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GI & Hepatology News

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June 2026 | news.gastro.org



By Doug Brunk

Gluten found to trigger immune response at very low doses

Even trace exposures below labeling standards activate immune pathways while symptoms fail to signal risk.

Very small amounts of gluten can trigger measurable immune activation in patients with celiac disease, even at doses below current international food-labeling thresholds, according to the results of a randomized controlled trial published in *Gastroenterology*.

In a double-blind, placebo-controlled dose-response study of

51 adults with biopsy-confirmed celiac disease on a gluten-free diet, investigators in Australia found that doses as low as 3 mg induced immune responses in some patients. Symptoms did not reliably distinguish gluten exposure from placebo.

For the trial, researchers evaluated single-dose gluten

challenges ranging from 1,000 mg down to 1 mg. Participants at a single tertiary center in Brisbane underwent three challenges each, spaced 4 weeks apart, with immune activation defined as at least a twofold increase in serum interleukin-2 (IL-2) within 6 hours, reported A. James M. Daveson, MBBS, Director of

Early-onset CRC deaths rising fast, analysis finds

Early-onset colorectal cancer is no longer rare — it's becoming deadly. New US data show rectal cancer deaths are rising fastest among adults under 45, especially in Hispanic and White populations, with delayed diagnosis a factor. Experts warn symptoms like rectal bleeding and bowel changes are often dismissed, allowing cancers to advance unchecked.

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Credit: AdobeStock.com

the Celiac Disease and Immune Health Research Program at Wesley Research Institute in Auchenflower, Queensland, Australia, and colleagues.

Dose-dependent immune activation

Gluten exposure produced a clear dose-response relationship in IL-2 levels, peaking at 4 hours. At higher doses, most patients showed immune activation: 83% responded at 610 mg and 56% at 1,000 mg. However, responses were also observed at lower doses, including 36% at 90 mg, 27% at 8 mg, and 17% at both 13 mg and 3 mg.

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Clinical practice update: New hemorrhoid care tips

A new AGA update says most hemorrhoids can be effectively diagnosed and treated right in the office using added fiber, simple lifestyle changes, and minimally invasive procedures — with surgery reserved only for more advanced cases.

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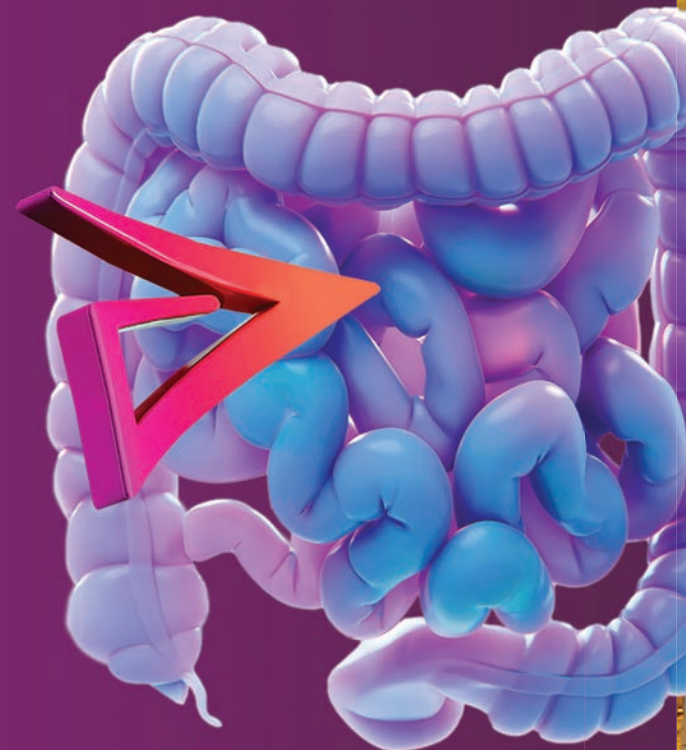


For adults with moderately to severely active ulcerative colitis (UC) or Crohn's disease.

Discover how the only gut-focused biologic*

for Crohn's and UC helps block certain inflammation-causing lymphocytes from entering the gut

*ENTYVIO specifically binds to the $\alpha 4 \beta 7$ integrin and blocks its interaction with MAdCAM-1, which is mainly expressed on gut endothelial cells.¹



IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ENTYVIO is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients.

WARNINGS AND PRECAUTIONS

- **Infusion-Related and Hypersensitivity Reactions:** Infusion-related reactions and hypersensitivity reactions, including anaphylaxis, dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate, have been reported. These reactions may occur with the first or subsequent infusions and may vary in their time of onset from during infusion or up to several hours post-infusion. If anaphylaxis or other serious infusion-related or hypersensitivity reactions occur, discontinue administration of ENTYVIO immediately and initiate appropriate treatment.
- **Infections:** ENTYVIO increases the risk for developing infections. Serious infections in clinical trials included anal abscess, sepsis (some fatal), tuberculosis (TB), salmonella sepsis, Listeria meningitis, giardiasis, and cytomegaloviral colitis. Postmarketing reports include systemic bacterial, fungal, viral, and parasitic opportunistic infections. Do not start ENTYVIO in patients with a clinically important active infection until resolved or adequately treated. In patients with chronic infection or history of recurrent infection, consider risks and benefits prior to ENTYVIO. Instruct patients to seek medical

advice if signs or symptoms of acute or chronic infection occur. If a serious infection develops or does not respond to therapy, monitor closely and do not administer ENTYVIO until resolved. *Tuberculosis:* Consider evaluating for TB prior to ENTYVIO. Do not administer ENTYVIO to patients with active TB. Before starting ENTYVIO, treat latent TB and consider anti-TB therapy in patients with a history of TB if adequate course of treatment cannot be confirmed. Monitor for active TB during and after ENTYVIO.

- **Progressive Multifocal Leukoencephalopathy (PML):** PML, a rare and often fatal opportunistic infection of the central nervous system (CNS), has been reported with systemic immunosuppressants, including another integrin receptor antagonist. PML typically only occurs in patients who are immunocompromised. One case of PML in an ENTYVIO-treated patient with multiple contributory factors has been reported. Although unlikely, a risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs or symptoms that may include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. If PML is suspected, withhold dosing with ENTYVIO and refer to neurologist; if confirmed, discontinue ENTYVIO dosing permanently.
- **Liver Injury:** There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO. ENTYVIO should be discontinued in patients with jaundice or other evidence of significant liver injury.



- **Immunizations:** Prior to initiating treatment with ENTYVIO, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving ENTYVIO may receive non-live vaccines and may receive live vaccines if the benefits outweigh the risks.

ADVERSE REACTIONS

The most common adverse reactions (incidence $\geq 3\%$ and $\geq 1\%$ higher than placebo) were: nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, pain in extremities, and injection site reactions with subcutaneous administration.

DRUG INTERACTIONS

Because of the potential for increased risk of PML and other infections, avoid the concomitant use of ENTYVIO with natalizumab products and with TNF blockers. Upon initiation or discontinuation of ENTYVIO in patients treated with CYP450 substrates, monitor drug concentrations or other therapeutic parameters, and adjust the dosage of the CYP substrate as needed.

INDICATIONS

ENTYVIO is indicated in adults for the treatment of:

- moderately to severely active ulcerative colitis (UC)
- moderately to severely active Crohn's disease (CD)

DOSAGE FORMS & STRENGTHS

- ENTYVIO Intravenous Infusion: 300 mg vedolizumab;
Subcutaneous Injection: 108 mg vedolizumab

Please see accompanying Brief Summary of Full Prescribing Information on adjacent pages.

MAdCAM-1=mucosal addressin cell adhesion molecule-1.

Reference: 1. ENTYVIO (vedolizumab) prescribing information. Takeda Pharmaceuticals.



Walk through the MOA and review clinical data of this biologic at [ENTYVIOHCP.com](https://www.entyviohcp.com)

If you are a Colorado prescriber, please see the Colorado WAC disclosure form at [Takeda.info/ENTYVIOCPricing](https://www.takeda.info/ENTYVIOCPricing).

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

Consult the Full Prescribing Information for complete product information.

ENTYVIO (vedolizumab) for injection, for intravenous use

ENTYVIO (vedolizumab) injection, for subcutaneous use

ENTYVIO PEN (vedolizumab) injection, for subcutaneous use

INDICATIONS AND USAGE

ENTYVIO is indicated in adults for the treatment of:

- moderately to severely active ulcerative colitis (UC).
- moderately to severely active Crohn's disease (CD).

CONTRAINDICATIONS

ENTYVIO is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients (such as dyspnea, bronchospasm, urticaria, flushing, rash and increased heart rate) [see *Warnings and Precautions*].

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions and Hypersensitivity Reactions

Infusion-related reactions and hypersensitivity reactions have been reported, including anaphylaxis, dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate [see *Adverse Reactions*]. These reactions may occur with the first or subsequent infusions of ENTYVIO and may vary in their time of onset from during infusion or up to several hours post-infusion.

If anaphylaxis or other serious infusion-related or hypersensitivity reactions occur, discontinue administration of ENTYVIO immediately and initiate appropriate treatment.

Infections

Patients treated with ENTYVIO are at increased risk for developing infections [see *Adverse Reactions*]. Serious infections reported in clinical trials include anal abscess, sepsis (some fatal), tuberculosis (TB), salmonella sepsis, Listeria meningitis, giardiasis, and cytomegaloviral colitis. Postmarketing cases of systemic bacterial, fungal, viral, and parasitic opportunistic infections have been reported.

Treatment with ENTYVIO should not be initiated in patients with a 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 ENTYVIO. During treatment with ENTYVIO, instruct patients to seek medical advice if signs or symptoms of clinically important acute or chronic infection occur. If a serious infection develops or an infection is not responding to standard therapy, monitor the patient closely. ENTYVIO should not be administered until the infection resolves.

Tuberculosis

Consider evaluating patients for TB infection prior to initiating treatment with ENTYVIO. Treatment with Entyvio should not be administered to patients with active TB infection. Initiate treatment of latent TB prior to administering ENTYVIO. Consider anti-TB therapy prior to initiation of ENTYVIO 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 ENTYVIO treatment.

Progressive Multifocal Leukoencephalopathy

PML, a rare and often fatal opportunistic infection of the central nervous system (CNS), has been reported with systemic immunosuppressants, including another integrin receptor antagonist. PML is caused by the John Cunningham (JC) virus and typically only occurs in patients who are immunocompromised. One case of PML in an ENTYVIO-treated patient with multiple contributory factors has been reported in the postmarketing setting (e.g., human immunodeficiency virus [HIV] infection with a CD4 count of 300 cells/mm³ and prior and concomitant immunosuppression). Although unlikely, a risk of PML cannot be ruled out.

Monitor patients on ENTYVIO for any new onset, or worsening, of neurological signs and symptoms. Typical signs and symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. The progression of deficits usually leads to death or severe disability over weeks or months. If PML is suspected, withhold dosing with ENTYVIO and refer to a neurologist; if confirmed, discontinue dosing permanently.

Liver Injury

There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO. In general, the combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that may lead to death or the need for a liver transplant in some patients. ENTYVIO should be discontinued in patients with jaundice or other evidence of significant liver injury [see *Adverse Reactions*].

Immunizations

Prior to initiating treatment with ENTYVIO, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving ENTYVIO may receive non-live vaccines (e.g., influenza vaccine injection) and may receive live vaccines if the benefits outweigh the risks. There are no data on the secondary transmission of infection by live vaccines in patients receiving ENTYVIO [see *Adverse Reactions*].

ADVERSE REACTIONS

The following topics are also discussed in detail in the Warnings and Precautions section:

- Infusion-Related Reactions and Hypersensitivity Reactions [see *Warnings and Precautions*]
- Infections [see *Warnings and Precautions*]
- Progressive Multifocal Leukoencephalopathy [see *Warnings and Precautions*]
- Liver Injury [see *Warnings and Precautions*]

Clinical Trials Experience

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

The data described below reflect exposure to intravenous ENTYVIO in 3,326 patients and healthy volunteers in clinical trials, including 1,396 exposed for greater than one year, and 835 exposed for greater than two years.

Intravenous Infusion

The safety data described in *Table 1* are derived from four controlled Phase 3 trials (UC Trials I and II, and CD Trials I and III); data from adult patients receiving open-label intravenous ENTYVIO treatment at Weeks 0 and 2 (prior to entry into UC Trial II and CD Trial III) and from Weeks 6 to 52 (non-responders at Week 6 of UC Trial I and CD Trial I) are included.

In these trials, 1,434 patients received ENTYVIO 300 mg intravenously for up to 52 weeks, and 297 patients received placebo for up to 52 weeks. Of these, 769 patients had ulcerative colitis and 962 patients had Crohn's disease. Patients were exposed for a mean duration of 259 days (UC Trials I and II) and 247 days (CD Trials I and III).

Adverse reactions were reported in 52% of patients treated with intravenous ENTYVIO and 45% of patients treated with placebo (UC Trials I and II: 49% with ENTYVIO and 37% with placebo; CD Trials I and III: 55% with ENTYVIO and 47% with placebo). Serious adverse reactions were reported in 7% of patients treated with intravenous ENTYVIO compared to 4% of patients treated with placebo (UC Trials I and II: 8% with ENTYVIO and 7% with placebo; CD Trials I and III: 12% with ENTYVIO and 9% with placebo).

The most common adverse reactions (reported by ≥3% of patients treated with intravenous ENTYVIO in the UC Trials I and II and CD Trials I and III combined group and ≥1% higher than in combined placebo group) were nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain and pain in extremities (*Table 1*).

Table 1. Adverse Reactions in ≥3% of Intravenous ENTYVIO-Treated Adult Patients and ≥1% Higher than in Placebo (UC Trials I and II* and CD Trials I and III*)

Adverse Reaction	ENTYVIO IV† (N=1434)	Placebo‡ (N=297)
Nasopharyngitis	13%	7%
Headache	12%	11%
Arthralgia	12%	10%
Nausea	9%	8%
Pyrexia	9%	7%
Upper respiratory tract infection	7%	6%
Fatigue	6%	3%
Cough	5%	3%
Bronchitis	4%	3%
Influenza	4%	2%
Back pain	4%	3%
Rash	3%	2%
Pruritus	3%	1%
Sinusitis	3%	1%
Oropharyngeal pain	3%	1%
Pain in extremities	3%	1%

* Data from patients receiving open-label intravenous ENTYVIO treatment at Weeks 0 and 2 (prior to entry into UC Trial II and CD Trial III) and from Weeks 6 to 52 (non-responders at Week 6 of UC Trial I and CD Trial I) are included.

† Patients who received ENTYVIO for up to 52 weeks.

‡ Patients who received placebo for up to 52 weeks.

Safety data for patients (n=279) in UC Trials I and II and CD Trials I and III who received intravenous ENTYVIO at Weeks 0 and 2 and were then randomized to placebo at Week 6 for up to 52 weeks, and for patients (n=416) in CD Trial II, a 10-week Crohn's disease trial, are similar to those listed in *Table 1*.

Infusion-Related Reactions and Hypersensitivity Reactions

Serious infusion-related reactions and hypersensitivity reactions including anaphylaxis have been reported following intravenous ENTYVIO administration in clinical trials [see *Warnings and Precautions*]. In UC Trials I and II and CD Trials I and III, one case of anaphylaxis [one out of 1,434 patients treated with intravenous ENTYVIO (0.07%)] was reported by a Crohn's disease patient during the second infusion (symptoms reported were dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate) and was managed with discontinuation of infusion and treatment with antihistamine and intravenous hydrocortisone.

