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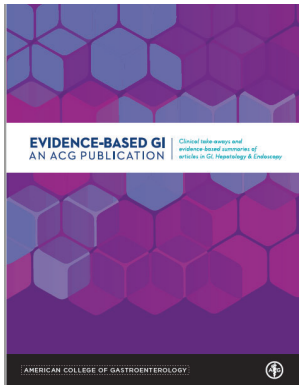

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EUS-Guided Versus Surgical Gastroenterostomy: Which Endures? The *ENDURO* trial

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Associate Editor

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This summary reviews This article reviews Bang JY, Puri R, Lakhtakia S, et al. Endoscopic or surgical gastroenterostomy for malignant gastric outlet obstruction: A randomised trial. Gut 2026;75:24-32.

Correspondence: Margaret J. Zhou, MD. Associate Editor. Email: EBGI@gi.org
Keywords: EUS, gastroenterostomy, endoscopy

STRUCTURED ABSTRACT

Question: In patients with malignant gastric outlet obstruction, is endoscopic ultrasonography-guided gastroenterostomy (EUS-GE) compared with surgical gastroenterostomy (GE) associated with improved outcomes?

Design: Randomized controlled trial (RCT).

Setting: Twelve academic and teaching hospitals in the Netherlands. The study required that each hospital have experience in at least 20 lumen-apposing metal stents (LAMS) of any indication, at least 10 endoscopic gastroenterostomies, and competence approved by 2 experienced interventional endoscopists from the study steering committee.

Patients: Adult patients presenting with malignant gastric outlet obstruction (GOO) presenting with nausea, vomiting, or inability to eat, defined by the Gastric Outlet Obstruction Scoring System (GOOSS) score of 0 (no oral intake) or 1 (liquids only).

Interventions: Patients were randomly assigned 1:1 to endoscopic gastroenterostomy or surgical gastroenterostomy.

Outcomes: Primary outcomes included: 1) time to resumption of soft oral intake (GOOSS score of 2 or higher, without vomiting) and 2) non-inferiority in the rate of persistent or recurrent obstructive symptoms requiring reintervention. The outcome of first day of oral intake was assessed by patient diaries or phone calls from staff. Reintervention was defined as any endoscopic, surgical, or radiological intervention after the study procedure aimed to improve nutritional intake. Multiple secondary outcomes were also assessed including clinical success.

Data Analysis: Intention-to-treat analysis, time to oral intake was compared using a Cox proportional hazards model adjusted for WHO performance status. Patients were censored at the end of follow-up (6 months) or death. For the non-inferiority analysis, a maximum re-intervention risk difference of 20% was set because the study authors believed the expected benefits of endoscopic as opposed to surgical intervention would outweigh a possible difference in reintervention rate (i.e. less invasiveness, fewer adverse events).

Funding: KWF Dutch Cancer Society.

Results: Between February 2022-February 2024, 98 patients were assigned to endoscopic gastroenterostomy (n=48) or surgical gastroenterostomy (n=50). Mean age of the cohort was 69-70 years, over 50% of patients were male, and the predominant cancer type was pancreas cancer (comprising 58% of patients in the EUS-GE group and 50% of patients in the surgical GE group). The obstruction was localized to the proximal duodenum in most cases. Six-month follow-up was completed in 11 (23%) patients in the EUS-GE group and 12 (24%) patients in the surgical GE group. At the time of follow-up, 77% and 76% of patients had died in the EUS-GE and surgical groups, respectively.

In the EUS-GE group, patients were able to resume solid oral intake after a median of 1 day (interquartile range [IQR] 1-3) compared with 3 days (IQR 1-6) in the surgical GE group (hazard ratio [HR] 2.21; 95% CI 1.43-3.42; P=0.0003). Reintervention for persistent/recurrent obstructive symptoms was required in 5 (10%) patients after EUS-GE and in 6 (12%) patients after surgical GE (risk difference 1.6%; upper limit of 90% CI 8.9, which was consistent with non-inferiority)

Multiple secondary endpoints were evaluated. Clinical success, defined by tolerating soft solid foods without vomiting (GOOSS score ≥2) was achieved in 96% of the EUS-GE group vs 80% of the surgical GE group (relative risk [RR] 1.20 [95% CI 1.03-1.39]). Gastroenterostomy dysfunction occurred in 4% of the EUS-GE vs 10% of the surgical GE group (RR 0.42; 95% CI 0.09-2.02), and reintervention was required in 21% vs 28%, respectively (RR 0.74; 95% CI 0.37-1.51). Time to initiation of systemic therapy was similar between the 2 groups. Median length of hospital stay in the EUS-GE group was 1 day (IQR 1-3) vs 4 days (IQR 2-7) in the surgical GE group (risk difference 0.46; 95% CI 0.20-0.78). Median overall survival after EUS-GE vs surgical GE was 91 days (IQR 56-165) vs 74 days (IQR 29-157), respectively.

