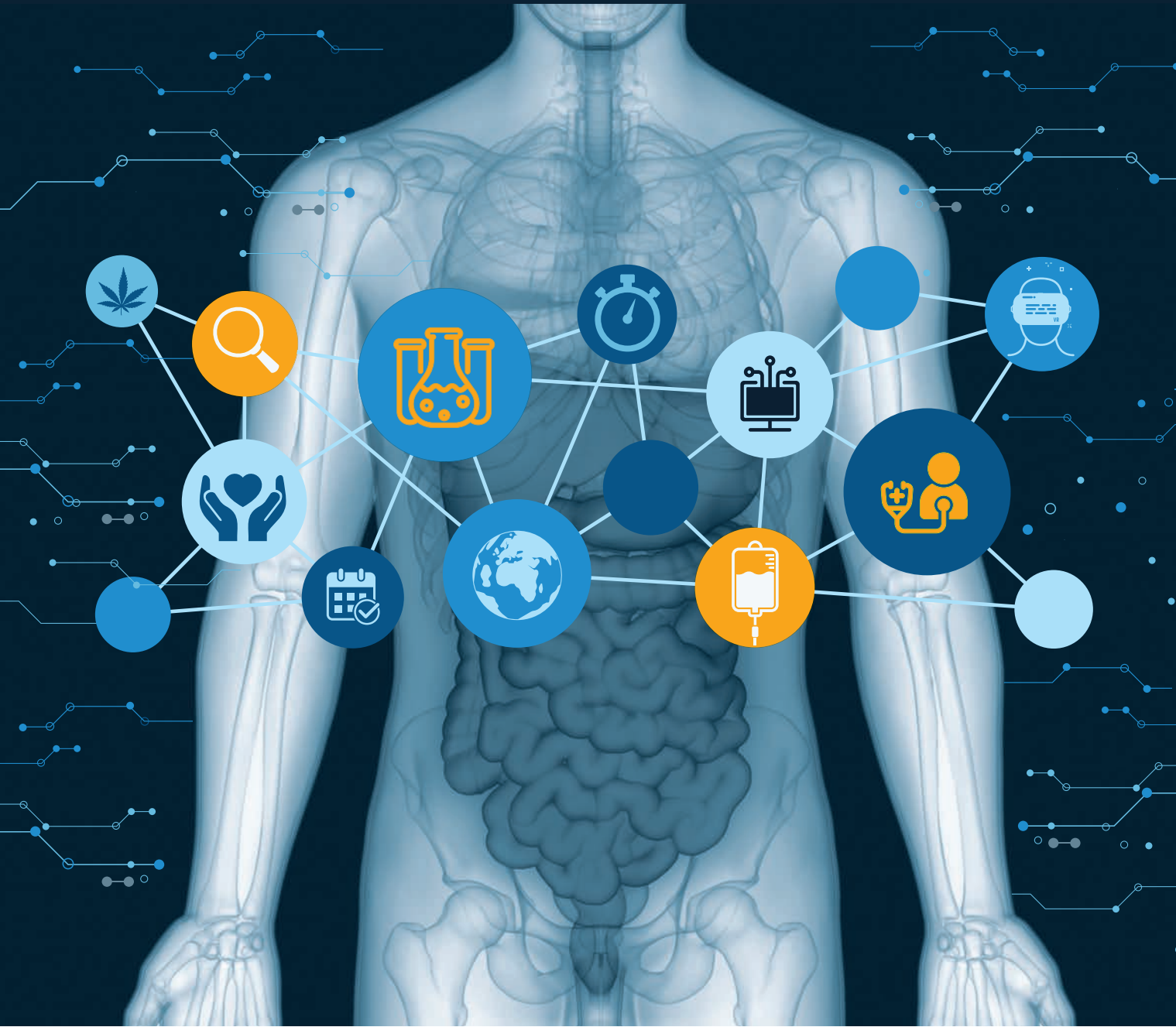


A SUPPLEMENT TO GI & HEPATOLOGY NEWS®

# GASTROENTEROLOGY

## DATA TRENDS 2024 ▶ aga



 American Gastroenterological Association

Official newspaper of the AGA Institute  
[mdedge.com/gihepnews](http://mdedge.com/gihepnews)

# GI & Hepatology News

May 2024

# GASTROENTEROLOGY DATA TRENDS 2024



**Editor in Chief, GI & Hepatology News**  
Megan A. Adams, MD, JD, MSc

**AGA Staff**

**Vice President of Communications**  
Jessica Willocks Duncan

**Creative Director**  
Chris Kaczmarek

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**Editorial Directors**  
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**Creative Director**  
Louise A. Koenig

**Senior Art Director**  
Karen Blackwood

**Senior Production Manager**  
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**Director, Business Development**  
Cheryl Wall 212-417-9655  
cwall@mdedge.com

**Frontline Medical Communications Corporate**

283-299 Market St  
(2 Gateway Building)  
4th Floor  
Newark, NJ 07102  
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**VP, Sales**  
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# Contributing Authors

*GI & Hepatology News* and the American Gastroenterological Association would like to thank the following experts for their contributions to this issue.



**Shirley Cohen-Mekelburg, MD, MS**

Assistant Professor  
Division of Gastroenterology  
Michigan Medicine  
Director of IBD  
VA Ann Arbor Health Care System  
Ann Arbor, Michigan

Dr. Cohen-Mekelburg has disclosed no relevant financial relationships.



**Nirmala Gonsalves, MD, AGAF, FACC**

Professor of Medicine  
Division of Gastroenterology & Hepatology  
Northwestern University  
Feinberg School of Medicine  
Co-Director of Eosinophilic Gastrointestinal Disorders Program  
Northwestern Memorial Hospital  
Chicago, Illinois

Disclosures:  
Serve(d) as a consultant for: AstraZeneca; Allakos; AbbVie; BMS; Sanofi-Regeneron  
Serve(d) as a speaker or a member of a speakers bureau for: Sanofi-Regeneron



**Gilaad G. Kaplan, MD, MPH, AGAF**

Professor  
Gastroenterologist  
Department of Medicine  
University of Calgary  
Alberta, Canada

Disclosures:  
Serve(d) as a speaker or a member of a speakers bureau for: AbbVie; Janssen; Pfizer  
Received research grant from: Ferring



**Jami A. Kinnucan, MD, AGAF, FACC**

Senior Associate Consultant  
GI Practice Chair  
Director of Digital Health and Practice Integration  
Division of Gastroenterology and Hepatology  
Department of Medicine  
Mayo Clinic  
Jacksonville, Florida

Disclosures:  
Serve(d) as a director, officer, partner, employee, advisor, consultant, or trustee for: Abbvie (Advisor, consultant); BMS (Advisor); Fresenius kabi (Advisor, consultant); Janssen (Advisor); Takeda (Advisor, consultant); Pfizer (Consultant)



**Paulo Kotze, MD, MS, PhD**

Professor  
Cajuru University Hospital  
Curitiba, Puerto Rico

Disclosures:  
Serve(d) as a director, officer, partner, employee, advisor, consultant, or trustee for: AbbVie; Pfizer; Janssen; Takeda



**David Lieberman, MD, AGAF**

Professor  
Department of Medicine  
Division of Gastroenterology  
Oregon Health and Science University  
Staff Physician  
Department of Medicine  
Portland VA Medical Center  
Portland, Oregon

Disclosures:  
Serve(d) as a consultant for: UDX; Geneoscopy  
Received income in an amount equal to or greater than \$250 from: Geneoscopy

# Contributing Authors

*GI & Hepatology News* and the American Gastroenterological Association would like to thank the following experts for their contributions to this issue.



**Jorge D. Machicado, MD, MPH**

Clinical Assistant Professor  
Division of Gastroenterology and Hepatology  
University of Michigan  
Ann Arbor, Michigan

Disclosures:

Serve(d) as a speaker for: Mauna Kea Technologies (Paris, France 10/21)  
Received income in an amount equal to or greater than \$250 from: Mauna Kea Technologies (Paris, France 10/21)



**Siew Chien Ng, MBBS, PhD, AGAF**

Professor, Department of Medicine and Therapeutics  
The Chinese University of Hong Kong  
Professor, Department of Medicine and Therapeutics  
Division of Gastroenterology and Hepatology  
Prince of Wales Hospital  
Hong Kong

Disclosures:

Serve(d) as a director, officer, partner, employee, advisor, consultant, or trustee for: The Chinese University of Hong Kong; GenieBiome Limited  
Serve(d) as a speaker or a member of a speakers bureau for: AbbVie; Ferring; Janssen; Menarini; Takeda; Tillotts; Pfizer  
Received research grant from: AbbVie; Ferring; Olympus; Janssen  
Have a 5% or greater equity interest in: GenieBiome Limited  
Received income in an amount equal to or greater than \$250 from: The Chinese University of Hong Kong; GenieBiome Limited



**Richa Shukla, MD**

Assistant Professor  
Margaret M. and Albert B. Alkek Department of Medicine  
Section of Gastroenterology and Hepatology  
Baylor College of Medicine  
Houston, Texas

Disclosures:

Serve(d) as a speaker or a member of a speakers bureau for: AbbVie  
Received income in an amount equal to or greater than \$250 from: AbbVie



**Julia J. Wattacheril, MD, MPH**

Associate Professor  
Department of Medicine  
Director, MASLD Program  
Division of Digestive and Liver Disease  
Center for Liver Disease and Transplantation  
Columbia University Irving Medical Center  
New York Presbyterian Hospital  
New York, New York

Disclosures:

Serve(d) as a director, officer, partner, employee, advisor, consultant, or trustee for: AlphaSights, GlaxoSmithKline  
Received research grant from: Galectin Therapeutics; Intercept Pharmaceuticals; AMRA Medical