In UC Trials I and II and CD Trials I and III, 4% of patients treated with intravenous ENTYVIO and 3% of patients treated with placebo experienced an infusion-related reaction (IRR). The most frequently observed IRRs in the patients treated with intravenous ENTYVIO (reported more than twice) were nausea, headache, pruritus, dizziness, fatigue, infusion-related reaction, pyrexia, urticaria, and vomiting (each of these adverse reactions occurred in <1% in all patients treated with intravenous ENTYVIO) and no individual adverse reaction reported occurred at a rate above 1%. These reactions generally occurred within the first two hours after the infusion and resolved with no treatment or following antihistamine and/or IV hydrocortisone treatment. Less than 1% of patients treated with intravenous ENTYVIO had IRRs assessed by the investigator as severe, and IRRs requiring discontinuation of study treatment occurred in <1%.

In clinical trials, for patients with mild IRRs or hypersensitivity reactions, physicians were allowed to pretreat with standard medical treatment (e.g., antihistamine, hydrocortisone, and/or acetaminophen) prior to next infusion.

Infections

In UC Trials I and II and CD Trials I and III, the rate of infections was 0.85 per patient-year in the patients treated with intravenous ENTYVIO and 0.7 per patient-year in the patients treated with placebo [see *Warnings and Precautions*]. The infections consisted primarily of nasopharyngitis, upper respiratory tract infection, sinusitis, and urinary tract infection. Two percent of patients discontinued intravenous ENTYVIO due to infections.

In UC Trials I and II and CD Trials I and III, the rate of serious infections was 0.07 per patient-year in patients treated with intravenous ENTYVIO and 0.06 per patient-year in patients treated with

placebo. Serious infections were more common in Crohn's disease patients than ulcerative colitis patients, and anal abscesses were the most frequently reported serious adverse reaction in Crohn's disease patients. Over 48 months, there was no increase in the rate of serious infections.

In controlled- and open-label long-term extension trials in adults treated with intravenous ENTYVIO, serious infections have been reported, including anal abscess, sepsis (some fatal), tuberculosis, salmonella sepsis, *Listeria meningitis*, giardiasis, and cytomegaloviral colitis.

In UC Trials I and II and CD Trials I and III, sepsis, including bacterial sepsis and septic shock, was reported in four of 1,434 (0.3%) patients treated with intravenous ENTYVIO and in two of 297 patients treated with placebo (0.7%). During these trials, two Crohn's disease patients treated with intravenous ENTYVIO died due to reported sepsis or septic shock; both patients had significant comorbidities and a complicated hospital course that contributed to the deaths. In an open label, long-term extension trial, additional cases of sepsis (some fatal), including bacterial sepsis and septic shock, were reported. The rate of sepsis in patients with ulcerative colitis or Crohn's disease receiving intravenous ENTYVIO was two per 1,000 patient-years.

In clinical trials, all patients were screened for tuberculosis. One case of latent, pulmonary tuberculosis was diagnosed during the controlled trials with intravenous ENTYVIO. Additional cases of pulmonary tuberculosis were diagnosed during the open-label trial. All of these observed cases occurred outside the United States (U.S.), and none of the patients had extrapulmonary manifestations.

Liver Injury

There have been reports of elevations of transaminase and/or bilirubin in patients receiving intravenous ENTYVIO [see *Warnings and Precautions*]. In UC Trials I and II and CD Trials I and III, three patients reported serious adverse reactions of hepatitis, manifested as elevated transaminases with or without elevated bilirubin and symptoms consistent with hepatitis (e.g., malaise, nausea, vomiting, abdominal pain, anorexia). These adverse reactions occurred following two to five intravenous ENTYVIO doses; however, based on case report information it is unclear if the reactions indicated drug-induced or autoimmune etiology. All patients recovered following discontinuation of therapy with some requiring corticosteroid treatment. In controlled trials, the incidence of ALT and AST elevations $\geq 3 \times$ ULN was $< 2\%$ in patients treated with intravenous ENTYVIO and in patients treated with placebo. In the open-label trial, one additional case of serious hepatitis was observed.

Malignancies

In UC Trials I and II and CD Trials I and III, malignancies (excluding dysplasia and basal cell carcinoma) were reported in six of 1,434 (0.4%) patients treated with intravenous ENTYVIO, including colon cancer (n=2), transitional cell carcinoma (n=1), breast cancer (n=1), carcinoid tumor of the appendix (n=1) and squamous cell carcinoma (n=1). Malignancy was reported in one of 297 (0.3%) patients treated with placebo (squamous cell carcinoma).

Malignancies (excluding dysplasia and basal cell carcinoma) observed during the ongoing open-label long-term extension trial included B-cell lymphoma, breast cancer, colon cancer, malignant hepatic neoplasm, malignant lung neoplasm, malignant melanoma, lung cancer of primary neuroendocrine carcinoma, renal cancer and squamous cell carcinoma. Overall, the number of malignancies in the clinical trials was small; however, long-term exposure was limited.

Subcutaneous Injection after Two Intravenous Doses of ENTYVIO

ENTYVIO was administered as a subcutaneous injection in adult patients with ulcerative colitis and Crohn's disease in double-blind, placebo-controlled clinical trials (SC UC Trial and SC CD Trial, respectively). Patients who achieved clinical response following two doses of ENTYVIO administered as an intravenous infusion at Week 0 and Week 2 were randomized 2:1 at Week 6 to ENTYVIO as a subcutaneous injection (N=106) or placebo (N=56) (SC UC Trial) and as subcutaneous injection (N=275) or placebo (N=134) (SC CD Trial).

The safety profile for up to 52 weeks of total treatment was similar between patients who were switched to ENTYVIO as a subcutaneous injection in SC UC and SC CD clinical trials and patients in UC and CD clinical trials who received ENTYVIO as an intravenous infusion (*Table 1*) except for injection site reactions, which were reported with subcutaneous ENTYVIO. Injection site reactions with subcutaneous ENTYVIO were reported in 10% (11/106) of patients in SC UC Trial, including injection site erythema, rash, pruritus, swelling, bruising, and hematoma. Injection site reactions with subcutaneous ENTYVIO were reported in 3% (8/275) of patients in SC CD Trial, including injection site erythema, pruritus, urticaria, pain, rash, and edema.

Live and Oral Vaccines

There are no data on the secondary transmission of infection by live vaccines in patients receiving ENTYVIO.

In a placebo-controlled study of healthy volunteers, 61 subjects were given a single intravenous ENTYVIO 750 mg dose (2.5 times the recommended dose), and 62 subjects received placebo followed by intramuscular vaccination with Hepatitis B surface antigen and oral cholera vaccine. After intramuscular vaccination with three doses of recombinant Hepatitis B surface antigen, those treated with intravenous ENTYVIO did not have lower rates of protective immunity to Hepatitis B virus. However, those exposed to intravenous ENTYVIO did have lower seroconversion rates and anti-cholera titers relative to placebo after receiving the two doses of a killed, oral cholera vaccine. The impact on other oral vaccines and on nasal vaccines in patients is unknown.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of ENTYVIO. 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 drug exposure.

Immune system disorders: Anaphylaxis [see *Warnings and Precautions*]

Gastrointestinal system disorders: Acute Pancreatitis

Respiratory, thoracic, and mediastinal disorders: Interstitial lung disease, pneumonitis.

DRUG INTERACTIONS

Natalizumab Products

Because of the potential for increased risk of PML and other infections, avoid the concomitant use of ENTYVIO with natalizumab products.

TNF Blockers

Because of the potential for increased risk of infections, avoid the concomitant use of ENTYVIO with TNF blockers.

CYP450 Substrates

The formation of CYP450 enzymes may be suppressed by increased levels of certain cytokines (e.g., IL-6, IL-10, TNF α , IFN) during chronic inflammation. Therefore, use of ENTYVIO may normalize the formation of CYP450 enzymes by modulating the underlying disease. Upon initiation or discontinuation of ENTYVIO in patients treated with CYP450 substrates, monitor drug concentrations or other therapeutic parameters, and adjust the dosage of the CYP substrate as needed. See the prescribing information of specific CYP substrates.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Available data from the Organization of Teratology Information Specialists (OTIS)/MotherToBaby ENTYVIO Pregnancy Registry, published literature and pharmacovigilance in pregnant women have not reliably identified an ENTYVIO-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes (*see Data*). There are risks to the mother and the fetus associated with inflammatory bowel disease in pregnancy (*see Clinical Considerations*).

No fetal harm was observed in animal reproduction studies with intravenous administration of vedolizumab to rabbits and monkeys at dose levels 20 times the recommended human dosage (*see Data*).

The background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. 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 miscarriage is 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 (IBD) 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

ENTYVIO administered during pregnancy could affect immune responses in the in utero-exposed newborn and infant. The clinical significance of low levels of ENTYVIO in utero-exposed infants is unknown. The safety of administering live or live-attenuated vaccines in exposed infants is unknown.

Data

Human Data

The vedolizumab pregnancy exposure registry conducted by OTIS/MotherToBaby study in the United States and Canada collected prospective observational data between 2015 and 2022 to assess the risk of major birth defects in live-born infants of women with ulcerative colitis (UC) or Crohn's disease (CD) treated with vedolizumab during pregnancy. The study compared pregnant patients with UC or CD exposed to vedolizumab with pregnant patients with UC or CD treated with other biological products. The registry included 99 women (58 with UC, 41 with CD) treated with vedolizumab during pregnancy, and 76 women (27 with UC, 49 with CD) exposed to other biological products during pregnancy.

The proportion of major birth defects among live-born infants in patients with UC or CD treated with vedolizumab and patients with UC or CD treated with other biological products was 7.4% (7/94) and 5.6% (4/71), respectively. Overall, there was no evidence of increased risk for major structural birth defects (adjusted RR 1.07, 95% CI: 0.33, 3.52).

The methodological limitations of the registry, including small sample size and the non-randomized design, resulted in a limited ability to estimate the risk of major birth defects and other maternal and infant outcomes. The conclusions from the pregnancy registry were consistent with the published literature and pharmacovigilance.

Animal Data

A reproduction study has been performed in pregnant rabbits at single intravenous doses up to 100 mg/kg administered on gestation Day 7 (about 20 times the recommended human dosage) and has revealed no evidence of impaired fertility or harm to the fetus due to vedolizumab. A pre- and post-natal development study in monkeys showed no evidence of any adverse effect on pre- and post-natal development at intravenous doses up to 100 mg/kg (about 20 times the recommended human dosage).

Lactation

Risk Summary

Data from a clinical lactation study show the presence of vedolizumab in human milk. The mean calculated daily infant dosage was 0.02 mg/kg/day orally (*see Data*). Systemic exposure in a breastfed infant is expected to be low because monoclonal antibodies are largely degraded in the gastrointestinal tract. There are no data on the effects of vedolizumab on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ENTYVIO and any potential adverse effects on the breastfed infant from ENTYVIO or from the underlying maternal condition.

Data

A milk-only lactation study was conducted in 9 adult lactating women being treated for active ulcerative colitis or Crohn's disease with intravenous ENTYVIO every 8 weeks after reaching steady state and completing the induction phase (ENTYVIO administration at 0, 2, and 6 weeks). Mean concentrations of ENTYVIO in human milk ranged from 0.03 to 0.26 mcg/mL. The mean calculated daily infant oral dosage was 0.02 mg/kg/day calculated as a product of the average concentration over the 8-week dosing interval and the standardized milk consumption of 150 mL/kg/day.

Pediatric Use

Safety and effectiveness of ENTYVIO in pediatric patients have not been established.

Geriatric Use

Clinical trials of ENTYVIO did not include sufficient numbers of patients aged 65 and over (72 patients with Crohn's or ulcerative colitis patients aged 65 and over were treated with ENTYVIO during controlled Phase 3 trials) to determine whether they respond differently from younger adult patients. However, no overall differences in safety or effectiveness were observed between these patients and younger adult patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients.

Manufactured by:

Takeda Pharmaceuticals U.S.A., Inc.

Cambridge, MA 02142

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Revised: February 2026

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For more information, go to www.ENTYVIO.com or call 1-877-TAKEDA7 (1-877-825-3327).

US-VED-4326 03/26

Fellows as force multipliers

Graduating fellows are already reshaping care delivery through quality improvement work that makes everyday care safer and more reliable.



June marks an important milestone in gastroenterology: fellowship classes graduate, new colleagues prepare to enter independent practice, and teams across the country adjust to the annual transition in roles and responsibilities. It's a time of celebration, but also a moment to recognize that fellows are not only the future of our field — they are already shaping and improving it in meaningful ways.

This reality was reflected in the many fellow-driven quality improvement projects presented at Digestive Disease Week® (DDW), which showcased the impact trainees are already having on care delivery. These projects offered a snapshot of the workforce we are welcoming: clinicians fluent not only in diagnosis and procedures, but also in measurement, implementation, and the disciplined work of building more reliable systems of care. What these projects made visible was the everyday work behind better, safer care. Rather than focusing on new devices or high-profile interventions, these projects addressed the practical steps that make care safer, more reliable, and more accessible: clearer bowel prep instructions that reduce inadequate preps and same-day cancellations; more reliable follow-up after abnormal screening tests; standardized pathways that shorten time to appropriate endoscopy; more consistent documentation and handoffs that prevent missed anticoagulation plans or delayed pathology follow-up; and smoother workflows for initiating and monitoring therapies for chronic GI disease. Across academic and community practice, we know that quality and access often depend on getting these details right.

As we congratulate our graduating fellows, we should also thank the teams who make fellow-led quality improvement (QI) possible: program leadership, QI mentors, nurses, endoscopy techs, schedulers, anesthesia colleagues, pathologists, IT partners, and many others. Their work is a reminder that meaningful improvement depends on collaboration. To our graduating GI fellows: thank you for the work you have done to improve care. I hope you will continue to bring that same curiosity and discipline wherever you practice next.

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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Director of Business Development – Advertising Sales Trevor Deal

Contact Information +1 908-463-3825 trevor.deal@conexiant.com

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"This study provides the most comprehensive nationwide description to date of the natural history of hereditary pancreatitis caused by pathogenic trypsinogen gene variants."

Guillaume Cléry, MD • See Page 9



AGA president maps innovation agenda at DDW® 2026

Dr. Lawrence Kim called for a unified approach to innovation spanning AI, genomics, workforce development, and policy advocacy.

By [Doug Brunk](#)

More than two decades after AGA outlined its vision for the future of GI care, many predictions have materialized, but not always as expected.

At Digestive Disease Week® (DDW) 2026, AGA President Lawrence Kim, MD, AGAF, drew on that perspective to call for a broader, more integrated approach to innovation, one that spans technology, care delivery, and workforce development.

Dr. Kim, a partner at South Denver Gastroenterology in Colorado, framed his presidential address around a retrospective analysis of priorities identified by AGA leadership in the early 2000s, highlighting how past predictions have translated into current practice. Colorectal cancer screening remains a dominant focus, with colonoscopy continuing as the primary modality despite earlier expectations that computed tomography colonography or molecular stool testing might replace it.

“These alternatives have limitations, leaving colonoscopy the most effective and reliable screening method,” Dr. Kim said.