There was no difference in technical success, GE dysfunction, time to reintervention, 1-month weight change, or 30-day readmissions between the 2 groups. Quality of life, as measured by the European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30), was similar in the first 3 months but was better in the surgical group than in the EUS-GE group at 6 months.

Adverse events occurred in 58% vs 64% in the EUS-GE vs surgical GE groups, respectively (RR 0.91; 95% CI 0.66-1.25). Serious adverse events occurred in 4 (8%) of patients in the EUS-GE group, which included surgical GE due to obstruction distal to the ligament of Treitz and due to LAMS maldeployment, ICU admission due to LAMS maldeployment and death due to pneumonia and clinical deterioration vs 6 (12%) in the surgical GE groups (including endoscopy for anastomosis assessment under general anesthesia, surgical gastrostomy due to persistent gastropareiss, ICU admission due to severe hypokalemia, and death due to major abdominal bleeding, clinical deterioration or pneumosepsis).

COMMENTARY

Why Is This Important?

This is one of the first RCTs comparing EUS-GE and surgical GE for the management of malignant GOO. Recently, another multi-center RCT conducted at 6 centers in the USA, Germany and India randomized 74 patients to EUS-GE or surgical GE.[1] This trial was similarly performed at expert centers requiring endoscopists to have experience of at least 20 EUS-GE procedures. GOOSS of 0 or 1 at the time of hospital discharge was achieved in 8% vs 39% among patients who underwent EUS-GE vs surgical GE,