# Eosinophilic Gastrointestinal Diseases: Beyond EoE

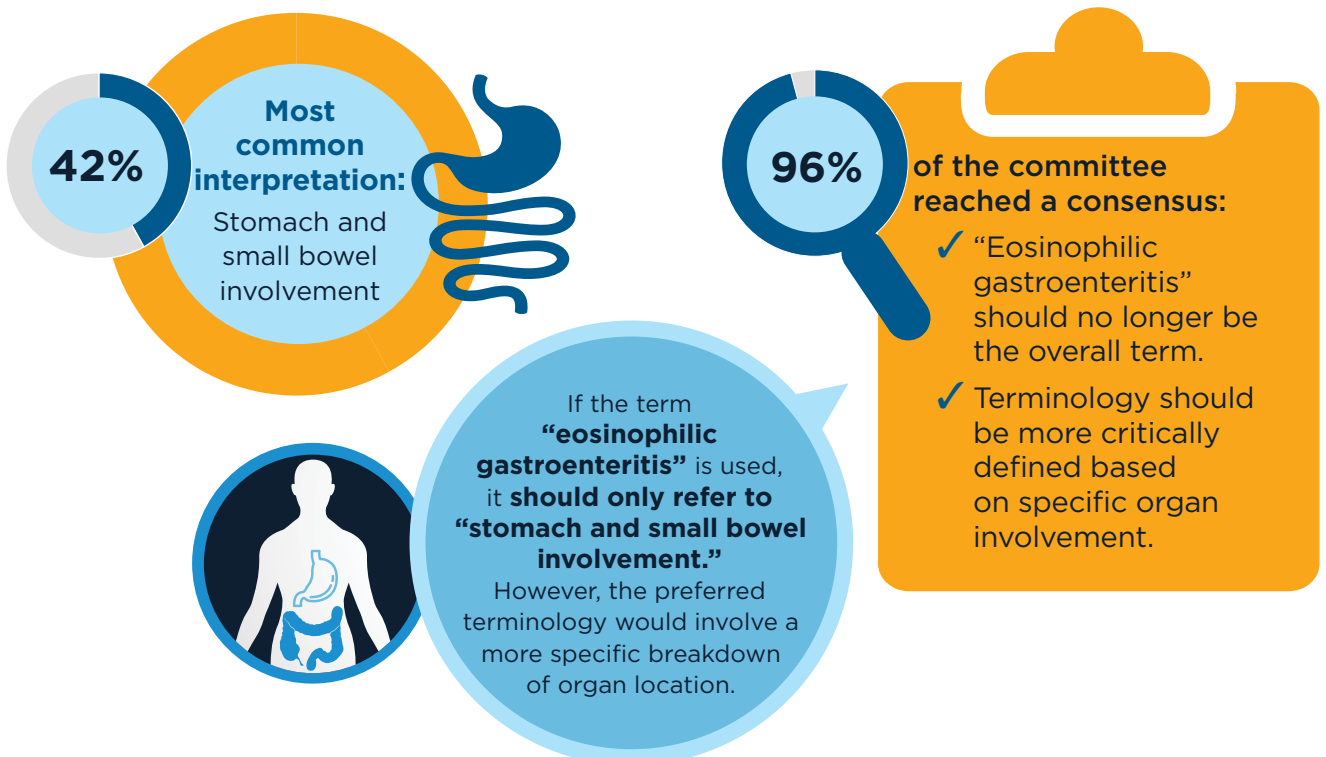
Nirmala Gonsalves, MD, AGAF, FACG

While great strides have been made in the last few decades to improve our understanding of the diagnosis and treatment of eosinophilic esophagitis (EoE), there is much to be learned about treating other non-EoE eosinophilic gastrointestinal diseases (EGIDs). One of the first challenges in diagnosing these rare conditions was developing a consistent nomenclature. For instance, previously, the term "eosinophilic gastroenteritis" was used broadly to encompass diverse instances of eosinophilic infiltration within the gastrointestinal tract. However, this broad application and lack of standardized criteria resulted in diagnostic

ambiguity and confusion. To help improve clinical and research advances in disorders of eosinophils below the diaphragm, in 2022 an international committee convened to create a consensus on standardizing EGID nomenclature. This important milestone created an EGID nomenclature system to specify the location of inflammation in a more precise and defined way.<sup>1</sup> Additional challenges with diagnosing and managing the non-EoE EGIDs include the heterogenous symptom presentation, which can lead to delay in diagnosis. Furthermore, the lack of an FDA-approved treatment for non-EoE EGIDs creates additional hurdles for treatment.

## Standardizing EGID Nomenclature<sup>1</sup>

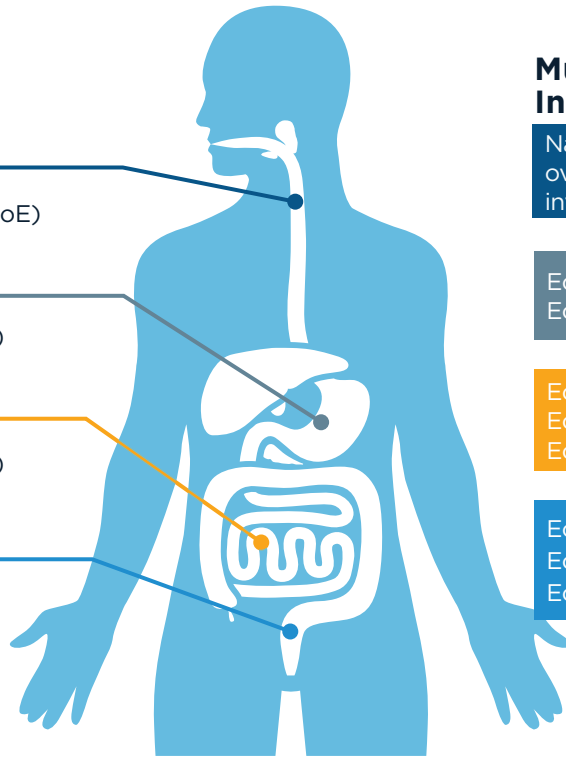
The first step in developing these guidelines was convening a multidisciplinary committee that included 91 experts from 5 continents, spanning the fields of adult/pediatric gastroenterology, allergy, and pathology, as well as other key stakeholders. The first observation was that within the committee alone, **there were 15+ interpretations for the term "eosinophilic gastroenteritis."**





### EGID Location and Condition

- Esophagus →**  
Eosinophilic Esophagitis (EoE)
- Stomach →**  
Eosinophilic Gastritis (EoG)
- Small bowel →**  
Eosinophilic Enteritis (EoN)
- Colon →**  
Eosinophilic Colitis (EoC)



### Multiple Areas of Involvement

Naming consensus not reached for overlapping stomach and esophageal involvement.

Eosinophilic Gastritis and Enteritis  
Eosinophilic Gastritis and Duodenitis

Eosinophilic Duodenitis (EoD)  
Eosinophilic Jejunitis (EoJ)  
Eosinophilic Ileitis (EoI)

Eosinophilic Gastritis and Colitis  
Eosinophilic Duodenitis and Colitis  
Eosinophilic Ileitis (EoI)




Multiple naming convention applies when both possible locations are affected.

### EoE vs non-EoE EGIDs<sup>2</sup>

<b>EoE</b>	<b>Both</b>	<b>Non-EoE EGIDs</b>
Two FDA-approved treatments available Male predominance	Similar pathophysiology Affect patients at any age	No FDA-approved treatments Heterogeneous symptoms No male/female predominance

### Clinical Presentation of Non-EoE EGIDs<sup>2,3</sup>

	Signs and Symptoms	Characteristic		
		Mucosal	Muscularis	Serosal
<b>EoG</b>	<ul style="list-style-type: none"> <li>• Early satiety</li> <li>• Epigastric pain</li> <li>• Dyspepsia</li> <li>• Failure to gain weight</li> <li>• Oral aversion</li> <li>• Vomiting</li> </ul>	<ul style="list-style-type: none"> <li>• Weight loss</li> <li>• Ulcerations</li> </ul>	<ul style="list-style-type: none"> <li>• Gastric outlet obstruction</li> </ul>	<ul style="list-style-type: none"> <li>• Ascites</li> <li>• Bloating</li> </ul> 
<b>EoN</b>	<ul style="list-style-type: none"> <li>• Abdominal pain</li> <li>• Bloating</li> <li>• Diarrhea</li> <li>• Dyspepsia</li> <li>• Hematemesis</li> <li>• Vomiting</li> </ul>	<ul style="list-style-type: none"> <li>• Anemia</li> <li>• Malabsorption</li> <li>• Protein-losing enteropathy</li> </ul>	<ul style="list-style-type: none"> <li>• Dysmotility</li> <li>• Intussusception</li> <li>• Bowel obstruction</li> </ul>	<ul style="list-style-type: none"> <li>• Ascites</li> <li>• Bloating</li> </ul>
<b>EoC</b>	<ul style="list-style-type: none"> <li>• Abdominal pain</li> <li>• Diarrhea or constipation</li> <li>• Lower GI bleeding</li> <li>• Tenesmus</li> </ul>	<ul style="list-style-type: none"> <li>• Bleeding</li> <li>• Protein-losing enteropathy</li> </ul>	<ul style="list-style-type: none"> <li>• Dysmotility</li> <li>• Intussusception</li> <li>• Bowel obstruction</li> </ul>	<ul style="list-style-type: none"> <li>• Ascites</li> <li>• Edema</li> </ul>

## Non-EoE EGID Treatment Outcomes<sup>3-5</sup>

### Clinical Improvement With Dietary Therapy

A prospective study of an elemental diet in adult patients with EoG and EoN showed **histologic remission and improvement** in endoscopic change, symptoms, molecular parameters, and quality of life.

In one small study, patient compliance with **elemental diet** reached 100%, with perceived effort decreasing from 81% to 37% by week 5.

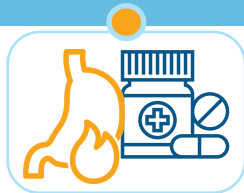


### Proton Pump Inhibitor (PPI) Therapy

Thought to **suppress acid-related aggravation** of gastroduodenal lesions.

In a retrospective series of adult and pediatric patients with non-EoE EGIDs, > 60% were initially treated with a PPI.

Efficacy and response mechanisms need to be further tested and confirmed.



### Systemic Glucocorticoid

Doses of 20-40 mg daily are **effective at achieving remission**.

However, relapse is common with dose reduction.