He added that newer technologies have helped improve decision-making and workflow, rather than replace current standards.

The address summarized past trends, program results, and new innovations shaping the field. It focused on areas like advances in genomics and proteomics, workforce growth, and the use of artificial intelligence (AI).

He said genomic and molecular diagnostics have improved screening and risk assessment for patients with gastrointestinal conditions, but they’re not yet fully part of routine care. He also noted that earlier workforce predictions from AGA have come true, with nurse practitioners and physician associates taking on bigger roles, now leading to the creation of formal certification pathways.

Dr. Kim highlighted several AGA initiatives designed to accelerate innovation. The AGA Tech Summit and



Lawrence Kim, MD, AGAF

the Committee for GI Innovation and Technology bring together physicians, researchers, investors, and industry partners to support early-stage development. The AGA Incubator provides structured mentorship for startup companies, while the GI Opportunity Fund offers seed investment in emerging technologies.

One example cited was Edulis Therapeutics, this year’s “Shark Tank” competition winner focused on improving treatment options for patients with Crohn’s disease.

AI was another major focus, particularly the introduction of a point-of-care clinical decision support tool called Next-Gen Intelligence for GI and Liver (NIGEL). The tool

is designed to deliver guideline-based recommendations tailored to gastroenterology practice.

“It doesn’t replace clinical judgment — think of it as an on-call AI colleague,” Dr. Kim said.

Beyond technology, the address underscored the importance of leadership development and policy advocacy. Since 2015, the AGA Future Leaders Program has trained physicians who now contribute to guideline development and organizational leadership.

On the policy front, AGA advocacy efforts have focused on Medicare reimbursement, federal research funding, and prior authorization. According to Dr. Kim, these efforts

contributed to preventing proposed cuts to research funding and maintaining the structure of National Institutes of Health programs relevant to digestive disease.

Research funding remains a central limitation to innovation, he noted. The AGA Research Foundation awarded \$2.9 million to 84 investigators and added 10 pilot grants in response to funding constraints.

Incoming President of the AGA Institute, Byron L. Cryer, MD, AGAF, highlighted emerging research areas presented during the plenary session, including regenerative approaches using enteric neural stem cells for Hirschsprung disease, AI-based endpoints in ulcerative colitis trials to improve detection of treatment effects, and environmental sustainability analyses of endoscopy units.

These efforts show a move toward teamwork across different fields, bringing together areas like translational science, digital health, and systems engineering.

Dr. Kim concluded by emphasizing that new ideas should not be judged just because they’re new, but by how much they improve patient care and everyday clinical practice.

“Our job isn’t to predict the future perfectly,” he said. “It’s to make sure gastroenterology is ready for it.”

Dr. Kim reported having no financial disclosures.

DDW is AGA’s annual meeting, jointly sponsored by AGA, AASLD, ASGE, and SSAT. Learn more at [ddw.org](#).

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Early-onset CRC deaths rising fast, analysis finds

“Rectal cancer is striking younger Americans earlier and killing faster.”

By [Doug Brunk](#)



Mythili Menon Pathiyil, MBBS

Mortality from early-onset colorectal cancer is rising among US adults younger than 45, with the steepest increases seen in rectal cancer and among Hispanic and White patients, according to a national analysis of data from 1999 to 2023 with projections through 2035.

“This is a drastic shift from prior generations, and it’s concerning because these individuals are not routinely screened,” the study’s lead author, Mythili Menon Pathiyil, MBBS, a gastroenterology fellow at SUNY Upstate Medical University, Syracuse, said during a press briefing in advance of Digestive Disease Week® (DDW) 2026.

Research indicates that young adults take about seven months on average to

seek treatment after their first symptoms appear, she added, while older patients typically do so within about one month. “This delay can be the difference between an early and a late-stage diagnosis,” she said.

Using CDC WONDER data, Pathiyil and colleagues assessed age-adjusted mortality rates in patients ages 20 to 44 and examined trends by sex, race and ethnicity, region, and age group. They used joinpoint regression to estimate average annual percentage change and an autoregressive integrated moving average model to generate forecasts.

Across most subgroups, mortality increased over the study period. Colon cancer mortality rose more in males than females, with average annual increases of about 0.4% versus 0.2%. By 2035, deaths are projected to reach 834 in males and 667 in females, representing increases of 42 and 19 deaths compared with 2023. Deaths from rectal cancer rose faster in both men and women, increasing by about 1.8% each year. The number of deaths is expected to reach 459 in men and 304 in women, which is about 90 more and 60 more than before, respectively.

Differences by race and ethnicity were observed. Hispanic patients had the fastest increases in mortality, with colon cancer rising by about 1.1% annually and rectal cancer by 2.2%, corresponding to projected increases of 35 and 31 deaths by 2035. White patients also had sustained increases, with colon cancer rising 0.7% annually and rectal cancer 1.7%, translating to projected increases of 94 and 108 deaths. In contrast, colon cancer mortality declined among Black patients and Asian or Pacific Islander patients,

with annual decreases of about 0.8% and 0.6%, respectively. However, both groups experienced rising rectal cancer mortality, increasing about 0.8% in Black patients and 1% in Asian or Pacific Islander patients.

Regional patterns showed the West had the steepest increases in both colon and rectal cancer mortality, rising by about 0.9% and 2% annually, respectively. The Northeast showed declining colon cancer mortality but rising rectal cancer mortality, increasing about 1.2% annually. The Midwest and South had modest increases in colon cancer mortality but substantially higher rectal cancer mortality trajectories, with annual increases of about 2% and 1.1%, respectively.

Age-specific analyses indicated a shifting burden toward older patients within the younger cohort. Patients ages 35 to 39 and 40 to 44 had the highest increases in mortality. Colon cancer mortality rose about 0.7% and 0.6% annually in these groups, while rectal cancer mortality increased about 1.8% and 1.7%. In contrast, colon cancer mortality declined among patients ages 20 to 24 years and 25 to 29 years, and rectal cancer mortality declined only in the 25 to 29 age group.

Overall, rectal cancer mortality was two to three times higher than colon cancer mortality across most subgroups, highlighting a disproportionate burden. Loren Laine, MD, a gastroenterologist at Yale University School of Medicine, who moderated the briefing, asked Pathiyil what might be driving this trend. She suggested the increase may stem from a combination of factors. Symptoms like rectal bleeding are frequently misattributed, often to hemorrhoids,

DDW 2026

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leading to missed or delayed diagnoses.

Patient behavior also plays a role, particularly among men under 50, who may lack a primary care physician, insurance, or may delay seeking care until symptoms become severe. In addition, broader gaps in the healthcare system “is one of the reasons why Hispanic populations have such a higher rate,” Pathiyil said. “This critical delay in diagnosis in itself might be one of the contributing factors about the rise in mortality, despite all advances in therapy.”

She concluded that the findings “reinforce that rectal cancer is striking younger Americans earlier and killing faster, and it is doing so at an accelerating pace. This is not a problem we can afford to ignore, which is why we need to revisit screening strategies, especially in high-risk subgroups. We [also] need to change how clinicians think about symptoms in younger patients. Rectal bleeding in people less than 45 years old should not be automatically attributed to hemorrhoids.”

Dr. Pathiyil reported having no disclosures.

GLP-1s found to outperform surgery for cirrhosis

A large US database study finds GLP-1 initiation within one year of cirrhosis diagnosis was associated with dramatically lower odds of ascites, hepatic encephalopathy, hepatorenal syndrome, and liver transplantation.

By [Doug Brunk](#)

Early use of glucagon-like peptide-1 receptor agonists was associated with

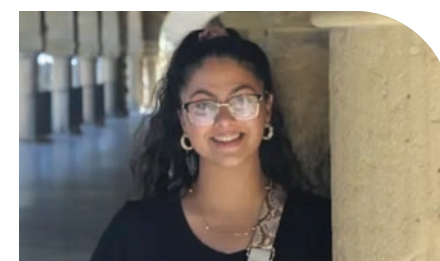
fewer liver-related complications and lower transplant risk compared to metabolic bariatric surgery in patients with metabolic-dysfunction associated steatohepatitis (MASH) cirrhosis and obesity without diabetes, according to a large US database study.

“The incidence of [metabolic dysfunction-associated steatotic liver disease (MASLD)] is rising, and it is projected to be a leading cause of liver transplantation in the US,” study author Charanpreet Sasan, MD, told *GI & Hepatology News* in advance of Digestive Disease Week® (DDW) 2026, where the work was presented. “Given increased risks from surgical procedures, associated recovery times and cost, being able to provide a non-surgical effective alternative option like GLP-1s can help to expand our therapeutic toolkit significantly.”

For the analysis, Dr. Sasan, a resident physician at UMass Chan Medical

School, Worcester, Mass., and colleagues evaluated outcomes in patients with MASH cirrhosis and obesity who did not have type 2 diabetes mellitus. They compared patients who initiated the glucagon-like peptide-1 receptor agonists (GLP-1s) semaglutide, tirzepatide, or liraglutide within one year of a cirrhosis diagnosis with those who underwent metabolic bariatric surgery (MBS) during the same period. Data were sourced from TriNetX, a network of 70 US health care organizations, using diagnostic codes to identify eligible patients while excluding those with hepatocellular carcinoma or cholangiocarcinoma.

The investigators used Kaplan-Meier methods to evaluate outcomes over time. Matching accounted for age, sex, race, ethnicity, body mass index, liver enzymes, serum creatinine, and cardiometabolic risk factors to reduce baseline differences between groups.



Charanpreet Sasan, MD

Before matching, the 2,475 patients treated with GLP-1s were older on average (51 vs 49 years), with slightly higher body mass index and higher lipid and glycemic markers than the 2,079 patients who underwent MBS. After propensity score matching to balance demographic, metabolic, and laboratory variables, the final cohort included 3,074 patients.

Over up to 10 years of follow-up, GLP-1 therapy was associated with lower rates of cirrhosis complications compared with surgery. Patients receiving GLP-1

had about 43% lower odds of developing portal hypertension. The risk reductions extended across multiple complications: ascites occurred at about 80% lower odds, hepatorenal syndrome at 89% lower odds, hepatic encephalopathy at 71% lower odds, and esophageal varices at 39% lower odds compared with MBS.

The need for liver transplantation also differed between groups. Patients treated with GLP-1 had about 55% lower odds of requiring transplant compared with those who underwent surgery.

“The most surprising finding was that the benefits of GLP-1 extended far beyond

the reduction in decompensating events like ascites, variceal bleeding, hepatorenal syndrome and hepatic encephalopathy, particularly altering liver transplantation risk,” Dr. Sasan said. “Early initiation of the medication, within one year of a cirrhosis diagnosis, resulted in a significant decrease and delay in the need for transplantation further stressing their benefit.”

She added that the findings address a gap in evidence for patients with MASH cirrhosis who do not have diabetes, and advocate for a shift towards earlier and more proactive therapeutic intervention. “While prior studies have demonstrated

the benefit of GLP-1 in the earlier stages of steatotic liver disease to prevent progression, our data shows that, even after development of cirrhosis, there are benefits from initiating GLP-1 therapy,” Dr. Sasan said. “The results emphasize that starting the GLP-1 therapy early, within the first year of a cirrhosis diagnosis, can help provide substantial protection against further MASH cirrhosis decompensations and decrease liver transplantation risk.”

During a question-and-answer session at the meeting, an attendee asked Dr. Sasan whether she and her colleagues had observed any differences in effects

among the various GLP-1 drugs. “We had wondered about that, but we weren’t able to run subgroup analyses because the N would get too small between the three GLP-1s that we included,” she said.

Despite the large sample size and long follow-up, the study has limitations. The retrospective design relies on coded data and may be subject to misclassification. Residual confounding is possible even after matching, particularly for factors such as medication adherence and lifestyle changes.

Dr. Sasan reported having no disclosures.

Largest cohort to date clarifies natural history of hereditary pancreatitis

“Our results support the need for long-term follow-up of all individuals carrying pathogenic trypsinogen gene variants, not only those with chronic pain or recurrent pancreatitis.”

By [Bob Alaburda](#)



Guillaume Cléry, MD

Patients with hereditary pancreatitis caused by pathogenic variants of the PRSS1 gene experience high rates of exocrine and endocrine complications across their lifespan and face a markedly elevated risk of pancreatic ductal adenocarcinoma (PDAC), according to a nationwide French cohort study presented at Digestive Disease Week® (DDW) 2026.

“This study provides the most comprehensive nationwide description to date of the natural history of hereditary pancreatitis caused by pathogenic trypsinogen gene variants,” study author Guillaume Cléry, MD, told *GI & Hepatology News*. “It includes nearly three decades of follow-up and, importantly, incorporates

individuals identified through family screening before symptom onset, allowing a more accurate estimation of disease penetrance and long-term complications. Because genetic testing for this condition is centralized in France, we were also able to obtain a reliable estimate of prevalence at the population level. Finally, our results confirm the increased risk of pancreatic cancer with greater precision than previous studies, with narrower confidence intervals reflecting the robustness of this large national cohort.”

For the PARADISIO-1 study, Dr. Cléry, a pancreatologist in the Department of Pancreatology and Digestive Oncology at Beaujon University Hospital, AP-HP Nord – Université Paris Cité, Clichy, France, and colleagues constructed the cohort using exhaustive listings from the three French genetic laboratories that perform PRSS1 testing nationwide. Eligible patients carried a confirmed pathogenic variant of PRSS1 identified between 1996 – the year the gene was first described – and 2025. Both living and deceased patients were included, with informed consent obtained from patients or their relatives. Data collection was carried out by the attending clinician for each patient.

Across France, 726 patients had been diagnosed with a pathogenic PRSS1 variant since 1996, corresponding to a cumulative prevalence of 1.1 cases per 100,000 inhabitants. Of these, 455 were enrolled in the study between October 2024 and October 2025, representing 4,380 person-years of follow-up. The estimated penetrance, defined by a clinical or morphological manifestation attributable to the PRSS1 mutation, was 77.6%. Median age at symptom onset was 12.5 years. The most prevalent variant was R122H, identified in 178 patients (39.1%).

Mean age at diagnosis was 32.3 years for pancreatic exocrine insufficiency (PEI) and 42.7 years for diabetes mellitus. By age 50, the cumulative incidence

of PEI was 27.5% and the cumulative incidence of diabetes was 20.4%. The R122H and N29I variants were linked to an elevated risk of developing diabetes, with hazard ratios (HRs) of 2.2 and 3.3, respectively.

Nineteen cancers were identified in the cohort, at a median age at diagnosis of 63.8 years. The standardized incidence ratio (SIR) for PDAC was 32.2 compared with the general population. The cumulative incidence of PDAC remained low through the first four decades of life and rose steeply thereafter, reaching 2% by age 50, 5.9% by age 60, 12.9% by age 70, and 14.5% by age 75. Diabetes was associated with a markedly increased risk of PDAC, with an HR of 6.75.

Dr. Cléry pointed to several findings he considered particularly noteworthy. “One finding that stood out was the high proportion of patients with a history of smoking, despite the known association between smoking and pancreatic cancer risk in hereditary pancreatitis,” he said. “This highlights an important opportunity for preventive interventions in this population. Another notable observation was that many individuals identified through family screening, although initially asymptomatic, developed pancreatic abnormalities or metabolic complications over time, reinforcing the importance of systematic follow-up even in apparently unaffected carriers.”

