during biliary access. Stents were placed to prevent post-ERCP pancreatitis or to facilitate difficult biliary cannulation. Patients were randomly assigned to have an abdominal X-ray two or four weeks after ERCP to determine whether the stent had passed spontaneously. Those with retained stents underwent endoscopic removal.

Of 182 patients screened, 160 were randomly assigned to one of the two follow-up groups. A total of 156 completed follow-up and were included in the analysis. The groups had similar baseline characteristics. The average age was about 62 years, about half of the patients were men, and the most common reason for ERCP was choledocholithiasis. About two-thirds of patients received a pancreatic duct stent to help prevent post-ERCP pancreatitis, while one-third received a stent to make biliary cannulation easier.

The primary outcome favored the four-week follow-up strategy. Only 7% of patients in the four-week group required endoscopic stent removal, compared with 19% in the two-week group. That means about one endoscopic removal procedure was avoided for every eight patients managed with the longer follow-up interval.

The lower rate of endoscopic stent removal was due to more patients passing their stents on their own. By the scheduled follow-up visit, 92% of patients in the four-week group had passed the stent spontaneously, "which exceeded our initial assumptions," Dr. Jang said, compared with 81% of those in the two-week group.

Importantly, waiting four weeks to assess stent passage did not appear to increase the risk of complications. Post-ERCP pancreatitis occurred in 11% of patients in the four-week group and 15% of those in the two-week group, a difference that was not statistically significant. Most cases were mild. Two patients in each group developed moderate pancreatitis, and no patients developed severe pancreatitis. The median time to pancreatitis onset was one day after ERCP, suggesting that most cases occurred soon after the procedure rather than during the longer period of stent retention.

The investigators found no cases of stent-associated pancreatitis, defined as pancreatitis that developed more than 48 hours after ERCP while the stent was still in place. No patients developed pancreatitis more than two weeks after the procedure or experienced other serious complications requiring emergency care. Hospital stays and postprocedure amylase and lipase levels were also similar between the groups.

Subgroup analyses showed similar results. Outcomes did not differ between patients who received stents to prevent post-ERCP pancreatitis and those who received stents to help with difficult biliary cannulation. Rates of endoscopic stent removal, spontaneous stent passage, and pancreatitis were similar regardless of the reason for stent placement.

"These findings support shifting to a four-week assessment interval, which can safely reduce unnecessary endoscopic removal procedures and associated health care burdens," Dr. Jang said.

The authors noted several limitations. All patients were treated at tertiary hospitals in South Korea, so the findings may not apply to other practice settings. The results are specific to the 5-French, 5-cm, single-pigtail pancreatic duct stent without an internal flange used in the study and may not apply to other stent designs. "Additionally, longitudinal studies are needed to further confirm long-term safety regarding rare, late-onset complications," Dr. Jang said.

The researchers reported having no disclosures.

GI & Hepatology News invited Sumant Inamdar, MD, MPH, an interventional gastroenterologist in the division of gastroenterology and hepatology at the University of Arkansas for Medical Sciences, Little Rock, to comment on the study.

What are the potential clinical implications of the research?

Dr. Inamdar: The main clinical implication is that, for the specific stent studied (a 5-Fr, 5-cm, single-pigtail, unflanged prophylactic pancreatic duct stent), a four-week assessment strategy may be safe and more efficient than routine two-week assessment. Waiting longer increased spontaneous stent passage from 81.3% to 92.1% and reduced the need for endoscopic removal from 18.8% to 6.6%. For patients, this could mean fewer repeat endoscopies, less anesthesia exposure, fewer visits, and lower cost. For endoscopy units, it may reduce avoidable procedures and free capacity for higher-priority therapeutic cases. Importantly, these findings support a selective, stent-specific approach, not a universal 4-week strategy for all pancreatic stents. The results are most applicable to short, unflanged prophylactic stents designed to pass spontaneously, and should not be automatically extrapolated to flanged, longer, therapeutic, or otherwise higher-risk pancreatic duct stents.

What additional research may be needed?

Dr. Inamdar: Several questions remain. First, the study was performed in tertiary centers in South Korea, so it would be helpful to see whether the same findings hold across other health systems and practice environments. Second, the results are highly dependent on the stent design. Different stent lengths, diameters, flanged stents, or internally anchored stents may have very different migration and retention behavior. Third, the study was not designed to evaluate longer-term pancreatic duct changes after delayed stent passage or retention. Although no stent-associated pancreatitis was observed, the sample size may not be large enough to detect rare adverse events. Additional studies with longer follow-up could help clarify whether prolonged retention has any delayed ductal consequences. Finally, contemporary post-ERCP pancreatitis prevention often includes rectal NSAIDs and protocolized hydration, but rectal NSAIDs were not used in this trial because they were not available in South Korea. That makes the study internally consistent, but it raises the question of how these results translate to centers where rectal indomethacin and other prophylactic strategies are routinely used.

Is there anything else you'd like to say about this work?

Dr. Inamdar: This is a pragmatic and clinically useful study because it answers a question that advanced endoscopists face frequently. Its strength is not only that it is randomized and multicenter, but that it focuses on an outcome that matters to patients and endoscopy units: the need for an additional endoscopic procedure. The findings should encourage guideline committees and endoscopy practices to think more carefully about stent-specific follow-up intervals rather than applying a single removal timeline to all pancreatic duct stents.

Dr. Inamdar reported having no disclosures.

AI colonoscopy tool boosts adenoma detection in VA network, study finds

In a cluster-randomized study of more than 334,000 colonoscopies across the Veterans Health Administration, facilities equipped with computer-aided detection raised adenoma detection rates by about 4 percentage points without lengthening withdrawal times.

By Doug Brunk

Making computer-aided detection devices available during colonoscopy was associated with higher adenoma detection rates across a large Veterans Health Administration network, according to a cluster-randomized study of more than 334,000 colonoscopies.

Facilities that adopted AI-assisted computer-aided detection during colonoscopy saw adenoma detection rates increase by 4 percentage points, while rates fell slightly at sites that did not use the technology. The findings suggest that making computer-aided detection (CADe) available may improve ADR, a colonoscopy quality metric, in routine VA practice, even among endoscopists with high baseline ADRs.

"Studies have demonstrated that endoscopists with a higher adenoma detection rate protect their patients from colorectal cancer (CRC) incidence and death better than those with a lower adenoma detection rate," first author Jason A. Dominitz, MD, MHS, of the National Gastroenterology and Hepatology Program at the Veterans Health Administration, Washington, DC, told *GI & Hepatology News*. "Controlled clinical trials demonstrated that computer-aided detection CADe improves adenoma detection rates (ADR), but this benefit was not clearly demonstrated in real-world studies. Our study is important because we were able to conduct a pragmatic study in a real-world setting that allowed for comparisons of colonoscopy quality with vs without availability of CADe."

The study, published in *Gastroenterology*, compared 42 VA facilities that received GI Genius CADe devices with 97 control facilities. Randomized deployment occurred between October 2022 and February 2023, and outcomes were assessed using national administrative, pathology and colonoscopy databases.

The analysis included data from 269 endoscopists at CADe facilities and 547 endoscopists at control facilities. Investigators evaluated 71,594 colonoscopies before and 35,399 after deployment at CADe sites, along with 151,792 predeployment and 75,415 postdeployment procedures at control facilities.

