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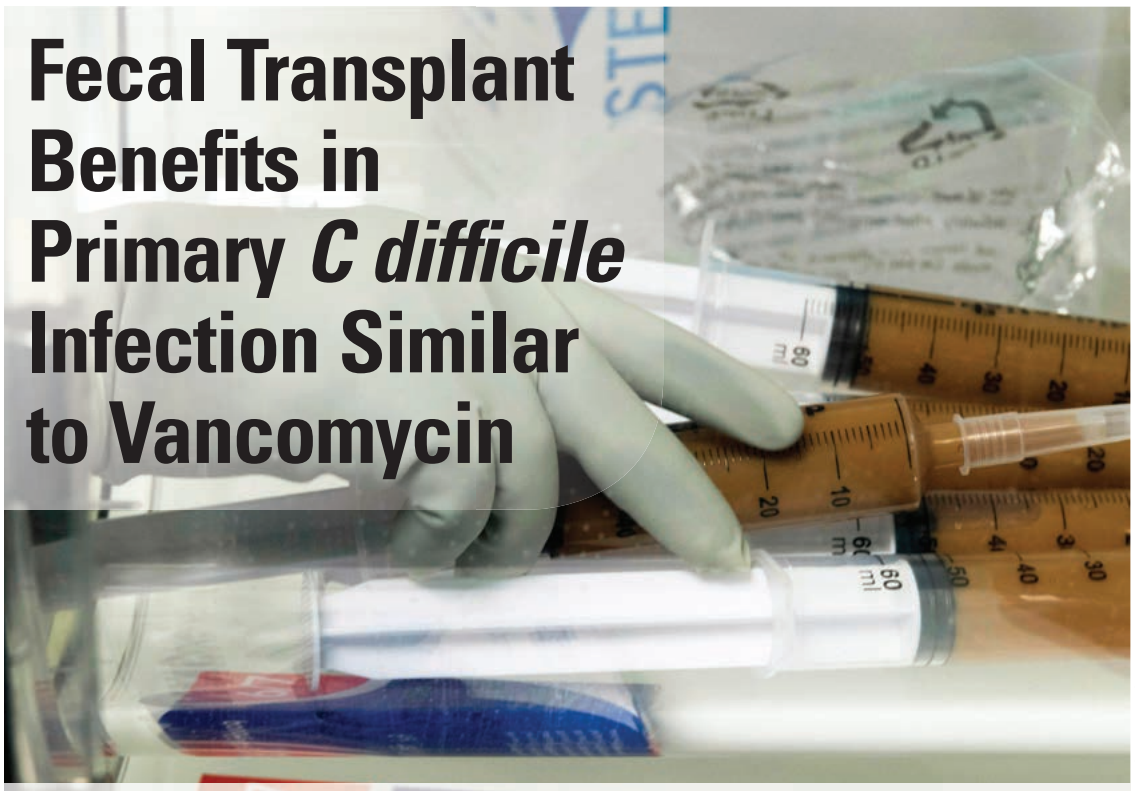
GI&Hepatology News

December 2025 Volume 19 / Number 12

Fecal Transplant Benefits in Primary *C difficile* Infection Similar to Vancomycin



THIERRY ZOCCOLAN/AFP VIA GETTY IMAGES

Fecal microbiota transplantation specifically consists of direct instillation of fecal matter to the upper gastrointestinal tract, via capsules or duodenal infusion, or the lower gastrointestinal tract via colonoscopy or enema.

BY NANCY A. MELVILLE

Fecal microbiota transplantation (FMT), shown to be effective in the treatment of recurrent *Clostridioides difficile* infection (CDI), also demonstrates significant benefit in the treatment of primary CDI, with efficacy that is comparable to the standard treatment of vancomycin, and in some measures, with even stronger efficacy, new research revealed.

"FMT, prepared and administered according to international guidelines, is an effective and safe treatment option for *C difficile* infections, which should be considered for all patients with the infection," first author Frederik Emil Juul, MD, PhD, of the Clinical Effectiveness Research Group, University of Oslo in Norway, told *GI & Hepatology News* in an interview.

FMT even showed a numerical superiority to vancomycin, which, though not statistically significant, "indicates that FMT has the potential to change the current practice of antibiotic therapy and may establish FMT as a first-line treatment for primary CDI," the authors further asserted in the study, published recently in the *Annals of Internal Medicine* (2025 Jun. doi: 10.7326/ANNALS-24-03285).

See **Transplant** · *page 16*

Healthy Diet, Exercise Cut Liver Death Risk in Drinkers

BY CAROLYN CRIST

Following a healthy diet and engaging in a high level of physical activity can significantly lower the risk for alcohol-related liver mortality, even among all drinking patterns, including heavy and binge drinking, according to a new study from Indiana University researchers.

Notably, any amount of daily alcohol intake or binge drinking increases the liver mortality risk, the researchers found. However, that risk can be reduced somewhat with healthy dietary patterns and increased physical activity.

Although previous studies suggested that one or two drinks per day could be associated with lower risks for cardiovascular disease, cancer, or liver-related outcomes, other confounders and unmeasured lifestyle behaviors could vary significantly between consumers and influence their health risks, the researchers said.

Dr. Chalasani

"A significant knowledge gap exists regarding the interplay of dietary patterns and physical activity with alcohol-attributable liver-specific mortality," said senior author Naga Chalasani, MD, AGAF, professor of gastroenterology and hepatology at the Indiana University School of Medicine in Indianapolis.

"It is not well understood whether healthy diets or

See **Healthy Diet** · *page 21*

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THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

LETTER FROM THE EDITOR

Is AI a Cure for Clinician Burnout?

The practice of medicine is evolving rapidly, with clinicians facing enhanced pressure to maximize productivity while managing increasingly complex patients and related clinical documentation. Indeed, clinicians are spending less time seeing patients, and more time in front of a computer screen.

Despite the many rewards of clinical medicine, rates of clinical practice attrition have increased among physicians in all specialties since 2013 (Ann Intern Med. 2025 Oct. doi: 10.7326/ANNALS-25-00564) with enhanced administrative burdens identified as a prominent driver. Among its many applications, artificial intelligence (AI) has immense potential to reduce the administrative and cognitive burdens that contribute to clinician burnout and attrition through tools such as AI scribes — these technologies have been rapidly adopted across healthcare systems and are already in use by ~30% of physician practices. The hope is that AI scribes will significantly reduce documentation time, leading to improvements in clinician well-being and expanding capacity for patient care. Indeed, some studies have shown up to a 30% improvement in documentation efficiency.

So, is AI a cure for physician burnout? The answer depends on what is done with these efficiency gains. If healthcare organizations respond to this enhanced efficiency by increasing patient volume expectations rather than allowing clinicians to recapture some of this time for meaningful work and professional well-being, it could create a so-called "workload paradox" where modest time savings are offset by greater productivity demands and the cognitive burden of reviewing AI-generated errors. While AI offers substantial promise as a tool to reduce administrative burdens, its success will depend on thoughtful and responsible implementation that prioritizes clinician well-being and patient safety in addition to productivity.


Dr. Adams

'While AI offers substantial promise as a tool to reduce administrative burdens, its success will depend on thoughtful and responsible implementation.'

In our final issue of 2025, we highlight a recent RCT from *Annals of Internal Medicine* finding that fecal microbiota transplantation is at least as effective as vancomycin in treating primary *C difficile* infection. In this month's Member Spotlight, we feature Andrew Ofosu, MD, MPH (University of Cincinnati Health), who stresses the importance of transparency and compassion in communicating effectively with patients, particularly around complex diagnoses. We hope you enjoy this and all the exciting content in our December issue. ■

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Approach to Weight Management in GI Practice

In Focus
Brought To You By The New Gastroenterologist

BY COLLEEN R. KELLY, MD, AGAF

Dr. Kelly is based in the Department of Medicine, Division of Gastroenterology, Brigham and Women's Hospital, and Harvard Medical School, both in Boston. She reported serving on the clinical advisory board for OpenBiome (unpaid) and has served on an advisory board for Eli Lilly.

Introduction

The majority of patients in the United States are now overweight or obese, and as gastroenterologists we treat a number of conditions that are caused or worsened by obesity. Cirrhosis related to metabolic-associated fatty liver disease (MAFLD) is now a leading indication for liver transplantation in the US, and obesity is a clear risk factor for all major malignancies of the gastrointestinal (GI) tract, including esophageal, gastric cardia, pancreatic, liver, gallbladder, colon, and rectum. Obesity is associated with dysbiosis and impacts barrier function: increasing permeability, abnormal gut bacterial translocation, and inflammation. It is more common than malnutrition in our patients with inflammatory bowel disease (IBD), where it impacts response to biologic drugs, increases the technical difficulty of surgeries, such as ileal pouch-anal anastomosis, and is associated with worse surgical outcomes. Furthermore, patients with obesity may be less likely to undergo preventative cancer screenings and are at increased risk related to sedation for endoscopic procedures. With over 40% of Americans suffering from obesity, and increasingly effective treatments available, the integration of weight management into a gastroenterology practice is essential to optimize outcomes.