The genotype-phenotype patterns observed in the cohort may also help explain why certain PRSS1 variants dominate clinical case series, he said. “[An] interesting observation was that the most frequent PRSS1 variants, particularly p.R122H and p.N29I, were associated with a higher risk of pancreatic insufficiency. This may partly explain why these variants are more commonly identified in clinical cohorts, as their greater clinical impact likely increases the probability of genetic

testing and diagnosis.”

Dr. Cléry said the data argue for sustained monitoring across the full mutation-carrier population, not only those with overt pancreatic disease. “Our results support the need for long-term follow-up of all individuals carrying pathogenic trypsinogen gene variants, not only those with chronic pain or recurrent pancreatitis. Pancreatic exocrine insufficiency and diabetes occur frequently and can have significant consequences such as malnutrition and bone disease if not recognized early. In addition, the observed increase in pancreatic cancer risk after age 60 years, particularly in patients with diabetes, suggests that surveillance strategies could be adapted according to individual risk profiles while maintaining monitoring throughout adulthood.”

Limitations of the analysis are inherent to retrospective, registry-based work, including reliance on clinician-entered data and the possibility of residual confounding in genotype-phenotype comparisons. The investigators noted that the size and completeness of the national cohort yielded narrower confidence intervals around the PDAC risk estimate than had been reported in earlier studies of hereditary pancreatitis.

“This study illustrates the value of nationwide collaboration in rare diseases,” Dr. Cléry said. “By combining genetic and clinical data collected over several decades, we were able to provide a more complete picture of disease evolution across the full spectrum of mutation carriers, including those identified before symptom onset. We hope these findings will help improve genetic counselling, patient education, and long-term management strategies for hereditary pancreatitis.”

Dr. Cléry reported having no relevant disclosures.



Key clinical takeaways

Early GLP-1 initiation within 1 year of MASH cirrhosis diagnosis was associated with fewer liver-related complications than bariatric surgery in patients without diabetes.

GLP-1 therapy significantly reduced odds of decompensation events, including ascites, hepatorenal syndrome, hepatic encephalopathy, portal hypertension, and varices.

GLP-1 use was linked to an approximately 55% lower odds of liver transplantation, suggesting a potential role in delaying progression and transplant need.

Investigational endoscopic therapy maintains weight after GLP-1 discontinuation

The treatment could provide an “off-ramp for patients who either can’t or don’t want to be on these drugs long-term.”

By [Doug Brunk](#)

“Nearly one in five adults report having taken a GLP-1 receptor agonist drug at some point, and the results can be dramatic. However, an estimated 60-70% of patients discontinue these drugs within the first year for a variety of reasons, including cost, side effects, or simply not wanting to stay on a medication long-term,” said lead author Shelby Sullivan, MD, during a press briefing ahead of Digestive Disease Week® (DDW) 2026.

In an ongoing multicenter,



Shelby Sullivan, MD

randomized, double-blind, sham-controlled trial known as REMAIN-1, Dr. Sullivan and colleagues are evaluating whether DMR can help maintain weight loss achieved with tirzepatide. DMR is an investigational endoscopic procedure that uses hydrothermal ablation to remove the duodenal mucosa, an area linked to metabolic problems, with the goal of producing lasting metabolic benefits.

Dr. Sullivan reported findings from the midpoint cohort of the trial, which enrolled GLP-1-naïve patients ages 21 to 70 without diabetes and with a body mass index of 30 to 45 kg/m². After a tirzepatide run-in, eligible patients who achieved at least 15% total body weight loss stopped the medication and were randomized in a 2:1 ratio to DMR or sham at least one week later. All patients received structured lifestyle counseling.

“Participants really could not tell if they had had the sham or the real procedure because they really don’t have much in the way of symptoms after the procedure,” noted Dr. Sullivan of director of the Endoscopic Bariatric and Metabolic Program at Dartmouth Health Weight Center and professor of medicine, Dartmouth Geisel School of Medicine,

A total of 45 patients achieved the weight-loss threshold. Of these, 30 underwent DMR and 15 received a sham procedure. The groups were similar at baseline: the average age was 43, 80% were women, and 42% had prediabetes.

All trial participants lost about 40 pounds on GLP-1 therapy. However, six months after stopping the drug, patients in the sham control group gained back about 40% more weight compared with their counterparts in the DMR group. There was also a clear dose-response effect: the more ablations performed, the greater the weight loss. “Those who had a longer length of resurfacing regained just 7 pounds, maintaining more than 80% of their weight loss, while the sham control group regained about twice that amount,” Dr. Sullivan said. “Importantly, there were no definite or probable treatment emergent [or] serious adverse events related to the device or procedure.”

If the results are validated in the full REMAIN-1 trial, DMR “could

fundamentally change how we think about GLP-1 therapy and potentially be approved for use in the US, providing an off-ramp for patients who either can’t or don’t want to be on these drugs long-term with a minimally invasive procedure to lock in the metabolic benefit,” she noted.

Loren Laine, MD, a gastroenterologist at Yale University School of Medicine, who moderated the briefing, said he finds the research compelling, both clinically and in terms of how the body works. He noted that it highlights the duodenum’s key role in metabolic processes, including insulin resistance, diabetes, and obesity. “Interestingly, other studies have shown that injuring the duodenum or even bypassing the duodenum can impact metabolic function and weight,” Dr. Laine said.

According to Dr. Sullivan, the REMAIN-1 trial is now fully enrolled with more than 300 participants, and top-line results are expected in the fourth quarter of 2026.

Dr. Sullivan reported research support from Fractyl Health, Nitinotes Surgical, and Viking Therapeutics, as well as consulting relationships with Biolinq and Olympus (with prior roles at Allurion Technologies and Fractyl Health). She also disclosed holding stock in Biolinq. Her colleagues reported no disclosures.

Antibiotics tied to early adenoma risk, study finds

A nested case-control study of nearly 24,000 patients finds cumulative exposure and timing both matter.

By [Doug Brunk](#)

Oral antibiotic use was associated with a higher risk of early-onset colorectal adenoma (EOCRA) in a large US population, with increasing exposure and longer intervals since use linked to greater risk, according to a nested case-control study of nearly 24,000 patients.

"In recent decades, there has been a striking increase in colorectal cancer (CRC) incidence in young adults <50 years of age, both in the US as well as globally," the study's lead researcher, Amanat Bal, MD, MS, of Kaiser Permanente San Francisco Medical Center, said in advance of Digestive Disease Week® (DDW) 2026, where the work was presented. "While multiple mechanisms have been proposed to help explain this, one hypothesis is that gut microflora perturbations could be influencing the colorectal adenoma-to-cancer pathway."

A wealth of published evidence has shown that antibiotics can disturb the normal bacteria living in the colon and rectum, she continued. When this balance is upset, harmful bacteria can grow more easily, which may increase the risk of tumors forming. "Prior studies have examined the link between antibiotic use and colorectal cancer, as well as antibiotic use and colorectal adenomas in older adults but not specifically among young adults," Dr. Bal said. "Our study extends prior findings by exclusively examining EOCRA incidence and antibiotic use in adults under 50 years of age."

Using Kaiser Permanente Northern California patient data, Dr. Bal, senior author Jeffrey K. Lee, MD, MPH, also of Kaiser Permanente, and colleagues evaluated the association between antibiotic exposure and EOCRA in 6,936 patients with EOCRA and 16,900 matched controls with normal colonoscopy findings from 2006 to 2023. EOCRA cases were comparable

to their matched controls, with a mean age of 45 years across both groups, 52% female, and similar distributions of race and ethnicity, duration of drug benefits (≥ 10 years), and colonoscopy date.

The investigators defined antibiotic exposure as oral use at least two years before the index date. In unadjusted analysis, antibiotic exposure was associated with 1.59 times the odds of EOCRA; after adjustment for confounders using conditional logistic regression, the odds were 1.45 times higher.

Risk was elevated across antibiotic types. Broad-spectrum agents were associated with 1.38 times the odds of EOCRA, while narrow-spectrum agents were associated with 1.16 times the odds. "We observed a particularly robust association with sulfonamide and trimethoprim use," Dr. Bal noted. "Recent studies have suggested that exposure to long-acting sulfonamides in utero may be linked to subsequent CRC in adult offspring, and our findings suggest a possible mechanistic link tying sulfonamide antibiotic use to a higher risk of adenoma and subsequent carcinoma development."

The researchers observed a dose-response relationship, with EOCRA risk rising with the number of antibiotic dispensations and peaking at seven to nine courses (1.60 times the odds vs no exposure).

Timing of exposure also influenced risk. The association strengthened as the interval since antibiotic use



Amanat Bal, MD, MS



Jeffrey K. Lee, MD

"Our findings suggest a possible mechanistic link tying sulfonamide antibiotic use to a higher risk of adenoma and subsequent carcinoma development."

increased, with the highest risk observed five to less-than-eight years after exposure, corresponding to 1.71 times the odds of EOCRA.

Although causality cannot be established from this observational study, Dr. Bal concluded that the overall findings support the hypothesis that antibiotic exposure may contribute to the development of EOCRA and underscore the need for judicious

antibiotic use in clinical practice. "We also observed a modest dose-response relationship, in which increasing antibiotic prescription burden was associated with increased EOCRA risk, which suggests that cumulative antibiotic exposure may be an important factor to take into account when engaged in clinical care," she said.

Dr. Bal reported having no disclosures.

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Electrosurgery guidance refines endoscopy practice

“An understanding of the principles of electrosurgery is fundamental for its safe and effective use.”

By [Doug Brunk](#)

A new AGA clinical practice update highlights that safe and effective electrosurgery in gastrointestinal endoscopy is determined not only by device settings, but also by operator technique and tissue factors, with no clear difference in major outcomes among commonly used types for polypectomy.

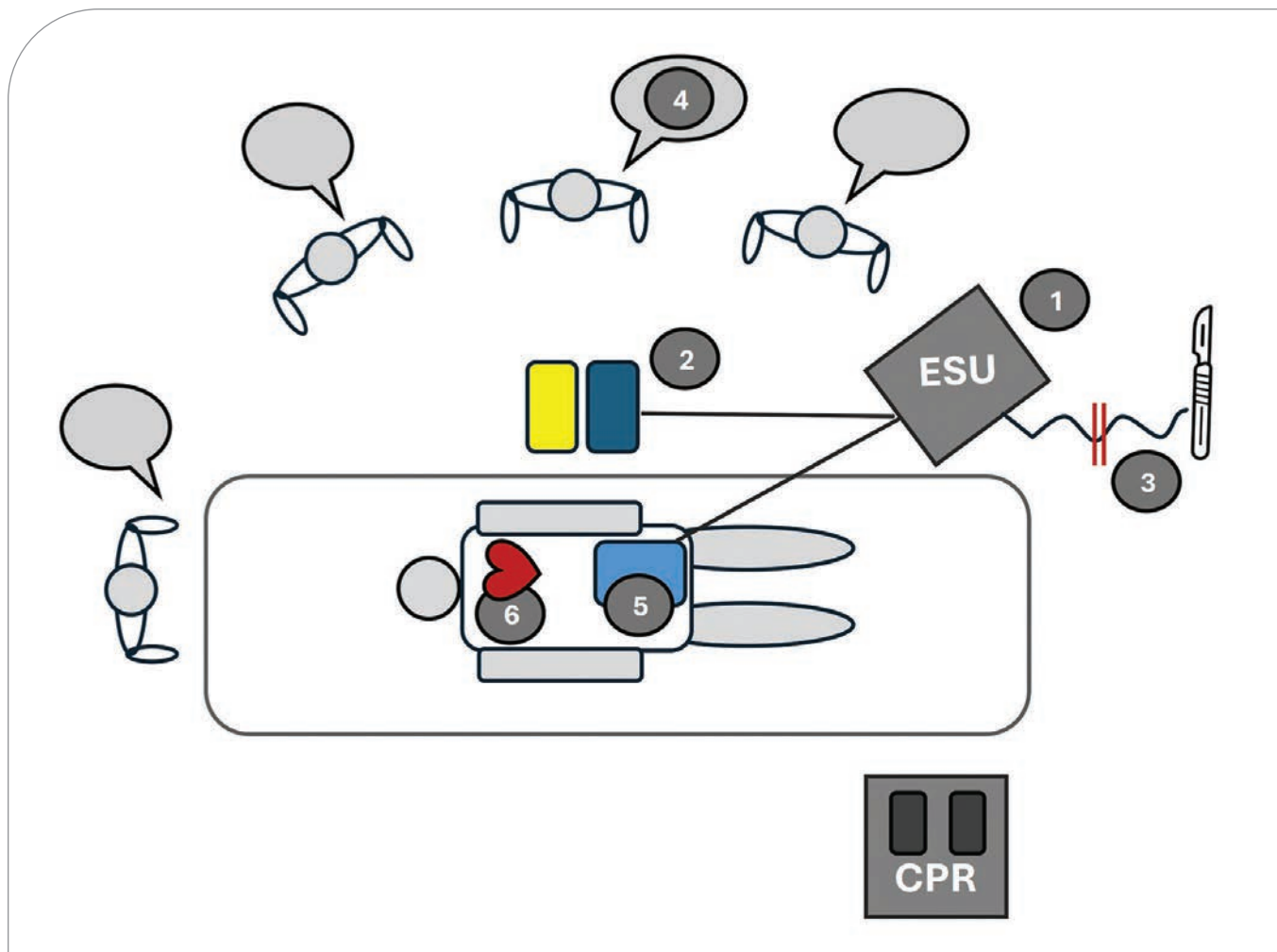
“Electrosurgery is extensively used in endoscopic therapeutic procedures,” Dennis Yang, MD, of the Center for Interventional Endoscopy at AdventHealth, Orlando, Florida, and coauthors wrote in the update, published in *Clinical Gastroenterology and Hepatology*. “An understanding of the principles of electrosurgery is fundamental for its safe and effective use across the various applications of this technology in gastrointestinal (GI) endoscopy.”

The update, based on expert review and 13 best practice advice statements, synthesizes current evidence and practical considerations for physicians using electrosurgical units (ESUs) across therapeutic endoscopy. The authors noted that multiple variables, including device type, contact area, tissue composition, and operator technique, interact to determine tissue effect.

Adjusting generator settings alone may not reliably achieve the intended outcome. Current density, defined as current per unit area, plays a key role. Smaller contact areas, such as thin snares, increase current density and favor cutting, while larger contact areas reduce density and promote coagulation.