Development of topical corticosteroids with crushed budesonide has been investigated, similar to the use of oral viscous budesonide in EoE.



### Other Medical Therapies

Biological therapies for non-EoE have shown promise to be effective for **improving eosinophil count** based on preliminary studies.

Immunomodulators, leukotriene inhibitors, and mast cell stabilizers have been used with **variable results**.



## Additional Considerations in Non-EoE EGID<sup>1,4,6-8</sup>

### Natural History Studies Suggest...

EGIDs are chronic in nature.



Most patients have a long duration of disease prior to presentation.



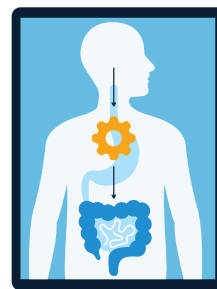
The patchy nature of the disease contributes to delay in diagnosis.



Multiple biopsies in the stomach and duodenum are required to accurately diagnose non-EoE EGIDs.



### Endoscopic Features of Non-EoE



- ✓ EGIDs that prompt biopsies
- ✓ Gastric erythema
- ✓ Erosions/ulcerations
- ✓ Nodularity
- ✓ Friability
- ✓ Granularity
- ✓ Thickened folds



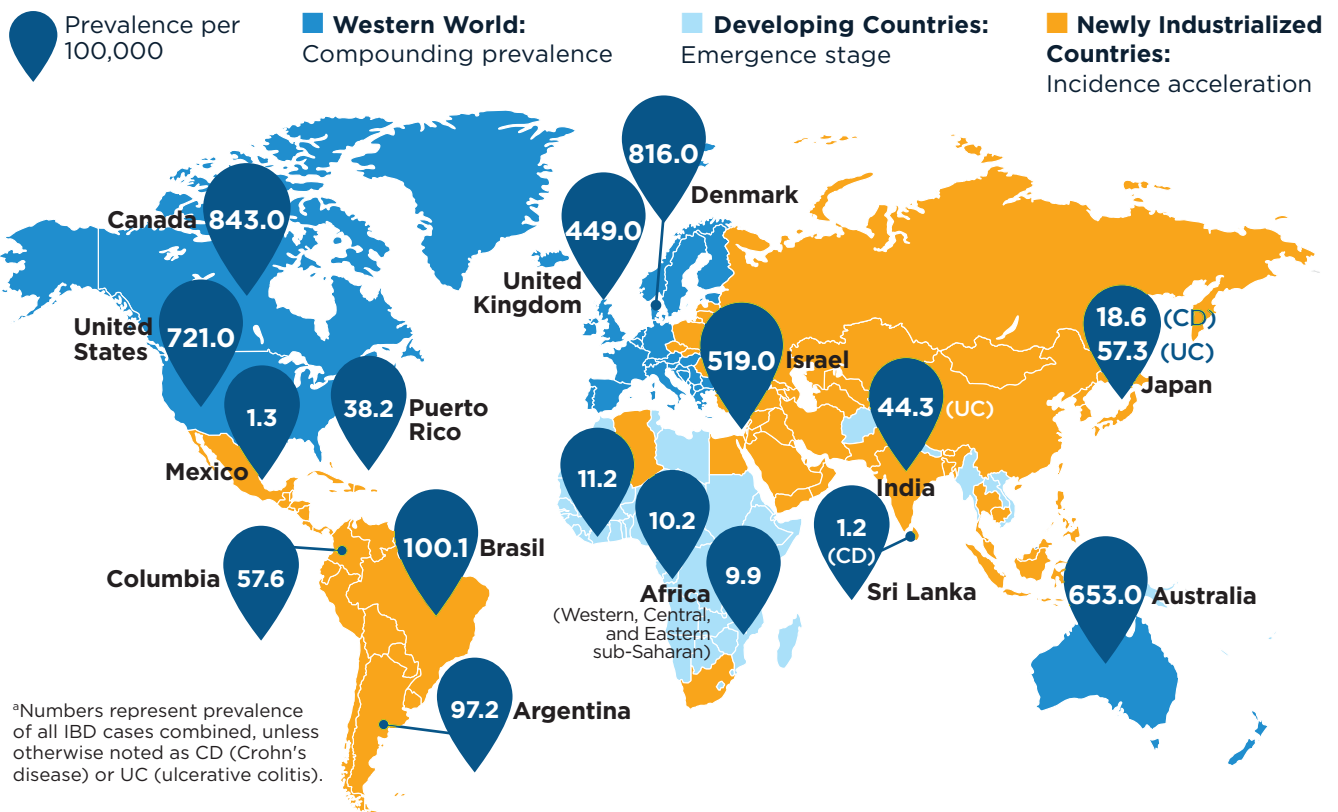
# The Changing Face of IBD: Beyond the Western World

Gilaad G. Kaplan, MD, MPH, Paulo Kotze, MD, MS, PhD, and Siew C. Ng, MBBS, PhD

Inflammatory bowel disease (IBD) has become a global disease, with rising incidence in non-Western cohorts such as Asia and Latin America.<sup>1</sup> These newly industrialized countries are in an “acceleration in incidence” stage, while Western countries are in a “compounding prevalence” stage as new cases level out, but prevalence climbs steadily.<sup>1</sup> Incidence is varied throughout Asia and remains comparatively lower than in Western countries; this discrepancy is influenced by environmental risk factors such as diets high in fat, animal protein, sugar, fast food, and food additives, which are common in the Western world.<sup>2</sup> In Latin America and the Caribbean, the incidence of

IBD is also increasing, but is still less than in Western countries, and variance between countries depends on the level of urbanization and industrialization.<sup>3</sup> Risk factors are like those of Asia, and also include inadequate living conditions, the absence of exposure to infectious diseases, treated water, and a limited ability to differentiate the diagnosis of infectious diseases, representing a key difference compared with the Western world.<sup>3</sup> Treatment within these groups seems to be similarly effective compared with the Western world, although some areas of Asia and Latin America face more barriers to accessing healthcare, which is a key area that global health care could target.<sup>3,4</sup>

## Global Trends in IBD<sup>1-3,5-16,a</sup>



### Globally Understood Risk Factors

Smoking history, ultra-processed foods, living in an urban environment



### Extraintestinal Manifestations

Ankylosing spondylitis, fatigue, arthritis, uveitis, sacroiliitis, primary sclerosing cholangitis (lower rates in Asia), pyoderma gangrenosum, erythema nodosum



## IBD in the Western World<sup>2,5-7,17-19</sup>



### Most Studied Risk Factors



Less active lifestyle



Oral contraceptive use



Ultra-processed food



Antibiotic use during childhood

### More Commonly Diagnosed in . . .



Younger patients



Female patients



### Genes Involved

- ✓ *NOD2*
- ✓ *IL-23R*
- ✓ *ATG16L*

Data indicate a weaker heritable component for ulcerative colitis, while *NOD2* is stronger for Crohn's disease.

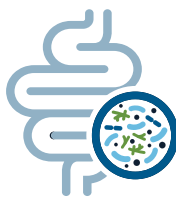
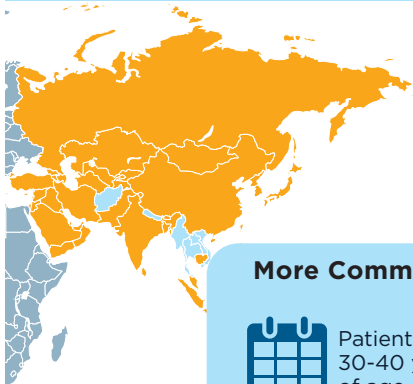
### Presentation of Disease

- ✓ IBD is diagnosed at all ages, but predominantly in young individuals.
- ✓ **Inflammatory Crohn's disease** is most common, but complications like perianal fistulizing disease and extra-intestinal manifestations may present at diagnosis.

### Differential Diagnosis

- Intestinal tuberculosis
- Yersiniosis
- Actinomycosis
- Sexually transmitted infections (STIs)
- Histoplasmosis
- Amoebiasis
- Helminthiasis
- Ischemic colitis
- Vasculitis

## IBD in Asia<sup>2,6,7,20-27</sup>



### Most Studied Risk Factors



Fat, cholesterol, and fatty acids



Eggs, meats, fish, and meat products



### More Commonly Diagnosed in . . .



Patients 30-40 years of age



Male patients



### Genes Involved

- ✓ *TNSF-F15*
- ✓ *NOD2* and *ATG16L1* are less common

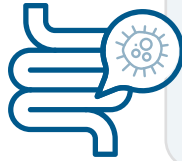
### Presentation of Disease

- ✓ The ratio of ulcerative colitis to Crohn's disease cases is **approaching 1:1**.
- ✓ About **1 in 3 patients** with Crohn's disease have complicated disease behavior/perianal manifestations at diagnosis.
- ✓ High rates of ileocolonic disease are observed.

### Differential Diagnosis

- Intestinal tuberculosis
- Infectious diseases (bacterial, protozoal, helminth infestations)
- Yersiniosis
- Actinomycosis
- Histoplasmosis
- Strongyloidiasis
- Amebiasis
- STIs
- Hepatitis B

## IBD in Latin America<sup>3,28</sup>



### Most Studied Risk Factors



Inadequate living conditions



Absence of infectious disease



Treated water

### More Commonly Diagnosed in . . .



Female patients



### Genes Involved

Not enough data exist at this time on the genetic basis and interaction with environment in this population, although a gene-environment interaction is suspected as a cause of disease.

### Presentation of Disease

- ✓ The most common Crohn's disease phenotypes are **inflammation**, stricturing, penetrating, and perianal disease.
- ✓ Extraintestinal manifestations occur in nearly **40% of patients**.

### Differential Diagnosis

- Parasitic infectious diseases (protozoa and helminths)
- Intestinal amebiasis (*Entamoeba histolytica*)
- Strongyloidiasis
- Tuberculosis

## Global Access to Treatment and Resources<sup>3,7,17,21</sup>



Despite the wide array of possible treatments for IBD—including mesalamine, immune system suppressors, biologics, oral small molecules, nutritional supplements, and surgery—**access to care varies greatly around the world.**

While these treatments are generally widely available for patients in the Western world, **Asian and Latin American populations have less extensive health care infrastructures**, making it much more difficult to receive proper diagnosis and therapy.