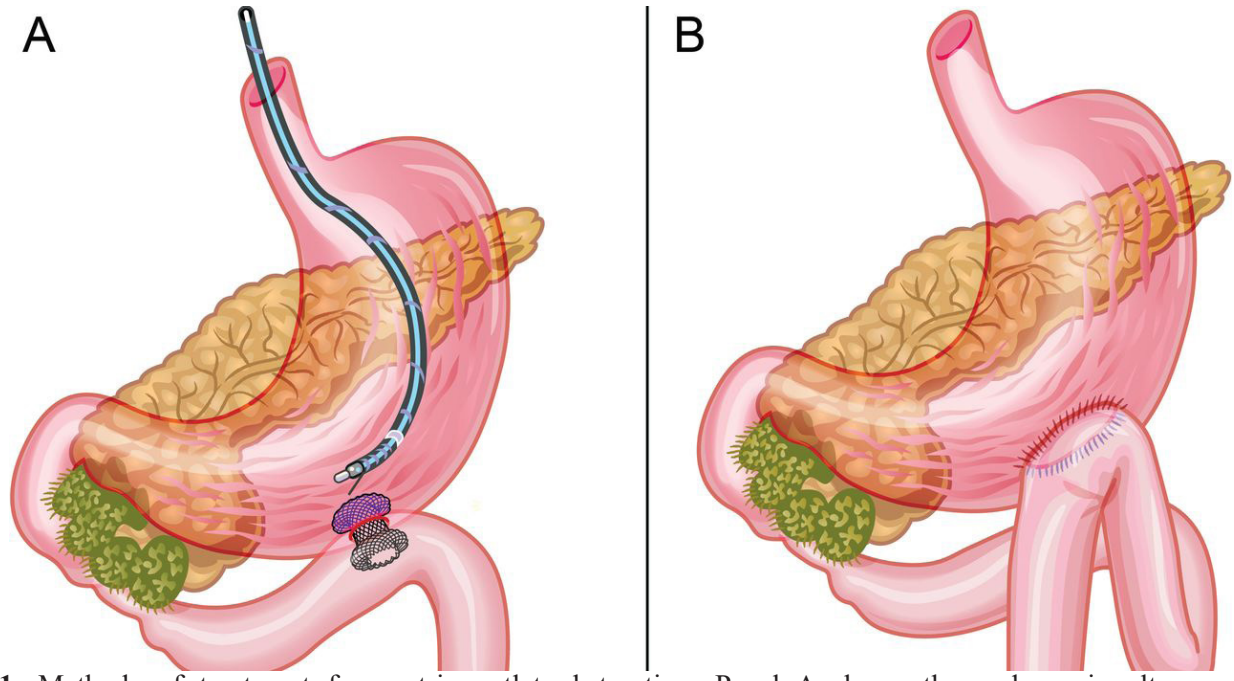

Figure 1. Methods of treatment for gastric outlet obstruction. Panel A shows the endoscopic ultrasound-guided gastroenterostomy approach, in which a lumen-apposing metal stent is placed into the jejunum from the gastric lumen. Panel B shows the surgical gastrojejunostomy approach.

Reproduced from Bang JY, Puri R, Lakhtakia S, et al. Endoscopic or surgical gastroenterostomy for malignant gastric outlet obstruction: A randomised trial. Gut 2026;75:24-32. with permission from BMJ Publishing Group Ltd.

respectively (risk difference -31.0%, 95% CI -47.6%-011.4%, P=0.002), and EUU-GE was associated with shorter time to solid diet (2 days vs 5 days, respectively) and shorter hospitalization (median 3 days vs 9 days, respectively). Quality of life assessed at the time of discharge also found higher quality of life score using the EORTC QLQ-C30 in the EUS-GE vs surgery group. Six-month mortality was 58% in the EUS-GE group and 42% in the surgical GJ group (P = 0.163). This study also evaluated mean total costs per admission to be lower for EUS-GE compared with surgery ($33,934 vs $51,437, respectively).

Prior to these RCTs, several observational studies had suggested that endoscopic GE could lead to shorter time to oral intake compared with surgical GE, although few studies were prospective. A recent systematic review/meta-analysis including a total of 484 patients found that EUS-GE had similar clinical success (defined as the ability to tolerate at least a liquid diet after the procedure) with fewer adverse events compared to surgical gastrojejunostomy, although surgical GE had higher technical success rates.[2] A subsequent network meta-analysis compared surgical gastrojejunostomy, EUS-GE, stomach-partitioning gastrojejunostomy (PGJ), and endoscopic stenting, which also found that EUS-GE was less likely to require reintervention than standard surgical GE, and EUS-GE and surgical GE had similar clinical success rates.[3]

While EUS-GE has been increasing in use over the last few years, current guidelines including those put forth by the American Society for Gastrointestinal Endoscopy (ASGE) in 2021 recommend surgical gastrojejunostomy or self-expanding metal stent (SEMS) placement in patients with malignant GOO undergoing palliative treatment but recommended surgical GJ in patients with a life expectancy of at least 6 months and good performance status.[4] At the time of that guideline creation the use of EUS-GE was not systematically assessed. This study provides needed evidence of the efficacy and durability of outcomes after EUS-GE compared with surgical GE in patients with limited life expectancy.

Key Study Findings

In patients with malignant GOO, EUS-GE resulted in shorter median time to resumption of oral intake compared with surgical GE (1 day vs 3 days, respectively) and was noninferior in terms of rates of reintervention (10% vs

Caution

Only about a quarter of patients were able to be followed up for 6 months in this study due to high rates of cancer-related mortality. These results may be less generalizable to patients with a longer life expectancy than those included in this study. Furthermore, surgical-GE is currently generally not recommended in patients with <6 month survival, and about 75% of the patients in this study died before the 6 month follow-up period. It is also important to note that the EUS-GEs performed in this study were done at high volume expert centers and thus may not be generalizable to centers with less expertise in this procedure. EUS-GE is a technically challenging procedure and adverse events with misdeployment can be very serious. The authors also note that this study did not include cancers extending into the distal stomach who also encounter issues with malignant GOO due to concerns about increased risk of anastomotic dysfunction so it is unclear how these results may apply to patients with these cancers.