Polypectomy: No clear winner for current type

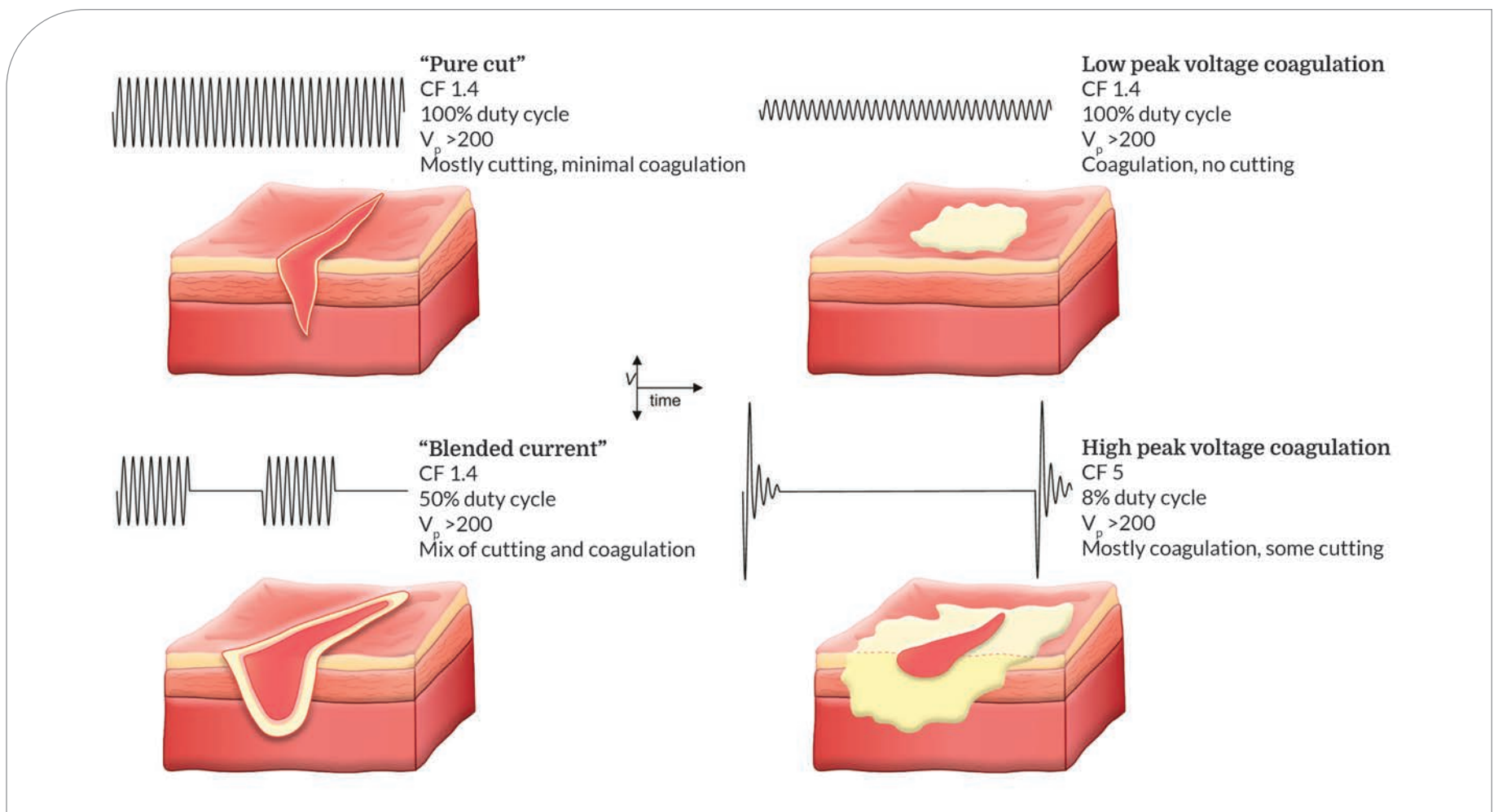
For colorectal polypectomy, the update authors reported that cut-predominant and coagulation-predominant currents can both be used without meaningful differences in major outcomes. In a randomized trial cited in the update, intraprocedural bleeding occurred more often with cutting current than coagulation current (17% vs 11%), but rates of severe adverse events (about 7% to 8% in both groups) and delayed bleeding (about 5% to 6%) were similar.



Credit: *Clinical Gastroenterology and Hepatology*

Best Safety Practices for ESU Operation

1	ESU generator should be positioned so that the display monitor featuring the power settings is clearly visible and within reach of operation
2	ESU activation pedals and other foot-equipment should be routinely aligned in the same manner to reduce the risk of inadvertently stepping on the wrong pedal during the procedure
3	ESU should remain on “standby” mode and all devices insulated and disconnected from the active cord when not in use or between applications to prevent unintentional activation
4	Closed loop communication should be used when operating the ESU: <ul style="list-style-type: none"> • Allows team members to acknowledge each step of the process via verbal confirmation, seeking clarification when necessary, and followed by verification that the task in hand has been correctly interpreted to close the loop prior to its execution
5	Endoscopy team should be knowledgeable on best practices for the placement and management of dispersive pads: <ul style="list-style-type: none"> • The pad should be placed over areas with good blood supply and avoid skin irregularities (e.g. scars, hair, implants, areas of moisture, sweat) that may be prone to failure and hinder current conduction). Body hair should be shaven at the chosen site to ensure uniform pad contact • The size of the dispersive pad should be appropriate to the patient’s age and weight • Dual-pads can be considered for select cases (e.g. larger patients)
6	Endoscopy team should be familiar and follow the protocols regarding the operation of cardiac (e.g. defibrillators, pacemakers) and other implantable devices (e.g. neurostimulators) [5]: <ul style="list-style-type: none"> • Standard practice should include obtaining detailed information of all implantable devices and consultation with cardiology and/or manufacturer when indicated • Cardiac devices should be continuously monitored during the procedure • If feasible, bipolar device should be considered as an alternative among patients with implantable defibrillators • Cardiac resuscitation equipment should be readily available



Credit: *Clinical Gastroenterology and Hepatology*

Complete resection and recurrence rates also did not differ between current types. However, the author’s noted findings were generated using modern microprocessor-controlled ESUs, which adjust power output in real time based on tissue impedance. Results may not be generalizable to older systems. Technique and tissue characteristics remain critical modifiers of outcomes, reinforcing that device settings should be individualized during procedures, noted Dr. Yang and colleagues.

Hot snare preferred for large pedunculated polyps

The update authors recommended hot snare polypectomy for large pedunculated polyps, which often contain sizable feeding vessels. Electrosurgical current facilitates vessel sealing and reduces immediate bleeding risk compared with cold snaring. For these lesions, a coagulation-predominant waveform may help seal vessels before transection. Proper snare positioning at the mid-stalk rather than near the base is also emphasized to limit thermal injury to the colonic wall.

Thermal margin ablation reduces recurrence

After piecemeal endoscopic mucosal resection (EMR), thermal ablation of

resection margins significantly lowers recurrence risk. Recent trials cited in the review show recurrence rates can be reduced to less than 5% at first follow-up when techniques such as snare tip soft coagulation (STSC) or argon plasma coagulation (APC) are applied to normal-appearing margins.

STSC and APC appear similarly effective, though STSC may be more cost-efficient. The update authors cautioned that thermal therapy should be limited to normal margins, with visible residual neoplasia treated separately.

Environment and technique

The environment you’re working in — gas versus fluid — changes how electrosurgery works. In saline, electricity flows more easily, so the energy spreads out and produces more coagulation rather than cutting. Because of this, endoscopists often need to use higher power settings to get a cutting effect. In the same way, the shape of the electrical waveform also affects the result. Settings with a higher duty cycle tend to cut tissue, while higher peak voltages can penetrate deeper and create stronger effects, even when the tissue has higher resistance.

Tissue resistance varies across the GI tract and changes during procedures,

particularly as tissue desiccates. Modern ESUs compensate for these changes, but real-time adjustment by the endoscopist remains necessary, noted the authors.

Safety practices and complications

Although ESU-related complications are uncommon, most adverse events are linked to operator or device factors. Recommended safety practices include preprocedural timeouts, proper placement of dispersive electrodes, and closed-loop team communication.

Extra care is required for patients with implanted heart devices, as electrosurgical currents can interfere with how the devices operate. Strategies include positioning return electrodes to avoid current pathways near devices and using bipolar energy when feasible.

Soft coagulation works well to stop bleeding, but using too much can cause deeper heat damage and may even lead to a delayed perforation. The authors recommended precise targeting, minimal contact area, and short activation times to mitigate risk.

Adjunct techniques and advanced procedures

Hot forceps avulsion was presented as an effective adjunct for fibrotic, non-

lifting lesions, particularly in the colon. This technique uses a concentrated electrical current applied in short bursts to remove attached tissue while limiting damage to surrounding areas.

For argon plasma coagulation (APC), physicians must balance power and gas flow. Too much fluid flow can spread the current and make it less effective, while poor bowel preparation can increase the risk of rare but serious complications, such as a colonic explosion.

In endoscopic retrograde cholangiopancreatography, optimal sphincterotomy depends more on technique than energy setting. Using light contact and positioning the wire correctly helps achieve effective cutting while lowering the risk of pancreatitis.

Electrosurgery is not a “set-and-forget” technology. Outcomes depend on a dynamic interplay of generator settings, device choice, tissue characteristics, and operator technique, concluded the update authors.

The update was commissioned and approved by AGA. Dr. Yang and several authors report consulting relationships with device manufacturers, including Boston Scientific, Olympus, Medtronic, and others.

New hemorrhoid care tips

The recommendations come from existing research and expert opinions.

By [Doug Brunk](#)

A new AGA clinical practice update reports that most patients with hemorrhoids can be effectively diagnosed and managed in the office, with dietary measures and minimally invasive procedures forming the backbone of care before surgery is considered.

The expert review, published in *Clinical Gastroenterology and Hepatology* and based on published literature and specialist consensus, provides 11 best practice advice statements for physicians on diagnosing and treating hemorrhoidal disease, a condition that affects more than 23 million people in the US and accounts for millions of annual visits.

The review's lead author, Waqar Qureshi, MD, of the Division of Gastroenterology at Baylor College of Medicine in Houston, told *GI & Hepatology News* the release of the update is timely because office-based management of hemorrhoid disease is a relatively recent development. "Incorporating hemorrhoid disease treatment in your practice can save both time and money since surgical referral is unnecessary for the majority of patients presenting with hemorrhoid disease," Dr. Qureshi said.

Diagnosis and initial evaluation

Hemorrhoids usually present with bleeding, itching, discomfort, or prolapse, with significant pain limited to acutely thrombosed cases or coexisting anal tears. Diagnosis mainly relies on the patient's history and a physical exam, and internal hemorrhoids are graded by symptoms and degree of prolapse.

The authors recommended performing anoscopy when available for all new patients who may have hemorrhoids to confirm the diagnosis and rule out other conditions, including cancer. A colonoscopy may also be needed in patients with rectal bleeding to check for more serious disease.

First-line therapy: Fiber and behavior

Diet and lifestyle changes remain the first-line treatment. Eating more fiber and avoiding straining or sitting on the toilet for long periods can help reduce symptoms like bleeding and prolapse.

Evidence from systematic reviews of seven studies supports fiber supplementation for symptom relief. In

one study of 102 patients with advanced disease, limiting toilet time to three minutes and consuming 20–30 grams of fiber daily improved outcomes.

Topical treatments such as anesthetics, corticosteroids, and vasoactive agents may provide short-term relief, but there isn't much strong evidence that they work well. Steroids should only be used for a short time because they can thin the skin, making it more sensitive.

Office-based procedures dominate

For patients with persistent symptoms, office-based interventions are recommended before surgery.

"Most grades of hemorrhoids can be treated by either a gastroenterologist or a surgeon equally effectively," Dr. Qureshi said. "In the case of advanced hemorrhoids that do not respond to rubber band ligation, surgery is necessary."

Rubber band ligation and infrared coagulation are both effective and safe for grades 1–3 hemorrhoids. Rubber band ligation has reported success rates ranging from 66% to 94%, with longer-lasting benefits for prolapse and recurrent bleeding compared with infrared coagulation.

Infrared coagulation, which uses heat to induce fibrosis and reduce blood flow, is particularly useful for smaller internal hemorrhoids and may be preferred in patients at higher bleeding risk, such as those on anticoagulants.

Complications from banding occur in about 2% of cases and include bleeding, urinary retention, and discomfort. "Side effects are rare and minor, except for pelvic sepsis, which is exceedingly rare but important to recognize quickly so that it can be treated promptly," Dr. Qureshi said.

When to escalate to surgery

The authors recommend surgical referral for patients with grade 3 hemorrhoids who do not respond to office procedures, as well as for those with grade 4 disease. Surgical hemorrhoidectomy remains the definitive treatment for advanced disease, with complication rates of 1% to 2%.

Other surgical options, like stapled hemorrhoidopexy, may cause less



Waqar Qureshi, MD

“Incorporating hemorrhoid disease treatment in your practice can save both time and money since surgical referral is unnecessary for the majority of patients presenting with hemorrhoid disease.”

pain after surgery but carry higher recurrence and complication risks, so they are used less often.

Special populations

The review highlighted tailored management in specific groups. In patients with inflammatory bowel disease, treatment should be delayed until remission due to higher complication risk.

Hemorrhoids occur in up to two-thirds of pregnant women, with conservative therapy preferred during pregnancy and procedural interventions deferred until after delivery unless necessary.

In patients with cirrhosis, distinguishing hemorrhoids from rectal varices is essential. Both banding and infrared coagulation remain viable options, although infrared coagulation may be safer in patients with coagulopathy.

Acute thrombosis and urgent care

Acute thrombosed hemorrhoids, which cause severe pain, are best managed with incision and drainage, which relieves symptoms faster than non-surgical treatments.

The authors noted that their

recommendations come from reviewing existing research and expert opinions, not from a formal systematic review or graded evidence. Because of this, the quality and strength of the evidence differ between recommendations, especially for topical treatments and care for special populations.

Dr. Qureshi emphasized one best practice statement from the update that resonates with him: "The diagnosis and treatment of hemorrhoids is within the purview of the gastroenterologist."

"Hemorrhoid disease is easily and safely managed by the gastroenterologist in the office setting," he added.

Coauthors were Sook Hoang, MD, Department of Surgery, University of Virginia Health System, Charlottesville; Jeanetta Frye, MD, Division of Gastroenterology, University of Virginia Health System; and Satish Rao, MD, PhD, Division of Gastroenterology/Hepatology, Medical College of Georgia, Augusta.

AGA commissioned the review. Dr. Rao reported consulting for multiple pharmaceutical companies and receiving research support. The other authors had no conflicts of interest to declare.

Ultrasound plus AFP remains the standard for HCC surveillance

Semiannual ultrasound plus AFP remains the preferred HCC surveillance strategy, even as blood-based biomarkers and abbreviated MRI show promise but await sufficient evidence.

By [Meg Barbor](#)

A new clinical practice update released by AGA and published in *Gastroenterology* shares the foundation of hepatocellular carcinoma (HCC) surveillance remains semiannual ultrasound plus alpha-fetoprotein (AFP), even as blood-based biomarkers, abbreviated MRI, and risk-based surveillance strategies are being evaluated for clinical use.

The expert review was led by Nicole E. Rich, MD, of the Division of Digestive and Liver Diseases at UT Southwestern Medical Center, with coauthors Augusto Villanueva, MD, PhD, Jorge A. Marrero, MD, and Fasiha Kanwal, MD, MSHS.

The review spans the full HCC surveillance pathway, beginning with an emphasis that the most effective strategy for reducing HCC morbidity and mortality is preventing cirrhosis. This includes addressing chronic viral hepatitis through vaccination and treatment, recognizing and treating alcohol use disorder, and managing metabolic risk factors and chronic liver disease earlier in their course.

Although viral hepatitis remains important, growing numbers of cases are tied to metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol-associated liver disease. At the same time, surveillance remains underused, and many tumors are still diagnosed too late for curative treatment.