Global disparities are also due to pharmaceutical pricing, access to biosimilars, and national drug policies and approvals. Investment in new drugs and technology is expensive and limits the distribution of drugs in some countries.



# The Role of Noninvasive Biomarkers: Evaluation and Management of MASLD

Julia J. Wattacheril, MD, MPH

**M**etabolic dysfunction-associated steatotic liver disease (MASLD), previously known as nonalcoholic fatty liver disease (NAFLD),<sup>1</sup> refers to a range of liver conditions characterized by the accumulation of fat in the liver due to metabolic factors. MASLD affects nearly 30% of the global population and is a prevalent cause of advanced liver disease.<sup>2</sup> This disease can progress from simple steatosis to metabolic dysfunction-associated steatohepatitis (MASH), which involves inflammation and liver cell damage—and unmitigated can lead to liver cirrhosis, liver failure, and liver cancer.

Clinicians' early identification and stratification of at-risk individuals may impact progression and regression, as only a minority of individuals with MASLD present with liver-related consequences.<sup>2</sup> Although early identification and risk stratification may occur in gastroenterology and hepatology clinics, disease

modifying interventions may occur outside of those settings. Continuously monitoring MASLD response to current treatments is also key. Histologic examination of the liver is the current established standard for assessing and monitoring this disease, grading necroinflammation, and staging hepatic fibrosis; however, the cost and invasiveness limit its routine and widespread use.<sup>2</sup> Drug approvals independent of histology-based outcomes lay the groundwork for further standardization and validation of noninvasive tests (NITs) in the evaluation and management of MASLD.

The latest AGA Clinical Practice Update (2023) can help healthcare professionals use NITs to identify patients who are at higher risk for MASLD progression for directed intervention.<sup>2</sup> Ongoing research continues to refine the use of NITs in evaluating and managing MASLD; therefore, the landscape is likely to evolve and advance over time.

## Utilization of Noninvasive Biomarker Testing<sup>3</sup>



## Noninvasive Biomarkers for MASLD Evaluation and Risk Stratification<sup>1,4-8</sup>

### Serum-Based Biomarkers<sup>1,5,6</sup>

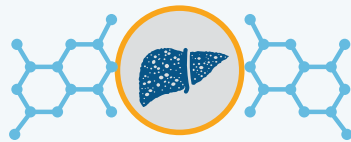


- ▶ Fibrosis 4 Index (FIB-4) score
- ▶ NAFLD fibrosis score
- ▶ Aspartate aminotransferase to platelet ratio index (APRI)

### Proprietary

- ✓ FIBROSpect®
- ✓ FibroTest®
- ✓ Enhanced Liver Fibrosis (ELF)®
- ✓ Hepamet Fibrosis Score®
- ✓ FibroMeter®
- ✓ NIS2+TM®
- ✓ NIS4®

### Imaging-Based Biomarkers<sup>4,5</sup>

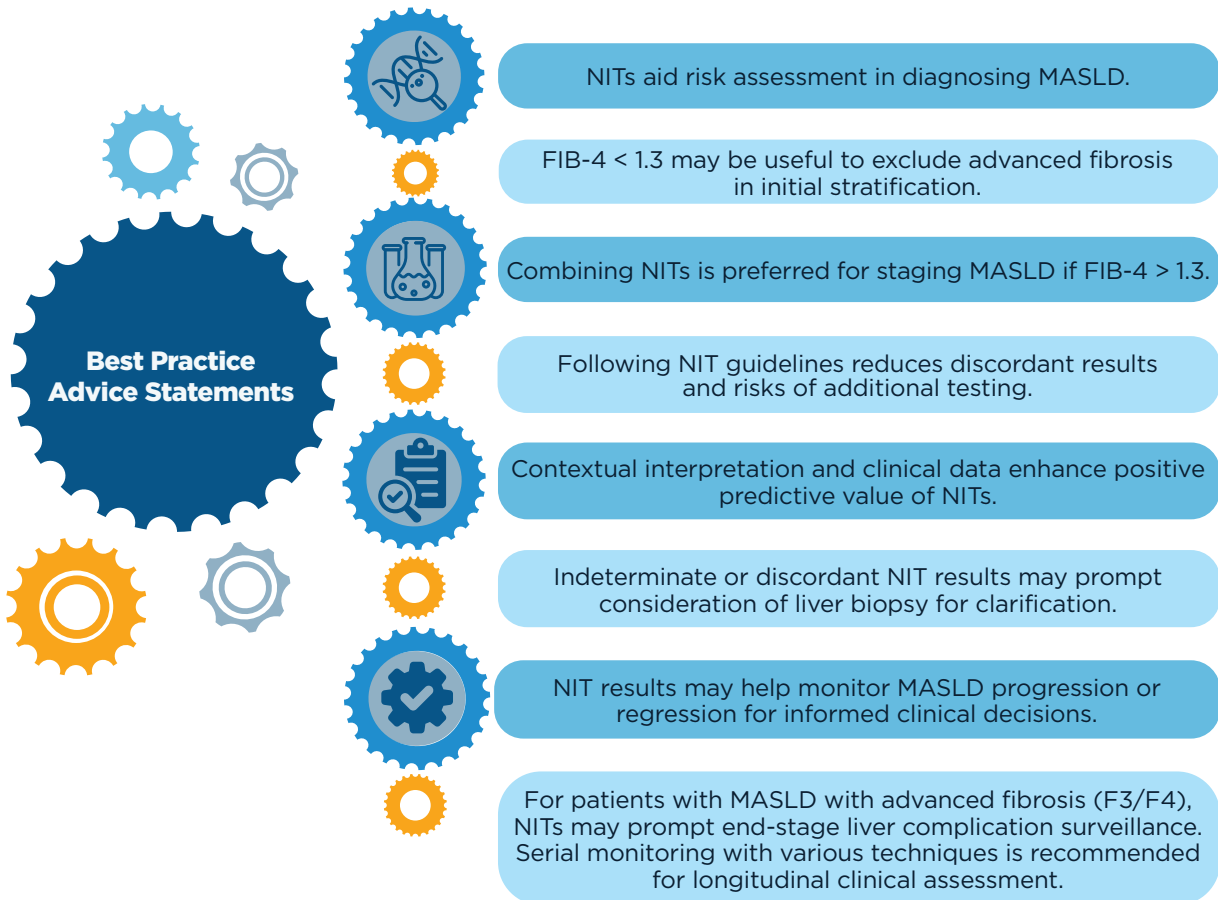


#### Measures liver stiffness, corresponding to fibrosis

- ✓ FibroScan®/vibration-controlled transient elastography (VCTE)
- ✓ Shear wave elastography (SWE)
- ✓ Magnetic resonance elastography (MRE)



## AGA Clinical Practice Update on Role of Noninvasive Biomarkers for MASLD<sup>2</sup>



## AGA Key Recommendations<sup>5</sup>

### Screening and Diagnostic Evaluation of MASLD Using NITs

	<p><b>Primary Suspicion</b></p>	<ul style="list-style-type: none"> <li>-Clinical suspicion for MASLD met</li> <li>-Primary assessment</li> <li>-Exclude alternative causes</li> </ul>
	<p><b>Fibrosis Risk Stratification</b></p>	<ul style="list-style-type: none"> <li>-Prioritize FIB-4 assessment with awareness of limitations</li> <li>-Determine diabetes status and metabolic risk factors</li> <li>-Sequential testing if high metabolic risk</li> </ul>
	<p><b>NITs for Advanced Fibrosis</b></p>	<ul style="list-style-type: none"> <li>-Serial monitoring (prefer imaging-based biomarkers)</li> <li>-Consider liver biopsy for discordant NITs</li> <li>-Clinical management on stage of disease</li> </ul>



# The Emerging Role of Liquid Biopsy in the Diagnosis and Management of CRC

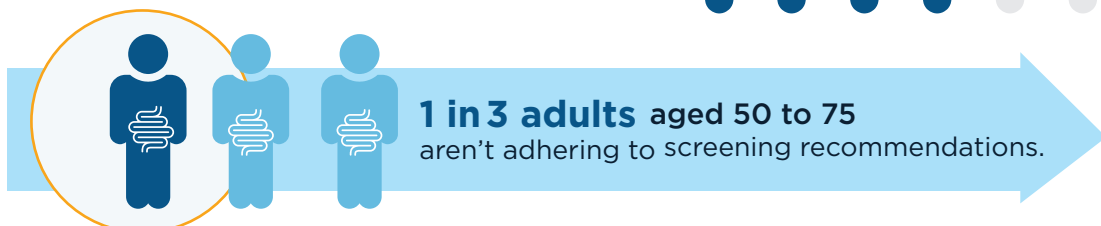
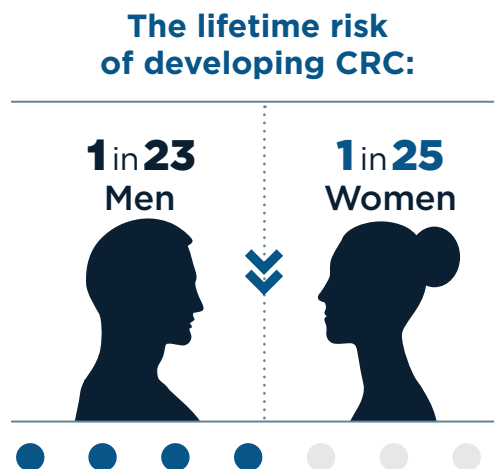
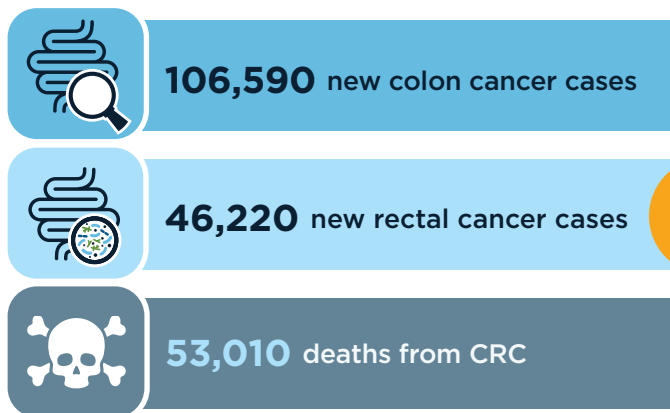
David Lieberman, MD, AGAF