My Practice

At my institution, interventional endoscopists work closely with the hepatobiliary surgery team to determine the optimal therapy for patients with malignant GOO. Both EUS-GE and uncovered duodenal stenting are typically considered in patients with more limited life expectancy and functional status, with EUS-GE considered more often in patients who may have closer to 3-6 months and duodenal stenting considered in patients with more limited life expectancy. Surgical GE may be more strongly considered in patients with at least 6 months life expectancy, but this may vary based on functional status and prior surgical history. Based on these

small trials, the existing data is likely not sufficient recommend endoscopic GE for all patients, but this certainly should be considered in patients with a life expectancy of around 6 months and especially as an alternative to duodenal stenting due to known issues with stent patency and reintervention.

For Future Research

Future study of patients with at least 6 months survival who could provide longer-term follow-up would be helpful to inform choice of therapy for patients who may have less limited life expectancy than those in this study and assess study outcomes such as reintervention in a larger population. The results of future cost-effectiveness studies that have been performed alongside this trial will also be helpful to inform therapy choices for health systems. Lastly, study on optimal endoscopist training to perform EUS-GE safely will also be critical as this procedure becomes more commonly performed given the technical expertise required.

Conflicts of Interest

The author has no reported conflicts of interest.

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REACTing Against Resistance: Fecal Microbiota Transplant Shows Safety and Promise in Long-Term Care Patients Cancer Risks in Familial Adenomatous Polyposis

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This article reviews Woodworth MH, Babiker A, Prakash-Asrani R, et al. Microbiota Transplantation Among Patients Receiving Long-Term Care: The Sentinel REACT Nonrandomized Clinical Trial. JAMA Netw Open. 2025;8(7):e2522740.

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Keywords: Fecal microbiota transplantation (FMT), multidrug-resistant organisms (MDROs), gut microbiome

COLON

STRUCTURED ABSTRACT

Question: Among long-term acute care hospital (LTACH) patients colonized with multidrug-resistant organisms (MDROs), is fecal microbiota transplantation (FMT) superior to no treatment (contemporaneous controls) for safety and infection-related outcomes?

Design: Single-center, open-label, nonrandomized pilot clinical trial with contemporaneous untreated controls; enrollment April–December 2023; follow-up 6 months.

Setting: Academic-affiliated LTACH in Atlanta, Georgia (Southeastern US); median ~50-patient census and ~28-day length of stay.

Patients: Participants were adults aged ≥18 years whom had a perirectal or stool culture positive for a target MDRO (extended-spectrum β-lactamase [ESBL] Enterobacterales, carbapenem-resistant Enterobacterales [CRE], multidrug-resistant [MDR] Pseudomonas, vancomycin-resistant Enterococcus [VRE], or toxigenic Clostridioides difficile); able/willing to receive FMT via feeding tube or retention enema; willing to discontinue antibiotics, probiotics/other microbiota therapies, and proton pump inhibitors (PPIs) ≥1 day before FMT through Day 28. Participants were excluded if: pregnant or breastfeeding, had a compromised immune system (e.g., AIDS with CD4<200 and detectable HIV load, ANC<1000, recent intensive chemo/radiotherapy or hematopoietic cell transplant) or had an inability to discontinue PPI therapy.

Interventions: Healthy-donor fecal microbiota (50–100 g stool suspended in 250 mL normal saline with 9% glycerol) instilled via gastrostomy tube or enema; no antibiotic or bowel-prep conditioning.

Outcomes: Primary: frequency and severity of adverse events (AEs) graded by CTCAE v5.0; solicited AEs assessed daily through Day 7; unsolicited AEs through 6 months. Secondary: proportion MDRO-positive perirectal/stool cultures at Weeks 2 and 4 after FMT. MDROs included ESBL Enterobacterales, CRE, MDR Pseudomonas, VRE, and toxigenic C. difficile. Exploratory: bloodstream infection, intestinal pathogen dominance by metagenomics, antibiotic days of therapy, and healthcare utilization over the 6 months before vs after prevalence sampling.

Data Analysis: Descriptive summaries; Wilcoxon rank-sum for continuous variables; Fisher exact for proportions; 2-sided α=0.05. Difference-in-differences model for antibiotic days of therapy; analyses in R. (Trial not powered for formal hypothesis testing.)

Funding: Emory Prevention Epicenter Program (CDC U54CK000601) and NIAID (K23AI144036, R38AI174306-01). Funders had no role in design, conduct, or analysis.