The update emphasized that standard surveillance has not changed. The preferred strategy remains ultrasound plus AFP every six months in patients at sufficient risk, particularly those with cirrhosis of any etiology and selected patients with chronic hepatitis B virus (HBV) infection without cirrhosis. This approach improves early-stage detection, expands access to curative therapy, and is associated with improved early detection and survival compared with annual surveillance.

The update also clarified where surveillance is not recommended. Among patients without cirrhosis, only a subset of those with chronic HBV infection should undergo routine surveillance. For patients without cirrhosis from other etiologies, including most with MASLD or cured hepatitis C, HCC incidence

remains too low to justify surveillance. The authors recommended leaving room for individualized discussion when fibrosis staging is uncertain or when additional risk factors, such as family history, complicate the picture.

Another key component of the update is consideration of the downsides of surveillance. Although ultrasound and AFP are noninvasive, false-positive results can trigger additional imaging, biopsy, patient anxiety, missed work, and financial burden. Surveillance is beneficial but is associated with potential harms. In patients with limited life expectancy or those who are not candidates for liver transplantation or HCC-directed therapy, the balance may shift away from routine surveillance.

The update authors described biomarkers as promising; however, current evidence does not support their routine use. Novel blood-based biomarkers, including GALAD and other composite panels, are described as promising but are not recommended for



Janice Jou, MD, MHS

routine surveillance. Some are already commercially available, yet the evidence remains insufficient for them to replace or routinely augment guideline-based surveillance.

Janice Jou, MD, MHS, Professor of Medicine in the Division of Gastroenterology and Hepatology at Oregon Health & Science University in Portland, and an associate editor of *GI & Hepatology News*, said the imperfection of current tests is itself a talking point. “One strategy to address this uncertainty in practice is to discuss it with the patient directly,” Dr. Jou said. “This is also an opportunity to discuss opportunities for our patients to participate in clinical trials to better our understanding of which HCC surveillance strategies are most effective.”

Similarly, multicancer early-detection blood tests are not recommended for HCC surveillance. Abbreviated MRI is also described as promising, but is not currently recommended for routine use in place of standard surveillance. Ongoing trials, including TRACER and PREMIUM, are expected to clarify whether biomarker-based and MRI-based approaches can improve outcomes enough to change practice.

The review authors also addressed the need for better risk stratification. Many HCC risk scores have been developed, but few have undergone

enough validation to support routine use. Risk stratification for cirrhosis remains an active area of development, but current models should not yet be used to routinely determine who should or should not undergo surveillance.

There is one important exception. In patients with chronic HBV infection without cirrhosis, the authors noted that PAGE-B and REAL-B scores can help stratify future HCC risk and may be useful in guiding surveillance decisions.

For practicing physicians, the message is both practical and cautionary: prevent cirrhosis when possible, use ultrasound plus AFP consistently, avoid overextending surveillance into low-risk groups, and resist adopting emerging tests before the evidence is available.

Dr. Jou pointed to under-surveillance, not over-surveillance, as the more pressing gap. “With the high burden of patients who are at risk for HCC and the diminishing hepatology workforce to care for liver disease patients, inconsistent surveillance in patients who need it is likely to be a significant ongoing issue,” she said.

A majority of HCC is still diagnosed either incidentally or when patients present with symptoms, she noted, adding that identifying at-risk patients and operationalizing recall systems requires infrastructure and funding that many practices lack.

Authors reported consulting and advisory roles with several pharmaceutical companies and research support from the NIH. One author also holds stock options and is listed on a related patent.

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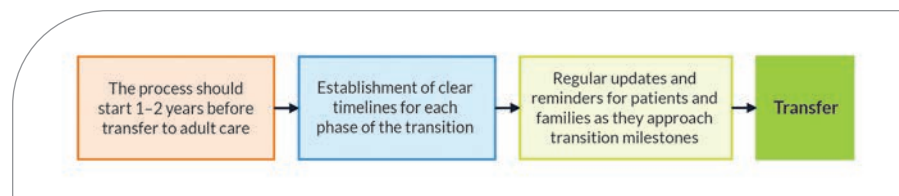
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Pediatric functional constipation: Societies release new clinical care pathway

Consensus guidance outlines stepwise diagnosis and treatment to streamline management and reduce unnecessary testing.

By [Doug Brunk](#)



Pediatric-to-adult transition care pathway

Credit: *Clinical Gastroenterology and Hepatology*

A new consensus clinical care pathway from two leading societies provides a standardized, stepwise approach to diagnosing and managing functional constipation in children.

Published in *Clinical Gastroenterology and Hepatology*, the pathway was developed by AGA and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition, based on a literature review and consensus from a panel of 13 multidisciplinary experts, and aims to reduce practice variation while improving care across primary and specialty settings.

Functional constipation affects about 10% of children worldwide and is a common reason for referral, yet management varies widely. The expert panel required at least 70% agreement on recommendations, ultimately reaching full consensus across diagnostic and treatment domains.

Diagnosis centers on history

The pathway prioritizes history and physical examination, reserving diagnostic testing for patients with alarm features or treatment-refractory disease. The authors recommend using Rome IV criteria as guidance but note that clinicians can diagnose constipation based on clinical judgment even if criteria are not fully met.

Routine imaging is discouraged. Abdominal radiography shows limited diagnostic accuracy and should be used selectively when examination is not feasible or findings are discordant.

Similarly, colonic transit studies and anorectal manometry are recommended only in select scenarios, such as when the diagnosis is unclear or a motility disorder is suspected.

Stepwise treatment approach

Treatment begins with diet, behavioral strategies, and pharmacologic therapy, escalating only when needed. Although

evidence for increased fiber intake is limited, a healthy diet is recommended, along with structured toileting and caregiver education.

Medical therapy is organized into three phases: disimpaction, maintenance, and withdrawal. Polyethylene glycol is recommended as first-line therapy, with doses of 1 to 1.5 g/kg daily for three to five days for disimpaction and lower doses for maintenance. Osmotic laxatives are the preferred initial maintenance therapy, with stimulant laxatives added if needed. Polyethylene glycol is more effective than alternatives such as lactulose or milk of magnesia, although differences are modest. Among newer agents, linaclotide showed benefit over placebo in pediatric trials and is approved for children older than six years, while lubiprostone did not outperform placebo in randomized trials.

For refractory cases, transanal irrigation achieved symptom improvement in 62% of patients in pooled analyses, and surgical options such as antegrade continence enemas are reserved for cases refractory to medical therapy.

Special populations and transition care

The pathway includes guidance for patients with neurodevelopmental disorders, who have higher rates of constipation and may present with atypical symptoms. Early referral to behavioral specialists is recommended.

The pathway outlines coordinated pediatric-to-adult care models and recommends starting transition discussions one to two years before transfer.

The work was supported by AGA and NASPGHAN, with funding from an independent medical education grant from Ironwood Pharmaceuticals. Several authors reported relationships with industry, including consulting and speaking roles.

GI & Hepatology News asked Leonel Rodriguez, MD, MS, lead author of the clinical care pathway and Section Chief of Pediatric Gastroenterology & Hepatology at Yale School of Medicine, to discuss its implications for practice.

Why is now a good time for publication of this clinical care pathway? What gap(s) in knowledge or therapeutics does it fill?

Dr. Rodriguez: Both the incidence and prevalence of functional constipation in children seem to be increasing over the last two decades (the former probably related to changes in dietary habits and behavioral disorders, and the latter probably due to lack of early detection and treatment and effective therapies leading to chronic symptoms). This makes constipation one — if not the most common — condition in the pediatric gastroenterologist's office. For these reasons, both AGA and NASPGHAN teamed up to develop a clinical care pathway that addresses common gaps in the evaluation and management of functional constipation, from early detection to prompt and proper therapy, to transition to adult care, in a more universal and real-world approach.

In your opinion, what are the top clinical takeaways from this work?

Dr. Rodriguez: We wanted to provide pediatric providers with a framework to empower them to detect and treat children early in the course of the disorder, a detailed but practical guide for medical therapy that includes aggressive use of stimulant laxatives early in treatment and for long-term maintenance. We also aimed to embrace the concept that transition can be multidirectional, depending on the course of the symptoms, allowing primary care providers to resume the care of patients when treatment is successful.

As you and your coauthors assembled this document, was there a topic, or perhaps more than one, that caused more deliberation than usual?

Dr. Rodriguez: We reached full agreement in all topics discussed, but perhaps the one that required debate and discussion the most was the definition of constipation. We wanted to be inclusive and create a tool that helps pediatric providers care for all children.

Did any aspect of your clinical practice change because of helping to form this clinical care pathway?

Dr. Rodriguez: I worked very closely with non-physician clinical providers during the development of this pathway. I work with such providers in my day-to-day clinical practice but during this process I became more cognizant of the importance of their role in the care of children with functional constipation.

What additional research may be needed/what questions remain unanswered on this topic?

Dr. Rodriguez: There is still so much we do not understand about functional constipation in children, but emphasis should be placed on developing and test strategies to increase early detection and early therapeutic interventions that have the potential to improve the long-term outcomes.

Dr. Rodriguez disclosed that he is a speaker for Medtronic.



Gluten found to trigger immune response at very low doses

Continued From Page 1 ➔

When the researchers used interval-censored modeling, the estimated dose triggering immune activation in 10% of patients (eliciting dose, ED₁₀) was 2.4 mg, and in 5% (ED₀₅) was 0.8 mg. The median eliciting dose (ED₅₀) was 111 mg. These findings suggest that immune activation can occur at gluten exposures below the 20 parts-per-million thresholds used in the US and Europe, which corresponds to roughly 3–5 mg per typical serving.

Symptoms do not track with exposure

Despite measurable immune activation, patient-reported symptoms were not dose dependent and did not differ from placebo at any gluten dose. Symptom severity scores increased modestly after challenges overall, but there was

no association between gluten dose and symptoms using multiple validated tools, including the Global Symptom Survey and Patient Gastrointestinal Symptoms survey.

This disconnect was evident even at higher doses, indicating that patients cannot reliably detect low-level gluten exposure based on symptoms alone.

Practical implications

For gastroenterologists, the findings highlight that current “gluten-free” labeling standards may not fully prevent immune activation in some patients with celiac disease. The study also reinforces that symptom-based assessment is insufficient for monitoring dietary adherence or inadvertent exposure, particularly at low doses. Objective biomarkers such as IL-2 may offer a more sensitive tool for detecting immune activation in both clinical practice and trials.

The prospective study enrolled adults aged 25–75 years who had maintained a gluten-free diet for more than two years. Participants completed 153 total challenges across four sequential cohorts,



with adaptive dose de-escalation and rigorous placebo control.

The researchers noted limitations of the study, including its single-center design, small sample size, and the exclusion of children and certain genetic subgroups, including patients homozygous

for HLA-DQ2.5. It also assessed acute immune responses rather than long-term outcomes such as mucosal injury.

The study was funded by Wesley Research Institute and Coeliac Australia. Dr. Daveson and several coauthors reported consulting roles, research funding, or patents related to celiac disease therapies.

GI & Hepatology News invited Dr. Daveson to elaborate on the study findings.

Why does this study matter?

Dr. Daveson: Global food labeling regulations vary around the world and are largely based on a study from 2007, where 50 mg of gluten a day resulted in a deterioration in people with celiac disease, though firm conclusions could not be drawn about doses of gluten below this level. Our study was the first to look at whether small amounts of gluten result in immune activation at very low doses — even below 10 mg and 50 mg. What we found is that immune activation was seen down to 3 mg.

When you had all the data in front of you, was there a finding, or perhaps more than one, that surprised you?

Dr. Daveson: At higher doses of gluten (3,000 mg to 6,000 mg), people with celiac disease on a strict gluten-free diet can develop pronounced nausea and vomiting when exposed, making it easier for them to recognize that they have ingested gluten. What was surprising in this study was that there was no difference in symptoms between the low doses and placebo, suggesting that people with celiac disease may not be able to recognize when they are inadvertently exposed to very small amounts of gluten. This is important for people with celiac disease who struggle to normalize their small bowel histology when trying to maintain a strict gluten-free diet. It may also have implications for the current FDA approval process of novel therapies for celiac disease, which currently require not only a demonstrable improvement in small bowel histology, but also an improvement in symptoms.

How might the findings influence clinical practice?

Dr. Daveson: They may influence global food labeling regulations regarding what is defined as “gluten-free” by regulatory bodies. It also answers a common question among people with celiac disease: what happens when they are inadvertently exposed to small amounts of gluten. It may also help explain why some studies suggest that patients take many years to enter mucosal remission despite adhering to a strict gluten-free diet.

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

Dr. Daveson: Global food labeling is based on a concentration which can be difficult to understand. We were also able to calculate an eliciting dose, (ED_p), where p indicates that dose is unsafe (in terms of IL-2 release) for p% of the population. An ED₀₅ would be safe in terms of IL-2 release for 95% of the population. In the United States and Europe, consuming 150–250 g of “gluten-free” food under the 20 ppm (or 20 mg/kg) standard may result in 3–5 mg of gluten exposure, exceeding the ED₁₀ (2.4 mg) estimated from our acute IL-2 endpoint. A comparable intake under the Australian and New Zealand “no detectable gluten” requirement (that sits at a threshold of ~3 ppm or 3 mg/kg) would be ~0.45–0.75 mg, below the ED₀₅ (0.8 mg) estimate and therefore predicted to be tolerated by most individuals with respect to acute immune activation.

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Simulation training may boost polypectomy technique

“There is no universal method for performing polypectomy, despite the high volume of procedures performed annually.”

By [Jess Allerton](#)

A simulation-based mastery learning (SBML) curriculum improved colonoscopic polypectomy performance among practicing gastroenterologists in a clinical validation study that evaluated real patient procedures before and after training. The findings, published in *Gastroenterology*, suggest that structured simulation-based education may help standardize technique and address variability in polypectomy performance in clinical practice.

“Colonoscopy with polypectomy is a core procedure performed by practicing gastroenterologists,” noted Srinadh Komanduri, MD, and colleagues in a research letter. “Yet, there is no universal method for performing polypectomy, despite the high volume of procedures performed annually.”

Incomplete resection of adenomatous tissue has been linked to colorectal cancers diagnosed after a previously negative colonoscopy, highlighting the importance of consistent procedural technique, reported Dr. Komanduri — of the Department of Medicine at Feinberg School of Medicine, Northwestern University, Chicago — and colleagues.

SBML is a competency-based training model in which participants must meet a defined minimum passing standard (MPS) to complete the curriculum. In this study, the program included a simulated skills pretest, an instructional video and lecture, expert-guided deliberate practice using an ex vivo bovine colon simulator with sessile and stalked polyps, and a simulated post-test in which participants were required to meet or exceed the MPS.

Investigators conducted a pre-post study at an academic medical center in Chicago. Nineteen practicing gastroenterologists participated, nearly two-thirds of whom had more than 10 years of clinical experience. Researchers analyzed videos of patient polypectomies



performed 12 months before and after completion of the SBML curriculum.

The analysis included procedures involving sessile or stalked polyps measuring at least 8 mm. A total of 168 polypectomies were reviewed from the pretraining period and 178 from the post-training period. Each procedure was evaluated using the 17-item modified Direct Observation of Polypectomy Skills (m-DOPyS) checklist, which assesses technical aspects of lesion evaluation, resection technique, and postresection management.