Colorectal cancer (CRC) is the third most common cancer in the United States, and early detection and monitoring are crucial for improving patient outcomes.<sup>1</sup> Liquid biopsy (LB) is a revolutionary approach that may offer a non-invasive way to diagnose and manage CRC. The history of LB for CRC reflects a progression from early attempts to detect biomarkers in blood to the current era of precise genetic analysis using circulating tumor deoxyribonucleic acid (ctDNA) and analyzed with next-generation sequencing. The technology has significantly improved over time, leading to the potential for integration into clinical practice and to provide more personalized and effective CRC management.<sup>2</sup>

LB offers several potential advantages for CRC screening compared to traditional non-invasive screening with a stool sample, or invasive screening

with colonoscopy. A blood test that could identify high-risk individuals who need colonoscopy is exciting, because it is possible that adherence to screening would be improved with LB. However, there are many challenges. Reduction of CRC mortality or incidence will depend on the ability of the test to accurately detect individuals with early-stage cancer or pre-cancerous advanced polyps. It is not clear if the biology of such lesions would result in an adequate signal in blood if the lesion were not invasive. Test performance also depends on completion of colonoscopy if individuals have an abnormal LB. Testing methods, cost consideration, and clinical validation of performance will need to be addressed.<sup>3</sup> As the technology advances, the role of LB in CRC screening will likely evolve and expand.

## The American Cancer Society CRC Estimates for 2024<sup>1,4</sup>



### FDA-Approved Liquid Biopsy Tests<sup>5-8</sup>

Name	Approval Year	Indication	Purpose	Significance
Cell Search <sup>®</sup> Circulating Tumor Cell (CTC) test <sup>5</sup>	2007	Patients with metastatic CRC	Assesses and monitors prognosis Tests blood to identify, isolate, and enumerate CTCs	First approved LB for enumerating CTCs
Epi proColon <sup>®</sup> Epigenomics <sup>6</sup>	2016	Average-risk patients who opt out of traditional screening for CRC	Detects Septin 9 methylated DNA in plasma	First approved LB for cancer-related single gene changes
Guardant360 <sup>®</sup> CDx <sup>7</sup>	2020	Those with solid CRC tumors, but not blood cancers	Tests blood for multiple cancer-related genetic changes	First approved LB for detecting multiple cancer-related genetic changes
FoundationOne Liquid CDx <sup>7</sup>	2020	A companion diagnostic to detect NTRK fusions in solid CRC tumors	Identifies those who may benefit from larotrectinib (FDA approval, 2018)	Only approved LB that analyzes 300+ genes
→ Expanded indication <sup>8</sup>	2023	A companion diagnostic for encorafenib + cetuximab for patients with <i>BRAF</i> V600E-mutated metastatic CRC	Tests blood for ctDNA	



### LB Benefits and Limitations<sup>2,3</sup>



#### Potential benefits in CRC screening and cancer management

1. Non-invasiveness and convenience could increase patient compliance for screening
2. May help identify a high-risk individual who should receive a colonoscopy
3. Can help tailor personalized and effective treatment plans based on genetic mutations or CRC biomarkers
4. Provides real-time data about the tumor's genetic profile and treatment response
5. Can predict relapses and metastases
6. Detects minimal residual disease



#### Limitations

1. Less accurate than other CRC screening tests for detection of early stage CRC or pre-cancerous advanced polyps
2. Could be less cost-effective for population-based screening compared to traditional methods based on the operating characteristics of the tests
3. Not as sensitive or specific as tissue biopsy or colonoscopy for detecting and characterizing genetics of CRC
4. Can't provide information about the specific location or extent of the primary tumor or metastases
5. Availability of reliable biomarkers is still limited
6. Currently lacking validation and standardization across labs

# Cannabinoids and Digestive Disorders

Jami A. Kinnucan, MD, AGAF, FACC

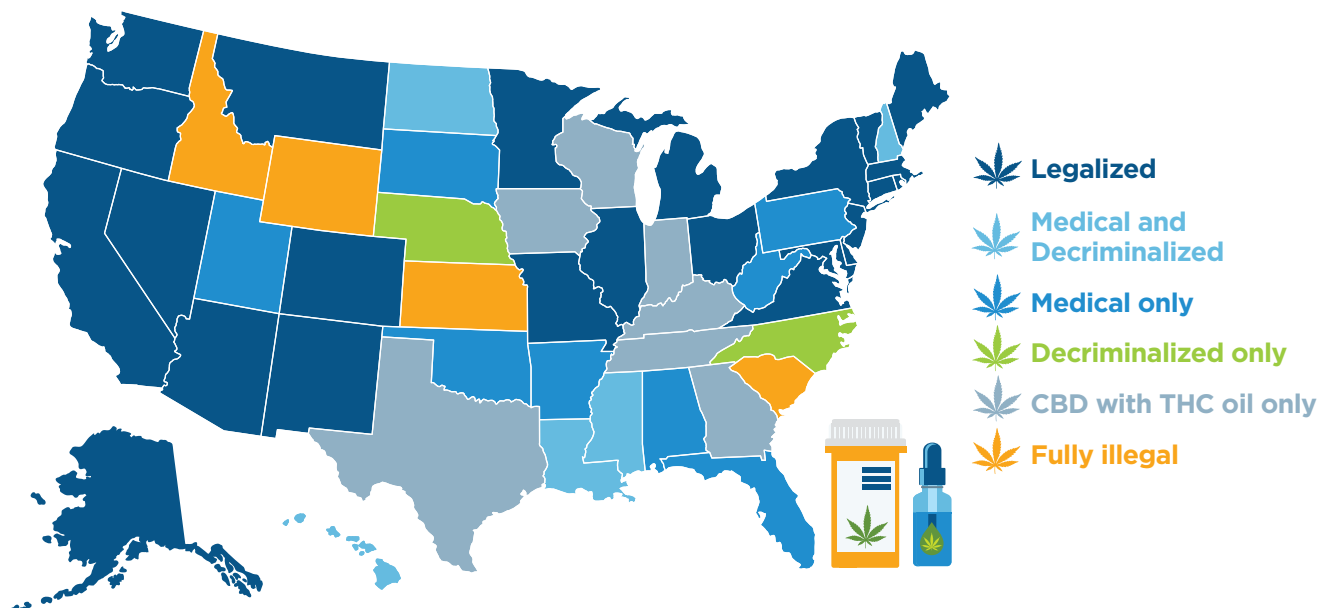
Complementary and alternative therapies are gaining interest in the gastrointestinal (GI) community. Up to 27% of adults in the United States and Canada report using cannabis for medical reasons, and up to 39% of patients with inflammatory bowel disease (IBD) report past use for symptom management.<sup>1-3</sup> Significant questions and challenges still remain surrounding the use of cannabis in GI disorders, including its varied legalization status globally.<sup>4,5</sup>

Cannabinoids can be broken down into endocannabinoids (naturally occurring substances within the body) such as 2-arachidonoylglycerol (2-AG) and anandamide (AEA), which act within the body at the cannabinoid receptors (CB) CB<sub>1</sub> and CB<sub>2</sub>.<sup>6</sup> There are also plant-based cannabinoids (phytocannabinoids) that include the most commonly known cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC). In addition, there are synthetic cannabinoids (manmade molecules that resemble THC or CBD), and synthetic receptor antagonists and agonists (manmade molecules that act directly at the cannabinoid receptors).

Studies have assessed cannabinoid use in many GI conditions—most notably IBD and irritable bowel syndrome (IBS)—however, medical marijuana use has only been approved in some states for Crohn’s disease or ulcerative colitis.<sup>4,7,8</sup> In patients with IBS, there have been conflicting results, with a recent clinical trial of a synthetic CB<sub>2</sub> agonist showing no significant change in abdominal pain scores.<sup>9</sup> In patients with IBD, results are also varied, with some trials showing improvement in clinical measures but not endoscopic remission.<sup>10</sup> These varied results could be due to differences in the formulation of cannabinoids studied and routes of administration.

While the endocannabinoid system is of high interest within the GI community due to its therapeutic potential, many challenges remain, such as legalization, widely varied compounds and doses of active ingredients, and a lack of large, high-quality randomized studies.<sup>5,11,12</sup> More research is needed to delineate the exact mechanism to best interact with the endocannabinoid system, and what GI disease states might be most affected.

## Marijuana Legalization in the United States<sup>4,5,a,b</sup>



<sup>a</sup>The recreational use of cannabis is illegal in most countries outside of the United States and Canada, with some moving toward decriminalization and medical marijuana legalization.