Results: Among 42 patients assessed (mean age ~64 years; 52% female overall), 10 received FMT and 32 served as contemporaneous MDRO-colonized controls. Routes among FMT recipients: 5 gastrostomy, 4 enema, 1 both (>30 days apart). No serious AEs were attributed to FMT; solicited post-FMT AEs were mild. At the final

visit, all FMT recipients remained MDRO culture–positive. Post hoc comparisons (underpowered) showed numerically fewer FMT recipients with positive blood cultures in the following 6 months (0/10 vs 6/32 [19%]; P=0.31), lower pathogen intestinal dominance (25% vs 50%; P=0.61), and fewer antibiotic days of therapy (median 12.6 vs 19.7 days per 1000 patient-days; P=0.38); a difference-in-differences analysis estimated 26 fewer antibiotic days per 1000 patient-days (95% CI, −64 to 12) after FMT.

Bottom line: In LTACH patients with MDRO colonization, single-dose FMT (via gastrostomy or enema) was acceptable and not associated with related serious adverse events (AEs); signals toward reduced bacteremia and antibiotic use did not reach statistical significance and warrant testing in larger randomized trials (**Table 1**).

Outcome	FMT Group (n=10)	Control Group (n=32)	*P* value	Interpretation
Serious adverse events related to FMT	**0**	—	—	No FMT-related serious AEs reported
Any adverse event (solicited, ≥7 days)	Mild, transient GI symptoms only	—	—	FMT well tolderated
MDRO colonization at final visit	**10/10 (100%)**	**32/32 (100%)**	—	Persistent MDRO colonization in all participants
Bloodstream infection within 6 mo	**0/10 (0%)**	6/32 (19%)	0.31	Trend toward fewer BSIs after FMT
Pathogen intestinal dominance	**25%**	50%	0.61	Numerically lower in FMT group
Antibiotic COT per 1,000 patient-days	**12.6**	19.7	0.38	Fewer antibiotic DOTs post-FMT
Difference-in-differences: DOT change (95% CI)	**−26 days (−64 to +12)**	Reference	—	Suggests reduced antibiotic exposure after FMT

Table 1. Clinical and microbiologic outcomes in the REACT trial comparing fecal microbiota transplantation (FMT) with contemporaneous controls among long-term acute care patients colonized with multidrug-resistant organisms (MDROs). FMT was well tolerated with no related serious adverse events and showed numerical reductions in bloodstream infections and antibiotic use, though not statistically significant. BSI, bloodstream infection; CI, confidence interval; DOT, days of therapy; GI, gastrointestinal.

*Dominance defined by metagenomic relative abundance > 30% of any MDRO species in stool.

COMMENTARY

Why Is This Important?

FAP is a difficult population to study because it is relatively rare, although it's clinical presentation is quite dramatic due to the burden of colorectal polyps. Many studies on FAP harken back to historical studies before the advent of routine high-definition colonoscopies for screening, as reflected in the increasing incidence of aFAP over time.[1] It is thus helpful to have a more contemporary description of cancer risks and outcomes in both cFAP and aFAP.

Key Study Findings

With presumed standard-of-care prophylactic colectomies and surveillance colonoscopies (in the United States), most FAP patients will fortunately not develop cancer, although the risk overall is still markedly higher than the average-risk patient without FAP.

There is still a subset of FAP patients that can develop rectal cancer after colectomy, thus frequent flexible sigmoidoscopy of the residual rectum (typically every 6-12 months depending on polyp burden) remains important.[2] The burden of duodenal adenomas is still substantial, particularly in the cFAP population, although we still do not fully understand risk factors for duodenal adenocarcinoma otherwise.

Caution

This study does not account for surveillance procedures such as colonoscopy prior to colectomy, as well as surveillance flexible sigmoidoscopy/ pouchoscopy (for those with an ileorectal anastomosis or ileo-anal pouch anastomosis) or ileoscopy (for those with an end ileostomy) after colectomy. Prior studies have observed that the risk of ileal adenomas is higher in those with a pouch compared to end ileostomy, which would be an important risk factor to understand given its potential impact on choice of surgery.[3] It is also curious that only about half of patients underwent surgery, which may be from inadequate observation time (i.e. the colectomy has not happened) rather than non-operative colonoscopic management of polyp burden, which is seldomly feasible with substantial resource and colonoscopic burden.[4]

FAP patients are not typically recognized as high risk for pancreatic adenocarcinoma in national guidelines.[5-7] As the authors note, these patients did not undergo genetic re-evaluation to assess for comorbid pathogenic variants. To recognize this as a FAP-associated cancer, future studies must account for differences in other risk factors for pancreatic cancer (alcohol, tobacco, chronic pancreatitis etc.). Finally, the study did not examine desmoid disease, which is a leading cause of

morbidity and mortality in FAP patients despite its non-malignant nature.