The primary outcome was the proportion of procedures meeting the checklist’s minimum passing standard. Before the training intervention, the median participant pass rate was 33.3%. After SBML training, the median pass rate increased to 80%.

Overall checklist scores also improved. The median mean score for each gastroenterologist increased from 78.8% of checklist items correct before training to 91.5% after training. When all procedures were analyzed together, median checklist scores increased from 86.7% to 100%.

The proportion of individual procedures meeting the minimum passing standard increased from 36.9% before training to 73.6% afterward. Improvements were seen across most technical domains of the checklist, including lesion visualization, snare placement, selection of resection technique, and post-polypectomy assessment.

For example, the proportion of

procedures in which endoscopists identified and treated residual polyp tissue increased from 49% before training to 80% after training. Photo documentation and retrieval of resected polyps also improved following the training intervention.

Patient and procedural characteristics were similar before and after the intervention. Mean polyp size was approximately 12.5 mm before training and 13.2 mm after, and average polypectomy time did not differ significantly between the two periods. Inter-rater reliability among blinded reviewers scoring the videos was substantial, with κ values ranging from 0.75 to 0.84.

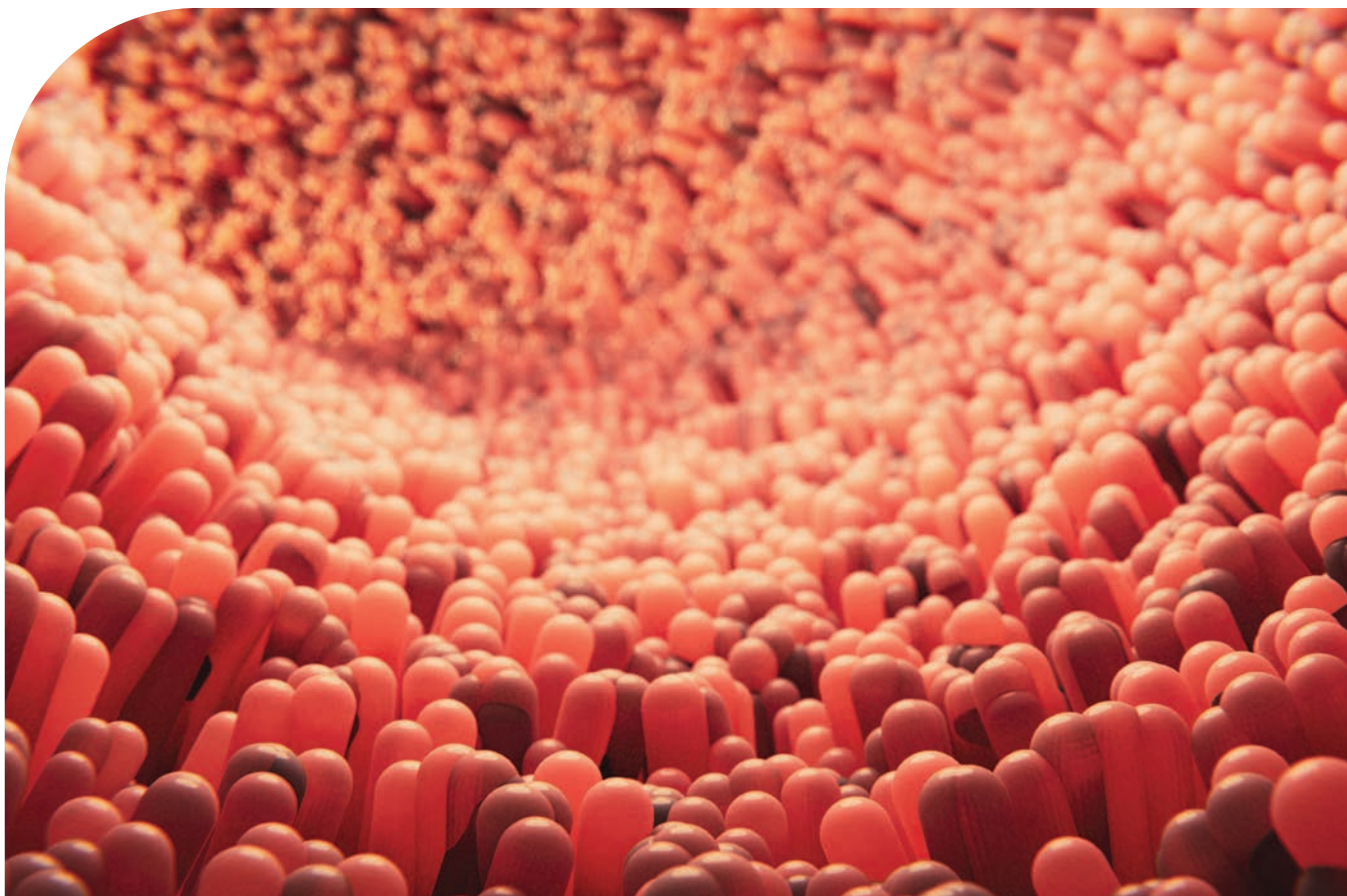
“Our study results highlight the urgent need for continuing procedural education for practicing gastroenterologists. The traditional model of skill acquisition during fellowship with limited ongoing assessment is insufficient. SBML is a promising component of continuing education for

polypectomy and warrants further study procedures,” wrote researchers.

Several limitations should be considered. The study used a pre-post design, which may introduce confounding factors. Video clips evaluated in the analysis included only the polypectomy segment of procedures, so some steps may not have been captured. In addition, the study was conducted at a single academic center, which may limit generalizability to other practice settings. Even after training, approximately one-quarter of procedures did not meet the minimum passing standard, suggesting that ongoing training or additional practice may be needed to achieve consistent proficiency.

The authors reported no conflicts of interest. The study was supported by a grant from the National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases.

“The traditional model of skill acquisition during fellowship with limited ongoing assessment is insufficient. SBML is a promising component of continuing education for polypectomy.”



Subcutaneous guselkumab shows strong remission in phase 3 UC trial

“Guselkumab provides an excellent choice for patients and clinicians where safety, efficacy, and convenience are priorities.”

By [Jess Allerton](#)

Subcutaneous guselkumab improved clinical, endoscopic, and histological outcomes in patients with moderately to severely active ulcerative colitis, according to results from the phase 3 ASTRO trial. The findings, published in *The Lancet Gastroenterology & Hepatology*, address a practical limitation of existing interleukin (IL)-23 inhibitors, which typically require intravenous induction before subcutaneous maintenance.

ASTRO was a double-blind, randomized, placebo-controlled, treat-through phase 3 trial conducted at 153 sites in 25 countries. The study enrolled adults with moderately to severely active ulcerative colitis (UC) (modified Mayo score 5–9) who had an inadequate response, intolerance, or dependence on conventional therapies or advanced treatments, including biologics, JAK inhibitors, or sphingosine 1-phosphate receptor modulators. A total of 418 participants were randomized to receive subcutaneous guselkumab (400 mg at weeks 0, 4, and 8 followed by maintenance dosing) or placebo. The primary endpoint

was clinical remission at week 12, with outcomes assessed through week 24.

“ASTRO shows that fully subcutaneous guselkumab induction achieved significantly higher week-12 clinical remission (28% vs 6%), endoscopic improvement (37% vs 13%), and histo-endoscopic mucosal improvement (30% vs 11%),” said corresponding author Millie Long, MD, MPH, in an interview with *GI & Hepatology News*. “In addition, ASTRO demonstrates sustained advantages across week-24 endpoints vs placebo, confirming that IL-23 blockade is sufficient to rapidly and durably control mucosal inflammation in moderate-severe UC. These data independently replicate and extend the prior QUASAR IV-induction findings. Targeting IL-23p19 with a dual-acting agent like guselkumab yields deep molecular, histologic, and clinical remission.”

By week 24, adverse event rates were similar or lower in the guselkumab groups

compared with placebo (53%–61% vs 65%), and serious adverse events occurred in 4% of guselkumab-treated patients versus 12% in the placebo group. The most commonly reported events were worsening ulcerative colitis, arthralgia, and upper respiratory tract infection. No new safety concerns were identified, and serious infections were infrequent.

“Guselkumab’s safety profile is at least as favorable — and in several domains potentially better — than current biologics, particularly compared with anti-TNFs (infection risk) and JAK inhibitors (potential for VTE, serious infection),” said Dr. Long, of the Division of Gastroenterology and Hepatology, University of North Carolina at Chapel Hill, NC. “It closely resembles the strong safety profile seen with the other IL-23p19 inhibitors. There is also minimal immunogenicity, thus no concomitant immunomodulators are required. Clinicians should consider the excellent safety, efficacy, and patient preference for modality of delivery when selecting patients for this therapy.”

The study is the first to demonstrate that an IL-23 inhibitor can be administered entirely subcutaneously for both induction and maintenance in ulcerative colitis. This may reduce reliance on infusion-based care and offer greater flexibility for patients and health care systems. The findings also support the role of IL-23 as a central pathway in ulcerative colitis pathogenesis and reinforce the therapeutic potential of IL-23p19 inhibition.

Looking ahead, Dr. Long explained

Key clinical takeaways

Fully subcutaneous guselkumab achieved higher rates of week-12 clinical remission (28% vs 6%), endoscopic improvement (37% vs 13%), and histo-endoscopic healing (30% vs 11%) versus placebo in moderate-severe UC.

Efficacy was sustained through week 24 with a favorable safety profile, including lower serious adverse events (4% vs 12%) and no new safety signals.

Guselkumab is the first IL-23 inhibitor effective as a fully subcutaneous induction and maintenance regimen, offering a convenient alternative that may shift IL-23 agents earlier in UC treatment sequencing.

these results may influence treatment sequencing in ulcerative colitis as therapeutic options continue to expand. “Guselkumab is one of the safest long-term advanced therapies for UC with strong evidence of achieving and maintaining deep remission. The fully subcutaneous regimen also enhances access and adherence. From a treatment sequencing perspective, I suspect that IL-23 agents will move earlier in the therapeutic algorithm for UC. Guselkumab provides an excellent choice for patients and clinicians where safety, efficacy, and convenience are priorities.”

The authors noted that the study excluded patients previously treated with IL-12 or IL-23 inhibitors, which may limit generalizability to this population. In addition, histological outcomes were not assessed at week 24, and placebo-treated patients were eligible for rescue therapy at week 16, which may affect longer-term comparisons with placebo.

The study was funded by Johnson & Johnson. Several authors reported financial relationships with industry, including consulting fees, research support, or employment with the sponsor. Full disclosures are detailed in the published findings.

Pancreatic cystic lesions: A case-based approach

By Ross Buerlein, MD, Vanessa Shami, MD, and Himesh Zaver, MD

The prevalence of pancreatic cysts increases with age, with recent meta-analyses demonstrating a range from 9% in individuals aged 50 to 59 years to as high as 38% in patients aged 80 years or older.¹⁻³

Pancreatic cysts represent a heterogeneous group of lesions, and their malignancy potential varies based on cyst type. These lesions are typically divided into two categories: inflammatory fluid collections and pancreatic cystic neoplasms (PCNs).

Inflammatory fluid collections arise as a complication of pancreatitis or pancreatic injury and lack a true epithelial lining. They can be challenging to distinguish from PCNs based on imaging alone. According to the Revised Atlanta Classification, these include acute peripancreatic fluid collections and pseudocysts arising after interstitial pancreatitis, as well as acute necrotic collections and walled-off pancreatic necrosis following necrotizing pancreatitis. The generally mature approximately four weeks after pancreatitis onset, though time to “maturity” can be variable.⁴

PCNs are divided into mucinous and non-mucinous lesions. Mucinous lesions are considered pre-malignant and are characterized by a mucin-secreting columnar epithelium, as seen in intraductal papillary mucinous neoplasms (IPMNs), mucinous cystic neoplasms (MCNs), and solid pseudopapillary neoplasms. In contrast, serous cystadenomas (SCAs) are benign, non-mucinous lesions composed of multiple small cysts lined by cuboidal epithelium and are thought to arise from pancreatic acinar cells. Less common serous lesions include solid serous adenomas, cystic neuroendocrine tumors, and cystic lesions associated with von Hippel-Lindau syndrome.

High-resolution cross-sectional imaging with contrast enhanced computed tomography (CT) or magnetic resonance imaging (MRI) allows for non-invasive assessment and characterization of pancreatic cystic lesions. Endoscopic ultrasound (EUS) is more invasive but provides superior spatial resolution and diagnostic cyst sampling. EUS-directed fine needle aspiration (EUS-FNA) can aid in differentiating serous from mucinous lesions. Mucinous fluid is typically more viscous and may demonstrate a positive “string sign,” which has been reported to have a specificity of approximately 95% for mucinous lesions.^{3,5}

The columnar epithelium of mucinous lesions secretes carcinoembryonic antigen (CEA), resulting in mucinous lesions typically having an elevated CEA level >192 ng/mL.⁶ More recent data have shown that a low cyst fluid glucose level (<50 mg/dL) has a significantly higher sensitivity for identifying a mucinous lesion when compared to CEA alone.⁷ Cyst fluid amylase level is often elevated in lesions with a connection to the pancreatic duct, which can be seen in IPMNs and pseudocysts. The 2024 international consensus guidelines on pancreatic cysts recommend consideration of molecular DNA markers in cases with diagnostic uncertainty, representing the first

major guideline to formally address the role of next generation sequencing in cyst evaluation.⁸ Microbiopsy forceps, passed through a 19-gauge needle, can be utilized to sample the cyst epithelium, improving diagnostic accuracy with a slight increased risk of post-procedure pancreatitis and bleeding.⁹ Lastly, confocal laser endomicroscopy, performed through a 19-gauge needle following intravenous injection of fluorescein, allows real time assessment of the cyst epithelium and may further enhance diagnostic accuracy, although its use remains limited to select centers.¹⁰

Case 1

An 81-year-old male was incidentally found on MRI to have a 4.3 cm x 2.1 cm cystic lesion in the head of the pancreas without upstream pancreatic duct dilation. He was overall healthy for his age. EUS confirmed no other high-risk features such as mural nodules, solid components, or main pancreatic duct dilation. Cyst fluid aspiration revealed an amylase level of 156 U/L, glucose of 20 mg/dL, and CEA of 139,340 ng/mL. Cytology evaluation supported the presence of mucin but no malignant cells.

Case 1 answer: Branch duct intraductal papillary mucinous neoplasms

Branch-duct intraductal papillary mucinous neoplasms (BD-IPMNs) are the most common PCNs. BD-IPMNs occur with similar frequency in men and women, and may present as solitary or multifocal lesions. By definition, all IPMNs communicate with the pancreatic duct, resulting in elevated cyst fluid amylase. Their columnar epithelium secretes carcinoembryonic antigen (CEA), leading to elevated cyst fluid CEA levels (>182ng/mL[VS]), while cyst fluid glucose is typically low (<50 mg/dL).⁷

Management of BD-IPMNs is guided by the presence of “high-risk” features, which vary slightly among guidelines but generally include^{3,6,8,11-13}:

- Malignant or dysplastic cytology
- IPMN-related symptoms (pain, jaundice, pancreatitis)
- Cyst size ≥3 cm
- Enhancing mural nodule or solid component
- Main pancreatic duct dilation ≥5 mm
- Elevated serum CA 19-9
- Rapid cyst growth (definitions range from ≥2.5 mm/year to ≥5 mm over 2 years)

When high-risk features are present, multidisciplinary discussion is recommended to determine the need for further assessment with EUS or surgical resection. In their absence, surveillance is advised, with imaging intervals determined by cyst size. If lesions are unchanged after 5 years, consideration to discontinue surveillance could be given. Patients who undergo surgical resection require ongoing imaging due to the risk of metachronous IPMNs and cancers.