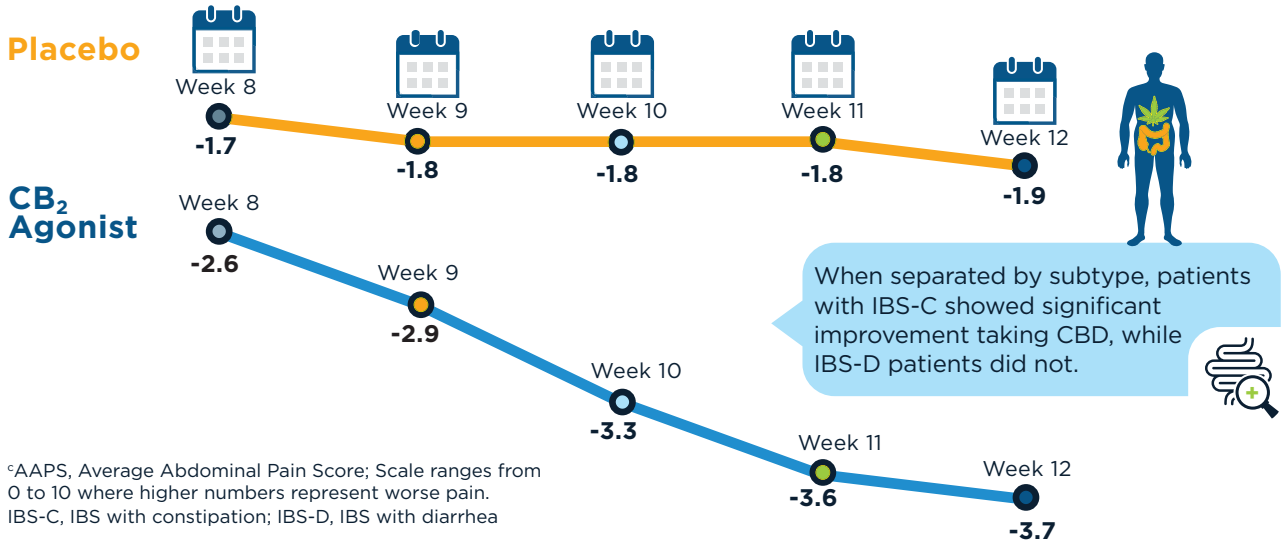
<sup>b</sup>CBD oil can be made with or without THC. This map refers to CBD oil with THC. CBD oil with THC is illegal in states marked as "Fully Illegal." All statuses are subject to state limits and CBD oil may be legal only up to 0.5% THC or marijuana may be legal only up to 1 ounce.

## Cannabinoid Treatment in IBS and IBD<sup>9,10,13,14</sup>

### CB<sub>2</sub> Receptor Agonist for IBS

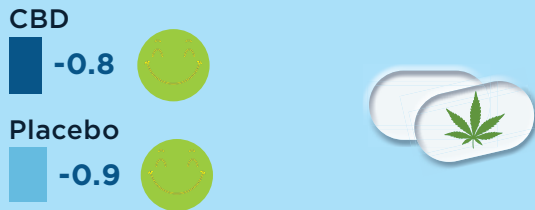
Although the weekly changes in average abdominal pain scores<sup>c</sup> were similar across study groups, CBD use showed significant improvement in a subgroup of patients who had moderate-to-severe pain at baseline.

#### Change from Baseline AAPS



### 50 mg CBD Chewing Gum for IBS

Change in Abdominal Pain Scores<sup>d</sup>



<sup>d</sup>Visual analog scale device with subjective pain faces and a 0-10 scale was used for abdominal pain score.

**No significant difference** in abdominal pain score between placebo and treatment group



**Cannabinoids in IBS:** Some studies have shown that cannabis use may increase risk for development of IBS, and studies on the use of cannabinoids have not shown significant results in reducing IBS symptoms, except in a small moderate-to-severe IBS subgroup.

### Meta-Analysis Data for IBD

15 nonrandomized studies



5 randomized studies (including 146 patients)

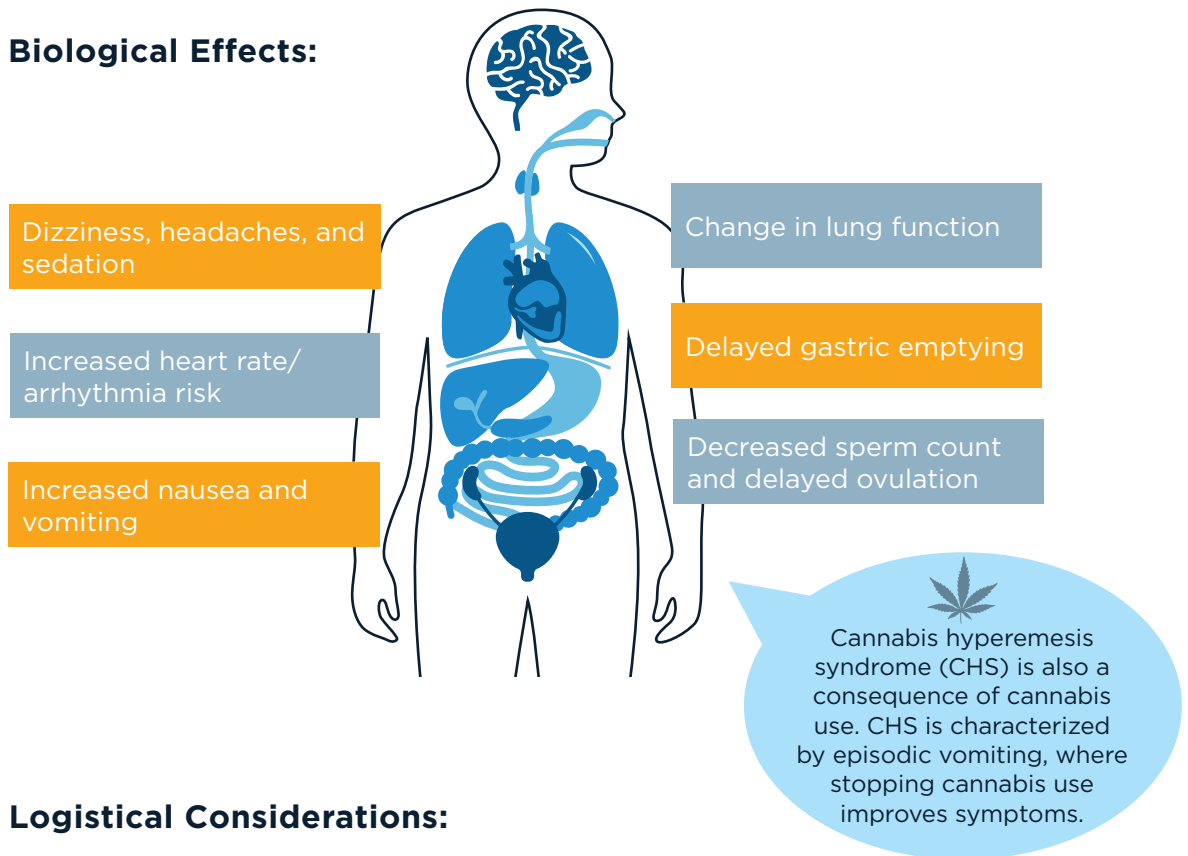
**Clinical remission:** Cannabinoids not effective (relative risk, 1.56) (0.99-2.46)

**Abdominal pain:** 68%-100% reported symptom relief (in the cannabinoid group)

**Cannabinoids in IBD:** Clinical symptoms, such as abdominal pain, nausea, diarrhea, poor appetite, and well-being, have been shown to improve in IBD, but studies have also used varied cannabinoid formulations. No change in inflammatory biomarkers has been observed.

Risks Involved in Cannabinoid Use<sup>11,15-17</sup>

**Biological Effects:**



**Logistical Considerations:**





# AI and Machine Learning in IBD: Promising Applications and Remaining Challenges

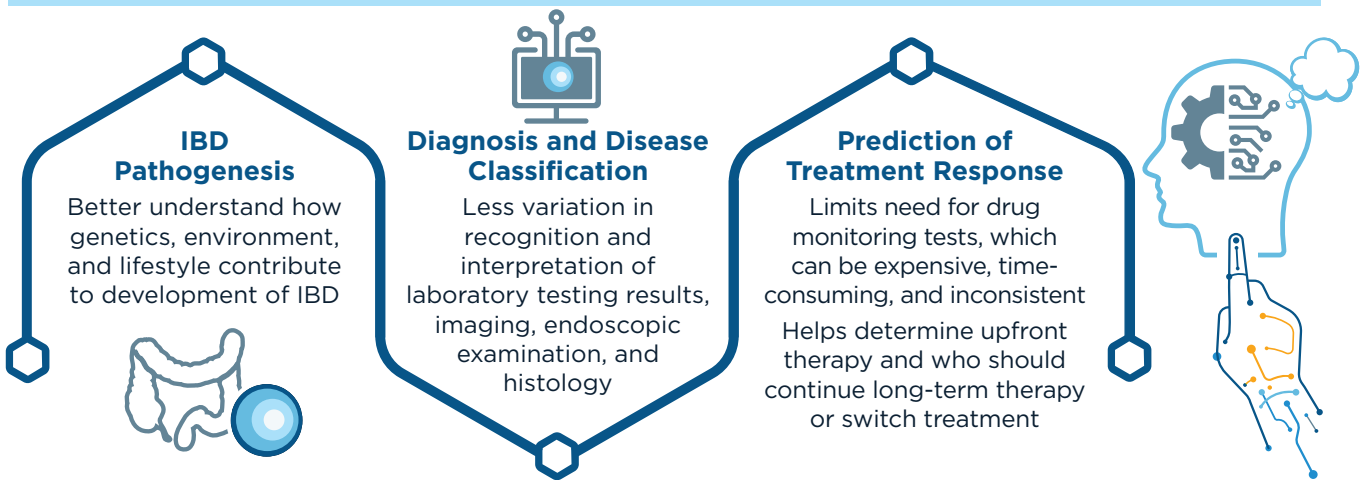
Shirley Cohen-Mekelburg, MD, MS

Nearly 1 in 100 Americans have inflammatory bowel disease (IBD), with up to 56,000 new cases being diagnosed each year.<sup>1</sup> IBD is a complex disease with a myriad of presentations, possible treatment approaches, and patient outcomes. Artificial intelligence (AI)—a field of technology which began in the 1950s—refers to the ability of computers to learn and perform tasks that would have typically required human intelligence, while “machine learning” refers to the development of the algorithms that help AI learn patterns from data.<sup>2,3</sup> The goal in many industries, including health care, is for AI to aid in and improve decision-making. Applications of AI including machine learning already greatly influence the oncology space, aiding in risk assessment, early diagnosis, prognosis, and treatment decision-making.<sup>4</sup>

Similar utilizations are being investigated to help improve the quality and efficiency of care for patients with IBD, but there is still much research to be done before we can fully leverage such tools in everyday practice.<sup>5</sup>