My Practice

Upon meeting a newly diagnosed FAP patient, I counsel the patient that although the risk of colorectal cancer is high, the risk can be dramatically reduced with colectomy and subsequent frequent lower endoscopies. Prior to colectomy, I find that the removal of most diminutive/small adenomas and counting the exact number of polyps is practically less useful. Given that the majority of FAP patients require extended or total colectomy, I perform colonoscopy with several diagnostic goals in mind: 1) masses concerning for cancer or advanced polyps; 2) estimating whether the rectal burden of polyps is "endoscopically manageable" over time with repeat procedures; 3) define the anatomic extent of endoscopically "un-manageable" polyposis in collaboration with colorectal surgery to inform whether the patient is a candidate for an ileorectal or even ileosigmoid anastomosis to improve post-operative quality of life. Finally, I do stress to the patient that even after surgery, frequent lower endoscopies are still critical to avoid the risk of rectal cancer.

For Future Research

Larger studies incorporating endoscopic data is still needed to understand how to manage the upper intestinal manifestations of FAP such as duodenal or gastric neoplasia, as well as medication interventions to help manage those with advanced duodenal neoplasia given the morbidity associated with duodenectomy.

Conflict of Interest

The author has no reported conflicts of interest.

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Chronic Hepatitis B: Treatment Criteria Expansion and Demystifying the "Grey Zone"

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This summary reviews Ghany MG, Pan CQ, Lok AS, et al. AASLD/IDSA Practice Guideline on treatment of chronic hepatitis B. Hepatology. 2025 Nov 4. doi: 10.1097/HEP.0000000000001549.

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Keywords: Chronic hepatitis B, Guideline, surveillance, infectious diseases

STRUCTURED ABSTRACT

Question: What are the evidence-based strategies for the prevention, surveillance, and treatment of chronic hepatitis B (CHB), including antiviral initiation thresholds, antiviral discontinuation criteria, and HCC surveillance protocols across multiple populations and clinical scenarios?

Design: This clinical practice guideline was developed by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA). The methodology employed 6 structured PICO (Population, Intervention, Comparison, Outcomes) questions and the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. Four de novo systematic reviews were conducted alongside the utilization of 2 existing systematic reviews. Multiple clinical trials were considered. Certainty of evidence was rated as high, moderate, low, or very low, with adjustments for risk of bias, imprecision, inconsistency, indirectness, and publication bias. Recommendations were classified as strong or conditional based on the balance of benefits and harms, evidence

certainty, patient values, and equity considerations.

Patients: The guideline applies to adults and children with chronic hepatitis B infection, including: HBsAg-positive pregnant individuals with high viremia (HBV DNA >200,000 IU/mL); persons in the immune-tolerant phase (HBeAg-positive, HBV DNA >10,000,000 IU/mL, normal ALT); individuals in the indeterminate or "grey zone" phase (HBeAg-positive or negative with ALT and HBV DNA levels outside of the defined immune-active or inactive thresholds); patients on long-term nucleos(t)ide analogue therapy with sustained HBV DNA suppression; individuals who have achieved HBsAg loss; and persons coinfected with hepatitis C virus (HCV), hepatitis D virus (HDV), and/or human immunodeficiency virus (HIV).

Interventions: Interventions evaluated include: maternal antiviral prophylaxis with tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) initiated at gestational week 28 (or week 16 when hepatitis B immune globulin is unavailable) to prevent mother-to-child transmission; antiviral therapy to reduce horizontal transmission in high-risk scenarios through shared decision-making; treatment initiation in immune-tolerant CHB for individuals over 40 years of age or with significant fibrosis (F2 or greater) or inflammation (grade 2 or higher); treatment initiation in patients who are HBeAg-negative and in the indeterminate phase using individualized risk assessment; continuation versus cessation of nucleos(t)ide analogue therapy in virally suppressed HBeAg-negative individuals without cirrhosis; and semiannual HCC surveillance with ultrasound and alpha-fetoprotein for at-risk populations including those with viral coinfections or older age at the time of HBsAg loss.