Understanding the Mechanisms of Obesity

There are complex orexigenic and anorexigenic brain pathways in the hypothalamus which control global energy balance. Obesity results when energy intake exceeds energy expenditure. While overeating and a sedentary lifestyle are commonly blamed, there are a number of elements that contribute, including genetics, medical conditions, medications, psychosocial factors, and environmental components. For example, sleep loss contributes to weight gain by several mechanisms including increasing ghrelin and decreasing leptin levels, thereby increasing hunger and appetite, as well as by decreasing insulin sensitivity and increasing cortisol. Subjects exposed to sleep deprivation in research settings take in 550 kcal more the following day. Medications used commonly in GI practice including corticosteroids, antihistamines, propranolol, and amitriptyline are obesogenic, and cannabis can impact hypothalamic pathways to stimulate hunger.

When patients diet or exercise to lose weight, as we have traditionally advised, there are strong hormonal changes and metabolic adaptations that occur to preserve the defended fat mass or "set point." Loss of adipose tissue results in decreased production of leptin, a hormone that stimulates satiety pathways and inhibits orexigenic pathways, greatly increasing hunger and cravings. Increases in ghrelin production by the stomach decreases perceptions of fullness. With weight loss, energy requirements decrease, and muscles become more efficient, meaning fewer kcal are needed to maintain bodily processes. Eventually a plateau is reached, while motivation to diet and restraint around food wane, and hedonistic (reward) pathways are activated.

These powerful factors result in the regain of lost weight within 1 year in the majority of patients.

Implementing Weight Management Into GI Practice

Given the stigma and bias attached to obesity, patients often feel shame and vulnerability about the condition. It is important to have empathy in your approach, asking permission to discuss weight and using patient-first language (eg, "patient with obesity" not "obese patient"). While BMI is predictive of health outcomes, it does not measure body fat percentage and may be misleading, such as in muscular individuals. Other measures of adiposity including waist circumference

Continued on following page

Table 1. 10 Pillars of Weight Management

Recommendation	Description
Prioritize Balanced Nutrition	Focus on vegetables, fruits, whole grains, lean proteins, and healthy fats. High-fiber, high-protein diets increase satiety and control calories. The Mediterranean diet promotes heart/brain health, reduces cancer risk, supports weight control, and lowers inflammation.
Avoid Ultra-Processed Foods	Limit foods high in added sugars, unhealthy fats, and refined carbs. These foods can trigger overeating by stimulating dopamine (similar to addictive drugs).
Aim for 150 Minutes of Exercise Weekly	Engage in moderate activities (walking, biking, dancing, swimming) for 150 minutes/week. Add strength training 2x/week to build muscle, support metabolism, aid long-term weight loss, and improves cardiovascular health and mood.
Increase NEAT (Non-Exercise Activity Thermogenesis)	Add more movement to daily routine: take stairs, walk during calls, stand more, take walking breaks, park farther away, fidget —find small ways to move more daily.
Prioritize Quality Sleep (7-8 Hours/Night)	Lack of sleep disrupts hunger hormones, increases cravings, and impairs decisions —contributing to weight gain. Avoid eating within 3 hours of bedtime.
Eat Enough Protein	Target 1 gram per kg body weight/day (or 1 g per 2.2 lbs). Include cottage cheese, Greek yogurt, lean meats. Protein drinks/bars can help — look at sugar/additive content.
Manage Stress Effectively	Use mindfulness, yoga, meditation, nature time, and deep breathing to manage stress, lead to emotional eating and weight gain.
Stay Hydrated	Drink water throughout the day. Thirst may be mistaken for hunger. Hydration supports satiety. Avoid sugary drinks and juice.
Eat Bread Last	Begin meals with salad (with olive oil) or protein. Eating carbs (bread, rice, potatoes) later reduces the glycemic and insulin response, helping reduce intake.
Set Realistic Goals and Track Progress	Set achievable weight and lifestyle goals. Use food diaries/apps to track meals and exercise. Weigh yourself daily (or at least weekly).

Source: Colleen R. Kelly, MD, AGAF

More gastroenterologists are expanding their practices to include nutrition and weight management, especially with highly effective medications on the market and the evolving field of bariatric endoscopy.

Dr. Colleen R. Kelly reviews the approach to weight management for gastroenterologists. This includes basic lifestyle modifications for weight loss, anti-obesity medications, bariatric surgeries, and endoscopic bariatric and metabolic therapies. ■

Judy Trieu, MD, MPH
Editor in Chief
The New Gastroenterologist

Continued from previous page

and body composition testing, such as with DEXA, may provide additional data. A BMI of 30 or above defines obesity, though newer definitions incorporate related symptoms, organ disfunction, and metabolic abnormalities into the term "clinical obesity." Asian patients experience metabolic complications at a lower BMI, and therefore the definition of obese is 27.5kg/m^2 in this population.

Begin by taking a weight history. Has this been a lifelong struggle or is there a particular life circumstance, such as working a third shift or recent pregnancy, which precipitated weight gain? Patients should be asked about binge eating or eating late into the evening or waking at night to eat, as these disordered eating behaviors are managed with specific medications and behavioral therapies. Inquire about sleep duration and quality and refer for a sleep study if there is suspicion for obstructive sleep apnea. Other weight-related comorbidities including hyperlipidemia, type 2 diabetes mellitus (T2DM), and MAFLD should be considered and merit a more aggressive approach, as does more severe obesity (class III, BMI ≥ 40). Questions about marijuana and alcohol use as well as review of the medication list for obesogenic medications can provide further insight into modifiable contributing factors.

Pillars of Weight Management

The internet is awash with trendy diet recommendations, and widespread misconceptions about obesity management are ingrained into how even physicians approach the disease. It is critical to remember that this is not a consequence of bad choices or lack of self-control. Exercise alone is insufficient to result in significant weight loss. Furthermore, whether it is through low fat, low carb, or intermittent fasting, weight loss will occur with calorie deficit. Evidence-based diet and lifestyle recommendations to lay the groundwork for success should be discussed at each visit (Table 1). The Mediterranean diet is recommended for weight loss as well as for several GI disorders and is the optimal eating strategy for cardiovascular health. Patients should be advised to engage in 150 minutes of moderate exercise per week, such as brisk walking, and should incorporate resistance training to build muscle and maintain bone density.

Anti-Obesity Medications

There are a number of medications, either FDA-approved or used off-label, for obesity treatment (Table 2). All are indicated for patients with a BMI of ≥ 30 kg/m^2 or for those with a BMI between 27-29 kg/m^2 with weight-related comorbidities and should be used in combination with diet and lifestyle interventions. None are approved or safe in pregnancy. Mechanisms of action vary by type and include decrease appetite, increase energy expenditure, improve insulin sensitivity, and interfere with absorption.

The newest and most effective anti-obesity medications (AOM), the GLP-1 receptor agonists (GLP-1 RA) are derived from gut hormones secreted in the distal small bowel and colon in response to a meal, which function to delay gastric emptying, increase insulin release from the pancreas, and reduce hepatic gluconeogenesis. Central nervous system effects are not yet entirely understood, but function to decrease appetite and increase satiety. Initially developed for treatment of T2DM, observed weight reduction in patients treated with GLP-1 RA led to clinical trials for treatment of obesity.

Semaglutide treatment resulted in weight reduction of 16.9% of total body weight (TBW), and one third of subjects lost ≥ 20% of TBW. Tirzepatide combines GLP-1 RA and a gastric inhibitory polypeptide (GIP) receptor agonist, which also has an incretin effect and functions to slow gastric emptying. In the pivotal SURMOUNT trial, approximately 58% of patients achieved ≥ 20% loss of TBW with 15-mg weekly dosing of tirzepatide. This class of drugs is a logical choice in patients with T2DM and obesity. Long-term treatment appears necessary, as patients typically regain two thirds of lost weight within a year after GLP-1 RA are stopped.

Based on tumors observed in rodents, GLP-1 RA are contraindicated in patients with a personal or family history of multiple endocrine neoplasia type 2 (MEN II) or medullary thyroid cancer. These tumors have not been observed in humans treated with GLP-1 RA. They should be used with caution in patients with history of pancreatitis, gastroparesis, or diabetic retinopathy, though a recent systematic review and meta-analysis suggests little to no increased risk for biliary events from GLP-1 RA. Side effects are most commonly gastrointestinal in nature (nausea, reflux, constipation, or diarrhea) and are typically most severe with initiation of the drug and with dose escalation. Side effects can be mitigated by initiating these drugs at lowest doses and gradually titrating up (every 4 weeks) based on effectiveness and tolerability. Antisecretory, antiemetic, and laxative medications can also be used to help manage GLP-1 RA–related side effects.

There is no reason to escalate to highest doses if patients are experiencing weight loss and reduction in food cravings at lower doses. Both semaglutide and tirzepatide are administered subcutaneously every 7 days. Once patients have reached goal weight, they can either continue maintenance therapy at that same dose/interval, or if motivated to do so, may gradually reduce the weekly dose in a stepwise approach to determine the minimally effective dose to maintain weight loss. There are not yet published maintenance studies to guide this process. Currently the price of GLP-1 RA and inconsistent insurance coverage make them inaccessible to many patients. The manufacturers of both semaglutide and tirzepatide offer direct-to-consumer pricing and home delivery.