At facilities using CADe, the adenoma detection rate increased from 50.7% before implementation to 54.9% afterward, a gain of 4.2 percentage points. In comparison, control facilities saw a slight decrease in adenoma detection rates, from 51.8% to 51.1% over the same period.

After accounting for differences in patient, physician, and facility characteristics, CADe use was associated with a 22% higher likelihood of detecting an adenoma compared with usual care.

The improvement was seen across endoscopists with a wide range of baseline performance levels. When investigators grouped endoscopists into five categories based on their adenoma detection rates before CADe implementation, they found improvements in every group.

Among endoscopists whose adenoma detection rates were below 40% at baseline, 55% at CADe facilities improved to meet or exceed the 40% benchmark after implementation, compared with 20% of endoscopists at control facilities.

The effect of CADe did not vary by physician specialty, sex, or years of experience. The benefits were also consistent across patient groups defined by sex, race, ethnicity and rural versus urban residence. The only factor that influenced the effect was patient age, with somewhat greater improvements seen in older patients.

Jason A. Dominitz, MD, MHS

In other findings, adenocarcinoma detection rates did not differ significantly between groups. Likewise, after accounting for baseline differences between the groups, CADe use was not associated with improved detection of sessile serrated lesions.

The technology also did not appear to increase false-positive alerts. Rates of non-neoplastic tissue sampling, which the investigators used as a proxy for false positives, were similar between the CADe and control groups after adjustment.

Procedure efficiency also appeared unchanged. In a subset of more than 13,000 colonoscopies with available withdrawal time data, adjusted analyses showed no significant difference in withdrawal times after CADe implementation.

A survey of 124 participating endoscopists found broad acceptance of CADe. Nearly 78% said they liked using the technology, and about three-quarters reported using it in more than 80% of screening and surveillance colonoscopies. Half, however, felt it generated too many false-positive alerts, and one-quarter worried about overreliance on the technology.

The investigators noted several limitations. Because procedure-level CADe usage data and information on colonoscopy indication, polyp size and advanced neoplasia were unavailable, the study could not determine whether higher adenoma detection led to greater detection of advanced lesions or improved long-term colorectal cancer outcomes. In addition, the study population was drawn from the VA and was predominantly male, which may limit generalizability.

The study was funded by the Veterans Health Administration Quality Enhancement Research Initiative. Tonya Kaltenbach, MD, MS, MEd, reported serving as a consultant for Olympus America but the remaining authors reported no relevant conflicts of interest.

Sustainability in endoscopy

Dear colleagues,

In this issue of Perspectives, we explore sustainability in the practice of endoscopy. Rising health care costs, growing demand for endoscopic services, and increasing concern for waste and its environmental impact have placed new emphasis on maximizing our resources. Drs. Deepak Agrawal and Zhouwen Tang discuss their approach and recommendations for minimizing waste and using supplies and equipment more efficiently. They challenge some long-standing dogma — such as the routine use of sterile water over tap water — and examine the limited evidence behind many of our more costly practices. Notably, many of these questions first arose out of necessity: national shortages of sterile water, or supplies placed on back order, forced practical reconsideration of habits long taken for granted.

Drs. Jehovan Fairclough and Melissa Arthurs-Wadsworth offer a complementary perspective, describing their day-to-day approach to practicing gastroenterology and endoscopy in Jamaica, where only 12 gastroenterologists serve a population of 2.8 million. In a setting where scarcity is not a periodic disruption but the everyday operating condition, sustainable practice becomes inseparable from good clinical judgment. They also make the case that sustainability extends beyond the procedure room, to the referral relationships, multidisciplinary discussions, and global partnerships that allow a small workforce to stretch scarce resources without compromising care. As always, we welcome your questions and comments.

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.

Sustainability in endoscopy: the why and how

By Deepak Agrawal, MD, FASGE, and Zhouwen Tang, MD

Medicine is rife with difficult decisions. Yet it is human nature to occasionally succumb to the easier path. It is often easier to order an endoscopy rather than explain why it is not needed. It is easier to follow the habits of an endoscopy unit than question them and risk alienation. It is lucrative to choose what provides financial benefit or convenience when someone else bears the cost. The immediate rewards often outweigh consideration of harms to the health system or society.

This is the case with sustainable practices in endoscopy — decreasing the carbon footprint of our procedures to meet tomorrow's needs. The increasing number of wildfires, flooding, and water scarcity across the US and the world indicates that tomorrow is already here. In 2009, The Lancet declared climate change the biggest threat to human health of the 21st century. More recently, 200 medical journals identified climate change as a health crisis, and the four major gastroenterology societies announced a commitment and strategic plan to promote sustainability in endoscopy. Since then, the carbon footprint of endoscopy has likely increased as more single-use accessories are introduced and adopted.

The total carbon footprint of endoscopy extends far beyond the procedure, but endoscopists influence a meaningful subset of those emissions. Recent life-cycle studies identify manufacturing, transportation, facility energy, reprocessing, anesthesia gases, water, and waste as major contributors. Our focus is on choices made by endoscopists, including endoscopic accessories and personal protective equipment, as well as waste segregation. Gastroenterology societies have put forth practical recommendations and solutions, but adoption remains limited.

Why have our actions significantly lagged our sustainability intentions?

Common to many wasteful practices is the seemingly unimpeachable pursuit of patient safety. Why not wash something twice to clean it more? Why wash it at all when you can throw it away? Who can argue when avoiding any theoretical risk of infection is treated as more important than the distant environmental harm that follows? This is the "zero-risk bias": the tendency to pay disproportionately to reduce a small risk to exactly zero. It offers psychological closure that "low enough" does not. But when the risk is already very low, eliminating the last fraction of risk comes at a disproportionate environmental cost.

It is easy to overlook environmental costs because market prices rarely capture negative externalities. A disposable device may appear cheaper or more efficient because its price excludes the costs of resource extraction, manufacturing, waste, disposal, and emissions. Those costs are instead shifted to society and future generations. Heat-related deaths in the United States, for example, have more than tripled from 2016 to 2023. Although our individual choices contribute to this broader problem, its multifactorial nature makes it difficult to attribute any particular outcome to any single action. That, however, does not make the cumulative impact of those choices inconsequential.

Categories	Examples of unsustainable practices	Points to ponder
Sedation and monitoring	• Routine use of IV fluids • Disposable EKG leads, BP cuffs, pulse oximeters	Are we following the most sustainable option? If not, is our practice based on evidence, convenience, fear over logic, marketing pressure? What can I do? How can I help implement change in the endoscopy unit?
Endoscopic instruments	• Disposable bougie dilators, dilation guidewires, balloon inflation device	
Endoscopic accessories	• Sterile water for irrigation during endoscopy • Single-use lubricant tubes • Disposable endoscopy buttons • Single-use gowns and face shields • Disposing of noninfectious waste in the red bin	
Endoscopy	• Guideline-discordant indications • Routine biopsies (e.g., gastric biopsies during every EGD)	

Table 1. Sustainability practices.

"The immediate rewards often outweigh consideration of harms to the health system or society. This is the case with sustainable practices in endoscopy — decreasing the carbon footprint of our procedures to meet tomorrow's needs."

Most endoscopy units do not measure the waste they generate, and we cannot control what we do not measure. Waste is that rare health care outcome for which no one is responsible and no data is recorded. Sustainability metrics are not recorded and do not drive any key performance indicators.