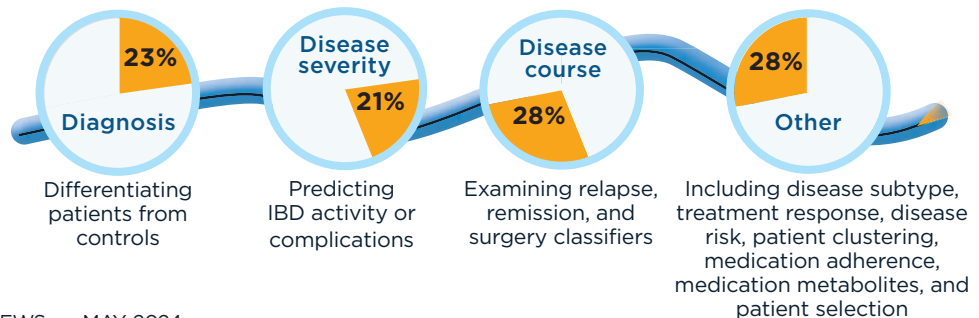
Although extensive progress in AI has been made since the turn of the century, several limitations remain. Poor-quality data sets may lead to inaccurate predictions, and it is difficult to generalize data sets to minority populations. In health care, clinicians must also understand and be able to interpret the algorithms in order to trust and apply them in practice. Lastly, and importantly, there are ethical concerns regarding patient privacy in data collection.<sup>6</sup>

## Potential Applications in IBD<sup>5</sup>

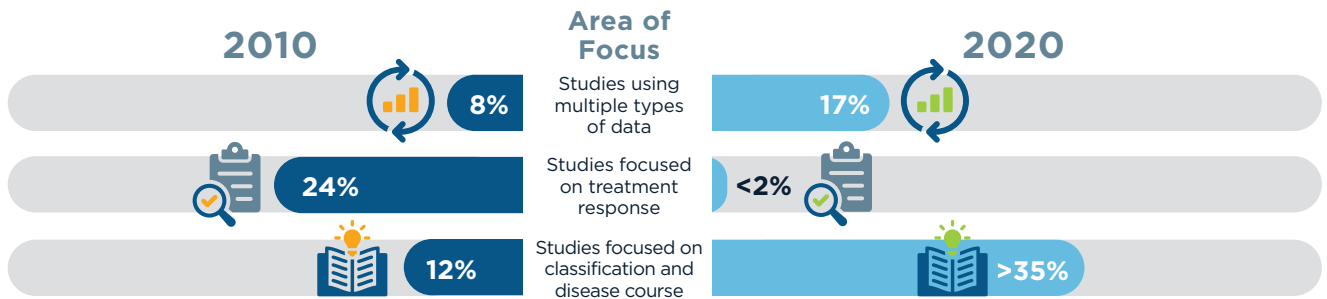


## Latest Research<sup>7</sup>

Between 2018 and 2021, there was a **68% increase** in published studies of machine learning techniques within IBD-related AI applications.




## Evolution of AI Research in IBD<sup>7</sup>



## What Do Clinicians Need to Know Right Now?<sup>7</sup>



Clinical expertise is still necessary to help interpret findings and detect nonrepresentative data, biased results, and poor generalization.

While variation in IBD practice is common, AI-enhanced decision support has the potential to reduce variability in treatment decisions and improve patient care.

## Limitations in AI Applications for IBD<sup>2,6,8</sup>

- |  |   |
|--|---|
| 1. Poor-quality data or lack of availability                         | Results in inaccurate algorithms, poor decision-making  |
| 2. Disproportionate representation in data samples                   | Creates algorithms that are trained based on specific demographics, which are not generalizable |
| 3. Difficult to explain or interpret algorithms                      | Compromises clinician trust in AI and confidence applying technology into practice              |
| 4. Collection of patient data to build algorithms                    | Leads to ethical concerns about protecting patient privacy                                      |
| 5. Complexity of integrating multiple data sets from various sources | Makes standardization of data difficult and inhibits seamless integration and analysis          |

# Simulation-Based Training in Endoscopy: Benefits and Challenges

Richa Shukla, MD

The methodologies used to train medical students and professionals are constantly evolving; centuries of studying anatomy with models and figurines—and then practicing on real patients—are now being reexamined in light of emerging technology. Simulation-based training offers a new, seemingly “risk-free” approach to learning because trainees can practice procedures in safe, realistic, patient-free environments. Early mistakes can be made with minimal consequence, training can be tailored to include highly specific clinical scenarios, and the evolving technology helps us accomplish these goals in extremely realistic simulations.<sup>1-3</sup> The COVID-19 pandemic further escalated the need for advanced training to be available virtually and helped to shape what these types of

programs should look like moving forward.<sup>4</sup>

As with every new piece of technology, some limitations still need to be addressed. Cost is the first one that comes to mind. While the long-term cost vs benefit debate is not yet settled, the upfront expense is substantial and immediately makes simulation-based training less accessible. The good news is that subsequent costs, such as those for software updates and upgrades, may be much lower. We are also at the mercy of possible technical issues and malfunctions, and the transferability of skills learned virtually into real-life practice may vary from person to person. Nevertheless, many promising elements make simulation-based training an exciting development for preparing the next generation of endoscopists.

## Types of Simulation-Based Training in GI Endoscopy<sup>1-3</sup>

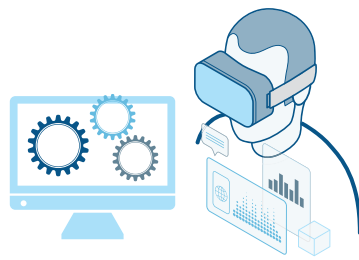


### Mannequins

**Immediate benefit:**  
Decreases training time

**Long-term benefit:**  
Reduces staff costs and increases learning opportunities

**Challenge:**  
Lacks authenticity and realism; relatively costly



### Virtual Reality

**Immediate benefit:**  
30% decrease in procedure time; Adaptable; Portable

**Long-term benefit:**  
Decreases complications, pain ratings, recovery time, and costs

**Challenge:**  
Technology is constantly becoming outdated



### Augmented Reality

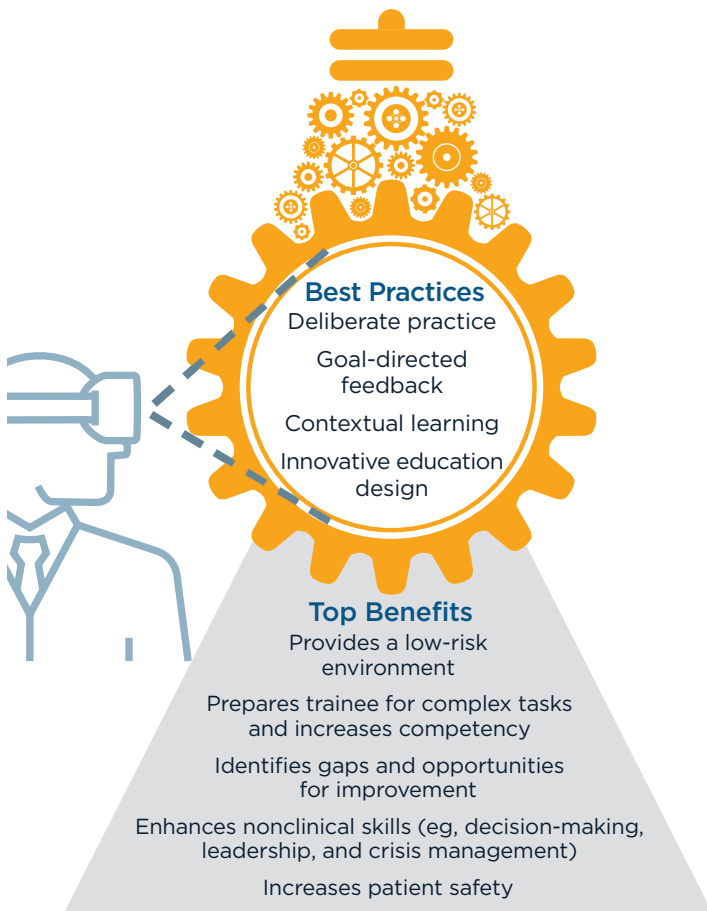
**Immediate benefit:**  
Resembles a real-life surgical experience

**Long-term benefit:**  
Improves efficiencies for inexperienced clinicians

**Challenge:**  
Cannot replace the mentor/mentee experience



## Improving Health Care Quality: Simulation-Based Training<sup>2-4</sup>



### Gaps in Training

While the implementation of simulation-based training has grown significantly in the 21st century, the COVID-19 pandemic was an unprecedented event that highlighted some remaining areas of unmet need.

### Results of the COVID-19 Lockdown

#### Skill deterioration

- In the absence of traditional in-person practice, simulation-based training can help both professionals and students maintain important daily skills.

#### Need for crisis-related training

- Simulation-based training can help health care professionals better prepare for less common, but highly critical scenarios.



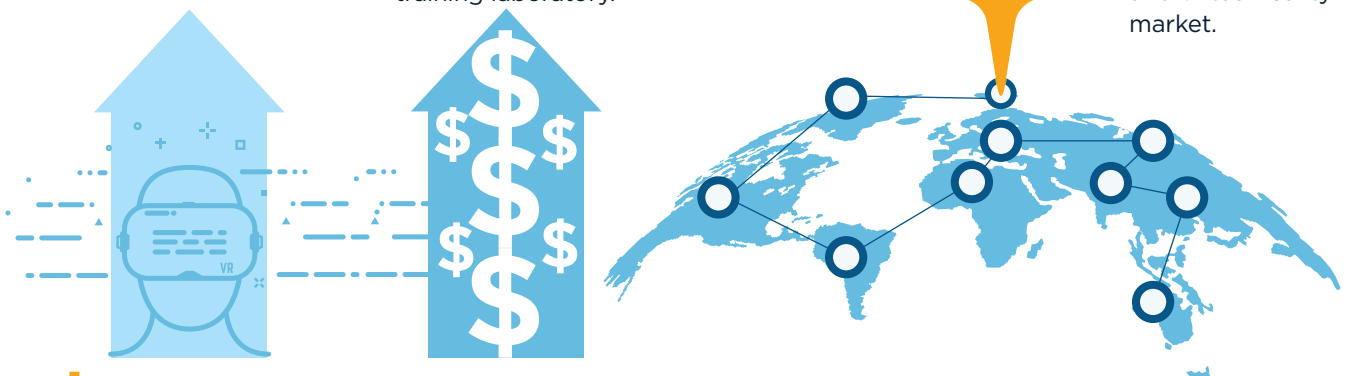
## Financial Implications<sup>3,5,6</sup>

Individual simulators cost upwards of **\$60,000 to \$100,000.**

**Costs increase exponentially** when funding a full simulation training laboratory.

**\$20.76 billion by 2032**

Projected forecast for the global health care augmented and virtual reality market.