Table 2. Anti-Obesity Medications

Medication	Mechanism / Notes
Olestra	Inhibits lipase; causes oily stools and fat-soluble vitamin malabsorption
Phentermine	Stimulates norepinephrine release; decreases appetite; FDA-approved for short-term use
Topiramate (off-label)	Enhances GABA activity; causes dysgeusia (especially to sweets/soda); carbonic anhydrase inhibitor also used for migraines
Qsymia™	Combination of phentermine + topiramate
Contrave™	Combination of bupropion + naltrexone; acts via pro-opiomelanocortin neurons to reduce appetite; impacts reward centers (hedonistic hunger); naltrexone blocks mu-opioid receptors and reduces alcohol cravings
Lisdexamfetamine	Approved for binge eating disorder
Metformin (off-label)	Used for metabolic syndrome, polycystic ovary syndrome, fatty liver; may help prevent antipsychotic-induced weight gain
Semaglutide, Liraglutide	GLP-1 RA approved for treatment of type 2 diabetes mellitus and obesity
Tirzepatide	Combined GLP-1 & GIP receptor agonist, results in loss of ≥ 20% body weight, also approved for type 2 diabetes mellitus and obstructive sleep apnea

Source: Colleen R. Kelly, MD, AGAF

Bariatric Surgery

In patients with higher BMI (≥ 35kg/m^2) or those with BMI ≥ 30kg/m^2 and obesity-related metabolic disease and the desire to avoid lifelong medications or who fail or are intolerant of AOM, bariatric options should be considered. Sleeve gastrectomy has become the most performed surgery for treatment of obesity. It is a restrictive procedure, removing 80% of the stomach, but a drop in circulating levels of ghrelin afterward also leads to decreased feelings of hunger. It results in 25%-30% TBW loss. It is not a good choice for patients who suffer from severe GERD, as this typically worsens afterward; also, de novo Barrett's has been observed in nearly 6% of patients who undergo sleeve gastrectomy.

Roux-en-Y gastric bypass is a restrictive and malabsorptive procedure, resulting in 30%-35% TBW loss. It has immediate metabolic effects, including increased release of endogenous GLP-1, which leads to improvements in weight-related T2DM. The newer single anastomosis duodenal-ileal bypass with sleeve gastrectomy (SADI-S) starts with a sleeve gastrectomy, making a smaller tube-shaped stomach. The duodenum is divided just after the stomach and then a loop of ileum is brought up and connected to the stomach (Figure 1). This procedure is highly effective, with patients losing 75%-95% of excess body weight and is becoming a preferred option for patients with greater BMI (≥ 50 kg/m^2). It is also an option for patients who have already had a sleeve gastrectomy and are seeking further weight loss. Because there is only one anastomosis, perioperative complications, such as anastomotic leaks, are reduced. The risk of micronutrient deficiencies is present with all malabsorptive procedures, and these patients must supplement with multivitamins,

Continued on following page

Needle-Knife Fistulotomy Is Safe During ERCP, Even for Trainee Endoscopists

BY WILL PASS
MDedge News

FROM TECHNIQUES AND INNOVATIONS IN GASTROINTESTINAL ENDOSCOPY

Needle-knife fistulotomy (NKF) is a safe and effective technique for primary biliary access during endoscopic retrograde cholangiopancreatography (ERCP), even among trainee advanced endoscopists, based on results of a randomized trial.

Across procedures conducted predominantly by trainees, safety outcomes were similar between NKF and standard cannulation, and all patients were successfully cannulated, suggesting this is a broadly accessible technique, reported Aleksey Novikov, MD, of the University of Florida College of Medicine, Gainesville, and colleagues.

Writing in *Techniques and Innovations in Gastrointestinal Endoscopy* (2025 Jul. doi: 10.1016/j.tige.2025.250941), the investigators noted that standard cannulation fails in 5%-20% of cases, which has led to development of various alternative techniques, including NKF. To perform the technique, the endoscopist makes a small incision in the intraduodenal biliary segment 3-6 mm above the papillary orifice, with cephalad extension until biliary access is achieved.

To date, four prospective studies have evaluated NKF in the hands of expert advanced endoscopists.

"These studies showed that NKF is a safe and useful technique that significantly reduces the risk of [post-ERCP pancreatitis] in the hands of expert advanced endoscopists," the investigators wrote. "The suggestion that NKF should be restricted to expert advanced endoscopists likely limits widespread use."

To determine whether NKF is a suitable technique for less experienced endoscopists, the investigators conducted a single-center, prospective randomized controlled trial at Thomas Jefferson University Hospital in Philadelphia.

Adults undergoing ERCP for biliary indications were randomly assigned in a 1:1 ratio to undergo primary cannulation via NKF or standard cannulation.

A total of 186 patients were randomized, with 137 ultimately included in the per-protocol analysis after exclusions for anatomic factors. Most procedures (72.3%) were performed by advanced endoscopy trainees under direct supervision, 26 procedures (19.0%) were performed by attending endoscopists without substantive prior NKF experience, and 12 (8.8%) by an attending endoscopist with NKF expertise.

"It is important to note that the majority of procedures performed in the context of this study were performed by an advanced endoscopy trainee with no NKF experience or an attending advanced endoscopist with minimal NKF experience," the investigators wrote.

All patients received prophylactic rectal indomethacin, and cannulation attempts were capped at 20 minutes before crossover to another technique was permitted. The primary endpoint was incidence of post-ERCP pancreatitis. Secondary endpoints included successful biliary access, time to access, and rates of bleeding and perforation.

Post-ERCP pancreatitis occurred at similar rate across groups: six cases (8.2%) in the standard cannulation arm and five cases (7.8%) in the NKF arm ($P = .93$). Rates of bleeding and perforation were also similar for both techniques.

Within the initial 20-minute window, biliary access rates were comparable between groups, at 75.3% and 82.2% for standard cannulation and NKF, respectively ($P = .89$). With additional attempts or crossover alowed, overall success rose to 100% in both arms.

Mean time to access was longer with NKF, averaging 380 seconds compared with 268 seconds for standard cannulation ($P < .05$).

"NKF was essentially equivalent to standard cannulation in many aspects," the investigators wrote, calling the two techniques "complementary."

They also suggested that the relative equivalence between techniques "carries more weight" after considering the low level of NKF experience among participating endoscopists.

"Overall, our data support teaching advanced endoscopy trainees NKF as a primary method of biliary access in patients with favorable anatomy," the investigators concluded. ■

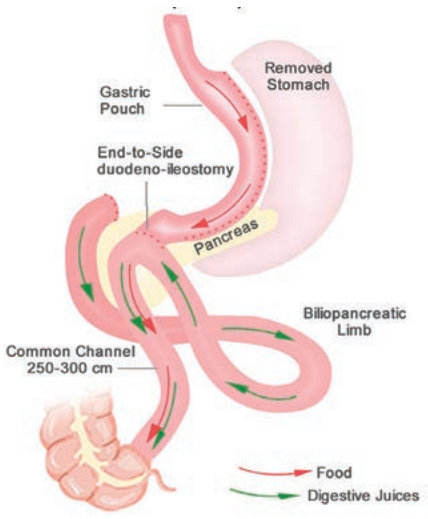
Continued from previous page

iron, vitamin D, and calcium.

Endoscopic Therapies

Endoscopic bariatric and metabolic therapies (EBMTs) have been increasingly studied and utilized, and this less invasive option may be more appropriate for or attractive to many patients. Intragastric balloons, which reduce meal volume and delay gastric emptying, can be used short term only (6 months) resulting in loss of about 6.9% of TBW greater than lifestyle modification (LM) alone, and may be considered in limited situations, such as need for pre-operative weight loss to reduce risks in very obese individuals.

Endoscopic gastric remodeling (EGR), also known as endoscopic sleeve gastrectomy (ESG), is a purely restrictive procedure in which the stomach is cinched to resize and reshape using an endoscopic suturing device (Figure 2). It is an option for patients with class I or II obesity, with data from a randomized controlled trial in this population

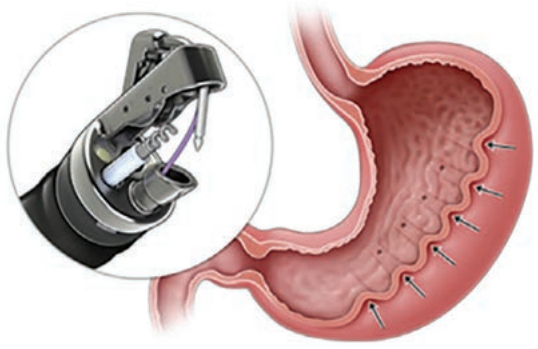


American Society for Metabolic and Bariatric Surgery

Figure 1. Single Anastomosis Duodeno-Ileal Bypass With Sleeve Gastrectomy

demonstrating mean percentage of TBW loss of 13.6% at 52 weeks compared to 0.8% in those treated with LM alone. A recent meta-analysis of 21 observational studies, including patients with higher BMIs (32.5-49.9 kg/m^2) showed pooled average weight loss of 17.3% TBW at 12 months with EGR.

This procedure has potential advantages of fewer complications, quicker recovery, and much less new-onset GERD compared to laparoscopic sleeve gastrectomy. Furthermore, it may be utilized in combination with AOMs to achieve optimum weight loss and metabolic outcomes. Potential adverse events include abdominal pain, nausea and vomiting, and rare instances of intra/extra luminal bleeding or abdominal abscess requiring drainage.