A reusable device is sold once; a disposable device creates recurring revenue. This economic reality drives industry investment in R&D and marketing. Breakthrough devices have unquestionably advanced medicine, but incremental variations are more often marketed as the newest and greatest — at the environmental cost of additional R&D, manufacturing, transportation, packaging, and disposal, even when a device goes unused. Our own entanglement plays a role. Advisory boards, consulting agreements, honoraria, and sponsored courses, while not inherently inappropriate, can create strong advocacy for newer devices, while restraint rarely has an equally organized voice.

Industry-sponsored studies, reviews, and opinion pieces about devices often outnumber unbiased literature. Some of the recommendations about devices also come from private, self-governed, standard-setting organizations whose membership includes device manufacturers and experts with ties to the industry. Both cursory manual research and large language models (such as ChatGPT, Gemini, and Claude) pick up on the sheer volume of this sponsored literature. All this drives the narrative toward practices that are lucrative for the industry and convenient for the staff, but unsustainable for the health system and society. As more endoscopy units adopt these practices, they become "standards of practice," forcing more endoscopy units to follow.

An example is the increasing number of endoscopy units switching from reusable to single-use EKG leads and endoscopy buttons. Internet searches and large language models cite numerous industry-written or sponsored articles claiming these reduce infection risk, despite no evidence to support this. A common theme is highlighting residual microbial contamination on equipment surfaces without demonstrating that it leads to infection.

Sustainability is a strategic and business imperative, not an option

lives. First, we must change our mindset. Negative externalities should not be ignored for convenience. Second, follow the available evidence (e.g., tap water is safe for irrigation, reusable EKG leads do not increase infection risk). Third, question the narrative (e.g., contamination does not mean infection, conflicts of interest among authors and sponsors). Fourth, move from passive observation to advocacy for sustainability (e.g., proper disposal of endoscopy accessories, use of reusable equipment when feasible). This also includes sending a message to device manufacturers to promote reuse and recycling. Finally, reduce unnecessary procedures, biopsies, and interventions. Many sustainable interventions offer sub-stantial financial benefits, and these should be shared with management. A few sustainability practices are given in Table 1.

Sustainability is *bonum* in se, or intrinsically good. Every resource we waste is one that cannot aid those in need. Our silence and inaction may have contributed to unsustainability, but we can show that we are bigger than that by choosing to be part of the solution.

Dr. Agrawal is a gastroenterologist at Premier Health and professor and chair of medicine at Wright State University, Dayton, Ohio.

Dr. Tang is a gastroenterologist and assistant professor of medicine at Dell Medical School, University of Texas at Austin.

Practicing gastroenterology and endoscopy in resource-poor settings

By Jehovan Fairclough, MBBS, MD, FRCP, FEBGH, and Melissa Arthurs-Wadsworth, BSc, MBBS, DM

There is great demand for gastroenterology care and gastroenterologists across the Caribbean, including Jamaica. Currently, Jamaica has 11 adult gastroenterologists and one pediatric gastroenterologist serving a population of over 2.8 million people. This stands in sharp contrast to the United States, where there are 4.6 gastroenterologists per 100,000 people — roughly one active specialist per 20,000 people — nearly all of whom have access to a dedicated endoscopy suite.

Beyond the sheer shortage of manpower, we face obstacles common to many developing nations: underdeveloped endoscopy infrastructure, limited capacity to build out new endoscopy units, and inconsistent access to supplies and equipment. Work is ongoing toward a national framework that would enable equitable access to care and reliable support services such as radiology, pathology, hepatobiliary surgery, and colorectal surgery. These realities directly shape our approach to patient care, where the focus remains on delivering the highest quality care possible within existing practice limitations.

“These realities directly shape our approach to patient care, where the focus remains on delivering the highest quality care possible within existing practice limitations.”

Performing advanced procedures such as endoscopic retrograde cholangiopancreatography (ERCP) in low- and middle-income countries like Jamaica presents a distinct set of challenges: a limited specialized workforce, financial and resource constraints, and delayed or late clinical presentations among the patients we serve.

Currently, only two formally trained advanced endoscopists serve the entire island of Jamaica. This acute workforce shortage places an immense burden on existing specialists, limits training opportunities, and creates severe bottlenecks in service delivery for a population whose need for complex biliary interventions continues to grow.

Compounding these structural deficits is a pattern of late clinical presentation. Driven by the insidious onset of disease — particularly biliary malignancies — along with poor health-seeking behaviors, patients frequently present with advanced pathology and significant physiological instability. These delayed presentations heighten technical difficulty, narrow the therapeutic window, and can elevate procedural risk.

Practice considerations

We place strong emphasis on our broad referral network, encouraging referring physicians to provide detailed clinical information with each gastroenterology consultation request. This allows for appropriate and equitable triage of patients.

In an era of rapid technological advancement, including the evolving role of artificial intelligence, we continue to rely on excellent clinical skills — thorough history taking, careful clinical examination, and judicious selection of appropriate testing. This tailored approach minimizes unnecessary, and often costly, testing without compromising the quality of patient care.

We actively foster close relationships with colleagues, allowing for open discussion of best practices appropriate to our local setting and consistent with accepted standards of care.

Critical, long-standing, and emerging global partnerships — with international GI societies, GI device companies, NGOs, and nonprofit organizations — support education and training, equipment and supply donations, and ongoing maintenance. These collaborations are actively pursued and have contributed significantly to the delivery of care in our local setting.

Procedural cost considerations

In a resource-poor setting, ensuring adequate indications for procedures and remaining creative and cost-conscious are essential to reducing costs.

This begins with discussion among referring colleagues, review of prior endoscopies and imaging, and consideration of previous procedural challenges. Cases requiring expert input are reviewed at our multidisciplinary meetings, where the optimal care pathway is determined.

Careful intraprocedural assessment guides the selection of appropriate strategies and disposables when intervention is required. For example: using a single snare rather than both a snare and biopsy forceps for multiple polypectomies; taking time to select the appropriately sized snare and ancillary tools for large polyp resections; carefully assessing stricture length and characteristics to guide stent selection; and performing single-session procedures for removal of multiple stones. These practices are important in minimizing procedural cost, and these skills are also taught to our gastroenterology fellows.

The use of noninvasive testing, and avoidance of unnecessary biopsies for histological assessment, is carefully considered where appropriate. Rapid urease testing, stool antigen testing, or urea breath testing for *Helicobacter pylori* is one such example: in low-risk patients, this strategy not only reduces cost but also helps bridge the gap created by long wait times for endoscopic procedures that may not be necessary to guide treatment.

Health care system considerations

The considerations discussed above reflect our day-to-day practical approach to care. We also recognize that policy change at the regional and national level is needed to address several ongoing systemic issues.

Improving health infrastructure throughout the country — building and strengthening facilities capable of delivering gastroenterology and endoscopy care at the community level — is essential. This would decentralize basic gastroenterology care away from urban centers and improve both access and efficiency. Studies to assess population needs, paired with a stepwise plan to support formal gastroenterology training and increase the number of specialists, will further improve access to quality care.

Local gastroenterology groups and cross-territory consortia are now being established to provide data-driven regional and national guidance on relevant systemic changes. These efforts will be pivotal in bridging existing gaps as we continue to deliver and advance the practice of gastroenterology.