EUS-guided fine needle injection of chemotherapy for ablation of mucinous pancreatic cystic lesions may also be offered in cases with high-risk



features. While initial chemoablation incorporated ethanol, a prospective randomized controlled trial demonstrated that elimination of ethanol significantly reduced adverse events, particularly pancreatitis, without compromising efficacy.¹⁴ Subsequent studies using ethanol-free protocols have shown that approximately 65%–70% of patients undergoing EUS-guided chemotherapy ablation achieve >95% cyst volume reduction on follow-up imaging, with the vast majority maintaining that response after many years of follow-up.^{15,16} Despite complete cyst resolution, continued radiographic surveillance is recommended. This outpatient procedure offers a less invasive alternative to surgery, including pancreaticoduodenectomy, with substantially lower procedural risk and no demonstrated adverse impact on quality of life compared with surgical management.^{15,16}

Case 2

A 68-year-old male presented with new-onset jaundice and elevated bilirubin (total bilirubin 3.3 mg/dL). CT demonstrated a 4.8 cm cystic lesion in the head of the pancreas communicating with the main pancreatic duct, with associated main duct dilation to 9 mm and common bile duct dilation to 15 mm. He subsequently underwent EUS which revealed mucin extruding from the pancreatic os, consistent with the classic “fish eye” appearance of mucorrhea. A thick walled, mucin filled cystic lesion was visualized in the pancreatic head, communicating with a dilated, mucin filled main pancreatic duct. As much as pathologists would like to provide a definitive answer, performing histochemical or immunohistochemical stains to highlight them does not change this fact. This also applies when a case is challenging microscopically. For any number of reasons, a biopsy can be difficult to interpret. Pathologists don’t want to give an equivocal answer if they can avoid it. If cancer is there, we want to say “positive for malignancy” rather than “atypical and suspicious,” but there are times where the latter can’t be avoided. This may necessitate a conversation and/or repeat sampling.

Case 2 answer: Mixed type IPMN

The patient subsequently underwent pancreaticoduodenectomy, and pathology revealed a mixed type IPMN with a focus of invasive adenocarcinoma. IPMNs are classified into three subtypes: main duct (MD-IPMN), branch duct (BD-IPMN), and mixed type. MD-IPMNs arise from the epithelium of the main pancreatic duct, leading to ductal dilation and a substantially higher risk of malignancy compared with BD-IPMNs. Surgical series report underlying malignancy in

up to 60% of resected MD-IPMNs; accordingly, most guidelines recommend multidisciplinary with strong consideration of surgical resection when the main pancreatic duct measures ≥ 5 mm, and particularly ≥ 10 mm, in patients with suspected mixed type or MD-IPMN.^{3,15} In this case, the presence of mucous extruding from the pancreatic os is pathognomonic for a main duct IPMN.

Case 3

A 37-year-old woman presented with a three-year history of intermittent right upper quadrant abdominal pain, chronic diarrhea, and episodic nausea and vomiting. CT revealed a 3.2×2.5 cm hypodense lesion in the pancreatic body with internal septations, concerning for a cystic neoplasm.

She subsequently underwent EGD and EUS, which revealed a solid appearing, round, well-defined 29 x 28 mm mass in the body of the pancreas. Cytology from fine needle aspiration showed papillary clusters of uniform cells with nuclear beta catenin and focal synaptophysin positivity.

Case 3 answer: Solid pseudopapillary neoplasm

Solid pseudopapillary neoplasms (SPNs) are rare pancreatic tumors that predominantly affect women in their second and third decades of life.¹¹ Patients may present with nonspecific symptoms such as abdominal pain, nausea, vomiting, or weight loss, although many lesions are discovered incidentally on imaging. SPNs typically appear as well-circumscribed, mixed solid and cystic lesions that may arise anywhere within the pancreas, usually as solitary masses.³

Histologically, SPNs are lined by cuboidal epithelial cells and lack communication with the pancreatic duct, resulting in normal cyst fluid amylase levels. Immunohistochemical staining is characteristically positive for beta-catenin, vimentin, alpha-1 antitrypsin, and synaptophysin.¹⁷ The histogenesis of SPNs remains uncertain, with acinar, endocrine, ductal, and multipotent progenitor cells all proposed as potential cells of origin. Although SPNs generally exhibit indolent behavior, malignant transformation can occur, with higher risk in larger lesions, particularly those measuring 5 cm or greater. Given their occurrence in younger patients and the potential for progression, surgical resection is typically recommended.³

Case 4

A 68-year-old woman presented with abdominal pain. A CT scan revealed an undifferentiated pancreatic lesion. The pain subsided with antacids. Outpatient MRI demonstrated a multicystic lesion in the pancreatic tail with enhancing internal septations and no definite communication with the main pancreatic duct. EUS revealed a 43 mm x 38 mm, anechoic, multicystic, septated lesion at the pancreatic body/tail junction. The lesion contained numerous thin septations without a solid component or mural nodule and did not appear to communicate with the main pancreatic duct.

Case 4 answer: Serous cystadenomas

Serous cystadenomas (SCAs) are typically asymptomatic and most commonly occur in women

in their fifth to seventh decades of life.^{3,11,18,19}

Imaging usually reveals a solitary, well-circumscribed microcystic lesion with a characteristic honeycomb pattern. A central stellate scar with “sunburst” calcification is considered pathognomonic, though it appears in only about 20%-30% of cases.¹¹ A less common macrocystic form exists and can be challenging to differentiate from mucinous cystic lesions, as illustrated in this case.

Multifocal SCAs are associated with von Hippel-Lindau (VHL) syndrome and may include a neuroendocrine component. Because SCAs do not communicate with the pancreatic duct, cyst fluid amylase levels are typically low. Diagnosis can often be established on imaging alone, though EUS is helpful when imaging findings are indeterminate. When aspirated, cyst fluid is characteristically thin and serous, with a typically very low CEA level (< 5 ng/mL) and often glucose > 50 mg/dL.

SCAs have an extremely low risk of malignant transformation (approximately 0.1%).^{18,19} As such, surgical resection is generally reserved for patients who develop symptoms such as pain or compression of adjacent structures.^{3,18,19}

Emerging technologies

EUS-directed pancreatic cyst ablation has emerged as a less invasive therapeutic option for select premalignant pancreatic cystic neoplasms, particularly in patients who are poor surgical candidates or who wish to avoid major surgery.

Multiple EUS-directed ablation techniques have been studied, with newer approaches demonstrating improved efficacy and lower rates of adverse events. These include chemotherapy ablation and radiofrequency ablation. Reported rates of complete cyst ablation vary widely across studies, highlighting the need for further investigation.

Ross C. D. Buerlein, MD; Himesh B. Zaver, MD; and Vanessa M. Shami, MD, are affiliated with the Division of Gastroenterology and Hepatology at the University of Virginia Health System in Charlottesville, Virginia.

Dr. Buerlein is an Assistant Professor of Medicine in the Division of Gastroenterology & Hepatology, Section of Interventional Endoscopy, at the University of Virginia Medical Center in Charlottesville, Virginia.

Dr. Zaver is with the Division of Gastroenterology & Hepatology at the University of Virginia Medical Center in Charlottesville, Virginia.

Dr. Shami is a Professor of Medicine, Director of Endoscopic Ultrasound, and Section Head of Interventional Endoscopy in the Division of Gastroenterology & Hepatology at the University of Virginia Medical Center in Charlottesville, Virginia.

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The new AGA President: Byron L. Cryer, MD's purpose-driven career

A child prodigy of remarkable focus, he became a concert violinist at the age of six.

The arc of the gastroenterology career of Byron L. Cryer, MD, is not defined by a single achievement, but by a steady accumulation of purpose-driven work spanning clinical care, scientific discovery, mentorship, and leadership. As the new president of AGA, Dr. Cryer stands as a figure whose influence reflects both intellectual rigor and a deeply rooted commitment to people. His journey offers a compelling portrait of how values, opportunity, and vision can converge to produce enduring impact.

Dr. Cryer's story begins with a foundation grounded in family, migration, and generational resilience. His parents were raised in Louisiana farming communities, where hard work and perseverance were not abstract ideals but daily necessities. Seeking broader opportunities, they settled in Miami, Florida. That decision, like many made quietly by families striving for progress, would shape the trajectory of their children's lives.

Growing up in Miami, Dr. Cryer was immersed in a culturally rich and diverse environment that broadened his worldview early. By the age of six, he had begun speaking Spanish, eventually achieving fluency. This early exposure to multiple cultures fostered an adaptability and ease of communication that would later distinguish him as both a clinician and a leader. It also instilled a perspective that would inform his lifelong commitment to equity and inclusion within medicine.

Before medicine, Dr. Cryer's first discipline was music. A child prodigy of remarkable focus, he became a concert violinist at the age of six, performing publicly while most children were just beginning to explore structured learning. His musical pursuits expanded to include piano and trumpet, but more importantly, they cultivated habits of precision, discipline, and pattern recognition. For Dr. Cryer, music was not merely an early interest but a framework for thinking. The transition from music to science, when it came, felt less like a pivot and more like a natural evolution, as both demanded rigor, creativity, and comfort with complexity.

Raised in the post-civil rights era, Dr. Cryer internalized a message that knowledge carried obligation: to act with integrity, to contribute meaningfully, and to help build institutions that expand opportunity for others. These principles have spanned his career, particularly in his work in mentorship and workforce development.

Dr. Cryer pursued his undergraduate studies at Harvard University, concentrating in biology, before enrolling at Baylor College of Medicine. Initially, his path within medicine was not predetermined. Like many students, he explored broadly, open to possibilities. Yet a single moment would alter the course of his career.

During his second year of medical school, Dr. Cryer attended a lecture delivered by Fred Sutton, MD — an African American gastroenterologist. Until that point, Dr. Cryer had not seen an African-American faculty member at his medical school. The impact of that one-hour lecture was immediate and profound. It crystallized not only his interest in gastroenterology, but also his understanding of representation and its power to shape aspirations. By the end of the lecture, he had decided on his specialty.

That moment would reverberate throughout his career, informing a deep commitment to mentorship and leadership development. For Dr. Cryer, the experience reinforced a simple but powerful truth: inspiration does not always come from grand gestures. It can emerge from a single, visible example of possibility.

A second pivotal experience followed during his residency, when he attended lectures on the emerging role of pharmacologic agents in preventing NSAID-induced gastrointestinal injury. The



Throughout his career, Dr. Cryer has paired scientific rigor with a deep commitment to mentorship and leadership.

concept of gastroprotection captured his curiosity. Soon after, he sought mentorship from Mark Feldman, MD, at the University of Texas Southwestern Medical Center, ultimately moving to Dallas to pursue fellowship training.

This decision marked the beginning of a career-long focus on the gastrointestinal effects of medications, particularly NSAIDs and aspirin. Over the ensuing decades, Dr. Cryer would become an internationally recognized authority in this domain. His body of work, comprising more than 150 peer-reviewed publications, spans translational science, clinical trials, epidemiology, and biomarker research. At a time when NSAIDs were among the most widely used medications worldwide, his research helped clarify both their benefits and their risks, advancing a more nuanced, patient-centered approach to care.

Rather than advocating for simplistic conclusions, Dr. Cryer's

Left: Dr. Cryer with his husband, Martin Balderrama. Middle: Dr. Cryer became a concert violinist at the age of six. Right: Dr. Cryer speaking at an FDA meeting on the safety of arthritis drugs.



Lightning round

What is your favorite GI organ and why?

The stomach, because it sits at the crossroads of physiology, pharmacology, and clinical impact. It's where some of the most elegant translational science has occurred, from acid suppression to *H. pylori*, and where therapeutics have fundamentally changed patient outcomes. It's also where I've spent much of my academic career, so there's both intellectual and personal investment.

What is the best piece of advice you've given or received?

"Be intentional about your trajectory. If you don't define your path, someone else will define it for you." That advice shaped how I approached leadership, research, and national engagement. I often translate that into mentoring others: find your lane, own your story, and deliver consistently.

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

The future of gastroenterology at the intersection of clinical excellence, innovation, and leadership, particularly how AI and emerging technologies will reshape how we deliver care, train physicians, and measure outcomes. I could also do the same on NSAID-related GI injury and prevention without much effort.

What is your favorite way to unwind after work?

For me, exercising creates a separation from the clinical and administrative intensity of the day. I start my days very early in the mornings, typically well before sunrise. For that reason, by the end of the workday

my brain is exhausted, and I can't further mentally challenge it. Therefore, exercising allows me to turn my brain off and do something entirely different than I have done all day.

If you could have dinner with anyone, who would it be and why?

I'd choose a small dinner with a mix of people rather than a single individual. First on the list would be someone like Atul Gawande, a Harvard surgeon and public health leader. I would invite him for a dialogue that would sharpen how to take big ideas (AI, quality, leadership) and actually embed them into everyday clinical practice at scale. I would also invite Yo-Yo Ma for the intersection of discipline and artistry, and a pioneering GI figure like Barry Marshall. That kind of cross-disciplinary conversation is where the most interesting ideas tend to emerge.

Who inspires you and why?

I've been shaped by mentors who combined intellectual rigor with humility, people who were not only outstanding clinicians and scientists, but also deeply committed to developing others. That combination of excellence and generosity is what I try to model in my own leadership roles.

What's a recent breakthrough or technology in the field you're excited about?

AI in endoscopy and clinical workflows. Not just detection algorithms, but systems that can augment decision-making, improve efficiency, and ultimately standardize high-quality care across environments. If AI is implemented thoughtfully, it has the potential to elevate both performance as gastroenterologists and patient outcomes at scale.

work emphasizes balance — risk stratification, individualized decision-making, and evidence-based mitigation strategies. His expertise extends beyond academia into national policy, including service on the U.S. Food and Drug Administration's Gastrointestinal Advisory Committee and as a consultant to the agency's Center for Drug Evaluation and Research. In these roles, he became known for his ability to communicate complex issues with clarity and precision.

Dr. Cryer is currently with Baylor University Medical Center, where he serves as chair of internal medicine and holds the Ralph Tompsett Endowed Chair in Medicine. In this role, he operates at the intersection of academic medicine and large-scale clinical practice, bringing a systems-oriented approach to leadership that reflects decades of experience.

Dr. Cryer's relationship with AGA spans more than three decades, beginning during his fellowship in 1989. Over the years, he has contributed across nearly every dimension of the organization's mission. His leadership roles have included service on the AGA Institute Governing Board, chairing the Underrepresented Minority Committee, and co-leading initiatives such as the AGA Equity Project and the Future Leaders Program. Through these efforts, he has helped shape pipelines for leadership development and broaden participation within the field.

As he steps into the presidency of AGA, Dr. Cryer brings not only a distinguished record of achievement, but also a leadership philosophy shaped by decades of experience and guided by enduring values. His approach is not defined by singular vision alone, but by stewardship.

This Member Spotlight is adapted from an article published in Gastroenterology by Rhonda F. Souza, MD, and Stuart J. Spechler, MD, AGAF, FACC.





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