American Society for Gastrointestinal Endoscopy - European Society of Gastrointestinal Endoscopy

Figure 2. Endoscopic Gastric Remodeling (or Endoscopic Sleeve Gastrectomy)

Recent joint American/European gastrointestinal endoscopy guidelines suggest the use of EBMTs plus LM in patients with a BMI of ≥ 30 kg/m^2, or with a BMI of 27.0-29.9 kg/m^2 with at least one obesity-related comorbidity. Small-bowel interventions are being investigated for patients with obesity and T2DM but not yet commercially available.

Conclusion

Given the overlap of obesity with many GI disorders, it is entirely appropriate for gastroenterologists to consider it worthy of aggressive treatment, particularly in patients with MAFLD and other serious weight-related comorbidities. With a compassionate and empathetic approach, and a number of highly effective medical, endoscopic, and surgical therapies now available, weight management has the potential to be extremely rewarding when implemented in GI practice. ■

For a full list of references, please visit www.mdedge.com/gihepnews.

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Potential 'First-Line Treatment'

Transplant *from page 1*

In the treatment of antibiotic-associated colitis due to CDI, vancomycin or fidaxomicin are the standard therapies, yet up to 20% of patients experience one or more symptom recurrences following successful initial antibiotic treatment, prompting the need for continued antibiotic regimens, resulting in increased costs and potential adverse events, while contributing to antibiotic resistance.

FMT, designed to restore a normal functional colonic microenvironment with the transfer of a healthy person's stool, though still somewhat controversial, has gained acceptance and favor in recent years in the treatment of recurrent CDI; however, research has been lacking on its efficacy in the treatment of primary CDI.

'Our results indicate that it is reasonable to treat patients with primary CDI with FMT and provide antibiotics only to patients with ongoing symptoms or recurrence after FMT.'

With a previous proof-of-concept trial and observational study showing promising results in primary CDI, Juul and colleagues conducted the current randomized, open-label noninferiority trial.

For the multi-center study, 100 adult patients with CDI, defined as *C difficile* toxin in stool and at least three loose stools daily, and no previous CDI within 1 year prior to enrollment, were randomized at 20 hospitals in Norway to receive either FMT, administered as an enema, without antibiotic pretreatment, or oral vancomycin at a dose of 125 mg, four times daily for 10 days.

The patients had a median age of about 70 years; more than 40% of patients had a Charlson Comorbidity Index score of ≥ 4, indicating severe comorbidity, and a third had severe CDI.

With the trial showing favorable results, a data and safety monitoring board recommended stopping the trial for efficacy and noninferiority after about half of the planned enrollment was reached.

The primary endpoint of a clinical cure, defined as firm stools or less than three bowel movements daily and no disease recurrence within 60 days without additional treatment, was observed in 34 of 51 patients who received FMT (66.7%) compared with 30 of 49 of those receiving vancomycin (61.2%; difference, 5.4 percentage points; *P* for noninferiority < .001).

The results contradict the theory that response to FMT is 25 percentage points lower than response to vancomycin, the authors noted.

The proportion of patients with clinical cure at day 14 was 70.6% in the FMT group and 77.6% in the vancomycin group, and among those patients, two (5.6%) in the FMT group had disease recurrence compared with eight (21.1%) in the vancomycin group between days 15 and 60.

In the FMT group, 11 patients received additional treatment compared with 4 in the vancomycin group, predominantly oral vancomycin in both groups.

Despite the high rates of severe comorbidity among the patients at baseline, a subgroup analyses showed no significant differences in treatment effects based on factors including sex, age group, Charlson Comorbidity Index score, or CDI severity.

Importantly, there were also no significant differences in adverse events between the groups.

"Our results indicate that it is reasonable to treat patients with primary CDI with FMT and provide antibiotics only to patients with ongoing symptoms or recurrence after FMT," the authors concluded.

Challenges in the US

FMT specifically consists of direct instillation of fecal matter to the upper gastrointestinal tract, via capsules or duodenal infusion, or the lower gastrointestinal tract via colonoscopy or enema.

While an AGA guideline issued in 2024 endorsed FMT for the prevention of recurrent, refractory, or fulminant CDI in select adults not responding to standard antibiotics (Gastroenterology. 2024 Mar. doi: 10.1053/j.gastro.2024.01.008), the association underscored important caveats, including a low quality of evidence, and concluded that FMT could not yet be recommended for other gastrointestinal conditions.

The treatment meanwhile has faced an uphill battle in the US. The provision of screened FMT inocula through the nonprofit OpenBiome, previously the country's largest stool bank, was recently suspended amid FDA policy changes.

And while other commercial-grade biotherapeutic products Rebyota and Vowst, have received FDA approval, cost and insurance coverage can be significant barriers, said Elizabeth Hohmann, MD, of the Infectious Disease Division at Massachusetts General Hospital, Boston, in an editorial published with the study (Ann Intern Med. 2025 Jun. doi: 10.7326/ANNALS-25-01868).

"Currently approved options are expensive and are not available to many who might benefit for various reasons, primarily cost," she said.

In Europe, and particularly Norway, acceptance of FMT for CDI and other indications has been more favorable, and while regulation of the treatment has varied among European countries, a new regulation to be implemented by the European Union in 2027 will improve standardization of the production, handling, storage, and other factors of FMT, Juul said.

"I believe the new regulations will make the treatment more available to patients, and a standardization of the FMT production will make future trials more comparable and useful across countries," he said.

Juul said he further expects that "our results will lower the threshold for choosing FMT as treatment in primary infections."

Quality of Life

Hohmann, who has treated many patients with recurrent CDI with FMT, noted that a key factor that should be underscored is how much better patients can feel after the treatment.

"Although there are no quality of life surveys in [the study], had they been done, I suspect quality of life might have been higher in the FMT group; in my experience, people feel better after microbiome restoration."

She added that her patients "report feeling much better, and that's why I keep doing it," she said. "I've had an 80-year-old patient tell me he's going back to snow shoveling; another saying she can return to yoga classes."

"When you have had bad gut microbiome dysbiosis that becomes normal, you feel a lot better," Hohmann said. In the treatment of primary CDI, however, she said the prospects, at least in the US, are likely slim.

"I do not believe that we in the United States will see FMT as a primary treatment of *C difficile* infection anytime soon," she predicted.

Nevertheless, Hohmann asserted that "FMT should remain available, with appropriate sources of carefully screened inocula for care and for further research into the many illnesses and therapies that are influenced by the health of the gut microbiome."

This study received funding from the South-East Norway Health Trust. Hohmann had no disclosures to report. ■

Withdrawing Anti-TNFs in IBD Remission: New Data

BY MEGAN BROOKS

Whether it's safe to stop anti-TNF treatment in patients with inflammatory bowel disease (IBD) in remission remains unclear.

In the Spanish EXIT study, anti-TNF withdrawal in selected patients with IBD in clinical, endoscopic, and radiological remission had no impact on sustained clinical remission at 1 year, although objective markers of activity were higher in patients who stopped treatment.

The discontinuation of anti-TNF treatment "could be considered as an option" for a selected group of patients, said the authors led by Javier Gisbert, MD, PhD, with Autonomous University of Madrid.

However, the higher proportion of patients with elevated fecal calprotectin and significant endoscopic lesions at the end of follow-up "calls for caution and should be considered when discontinuing treatment in patients," Gisbert and colleagues concluded.

The EXIT study results were published in the journal *Gut* (2025 Feb. doi: 10.1136/gutjnl-2024-333385).

Risky Business?

Anti-TNF drugs have reshaped IBD treatment but bring infection risks and costs, prompting interest in

Continued on following page

Pediatric Wilson's Disease: Higher Risk of Bad Outcomes

BY WILL PASS
MDedge News

FROM GASTRO HEP ADVANCES

Children with Wilson's disease (WD) are more likely than are adults to present with acute liver failure or acute-on-chronic liver failure and have lower transplant-free survival, according to data from a large single-center study in India.

These findings underscore the importance of early recognition and genetic evaluation in pediatric patients, and timely consideration of liver transplantation in severe presentations, reported lead author Anand V. Kulkarni, MD, of AIG Hospitals, Hyderabad, India, and colleagues.

"There is a lack of large cohort studies evaluating the clinical presentation of WD, along with a limited understanding of genotype–phenotype correlations in patients with WD presenting with liver disease and the absence of comprehensive comparisons between pediatric and adult outcomes," the investigators wrote in *Gastro Hep Advances* (2025 Jun. doi: 10.1016/j.gastha.2025.100717). "Additionally, data on living donor liver transplantation (LDLT) outcomes in WD remain scarce."

To address these gaps, Kulkarni and colleagues performed a single-center retrospective study of all patients with WD diagnosed and managed at AIG Hospitals between June 2020 and April 2024.

Diagnosis followed Leipzig criteria, incorporating clinical features, slit-lamp examination for Kayser–Fleischer rings, serum ceruloplasmin, 24-hour urinary copper, hepatic copper when available, and genetic testing when available.

'There is ... a limited understanding of genotype–phenotype correlations in patients with WD presenting with liver disease and the absence of comprehensive comparisons between pediatric and adult outcomes.'