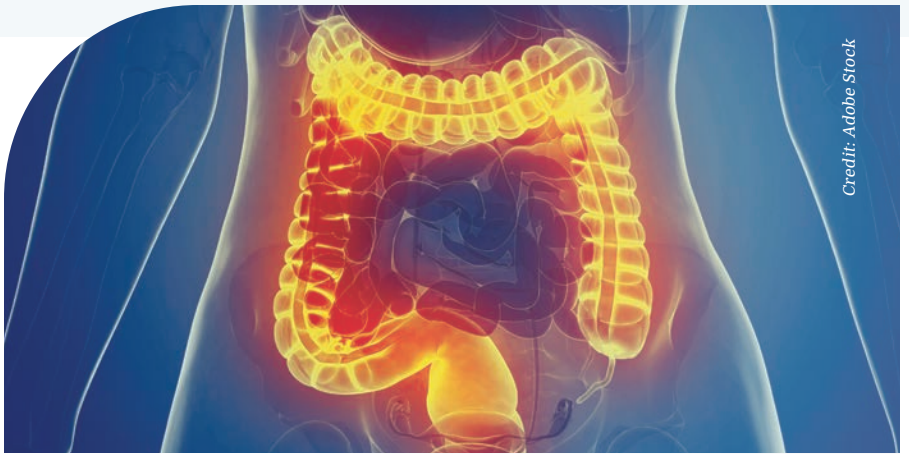
Dr. Fairclough is a gastroenterologist and interventional endoscopist at the University Hospital of the West Indies, Mona, Jamaica.

Dr. Arthurs-Wadsworth is a first-year gastroenterology fellow at the University Hospital of the West Indies, Mona, Jamaica.

Rome V criteria may miss some IBS cases in secondary care

New validation study found Rome V criteria were less sensitive than earlier Rome definitions in a UK secondary-care IBS clinic.

By Doug Brunk


Credit: Adobe Stock

The newly introduced Rome V criteria for irritable bowel syndrome may miss about one-third of patients who would meet a clinical reference standard for irritable bowel syndrome (IBS), according to a diagnostic accuracy study conducted in a UK secondary-care clinic. The diagnostic accuracy study included consecutive adults aged 16 years and older referred with suspected IBS to a specialist IBS clinic at Leeds Teaching Hospitals NHS Trust, Leeds, UK, from Sept. 22, 2016, to June 18, 2024.

The findings, published in *The Lancet Gastroenterology & Hepatology*, represent the first independent validation of the Rome V criteria since their introduction in May 2026. Although the revised criteria were intended to better distinguish irritable bowel syndrome (IBS) from centrally mediated abdominal pain syndrome, the investigators found that they identified a different group of patients than the Rome III and Rome IV criteria and excluded many patients who would likely still be diagnosed with IBS in routine clinical practice.

"IBS remains a clinical diagnosis," first author Kyle Staller, MD, MPH, of the division of gastroenterology at Massachusetts General Hospital and Harvard Medical School, Boston, told GI & Hepatology News. "The Rome criteria are valuable because they help us standardize that diagnosis, but they are not a substitute for clinical judgment. Rome V is an important step in the continuing evolution of IBS diagnosis, but our findings suggest that some refinement may be needed, particularly around how we separate IBS from continuous abdominal pain syndromes. For patients, the diagnosis has real meaning. It validates the symptom pattern, reduces the impulse toward endless testing, and allows us to focus on treatments that can improve quality of life."

Dr. Staller and colleagues evaluated the diagnostic performance of the Rome V criteria in 726 consecutive adults referred to a UK specialist clinic with suspected IBS between 2016 and 2024. Before undergoing guideline-recommended testing to rule out organic gastrointestinal disease, patients completed standardized symptom questionnaires. The investigators performing the diagnostic evaluations were blinded to the questionnaire results. The reference standard defined IBS as lower abdominal pain or discomfort associated with changes in stool frequency or stool form in patients without evidence of organic gastrointestinal disease after standardized testing. The investigators then compared the diagnostic performance of the Rome V criteria with that of the Rome IV and Rome III criteria using this reference standard.

Among the 726 patients with complete Rome V data, 417, or 57%, met the new diagnostic criteria. However, 590 patients met the reference standard for IBS, and only 390 of them also met the Rome V criteria, resulting in a sensitivity of 66%. The Rome V criteria had a specificity of 80%. By comparison, the Rome IV criteria achieved a sensitivity of 79% and a specificity of 81%, while the Rome III criteria had a sensitivity of 88% and a specificity of 75%.

The main reason patients were missed was the new Rome V requirement that abdominal pain not be continuous. Among the 200 patients who met the reference standard but did not meet the Rome V criteria, 71% were excluded for reporting abdominal pain every day of the week.

Agreement between the Rome V criteria and earlier diagnostic definitions was also limited. Agreement with the Rome III and Rome IV criteria ranged from fair to moderate, suggesting that the new criteria identify a different group of patients than the earlier versions.

Dr. Staller said the current analysis did not use the official Rome V questionnaires, which are now available for use in research settings. "Some subtle differences between the questionnaires used in the current study and the official questionnaires — particularly in regard to the definition of continuous abdominal pain—may affect the reported performance of the Rome criteria," he said. "Nevertheless, these findings may have important implications for the way in which these new criteria are applied."

Adding the Rome V supportive criterion that abdominal pain or discomfort in women should not occur only during menstruation had little effect on overall diagnostic performance. Only 11% of women who met the Rome V criteria reported symptoms exclusively during their menstrual periods. Including this criterion slightly improved specificity but reduced sensitivity further.

Patients who met the Rome V criteria also differed clinically from those identified by the earlier definitions. Compared with patients who met the Rome III or Rome IV criteria, they had lower IBS Severity Scoring System scores, indicating milder disease on average. They also reported lower levels of anxiety, depression, and extraintestinal somatic symptoms, suggesting that the Rome V criteria may preferentially identify patients with less severe illness. The authors suggested the criteria might perform better in primary care than in a secondary-care referral setting, but emphasized that this has not yet been demonstrated.

Only about 5% of patients who met any of the three Rome criteria were ultimately found to have an organic gastrointestinal disease after diagnostic testing. The most common alternative diagnosis was bile acid diarrhea, followed by exocrine pancreatic insufficiency, microscopic colitis, and Crohn's disease.