Outcomes: The guideline aims to optimize: reduction of vertical (mother-to-child) and horizontal HBV transmission; prevention of progression to cirrhosis, hepatic decompensation, and HCC; achievement of virologic suppression (undetectable HBV DNA), biochemical response (ALT normalization), and HBsAg loss (functional cure); reduction in liver-related mortality and need for liver transplantation.

Data Analysis: Data informing these recommendations were derived from randomized controlled trials, prospective and retrospective cohort studies, and observational analyses with systematic reviews. Meta-analyses quantified pooled incidence rates and, where appropriate, treatment effects. When high-quality direct evidence was

lacking, biological plausibility and indirect evidence informed recommendations. Strong recommendations indicate that most informed patients would choose the recommended intervention, while conditional recommendations suggest substantial variability in patient preferences necessitating shared decision-making.

Funding and Disclosures: This guideline was funded by AASLD and IDSA without external commercial support. Development adhered to National Academy of Medicine standards for transparency and methodological rigor.

Results: Chronic hepatitis B (CHB) remains an important global public health concern affecting approximately 296 million individuals worldwide.1 This updated 2025 guideline addresses critical topics including prevention of mother-to-child transmission and horizontal transmission, treatment in immune-tolerant and indeterminate phases ("grey zone"), treatment discontinuation, and hepatocellular carcinoma (HCC) surveillance.

Prevention of Mother-to-Child Transmission. A strong recommendation is provided for initiating TDF or TAF at gestational week 28 for pregnant individuals with HBV DNA >200,000 IU/mL, regardless of e-antigen status. If hepatitis B immune globulin is unavailable, TDF can be considered at gestational week 16, based on a recent randomized clinical trial demonstrating noninferiority in preventing transmission.3 TDF has a more extensive safety record in pregnancy than TAF. The choice of antiviral therapy should account for each medication's side-effect profile. Antiviral therapy can be discontinued at delivery, with monitoring for withdrawal flares every 1-3 months for up to 6 months post-partum.

Horizontal Transmission Prevention. AASLD addresses antiviral therapy to reduce horizontal transmission in high-risk scenarios (conditional recommendation, very low certainty). A shared decision-making approach is suggested for viremic individuals in high-risk settings, including those engaging in unprotected sex, injecting drugs with inconsistent harm reduction practices, living with susceptible household members, or healthcare workers performing exposure-prone procedures.

Immune-Tolerant Phase. Antiviral therapy is now conditionally recommended for persons in the immune-tolerant phase who are over the age of 40, or who have significant liver inflammation (grade 2 or higher) or fibrosis (F2 or greater), reflecting

subgroups. The most accurate non-invasive liver disease assessment is vibration-controlled transient elastography (VCTE). A cutoff threshold of ≥7kPa can identify patients with F2 fibrosis or higher. For individuals under 40 without significant fibrosis, treatment initiation should be based on shared decision-making. Providers should consider a family history of HCC. Close monitoring with HBV DNA and ALT testing at least every 6 months is suggested if treatment is not initiated.

HBeAg-negative Indeterminate Phase. There has been a paradigm shift from prior recommendations favoring monitoring alone to this guideline which now suggests antiviral therapy using a shared decision-making approach for HBeAg-negative adults without cirrhosis in the indeterminate phase (conditional recommendation, very low certainty). A meta-analysis demonstrated that antiviral treatment was associated with a 64% reduction in HCC incidence (adjusted incidence rate ratio 0.36, 95% CI 0.16-0.81). [2,4]

Nucleos(t)ide Analogue Discontinuation. The guideline conditionally recommends against discontinuing nucleos(t)ide analogue therapy until HBsAg loss is achieved. This recommendation reflects results from systematic reviews demonstrating modest rates of HBsAg loss (10.6% at 2 years) offset by substantial risks, including ALT flares (26.9% at 2 years), need for re-treatment (42% at 5 years).[5–10] Patients that can be considered to stop therapy should have no cirrhosis or hepatic decompensation, no HCC or extrahepatic HBV disease, no HIV or HDV coinfection, have ≥2 years of undetectable HBV DNA (after HBeAg seroconversion if initially HBeAg-positive), HBsAg <100 IU/mL, and be reliable for close monitoring.