Patients were stratified by age into pediatric and adult groups. The investigators compared clinical presentation, laboratory parameters, and outcomes across age groups.

Management reflected standard practice at the center: chelation with D-penicillamine or trientine, zinc therapy as monotherapy or adjunctive therapy, plasma exchange for acute liver failure or acute-on-chronic liver failure, and evaluation for living-donor liver transplantation when indicated. Genetic analysis was performed in approximately 70% of the cohort.

The final dataset included 156 patients, with a median age of 19 years (range, 2–57), and an approximately equal split between adult and pediatric groups.

Presentation differed markedly by age. Among pediatric patients, the most common presentations were acute liver failure (26.7%) and acute-on-chronic liver failure (20%). Adults most frequently presented with decompensated cirrhosis (30.9%). Kayser–Fleischer rings were more prevalent in the pediatric group, consistent with underlying disease despite acute presentation.

Outcomes also varied by age and presentation. On Kaplan–Meier analysis, transplant-free survival was 72% in children and 87.7% in adults after a median follow-up of 1.33 years (P = .01). Overall cohort transplant-free survival at 1.33 years was 80.1%. Thirteen percent of patients underwent LDLT, with 90% 1-year post-transplant survival. Among those who received plasma exchange for acute presentations, transplant-free survival was 40.5%.

Among the patients with genetic data, 54.1% were homozygous or compound heterozygous for combinations of pathogenic variants and variants of uncertain significance in ATP7B. The most frequently observed pathogenic variants were p.Gly977Glu, p.Cys271Ter, and p.Asn1186Ser. Several additional variants, including novel changes, were identified across the cohort.

No consistent genotype–phenotype correlation was observed. The investigators noted that the center's focus on liver disease likely enriched the cohort for hepatic presentations, and that some patients were included based on Leipzig scores of 2-3 with supportive clinical response to therapy.

"Further research should focus on identifying structural variants, variants in other genes, and epigenetic modulators of genetic expression," Kulkarni and colleagues concluded.

The genetic tests were performed with intramural funding support from the Asian Healthcare Foundation, provided to AIG Hospitals Hyderabad. The investigators disclosed no conflicts of interest. ■

Continued from previous page

planned withdrawal after stable remission.

Yet prior evidence has been mixed. A meta-analysis of 27 studies suggested higher relapse after stopping anti-TNF therapy. However, the results were heterogeneous and most of the studies were retrospective, with a low number of patients and without a control group to compare with.

Clinical trials that have assessed the risk for relapse after discontinuation of anti-TNF therapy generally favored maintenance but had notable limitations.

The EXIT trial was conducted at 33 IBD units across Spain. A total of 140 patients in steroid-free clinical remission for ≥ 6 months on standard-dose infliximab or adalimumab were randomized (1:1) to either continue anti-TNF or switch to placebo matched to the drug they had been taking. All patients continued on immunomodulator therapy.

At 1 year, the proportion of patients with sustained clinical remission (primary outcome) was similar between patients who continued anti-TNF therapy and peers who stopped the medication (76% and 84%, respectively).

However, the proportion of patients with significant endoscopic lesions at the end of follow-up was higher in those who withdrew anti-TNF therapy (19% vs 8.5%; P = .01). Elevated fecal calprotectin (> 250 µg/g) was more common after withdrawal (33% vs 13%; P = .01).

Fecal calprotectin > 250 µg/g at baseline predicted lower odds of sustained remission and higher risk for losing remission — and was the only factor associated with lower likelihood of sustained remission.

Common Clinical Question

"When a patient starts an advanced biologic therapy, they often ask — will I be able to stop it?" Jean-Frederic Colombel, MD, director of the Inflammatory Bowel Disease Clinical Center at the Icahn School of Medicine at Mount Sinai, New York City, who wasn't involved in the study, told *GI & Hepatology News*.

Generally speaking, Colombel said he tells patients, "If the drug is working well and you are in deep remission, they should try to avoid stopping because there is a risk of relapse. And with relapse, we never know if the drug will work again and maybe we'll have to switch to another medication."

"It's an individualized discussion and decision and patients who do opt to stop [anti-TNF therapy] need to be monitored closely," Colombel said.

'Even though it didn't translate yet to clinical relapse, there were more patients with subclinical active disease in the group that stopped as compared to the group that continued.'

Colombel cautioned that the study had a relatively short 1-year follow-up and those that stopped anti-TNF therapy had evidence of recurrent inflammation.

"Even though it didn't translate yet to clinical relapse, there were more patients with subclinical active disease in the group that stopped as compared to the group that continued," Colombel said.

He also noted that in the SPARE trial of patients with Crohn's disease in clinical remission, patients who stopped infliximab had a higher risk for relapse compared with patients who stopped azathioprine and those who continued the combination therapy (Lancet Gastroenterol Hepatol. 2023 Jan. doi: 10.1016/S2468-1253[22]00385-5).

The EXIT study was supported by grants from Instituto de Salud Carlos III, Grupo Español de Trabajo en Enfermedad de Crohn y Colitis Ulcerosa and AbbVie. Gisbert reported serving as speaker, consultant, and advisory member for or receiving research funding from MSD, AbbVie, Pfizer, Kern Pharma, Biogen, Mylan, Takeda, Janssen, Roche, Sandoz, Celgene/Bristol Myers, Gilead/Galapagos, Lilly, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Norgine and Vifor Pharma. Colombel had no relevant disclosures. ■

Real-World Pros & Cons of the New Liver Disease Nomenclature

BY MARILYNN LARKIN

FROM UEG 2025

VIENNA – Replacing the term nonalcoholic fatty liver disease (NAFLD) with metabolic dysfunction–associated steatotic liver disease (MASLD) has several important "pros" and "some minor cons," Maria Effenberger, MD, Medical University of Innsbruck, Berlin, told attendees at United European Gastroenterology (UEG) Week 2025 in Vienna.

In her presentation, "Sense and Nonsense of the New Nomenclature," Effenberger highlighted the clinical implications of the new liver disease terminology and pointed to a few factors still needing to be sorted out.

'MASLD is a systemic disease, and that term represents it much better than only looking at it as a hepatological disease. Many factors, especially inflammatory ones, influence steatosis, inflammation, and fibrosis.'

Both NAFLD and MASLD are steatotic liver diseases, and, notably, there are few differences between the two in clinical studies, which makes the terminology shift easier, said Effenberger. She cited a recent study showing demographic and clinical profiles of individuals classified as NAFLD and MASLD in the US were "strikingly similar," as were the accuracy of the noninvasive tests and all-cause and cause-specific mortality rates for both conditions.

However, "the important thing about MASLD is that the term is really connected to metabolic dysfunction," said Effenberger. To be diagnosed with MASLD, patients with liver disease need to have at least one of five cardiometabolic abnormalities: a high BMI — over 25 in White people and over 23 in Asian people; type 2 diabetes (T2D) or prediabetes; arterial hypertension; high levels of triglycerides; or a low level of high-density lipoprotein cholesterol.

"MASLD is a systemic disease, and that term represents it much better than only looking at it as a hepatological disease," Effenberger said. "Many factors, especially inflammatory ones, influence steatosis, inflammation, and fibrosis." These include influences from adipose tissue, the gut microbiome, the brain, and a hypocaloric diet, and from steatosis of the liver itself. Proinflammatory cytokines induced by the disease can lead to inflammation throughout the body, with clinical outcomes such as stroke, heart failure, arrhythmias, myocardial infarction, and chronic kidney disease.

MASLD, MetALD, or ALD?

"What is important now," said Effenberger, is that "every patient who has liver disease should be asked two questions." The first question is does the patient have any of the cardiometabolic criteria outlined above. Second, is the patient consuming alcohol?

If the patient has one of the cardiometabolic criteria but doesn't consume alcohol, "we are straight at the diagnosis of MASLD," she explained. If the patient does consume alcohol, it depends on how much.

Patients who have at least one cardiometabolic risk factor and consume 140-350 g for men and 210-420 g for women are considered to have Metabolic and Alcohol-Associated Liver Disease (MetALD). And those with steatotic liver disease who drink alcohol above the MetALD thresholds are considered to have ALD.

Effenberger pointed to two "cons" of the new nomenclature that need to be clarified. Although MetALD has poorer outcomes than MASLD, "it's really hard to differentiate between ALD and MASLD," she said. Yet the distinction is important because risks for cirrhosis, hepatocellular carcinoma (HCC), and overall mortality increase more for patients diagnosed with ALD vs MASLD.

"Do MASLD patients drink alcohol? Yes they do," Effenberger said. "And if you have MASLD and another trigger factor like alcohol, the rates of mortality, morbidity, and cancer go up."

Moderator Laurent Castera, MD, PhD, Université Paris-Cité, Paris, noted that a "pro" of the new nomenclature is that it is "shedding light on the importance of alcohol because when we discuss steatotic liver disease or MASLD, alcohol is always the elephant in the room," he said. "We need to increase the awareness that even in the absence of alcohol, you can still develop cirrhosis if you have severe metabolic risk factors."

On the other hand, he said, "We desperately need more statistics on the true prevalence of alcohol consumption. While studies suggest the prevalence is low, at around 4% or 5%, that does not match the reality, in my opinion."