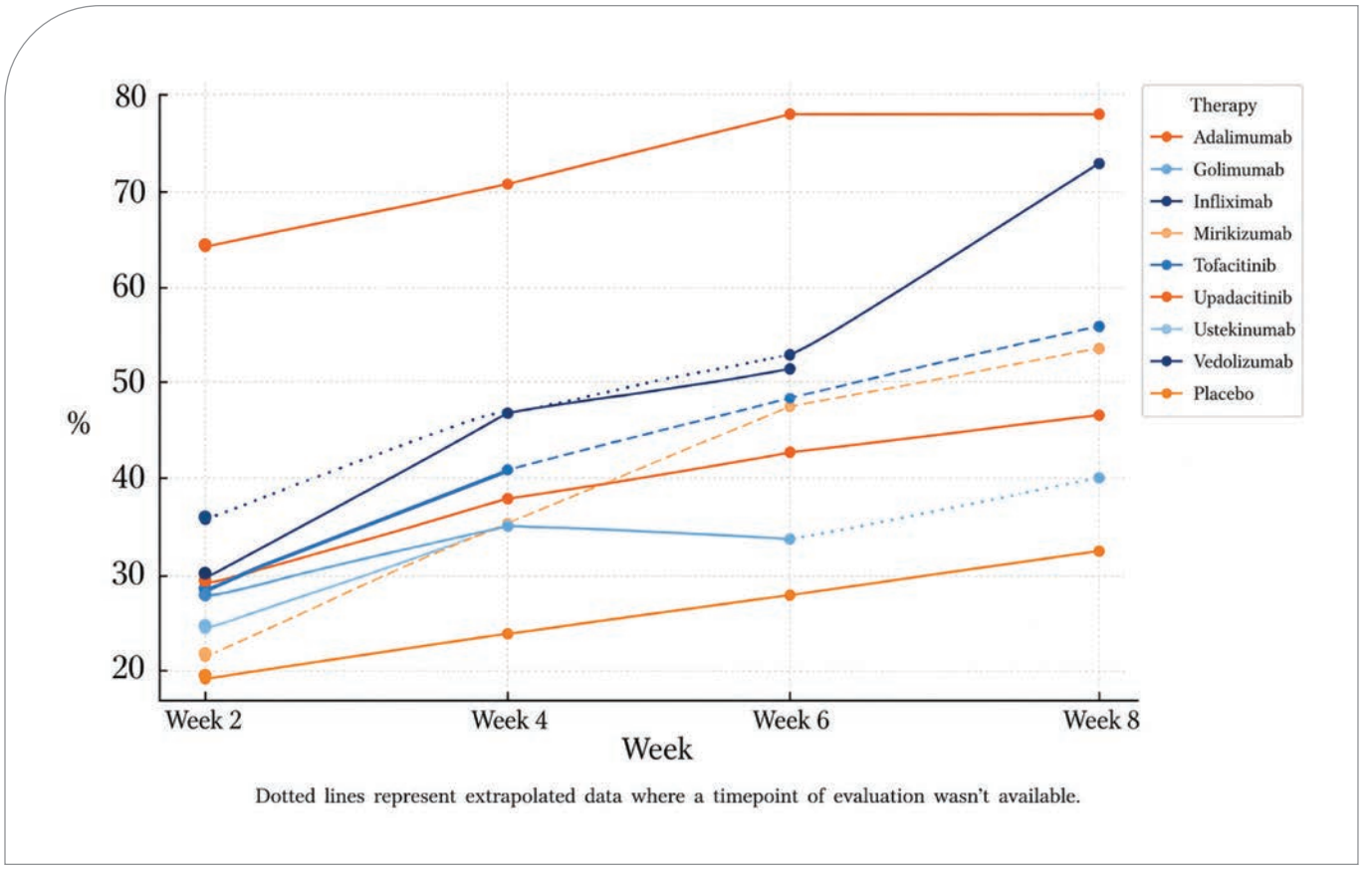
For clinicians, the findings suggest that patients should not be considered unlikely to have IBS simply because they do not meet the Rome V criteria, particularly if they have continuous abdominal pain.

Dr. Staller reported research support from Ardelyx and consulting relationships with AbbVie, Ardelyx, Atmo, Ferring, Gemelli, Laborie, Mahana, Mindset Health, Salix, and Takeda. The remaining authors reported no competing interests.

Upadacitinib, infliximab showed fastest symptom relief in ulcerative colitis, analysis found

A post hoc analysis suggests onset of action may help guide advanced therapy selection in moderate to severe ulcerative colitis.

By Meg Barbor



Time to achieve PRO-2 response among biologic-naïve participants. Figure courtesy of *Clinical Gastroenterology and Hepatology.*

Upadacitinib and infliximab showed the fastest early symptom relief among biologic-naive patients with moderate to severe ulcerative colitis, according to a post hoc analysis of individual patient-level data from 11 randomized trials published in *Clinical Gastroenterology and Hepatology.*

The analysis included 3,573 biologic-naive patients with moderate to severe ulcerative colitis who received standard induction doses of infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, mirikizumab, tofacitinib, upadacitinib, or placebo. Investigators compared early symptom improvement using Patient-Reported Outcome-2 (PRO-2) response, defined as at least a 50% reduction in stool frequency and rectal bleeding scores at week two. Infliximab was used as the active comparator in adjusted analyses.

"The biggest takeaway is that there's a clear hierarchy when it comes to how fast these drugs provide symptom relief," said senior author Neeraj Narula, MD, MPH, FRCPC, of McMaster University, in an interview with *GI & Hepatology News*. "Upadacitinib and infliximab are the clear frontrunners for rapid onset, showing significant patient-reported improvement by week two, though many other therapies definitely catch up by the end of induction."

Rapid response favored upadacitinib and infliximab

At week two, upadacitinib had the highest PRO-2 response rate, at 65.0%, followed by infliximab at 36.5%. Response rates for the other active therapies ranged from 24.9% with mirikizumab to 31.1% with vedolizumab, compared with 20.4% with placebo.

In adjusted analyses, upadacitinib was the only therapy associated with significantly higher odds of week two PRO-2 response compared with infliximab (adjusted odds ratio, 3.57; 95% CI, 2.40–6.20).

By the end of induction, upadacitinib and infliximab continued to show the highest PRO-2 response rates, at 79.0% and 72.6%, respectively. Upadacitinib showed no significant difference from infliximab in adjusted analyses at postinduction, whereas the other active therapies had significantly lower odds of response.

Neeraj Narula, MD, MPH, FRCPC

"The biggest takeaway is that there's a clear hierarchy when it comes to how fast these drugs provide symptom relief."

Clinical relevance: matching therapy to urgency

The study's clinical relevance, according to the authors, lies in matching treatment choice to the urgency of symptom control. For patients with severe symptoms or near-term hospitalization risk, rapid-onset options may be especially important. For more stable patients, the authors noted that therapies with more gradual onset may still be appropriate when safety profile, route of administration, convenience, or patient preference weigh more heavily.

"Clinicians can use this data to tailor treatment directly to how urgent a patient's situation is," Dr. Narula said. "If a patient is suffering severely and we need to keep them out of the hospital right now, upadacitinib or infliximab are the go-to options; if their disease is more stable, we can comfortably opt for therapies with a more gradual onset but perhaps a different safety or convenience profile."

Response and remission diverged

At week two, infliximab had the highest PRO-2 remission rate, at 34.9%, while upadacitinib, despite having the highest early response rate, had a week two remission rate of 19.7% and lower odds of remission compared with infliximab.

The investigators suggested this may reflect rapid symptom reduction across a broad group of patients who had not yet reached the stricter remission threshold within 14 days. By week 8, ustekinumab and infliximab had the highest unadjusted PRO-2 remission rates, at 53.9% and 51.9%, respectively, although adjusted analyses showed no significant difference between ustekinumab and infliximab.

Limitations and next steps

The analysis had several limitations. Although the investigators harmonized endpoints across trials and adjusted for baseline covariates, the included trials differed in design, induction duration, and assessment timing. Residual confounding remains possible, and the findings may not fully generalize to patients treated in routine clinical practice. The study also focused on biologic-naive patients, so the results may not apply to patients with prior advanced therapy exposure.

"Moving forward, we really need prospective, real-world studies to see if these speed-of-onset differences directly translate into other meaningful IBD-related outcomes, such as fewer hospitalizations and less corticosteroid use," Dr. Narula said.

Dr. Narula holds a McMaster University AFP Clinician Researcher Award and has received honoraria from Janssen, AbbVie, Takeda, Pfizer, Sandoz, Novartis, Iterative Health, Innomar Strategies, Fresenius Kabi, Amgen, Organon, Eli Lilly, and Ferring.