However, **maintenance of these training labs** should be cost-efficient once up and running.

# Fluid Management in Acute Pancreatitis

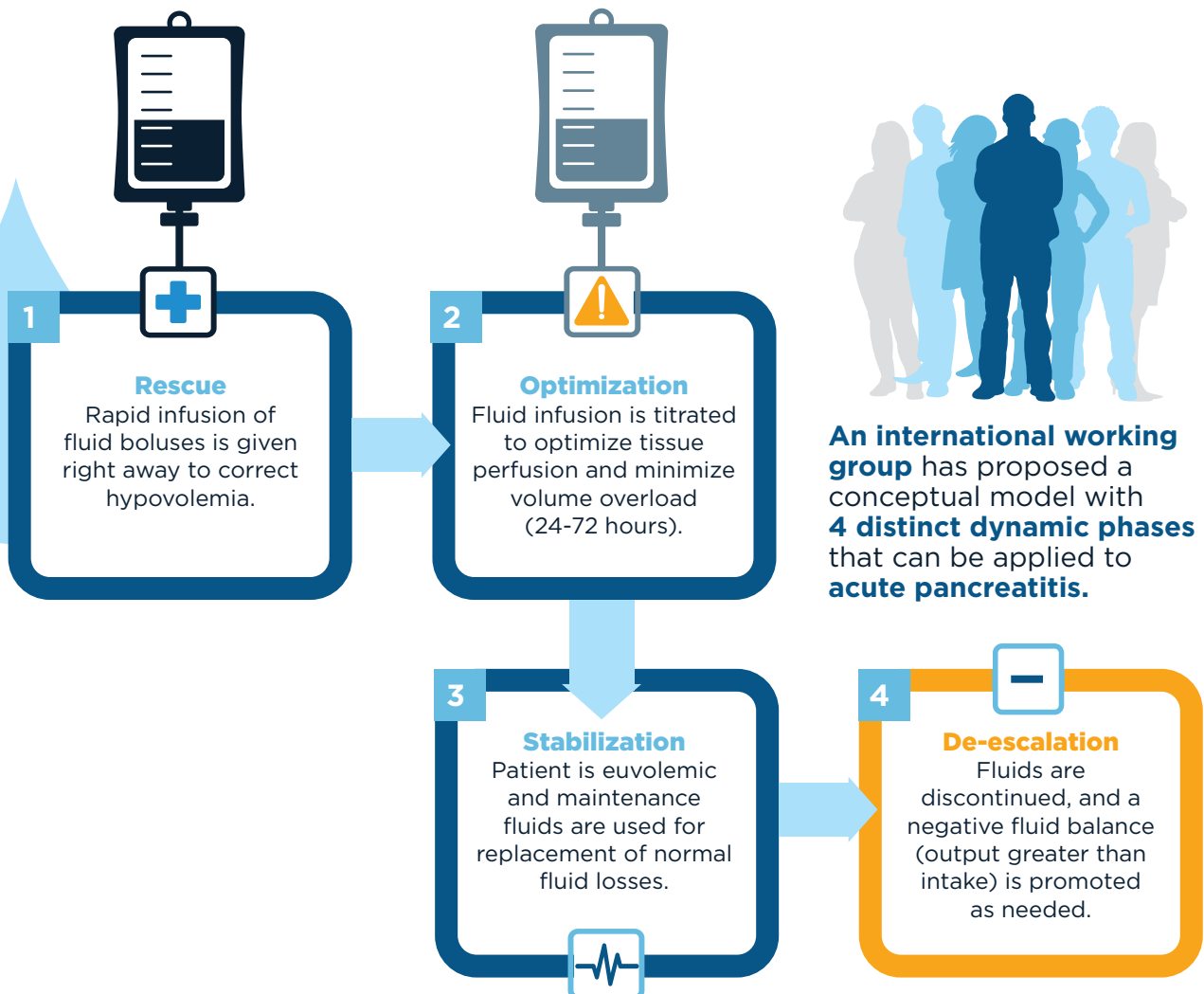
Jorge D. Machicado, MD, MPH

Acute pancreatitis is marked by inflammation of the pancreas, potentially leading to organ failure and pancreatic necrosis. Early management relies heavily on intravenous (IV) fluid resuscitation. Initiating fluid resuscitation at an early stage can enhance pancreatic perfusion and maintain adequate systemic circulation, reducing the risk of pancreatic necrosis, hypovolemic shock, and organ failure.<sup>1</sup>

Recently, a series of randomized controlled trials have provided a clearer understanding of the type and

rate of fluid administration that is the most beneficial for patients with acute pancreatitis.<sup>2-4</sup> The approach to managing fluids in cases of acute pancreatitis may vary depending on the severity of the condition and individual patient factors. Fluids should be prescribed considering their composition (type of fluid), dosing (rate of administration), goals, potential risks, and contraindications.<sup>2,3</sup> Close monitoring and assessment are essential components of effective fluid management of acute pancreatitis.<sup>2</sup>




## Phases of Fluid Therapy<sup>5</sup>





## Rate of Fluid Administration<sup>2</sup>

WATERFALL was a recent multinational, open-label, randomized controlled trial comparing early weight-based aggressive vs nonaggressive fluid resuscitation in patients with acute pancreatitis. This landmark study has helped clarify the question of the optimal rate of fluid administration in acute pancreatitis.

-  **744 patients** were planned to be randomized and assigned to aggressive (20 mL/kg bolus, followed by 3 mL/kg/h) or moderate (1.5 mL/kg/h, with a bolus of 10 mL/kg only if hypovolemia was present) fluid resuscitation protocols.
-  **Primary end point.** Detect a difference in the development of moderately severe or severe acute pancreatitis.
-  **Safety end point.** Evaluate fluid overload based on symptoms, physical signs, or imaging evidence of hypervolemia.



IV fluids should be initiated **at a moderate rate within 2 hours** after the acute pancreatitis diagnosis is made.

The study was terminated after first interim analysis of 249 patients.


There was **no significant difference** in incidence in moderately severe (MS) or severe acute (SA) pancreatitis by fluid rate:



However, fluid overload was **2.85x greater** with an aggressive vs moderate rate of resuscitation:




### Conclusion

 **Moderate fluid rate** is safer than aggressive fluid resuscitation, with similar efficacy.



 **Moderate fluid rate** (1.5 mL/kg/h) is recommended for patients with **acute pancreatitis** of any severity.

 **Fluid boluses of 10 mL/kg** over 1 to 2 hours are recommended for patients with **hypovolemia**.

## Fluid Types<sup>1,3,4,6</sup>



**Crystalloids or colloids? In severe acute pancreatitis** in 1 RCT of patients with severe acute pancreatitis, crystalloids showed:

- ▶▶ **Lower rates** of adverse events and organ failure
- ▶▶ **Similar survival**



**LR or NS?** In 4 RCTs (n=248), LR has shown to:

- ▶▶ **Reduce risk of ICU admissions**  
(RR, 0.42; 95% CI, 0.20-0.89)
- ▶▶ **Shorten hospital stay**  
(mean difference, -1.10; 95% CI, -1.92 to -0.28)<sup>4</sup>

**IV crystalloids** such as NS or LR are preferred over colloids.<sup>3</sup>

**Physiologic and clinical evidence** support using balanced crystalloids like LR over NS; however, a larger definitive RCT is needed.<sup>1,6</sup>



CI, confidence interval; LR, lactated ringer; NS, normal saline; RCT, randomized controlled trial; RR, risk ratio

## Assessing Fluid Volume Status<sup>7</sup>

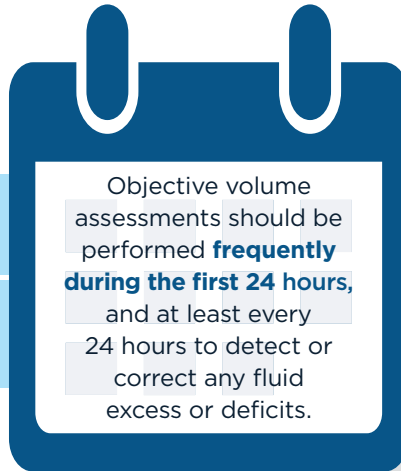
**Fluid resuscitation** should be guided by specific goals



Maintaining adequate blood pressure, urine output (>0.5 mL/kg/h)



Normalizing hematocrit and electrolyte levels



**Continuous monitoring** is essential to assess fluid status and response to treatment



Physical exam



Vital signs



Urine output



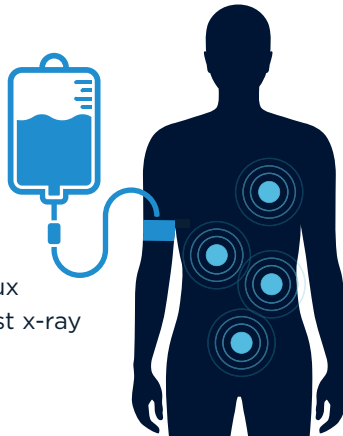
Laboratory values (hematocrit, blood urea nitrogen, creatinine, electrolytes)

## Fluid Overload<sup>2</sup>

### Diagnosis

#### Common indicators:

- Dyspnea
- Peripheral edema
- Pulmonary rales
- Increased jugular venous pressure or hepatojugular reflux
- Pulmonary congestion on chest x-ray
- Oxygen saturation < 92%



### If fluid overload is detected:

- ✓ **Decrease or stop fluids.**
- ✓ **Some patients may require diuretics.**

### If severe fluid overload:

- ✓ **Some patients may need mechanical ventilation and/or hemofiltration.**

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