Effenberger agreed. There's a problem in trying to zero in on alcohol consumption because of the stigma attached to it, she said. She pointed to an Austrian study assessing patients who are diagnosed with MASLD (J Hepatol. 2022 May. doi: 10.1016/j.jhep.2022.04.040). The researchers asked them, "Do you drink alcohol?" and all the participants said "no." However, after completing a questionnaire designed to identify alcohol use disorders, and undergoing glucuronide tests in the urine and hair, it became clear that 25%-30% of these patients actually drank alcohol on a regular basis.

'If a patient has MASLD and cardiometabolic risk factors, and a risk score that suggests the patient is at increased risk of CVD for 10 years, then a CT scan of the arteries of the heart is important.'

Cancer, Cirrhosis, CVD

MASLD is a trigger for cancer, especially HCC, Effenberger said. A recent review affirmed that MASLD is strongly associated with HCC, especially in Southeast Asia and India (Lancet Oncol. 2022 Mar. doi: 10.1016/S1470-2045[22]00078-X). The same study showed that many patients with MASLD are getting HCC without cirrhosis, and their cancer is often detected at a later stage; however, it's not yet clear why they are getting HCC, and further study is needed.

In addition, MASLD is associated with higher rates of extrahepatic cancers, including cancers of the skin and androgenic cancers. This, too, requires further investigation.

Regarding cardiovascular disease (CVD) risk, Effenberger emphasized that cardiometabolic diseases are strongly linked to each other. "Therefore, if you have diabetes and MASLD, the rates of atherosclerosis and of heart insufficiency and arteriosclerotic events like stroke and heart attacks go up, leading to the question of whether a CVD risk assessment is necessary in patients with MASLD."

One recent study suggests that yes, it is, she reported (Gut. 2024 Jan. doi: 10.1136/gutjnl-2023-330595). "If a patient has MASLD and cardiometabolic risk factors, and a risk score that suggests the patient is at increased risk of CVD for 10 years, then a CT scan of the arteries of the heart is important. The increased risk could also lead to intensified medical therapy, including GLP-1s or SGLT2s."

During the Q&A, one attendee asked whether all patients with noncirrhotic MASLD should be screened for HCC, given the increased risk. Effenberger agreed that would be the best way to identify those at high risk; however, she said, "I think science is not in a state where you can clearly define which patients will be at high risk, and so we don't have any guidelines for that."

Another attendee asked why HCC is more common in Indians and Asians. Effenberger said, "We don't know, but it is likely that there is an HCC-driven genetic risk factor."

Remaining Questions

And finally, there's the question of "what do we do with burntout MASLD?" Effenberger asked. "We know the fat content of the liver decreases when liver severity goes up. Therefore, we have a lot of patients with cirrhosis whose disease is not defined as steatotic liver because the liver fat content is no longer more than 5%."

The decrease in fat is an ongoing process, and therefore, these patients with MASLD and advanced hepatic disease need to be better represented in the nomenclature, she suggested.

No funding information was provided. Effenberger declared working with Ipsen as a potential conflict. ■

Polypectomy Best Practices Not Routinely Followed

BY MEGAN BROOKS

US endoscopists frequently stray from established best practices when removing colon polyps smaller than 1 cm, with fewer than 60% of procedures using the recommended cold snare technique, an analysis of more than 1.8 million colonoscopies found.

"We expected to find some variations in polypectomy technique, but the results were surprising; overall, cold snare usage was much lower than expected, given that this is the recommended method for removing most small polyps," Seth Crockett, MD, MPH, AGAF, professor of medicine, Division of Gastroenterology and Hepatology, Oregon Health & Science University, Portland, told *GI & Hepatology News*.

Dr. Crockett

'The results were surprising; overall, cold snare usage was much lower than expected, given that this is the recommended method for removing most small polyps.'

The study was published in the October issue of *The American Journal of Gastroenterology* (2025 Oct. doi: 10.14309/ajg.0000000000003461).

Using Gastroenterology Quality Improvement Consortium Registry data, Crockett and colleagues analyzed more than 1.8 million colonoscopies performed by 4601 endoscopists between 2019 and 2022 across 702 sites. All colonoscopies involved removal of polyps < 1 cm; lesions of this size are commonly found in screening colonoscopies, and detection is crucial to early cancer prevention.

The researchers found striking variation in polypectomy technique. Guideline-based cold snare polypectomy (CSP) was used in only 58% of cases (and as a single device in only 51%), whereas cold forceps polypectomy (CFP) accounted for 35% and hot snare polypectomy (HSP) for 11%.

The fact that CSP was used in fewer than 60% of cases represents "an important quality gap," the authors wrote, adding that the fact that more than 10% of colonoscopies used HSP suggests that "some patients harboring low-risk lesions may be exposed to excess risk related to these practice variations."

And while recommendations around the use of CFP are more nuanced (based largely on forceps type and polyp size), the "high frequency of CFP also suggests nonadherence to best practices," they noted.

Gastroenterologists More Likely to Follow Guidance

Polypectomy technique varied by polyp type. CFP was more common in cases where only hyperplastic polyps were removed compared with cases with tubular adenomas (45% vs 30%, respectively). CSP use was highest in cases where only sessile serrated lesions were removed (66%) compared with cases with only tubular adenomas (61%) or hyperplastic polyps (37%).

There was also considerable variation by provider specialty.

Gastroenterologists (compared with non-GI specialists) used HSP less (4% vs 8%) and CSP more (40% vs 34%). Colonoscopies performed with GI fellows were more likely to use CFP (31% vs 21%) and less likely to use HSP (1% vs 5%) compared with colonoscopies without fellows.

"It was somewhat reassuring that colonoscopies performed by gastroenterologists were more likely to adhere to guideline recommendations, which suggests that dedicated endoscopy training is likely an important factor driving high-quality colonoscopy," Crockett said.

"Unexpectedly," polypectomy technique also differed dramatically by geographic region, he said. CFP was used more than twice as often in the Northeast (31%) as in the Midwest (14%), whereas CSP was used more frequently in the Midwest (52%) than in the Northeast (32%).

"We suspect that much of the variation is related to differences in training, preferences, habits, and evolution of colonoscopy practice over time," Crockett said. "More research is needed on the underlying drivers of this variation, and how differences in polypectomy technique impact both the safety and efficacy of colonoscopy to prevent colorectal cancer," he said.

"As a specialty, we need to continue to work on disseminating guideline recommendations regarding colonoscopy quality, monitoring adherence to evidence-based practices, and working to address gaps in quality where they exist," he added.

'Concerning, Surprising, and Disappointing'

David Johnson, MD, professor of medicine and chief of gastroenterology at Eastern Virginia Medical School and Old Dominion University in Norfolk, called the results "concerning, surprising, and disappointing" and not consistent with the most current quality recommendations that advocate cold snare for most polyps less than 1 cm in size.

"Cold snare polypectomy has been shown not only to be more effective but also takes less time to perform, relative to cold biopsy," said Johnson, who wasn't involved in the study.

Johnson said, "Inadequate lesion resection and variation in resection quality are major issues for colonoscopy quality. Those who perform colonoscopies need to be up-to-date with evidence-based quality standards — as well as held accountable if [there is] discordant practice — if we are to optimize the cancer prevention benefits of quality colonoscopy."

'Inadequate lesion resection and variation in resection quality are major issues for colonoscopy quality. Those who perform colonoscopies need to be up-to-date with evidence-based quality standards.'

Limitations of the current analysis include lack of extensive patient information and inability to further stratify polyps < 1 cm by size.

The study had no commercial funding. Crockett had no disclosures. Johnson disclosed serving as a director, officer, partner, employee, adviser, consultant, or trustee for ISOThrive. ■

Dietary Trial Shows Benefits of a Low-Emulsifier Diet for Crohn's Disease

BY CHRISTINE KILGORE

FROM GMFH 2025

WASHINGTON, DC — A low-emulsifier–containing diet led to a threefold increased likelihood of improvement in symptoms of Crohn's disease compared with an emulsifier-containing diet in a randomized double-blind dietary trial involving 154 patients with mildly active disease living across the United Kingdom.

The findings were reported at Gut Microbiota for Health (GMFH) World Summit 2025 by Benoit Chassaing, PhD, of the Institut Pasteur, Paris, whose research leading up to the trial has demonstrated that food additive emulsifiers — ubiquitous in processed foods — alter microbiota composition and lead to microbiota encroachment into the mucus layer of the gut and subsequent chronic gut inflammation.

MONTICELLO/ISTOCK GETTY IMAGES

Patients in the ADDapt trial, which was also reported in an abstract earlier this year at the European Crohn's and Colitis Organization (ECCO) 2025 Congress, had a Crohn's disease activity index (CDAI) of 150-250 and evidence of inflammation (fecal calprotectin (FCP) ≥ 150 µg/g or endoscopy/radiology). All "had been exposed in their regular diets to emulsifiers," said Chassaing, a co-investigator, during a GMFH session on "Dietary Drivers of Health and Disease."

They were randomized to either a low-emulsifier diet or to a low-emulsifier diet followed by emulsifier "resupplementation" — a design meant to "account for the very strong placebo effect that is always observed with dietary studies," he said.