Home calprotectin monitoring fails to reduce ulcerative colitis flares

Proactive home monitoring alone didn't prevent flares, but the authors say pairing it with a standardized escalation protocol warrants further study.

By Doug Brunk

Routine home monitoring of fecal calprotectin every two months did not reduce symptomatic flares in patients with ulcerative colitis (UC) in remission compared with standard care, according to a multicenter randomized trial. However, patients whose treatment was adjusted after persistently elevated fecal calprotectin levels experienced numerically fewer flares, suggesting that biomarker monitoring may be more effective when elevated results prompt a predefined treatment change.

The findings, published in *Gastroenterology*, address a longstanding question about whether proactive biomarker monitoring can prevent relapse before symptoms appear. Fecal calprotectin, a marker of intestinal inflammation, often rises months before a clinical flare, and current guidelines recommend periodic testing for patients with UC who are in symptomatic remission. Although elevated fecal calprotectin levels have been linked to an increased risk of relapse, it has remained unclear whether frequent home testing improves patient outcomes.

"Home-based fecal calprotectin testing strongly correlates with lab-based ELISA testing, and high rates of patient acceptance have been reported with its use," wrote the investigators, who were led by first author Gregory Rosenfeld, MD, of the IBD Centre of BC, Vancouver, Canada.

For the trial, known as PROMOTE UC, researchers enrolled 716 adults with UC in symptomatic remission at 14 centers in Canada and Australia between November 2018 and December 2022. Participants were randomly assigned to standard care or home fecal calprotectin testing every two months for up to 18 months using a smartphone-based test. Patients with fecal calprotectin levels of at least 250 µg/g repeated the test within two weeks. Decisions about changing treatment were left to the treating physician. The primary endpoint was time to symptomatic flare.

After excluding patients lost to follow-up before receiving any intervention, the modified intention-to-treat analysis included 611 patients: 308 assigned to standard care and 303 to home monitoring. The average age was 42 years, 47% were men, and patients had lived with UC for an average of 11 years. About 45% were receiving advanced therapy at baseline. Disease extent and baseline fecal calprotectin levels were similar between the two groups.

By the end of follow-up, 32% of patients in both groups experienced a symptomatic flare, with 97 flares in the standard-care group and 96 in the home-monitoring group. Median time to flare was not reached in either group during the approximately 18-month follow-up. Flare rates were nearly identical, at about 0.29 flares per person-year, with no significant difference in the risk of flare between the two groups.

The findings were consistent across all predefined subgroup analyses. Home monitoring did not reduce flare risk in patients with proctitis, left-sided colitis, or pancolitis, or in those receiving either advanced therapies or conventional treatment. The results also did not change after excluding control patients who underwent fecal calprotectin testing outside the study protocol.

One unexpected finding emerged in a sensitivity analysis of patients' adherence to home testing. Nearly half of the patients assigned to home monitoring missed at least three scheduled tests. When investigators excluded patients after their third missed test, home monitoring was linked to a higher likelihood of symptomatic flare. The authors said this unexpected result may reflect detection bias, with more frequent testing leading patients to notice and report symptoms more often rather than indicating worse disease.

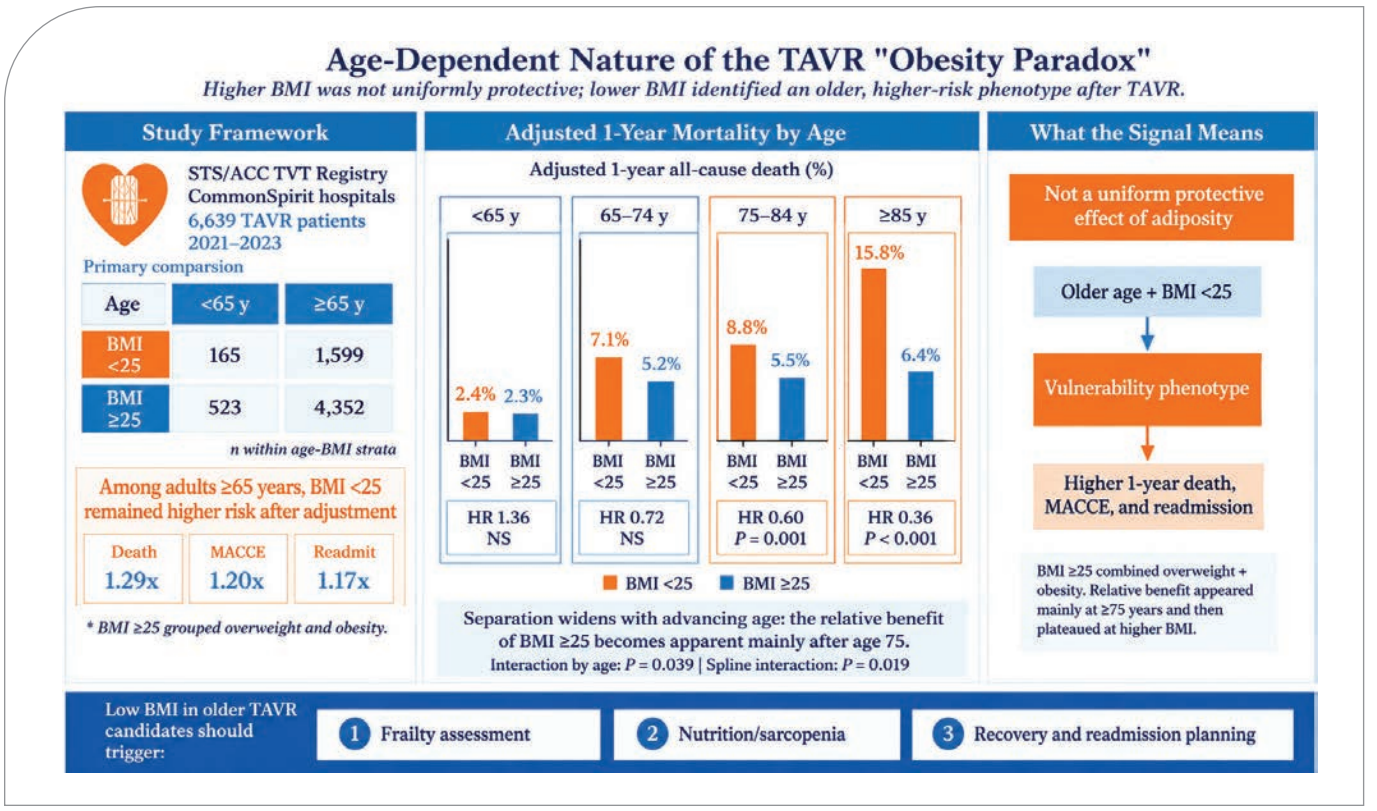
The study also examined whether patients with persistently elevated fecal calprotectin might benefit from earlier treatment changes. During follow-up, 88 patients developed confirmed elevations after initially having levels below the treatment threshold. Of those patients, 44% had their treatment changed at least two weeks before the end of the study. Symptomatic flares occurred in 49% of patients whose treatment was changed compared with 55% of those whose treatment remained the same, but the difference was not statistically significant.

None of the secondary outcomes differed between the groups. Rates of UC-related surgery and hospitalization were low and similar, as were new prescriptions for corticosteroids or advanced therapies, physician visits, medication adherence, quality-of-life scores, and missed work or school days. Patients successfully completed and transmitted 92% of home fecal calprotectin tests, although many missed multiple scheduled tests over time, highlighting the challenge of maintaining long-term adherence.

For practicing gastroenterologists, the findings suggest that routine biomarker monitoring alone may not improve outcomes if treatment decisions are left to physician discretion. Instead, the results support continued use of fecal calprotectin to assess inflammatory activity while underscoring the need for standardized treatment protocols when levels rise. "Our prospective study in patients with UC in symptomatic remission suggests that proactive monitoring without protocolized escalation utilizing home-based fecal calprotectintesting does not prevent symptomatic flares," the authors concluded. "Additional studies with clinician- and/or patient-directed protocolized interventions are needed to define the optimal use of proactive fecal calprotectinhome monitoring and the benefit of early intervention in patients with UC."

The investigators acknowledged several limitations. Symptomatic flares were not routinely confirmed by endoscopy, raising the possibility that some patients were misclassified. Treatment changes after elevated fecal calprotectin results were left to the treating physician rather than guided by a study protocol, making it difficult to assess the value of early intervention. Nearly half of patients in the home-monitoring group missed three or more scheduled tests, reducing the study's statistical power, and about 15% of enrolled patients were lost to follow-up before receiving the intervention. The trial also took place during the COVID-19 pandemic, which made patient retention and follow-up more difficult.

The study was funded by the Canadian Inflammatory Bowel Disease Research Consortium, Crohn's and Colitis Canada, Ferring, and Pfizer, with in-kind donations from AbbVie and Bühlmann. Dr. Rosenfeld and several coauthors reported research funding, consulting fees, speaker honoraria, or advisory relationships with pharmaceutical companies involved in IBD care.



Graphical abstract courtesy of *Gastroenterology*.

What it takes to build a gut-health service line

Two gastroenterologists on the staffing, billing, and payer decisions behind a nonendoscopic service line, and why both say it's worth the work.

Every gastroenterologist knows the patient: the scope is clean, the labs are unremarkable, and the symptoms persist. Meanwhile, colonoscopy reimbursement continues to decline, GLP-1 prescribing has made weight management and nutrition unavoidable in the GI clinic, MASLD occupies a growing share of the schedule, and patients are spending heavily on gut health outside the medical system. Together, those pressures are forcing practices to reconsider what GI care should include and how to make that care financially sustainable.

Supriya Rao, MD, DABOM, DABLM, and Vivian Asamoah, MD, spoke with *GI & Hepatology News* about what pushed them to build that care and what it actually required.

"The distinction between 'GI care' and 'metabolic and lifestyle care' is going to collapse over the next decade."

What made you decide to build out gut health, metabolic, and lifestyle care, when a GI practice's identity and economics have traditionally run through procedures?

Dr. Rao: Don't get me wrong — I still do a lot of procedures, and I'd say I'm still heavily skewed toward procedural volume. Early in my career, I was focused on getting really good at endoscopy and colonoscopy. But as time went on, I found myself scoping lots of patients with functional disorders, reflux symptoms, fatty liver — only to tell them everything is normal, all of your procedures are normal, while they were still having significant symptoms. The economics of running a GI practice run through the endoscopy suite and colonoscopy reimbursement, and there was this huge gap in care. Patients were coming to us saying, I'm having all these problems. We'd do the procedure. They were still having the problems. We didn't have a great plan for any of them.

So I started thinking: obviously something else is driving this. There have to be metabolic and lifestyle factors here. I convinced myself that in order to truly become better clinically, I needed to understand overall metabolic and gut health. In 2018, I went to my first obesity medicine conference — the Harvard Blackburn course — and I was shook. There was so much information there I knew nothing about. GI is a good springboard for this work: fatty liver and the metabolic diseases associated with it, plus reflux and functional disease, are all affected by obesity and lifestyle.

Dr. Asamoah: Endoscopy is essential. I perform procedures two to three days every week, and I take enormous pride in high-quality screening and diagnostics. But very early in practice, I kept running into the same wall: patients whose scopes and labs were normal, who were still sick. IBS, bloating, reflux, fatigue, food reactions, a lot of autoimmune conditions — and they really felt it was connected to their gut. All I could say was, your scope is normal. That's it. I could tell them what they didn't have, but I couldn't always tell them what to do next. Conventional GI training, even at the fellowship level, gave me very few tools for that conversation.

That gap is what pushed me toward integrative and functional medicine — not to replace conventional gastroenterology, but to extend it. Nutrition, the microbiome, sleep, stress physiology, and lifestyle are not adjacent to GI; they are GI.

What did it take to actually stand up a gut-health service line — staffing, referrals, and buy-in?

Dr. Rao: This began as a side interest, but I realized it was something that could benefit the practice if we could pilot it and then scale it. That took buy-in from my partners. I told them, look, I'm not going to be doing something in the wild, wild west — I'm going to get board certified; I'm going to be able to say I understand the metabolic consequences of all these things. You don't necessarily need to get board certified, but I felt I had to, otherwise I wasn't legit. I had to demonstrate that obesity medicine and lifestyle medicine weren't some soft add-on, but a clinical necessity that could also be financially viable.

Over time I started flirting with the idea of shared medical appointments — seeing 15 to 20 patients in a group, but being able to spend an hour with them and dig deeper. People have questions like, how much protein should I be eating? Should I be taking some peptide I got off the internet from a gym bro? Those are things we don't have time to dive into in a regular GI appointment, but we can spend 10 or 15 minutes on them in an hour-long shared appointment — and one person's question is usually somebody else's question too. The revenue on that was a no-brainer for my partners.

Dr. Asamoah: My situation is different from the typical group practice, and that's worth being honest about. I built Houston Gastro Institute as an independent, physician-owned practice more than a decade ago, so I don't answer to a hospital, to private equity, or to an institution. I didn't need partner buy-in. What I needed was patient buy-in and payor reality-testing, and those turned out to be the harder and more instructive problems.

The staffing piece came first. A nonendoscopic service line lives or dies on the team around the physician. We invested in four superb registered dietitians and trained advanced practice clinicians, and we built structured programs rather than one-off counseling visits — group nutrition visits, and defined programs for gut health and restoration, including what we call our Leaky Gut Program. The physician stays central, and patients are under my direct oversight, but the dietitian-led components are what make the model scalable and affordable.

Eventually I separated the work into two entities. The insurance-based GI practice handles conventional gastroenterology, including the nutrition services payors do reimburse — group nutrition visits and medical nutrition therapy among them. The integrative and functional medicine practice operates on a direct-pay model, because much of that work — extended visits, advanced testing interpretation, longitudinal coaching — simply isn't reimbursed adequately. I'd rather be transparent about that than pretend the current payment system supports this care, because it largely doesn't.

Referrals were the easiest part, honestly. Once patients experienced this model, they told other patients and their doctors.

Left: Supriya Rao, MD, DABOM, DABLM

- Managing partner, Integrated Gastroenterology Consultants, the largest independent private GI practice in Massachusetts; clinical assistant professor, Tufts University School of Medicine
- Board-certified in internal medicine, gastroenterology, obesity medicine, and lifestyle medicine.

Right: Vivian Asamoah, MD

- Founder & CEO, Houston Gastro Institute and Dr. Vivian Asamoah PLLC; Medical Director, Zazen Surgery Center- AAAHC
- Board-certified gastroenterology and hepatology, fellowship-trained at Johns Hopkins, certified in Integrative and Functional medicine (IFMCP).
- More than 12 years running an independent, physician-owned practice.