All patients received dietary counseling, a smart phone app and barcode scan to support shopping, and weekly support. They also received supermarket foods for 25% of their needs that were either free of emulsifiers or contained emulsifiers, and they were provided three snacks per day that were emulsifier-free or contained carrageenan, carboxymethycellulse (CMC), and polysorbate-80 (P80) — dietary emulsifiers that are commonly added to processed foods to enhance texture and extend shelf life.

In the intention-to-treat (ITT) analysis, 49% of patients in the intervention group reached the primary endpoint of a 70-point reduction or more in CDAI response after 8 weeks compared with 31% of those in the control group (P = .019), with an adjusted relative risk of response of 3.1 (P = .003), Chassaing shared at the GMFH meeting, convened by the American Gastroenterological Association and the European Society of Neurogastroenterology and Motility.

In the per-protocol analysis (n = 119), 61% and 47% of patients in the intervention and control groups, respectively, reached the primary outcome of CDAI response, with an adjusted relative risk of response of 3.0 (P = .018), he said.

Secondary endpoints included CDAI remission at 24 weeks, and according to the abstract for the ECCO Congress, in the ITT analysis, patients in the intervention group were more than twice as likely to experience remission.

Chassaing noted at the GMFH meeting that as part of the study, he and coinvestigators have been investigating the participants' gut microbiota with metagenomic analyses. The study was led by Kevin Whelan, PhD, head of the Department of Nutritional Sciences at King's College London.

Can Emulsifier-Sensitive Individuals Be Identified?

In murine model research 10 years ago, Chassaing showed that the administration of CMC and P80 results in microbiota encroachment into the mucus layer of the gut, alterations in microbiota composition — including an increase in bacteria that produce pro-inflammatory flagellin — and development of chronic inflammation.

Wild-type mice treated with these compounds developed metabolic disease, and mice that were modified to be predisposed to colitis had a higher incidence of robust colitis. Moreover, fecal transplantation from emulsifier-treated mice to germ-free mice reproduced these changes, "clearly suggesting that the microbiome itself is sufficient to drive chronic inflammation," he said.

In recent years, in humans, analyses from the large French NutriNet-Sante prospective cohort study have shown associations between exposure to food additive emulsifiers and the risk for cardiovascular disease, the risk for cancer (overall, breast, and prostate), and the risk for type 2 diabetes.

But to explore causality and better understand the mechanisms of emulsifier-driven changes on the microbiota, Chassaing and his colleagues also launched the FRESH study (Functional Research on Emulsifier in Humans), a double-blind randomized controlled-feeding study of the emulsifier CMC. For 11 days, 9 healthy patients consumed an emulsifier-free diet and 11 consumed an identical diet enriched with 15 g/d of CMC.

Patients on the CMC-containing diet had reduced microbiota diversity and depletions of an array of microbiota-related metabolites, but only a small subset had profound alterations in microbiota composition and increased microbiota encroachment into the mucus layer. "Some seemed to be resistant to CMC-induced microbiota encroachment, while some were highly susceptible," Chassaing said.

The pilot study raised the question, he said, of whether there is an "infectivity component" — some kind of "sensitive" gut microbiota composition — that may be associated with dietary emulsifier-driven inflammation and disease.

In other murine research, Chassaing and his team found that germ-free mice colonized with Crohn's disease–associated adherent-invasive *Escherichia coli* (AIEC) and subsequently given CMC or P80 developed chronic inflammation and metabolic dysregulation, "clearly demonstrating that you can convert resistant mice to sensitive mice just by adding one bacteria to the ecosystem," he said. "The presence of AIEC alone was sufficient to drive the detrimental effects of dietary emulsifiers."

(In vitro research with transcriptomic analysis then showed that the emulsifiers directly elicit AIEC virulence gene expression, Chassaing and his coauthors wrote in their 2020 paper, facilitating AIEC's "penetration of the mucus layer and adherence to epithelial cells and resulting in activation of host pro-inflammatory signaling.")

"We don't think it's solely the AIEC bacteria that will drive emulsifier sensitivity, though ... we think it's more complex," Chassaing said at the meeting. Overall, the findings raise the question of whether emulsifier-sensitive individuals can be identified.

This, he said, is one of his most recent research questions. His lab has led the development of an in vitro microbiota model built to predict an individual's sensitivity to emulsifiers. In a study published in April, the model recapitulated the differential CMC sensitivity observed in the earlier FRESH study, suggesting that an individual's sensitivity to emulsifiers can indeed be predicted by examining their baseline microbiota.

Interpreting the Epidemiology

Chassaing's research arch

Continued on following page

‘No Safe Level’ of Alcohol

Healthy Diet *from page 1*

increased physical activity levels explain differences in liver-specific mortality risks between lifetime abstainers and light-to-moderate alcohol consumers,” he said. “More importantly, it remains unclear whether a healthy diet and physical activity can lower liver-specific mortality in individuals engaging in high-risk alcohol consumption, such as heavy or binge drinking.”

The study was published online in the *Journal of Hepatology* (2025 Aug. doi: 10.1016/j.jhep.2025.06.033).

Analyzing Alcohol-Related Effects

Chalasani and colleagues analyzed data from more than 60,000 adults in the National Health and Nutrition Examination Surveys for 1984-2018 and linked data in the National Death Index through December 2019.

The research team looked at self-reported alcohol use, diet quality based on the Healthy Eating Index, and physical activity levels. Heavy drinking was defined as more than three drinks per day for women and more than four drinks per day for men, while binge drinking was defined as four or more drinks per day for women and five or more drinks per day for men.

Physically active participants had at least 150 minutes of moderate-intensity physical activity or 75 minutes of vigorous-intensity physical activity per week. Participants with healthier diets were in the top quartile of the Healthy Eating Index, which included diets high in vegetables, fruits, whole grains, seafood, plant-based proteins, and unsaturated fats, as well as diets low in solid fats, alcohol, and added sugars.

During a 12-year follow-up period, 12,881 deaths were reported, including 252 related to liver disease. An increased risk for liver-related death was associated with older age, smoking, diabetes, higher BMI, waist circumference, average daily alcohol intake, and binge drinking.

Compared to nondrinkers, those with daily alcohol intake had an increased liver-specific mortality risk, with an adjusted subdistribution hazard ratio (aSHR) of 1.04 for men and 1.08 for women.

Binge drinking had an even greater liver mortality risk, with an aSHR of 1.52 for men and 2.52 for women, than nonbinge drinking.

In contrast, a healthier diet — among those at the top quartile of the Healthy Eating Index — had a lower liver mortality risk in nonheavy drinkers (aSHR, 0.35), heavy drinkers (aSHR, 0.14), and binge drinkers (aSHR, 0.16).

In addition, physically active participants had a lower liver mortality risk for nonheavy drinkers (aSHR, 0.52), heavy drinkers (aSHR, 0.64), and binge drinkers (aSHR, 0.31).

Overall, the benefits of higher diet quality and physical activity were substantially greater in women than in men, the researchers found.

“The uniqueness of our study lies in its ability to simultaneously assess the moderating effects of two important lifestyle behaviors on liver mortality risk across different levels and patterns of alcohol consumption in a representative US population, offering a more nuanced and complete view of the risks of drinking,” Chalasani said.

Messaging From Clinicians to Patients

Despite some attenuation from a healthy diet and physical activity, alcohol consumption still carries an increased liver mortality risk, the researchers noted. Economically disadvantaged groups face higher exposure to high-risk alcohol use, unhealthy diets, and physical activity — and as a result, increased liver mortality.

“This study challenges the long-held belief that light-to-moderate drinking might be safe for the liver. It shows that any level of alcohol raises risk, but healthy diet and exercise can meaningfully reduce that harm,” said Joseph Ahn, MD, AGAF, assistant professor of medicine in the Division of Gastroenterology and Hepatology at the Mayo Clinic in Rochester, Minnesota.

Dr. Ahn

“The results should change how we think about alcohol — not as something potentially protective, but as a risk factor that can be partly mitigated by lifestyle,” he said.

“The key takeaway is that there is no safe level of alcohol for liver health. Clinicians should move away from reassuring patients about ‘moderate’ drinking and instead stress both alcohol reduction and the protective role of diet and physical activity,” Ahn added. “The next step is bringing these insights into guidelines and patient counseling, especially for populations at higher risk.”

The study was funded by departmental internal funding. Chalasani declared having no conflicts of interest for this paper, but he disclosed paid consulting agreements with numerous pharmaceutical companies. Ahn reported having no disclosures. ■

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illustrates the synergy between epidemiological research, basic/translational research, and clinical interventional research that’s needed to understand the diet-microbiome intersection in inflammatory bowel disease, said Ashwin Ananthakrishnan, MBBS, MPH, AGAF, associate professor of medicine at Massachusetts General Hospital, Boston, in an interview at the meeting.

“It’s a good example of how to really span the spectrum, starting from the big picture and going deeper to understand mechanisms, and starting from mechanisms and expanding it out,” Ananthakrishnan said.

In his own talk about research on inflammatory bowel disease (IBD), Ananthakrishnan said that epidemiological data have shown over the past 10-15 years that total dietary fiber is inversely associated with the risk for Crohn’s disease (with the strongest associations with fiber from fruits and vegetables). Studies have also shown that a higher intake of polyunsaturated fatty acids is associated with a lower risk for ulcerative colitis, whereas “an n-6-fatty acid–rich diet is associated with a higher risk of ulcerative colitis,” he said.