What's the through-line that connects gut, weight, metabolism, and lifestyle into one program rather than separate add-ons?

Dr. Rao: When I think about it, I think about the gut-brain-microbiome axis. These are not separate systems; they're all integrated into one, and gastroenterologists really need to capitalize on that. We are perfectly poised to take care of these patients.

Excess weight, excess adiposity, and metabolic syndrome drive systemic inflammation, and when your body has that inflammation, it manifests in the gut as changes in motility — constipation, diarrhea, IBS-type symptoms — as dysbiosis, as abdominal pain and visceral hypersensitivity, as fatty liver. We can't effectively treat those issues unless we're looking at insulin resistance and cholesterol. We can't manage severe IBS without looking at what a person is eating. Are they exercising? Are they sleeping well? Are they stressed out all the time? Treating those as separate silos ignores true physiology.

We still individualize it — it's not one-size-fits-all — but we're looking at the patient as a whole person, as opposed to, we're here to do your EGD and colonoscopy, and once that's done, go back to your PCP.

Dr. Asamoah: The through-line is that these are not separate organ systems with separate problems — they're one interconnected physiology. The gut microbiome influences metabolic signaling, satiety hormones, inflammation, and even mood. Insulin resistance and fatty liver disease walk into a GI clinic every single day. Sleep apnea has direct GI consequences. You cannot meaningfully treat MASLD without addressing metabolism, and you cannot address metabolism without addressing diet, sleep, movement, and stress.

In our practice, that thinking is organized under a framework I call The Complete Gut Approach: Explore, Investigate, Restore, Re-Center. Explore is a deep history — food, sleep, stress, medications, life context. Investigate is appropriate testing, both conventional and, where evidence supports it, advanced functional testing. Restore is targeted intervention: medical, nutritional, and lifestyle. Re-Center is maintenance, helping the patient sustain change rather than cycling back.

What I'd push back on is the idea that you can put it all in one bucket and develop one big program that everybody goes into. We're moving toward an evolution of care that is very personalized. Look at the disparities by gender alone — a woman's GI tract is very different from a man's, in terms of nutrition and in terms of where she is in her life and her health span. Is she perimenopausal? To bundle everyone into one gut health program that's going to fix everyone under one model, I don't think that will work. There are certain themes you can teach — whole foods, avoid ultra-processed foods — but beyond that, there has to be personalization of care.

How sustainable is a gut-health and metabolic service line inside a GI practice, and what would make it easier to build?

Dr. Rao: The current fee-for-service model still disproportionately rewards procedures and procedural volume over what you could call cognitive or lifestyle care — sitting with a patient and talking to them at length. What would make it easier is clearer reimbursement pathways and broadened insurance coverage for the medications. One thing that's crazy to me is that nutritionists often aren't covered by insurance. You're willing to pay for a gastric bypass for this patient, but not a nutritionist? That's beyond me.

Dr. Asamoah: I'll be direct: under current reimbursement, a nonendoscopic line is sustainable, but not on fee-for-service physician time alone. What makes ours work is a mix of models — reimbursed services like group nutrition visits and dietitian-delivered medical nutrition therapy, team-based care that doesn't require physician time for every touchpoint, structured self-paced patient programs, and a direct-pay integrative and functional medicine arm for the work insurance won't cover.

The group model is the key to the economics. If you onboard 20 or 30 patients into one group and you're billing an hour for 30 patients, that's a whole day's worth of visits done in an hour. And obesity is an epidemic, so you will have the patients. You can build around it — fatty liver evaluation with elastography, blood work every three months for patients with metabolic syndrome to document what you're reversing.

What would make it easier? Three things. First, reimbursement that reflects cognitive and preventive work: adequate payment for prolonged visits, intensive lifestyle intervention, and dietitian services across more diagnoses. Second, value-based arrangements — MASLD, IBS, and obesity-related disease are exactly where prevention saves money downstream, and ACO and risk-sharing models could recognize that. Third, training. Most GI fellows graduate with almost no formal education in nutrition, the microbiome, or lifestyle medicine, which means every practice that wants to do this has to build the expertise from scratch.

I'd also caution against overpromising. This is not a get-rich model, and it shouldn't be sold that way. It's a patient-retention, patient-outcome, and physician-fulfillment model that can be made financially sound with deliberate structure.

What would you tell a GI group that wanted to build a gut-health service line, and where do you see this model heading?

Dr. Rao: If you're interested in doing something like this, you need to start with a champion. For my group, that was me. In 2019, it seemed fringe — treating obesity, seeing patients for it. Now everyone knows somebody who's been on a GLP-1 in some fashion. You're not trying to force a practice to completely change its model overnight. Identify one person who's passionate about metabolic health, give them the time and bandwidth to get certified if that feels necessary, and build a pilot.

I started with a pilot shared medical appointment of 15 people in September 2022. It was successful not just in the sense that patients loved it, but in the metrics — decreases in blood pressure, decreases in hemoglobin A1c, improvement in the quality-of-life scores we gave patients. And the billing worked out. We've now taken care of thousands of patients in that program.

I obviously love doing procedures. But with reimbursements for colonoscopy going down a little every year, I don't think the practices that thrive in the coming years are going to be the ones relying solely on procedures. They need to be comprehensive digestive and metabolic health destinations — places where people go because they feel heard.

Dr. Asamoah: Start smaller than you think. Don't announce an "integrative program." It starts with great collaborations — one good registered dietitian in your area whose philosophy aligns with yours, embedded in your clinic, and a GI psychologist you can align with. Then build one structured offering around one condition you see constantly, whether that's IBS, MASLD, or post-infectious gut dysfunction. Not all three at once; you can't lump those together and call it gut health, because your outcomes will be different. Measure the outcomes. Let the results build the case before you scale. It could be one, two, three people, and in a year or two it could be a full-fledged team with different groups and programs.

Second, protect the science. Integrative and functional medicine has a credibility problem in some corners of our field, sometimes deservedly. Nutrition, lifestyle, integrative, functional, holistic — whatever you want to call it, it's still medicine, and I believe it should be led by physicians who have studied medicine. It must be evidence-informed. Hold this work to the same evidentiary standard as everything else we do, be willing to say "we don't have data for that," and keep the physician clinically accountable for the whole program.

As for where this is heading: I think the distinction between "GI care" and "metabolic and lifestyle care" is going to collapse over the next decade. MASLD is becoming the leading indication for liver transplant. The microbiome is moving from research curiosity to clinical tool. The practices that build the team and the framework now won't be adding a service line — they'll be positioned for what gastroenterology is becoming.

Lightning round

Tell us about a mentor and what you learned from them.

SR: He told me to always be curious and to continue to question when the picture is not clear.

VA: Dr. Gerard Mullin, a phenomenal attending physician at Johns Hopkins, was my mentor. He was one of the first people to show me that a gastroenterologist could also be an integrative medicine physician and that those two worlds didn't have to be in conflict. He was a pioneer well ahead of his time.

Favorite way to spend a day off?

SR: Being active all day and cooking a great meal at the end of it.

VA: With my family, doing anything, even just sitting at home. Talking, laughing, just being together is enough.

What topic could you give a 30-minute speech on with no preparation?

SR: How to incorporate obesity and lifestyle medicine in to a GI practice.

What advice would you wish you could give your younger self?

VA: Remove the fear. Nothing should lead to regret, because if it doesn't work out, you are learning and gaining wisdom. And if it does, you are succeeding into happiness. Either way, you come out ahead.

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