Dietary cohort studies, meanwhile, have shed light on the influence of dietary patterns — such as the Mediterranean diet and diets with high inflammatory potential —on IBD. A diet rich in ultra-processed foods has also been shown in a prospective cohort study to be associated with a higher risk for Crohn’s disease, with certain categories of ultra-processed foods (eg, breads and breakfast foods) having the strongest associations.

Such studies are limited in part, however, by inadequate assessment of potentially relevant variables such as emulsifiers, preservatives, and how the food is processed, he said.

And in interpreting the epidemiological research on fiber and IBD, for instance, one must appreciate that “there are a number of mechanisms by which fiber is impactful. ... There’s a big picture to look at,” Ananthakrishnan said. Fiber “can affect the microbiome, clearly it can affect the gut barrier, and it can affect bile acids; and there are detailed translational studies in support of each of these.”

But there are other constituents of fruits and vegetables “that could potentially influence disease risk, such as AhR ligands and polyphenols,” he said. “And importantly, people not eating a lot of fiber may be eating a lot of ultra-processed foods.”

Most interventional studies of fiber have not shown a benefit of a high-fiber diet, Ananthakrishnan said, but there are multiple possible reasons and factors at play, including potential population differences (eg, in inflammatory status or baseline microbiota), shortcomings of the interventions, and potentially inaccurate outcomes.

Abigail Johnson, PhD, RDN, associate director of the Nutrition Coordinating Center, University of Minnesota Twin Cities, Minneapolis, which supports dietary analysis, said during the session that the focus of dietary research is “moving toward understanding overall dietary patterns” as opposed to focusing more narrowly on vitamins, minerals, and macronutrients such as proteins, fats, and carbohydrates.

This is an improvement, though “we still don’t have good approaches for understanding [the contributions of] things like additives and emulsifiers, food preparation and cooking, and food processing,” said Johnson, assistant professor in the Division of Epidemiology and Community Health at University of Minnesota Twin Cities. “Perhaps by looking at things at the food level we can overcome some of these limitations.”

Ananthakrishnan reported being a consultant for Geneoscopy and receiving a research grant from Takeda. Chassaing did not report any financial disclosures. Johnson reported that she had no financial disclosures. ■

Member SPOTLIGHT

Balancing the Challenge of Research With the Joys of Clinical Care

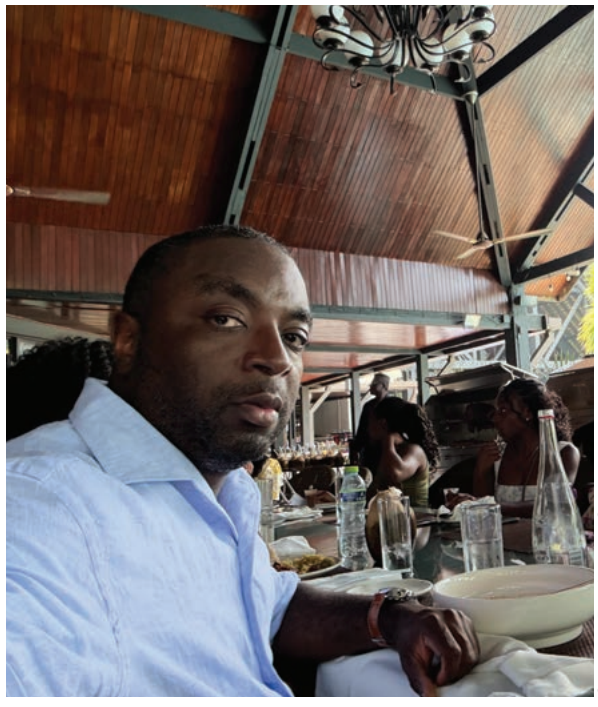
BY JENNIFER LUBELL
MDedge News

Andrew Ofosu, MD, MPH, loves the variety that gastrointestinal (GI) medicine offers on a day-to-day basis.

Some days are spent in the endoscopy suite, performing endoscopic retrograde cholangiopancreatography in patients with cholangitis, "which is usually a high-stakes situation," he said. Other days he might be in clinic, helping to manage a patient with chronic pancreatitis.

"The contrast of the immediate impact of a procedure combined with the continuity of long-term relationships is special to me," said Ofosu, an associate professor of medicine at the University of Cincinnati College of Medicine, in Cincinnati, Ohio. He's also a member of AGA's Future Leaders program, which provides early-career GI physicians with opportunities to network and develop leadership skills.

In an interview, he discussed his research pursuits in the areas of pancreatic cancer and artificial intelligence (AI), and his unique methods for connecting with patients. The art of listening to patient concerns is crucial, he says, especially following a difficult diagnosis.



Courtesy Dr. Andrew Ofosu

Dr. Andrew Ofosu of the University of Cincinnati

What's it like to be part of the AGA Future Leaders Class of 2025-2026? How has the experience enriched your career?
Dr. Ofosu: My time being part of this group has been very transformative. It's provided mentorship from national leaders. It's enabled me to collaborate with peers across different institutions and given me opportunities to refine my leadership skills. It's changed my perspective and created a network that has equipped me to contribute meaningfully to the gastroenterology community and to my institution.

'I aim for clarity and empathy. Some GI diagnoses can be intimidating ... so I use a lot of analogies and visuals to simplify complex conditions. I also ensure that patients understand what we are discussing because I found that what a patient hears isn't always what they think I explained.'

What is the most challenging clinical case you've encountered?
Dr. Ofosu: One case that stands out was a young patient with recurrent idiopathic pancreatitis. We went through all the potential differential etiologies that includes genetics, autoimmune disease, and structural etiologies. It became a long, diagnostic journey. The challenge wasn't just the medical aspect of it, but the emotional aspect of it ... when you don't have all the answers available. We were eventually able to figure out what the cause of the pancreatitis was. It was genetic, and the patient is doing great now.

One of your research interests has been developing innovative ways to use AI in endoscopic ultrasound to identify and characterize lesions. Can you discuss some of those innovations?
Dr. Ofosu: It's definitely an area that I'm looking to explore at this time — to leverage AI to improve diagnostic capability of endoscopic ultrasound. The whole idea is to be able to use AI to analyze images in real time that can help highlight features, which can ultimately help in distinguishing both benign and malignant tumors, and allowing AI to provide real-time diagnostic support, improving accuracy of diagnosis and reducing unnecessary treatment.

In 2021, you conducted a study to investigate the demographics, clinical outcomes and survival outcomes of patients diagnosed with early- and late-onset pancreatic adenocarcinoma *(Pancreatology. 2021 Jan. doi: 10.1016/j.pan.2020.12.007)*. What did your study reveal and what are the next steps?
Dr. Ofosu: Our study looked at over 136,000 patients with pancreatic adenocarcinoma [PAC] and compared those diagnosed under age 40 to older patients. We found that although pancreatic cancer is rare in the young, both groups are presenting more often with advanced disease, and incidence is rising. Younger patients tend to have tumors in the head of the pancreas, while older patients more often show growth in the body and tail. Survival overall remains very poor — about 6-7 months — but slightly better in younger patients.

I think the next step is to better understand the biological drivers of early-onset PAC to look at integrating molecular profiling to see if there are distinct genetic patterns that can guide therapy. Ultimately the goal is to improve early detection and tailor management strategy for this subset of patients.

What is your approach to patient communication and education?
Dr. Ofosu: I aim for clarity and empathy. Some GI diagnoses can be intimidating, with all the terminologies, and so I use a lot of analogies and visuals to simplify complex conditions. I also ensure that patients understand what we are discussing because I found that what a patient hears isn't always what they think I explained.

I believe being honest and compassionate should go hand in hand. I don't shy away from delivering difficult news, but I always take time to pause, listen, and acknowledge emotions. I found that patients and families appreciate transparency even when the prognosis is tough, as long as they know I'm fully present with them.

Can you share a memorable patient interaction that impacted you?
Dr. Ofosu: There was one patient with chronic

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LIGHTNING ROUND

What's your favorite season of the year?
Fall: I like the colors of changing leaves

What's your favorite way to spend a weekend?
Watching soccer with family and friends

If you could have dinner with any historical figure, who would it be?
Nelson Mandela

What's your go-to karaoke song?
Don't Stop Believin' by Journey

What's one thing on your bucket list?
Travel to Europe, experience different cultures

What's your favorite childhood memory?
When I learned how to fly a kite

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

Are you a planner or more spontaneous?
Planner

What's your favorite holiday tradition?
Sharing Christmas dinner with family

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pancreatitis due to alcohol who had limited economic and social support. Beyond the medical management, what made a difference was sitting and listening to the patient, helping them connect to resources and social support — a social network. I think this reinforces that medicine isn't just about lab values. It's all about restoring dignity and focus with the patient.


Dr. Ofosu

What do you think is the biggest misconception about your specialty?

Dr. Ofosu: That gastroenterology is all about procedures, that all we do is scope. In reality, it's a combination of technical expertise as well as the cognitive aspect of providing long-term management of complex diseases that affect patients, which takes a diverse skillset beyond endoscopy. ■

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