HCC Surveillance Expansion. Following HBsAg loss, continued surveillance is suggested for patients with cirrhosis, a family history of HCC, men with loss of HBsAg after age 40, and women with loss of HBsAg after age 50. For HDV coinfection, surveillance is suggested for all adults regardless of cirrhosis status, given that the annual rates of incident HCC are 1.87% even without cirrhosis. For HIV coinfection, surveillance is suggested for men ≥18 years and women ≥40 years. For HCV coinfection, DAA therapy is recommended with subsequent surveillance following HBV mono-infection criteria.

The presented information is summarized in **Table 1**.

Clinical Question	Key Recommendation	Strength	Certainty
Prevention of Mother-to-Child Transmission	Initiate TDF or TAF at gestational week 28 for pregnant individuals with HBV DNA >200,000 IU/mL; TDF has a more extensive safety record	Strong	Moderate
Horizontal Transmission Prevention	Shared decision-making for antiviral therapy in high-risk viremic individuals not meeting standard treatment indications	Conditional	Very Low
Immune-Tolerant Phase Treatment	Antiviral therapy suggested for persons >40 years or with significant inflammation (grade ≥2) or fibrosis (≥F2); shared decision-making for those <40 years	Conditional	Very Low
HBeAg-Negative Indeterminate Phase	Antiviral therapy suggested using shared decision-making approach; factors favoring treatment include age >40, male sex, platelet count <180k/mm3	Conditional	Very Low
NA Therapy Discontinuation	Suggests not withdrawing NA therapy until HBsAg loss; strict criteria for those desiring discontinuation including qHBsAg <100 IU/mL	Conditional	Very Low
HCC Surveillance After HBsAg Loss	Continue surveillance for those with cirrhosis, family history of HCC, men with HBsAg loss after age 40, women after age 50	Conditional	Very Low
HCC Surveillance in HBV-HDV Coinfection	Surveillance suggested for all adults independent of cirrhosis status; individualize decision for children	Conditional	Very Low
HCC Surveillance in HBV-HIV Coinfection	Surveillance suggested for men ≥18 years and women ≥40 years of age	Conditional	Very Low
HCC Surveillance in HBV-HCV Coinfection	Recommend DAA therapy for HCV; HCC surveillance per HBV mono-infection criteria	Conditional	Very Low

Table 1. Overview of AASLD/IDSA 2025 chronic hepatitis B guideline recommendations.

AASLD, American Association for the Study of Liver Diseases; DAA, direct acting antiviral; HBV, hepatitis B virus; HCC, hepatocellular carcinom; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDSA, Infectious Diseases Society of America; NA, nucleos(t)ide analogue; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

COMMENTARY

Why Is This Important?

CHB leads to an estimated 1.1 million deaths annually from cirrhosis and HCC. In the United States alone, the disease burden may reach 1.8 million persons, with approximately 50% unaware of their diagnosis. This guideline is important because it addresses several key clinical scenarios. AASLD now provides recommendations on antiviral therapy for prevention of horizontal transmission and a change in the management of patients in the indeterminate or "grey zone" phase (a population comprising up to 40% of CHB patients). Additionally, it adopts a more conservative stance on nucleos(t)ide analogue discontinuation. It also recommends the expansion of HCC surveillance to include viral coinfections and post-HBsAg clearance populations.

Key Study Findings

For mother-to-child transmission prevention, a systematic review of 31 studies demonstrated that TDF and TAF are equally effective (risk ratio 1.09, 95% CI 0.15-7.65) and safe when initiated at gestational week 28 for pregnant individuals with HBV DNA >200,000 IU/mL.[11] A recent randomized clinical trial further showed that TDF initiation at week 16 with infant vaccination was noninferior to week 28 initiation with HBIG (0.76% vs 0% transmission).[3] For the indeterminate phase, a meta-analysis of 37 cohorts involving 14,691 individuals found that antiviral treatment was associated with a 64% reduction in HCC incidence (adjusted aIRR 0.36, 95% CI 0.16-0.81) after adjusting for age, sex, HBeAg status, and platelet count.[4] Regarding nucleos(t)ide analogue discontinuation, evidence from four RCTs showed that while HBsAg loss rates were 10.6% at 2 years among those stopping therapy (versus 0% in those continuing), this benefit was offset by ALT flares in 26.9% and retreatment requirements in 42% at 5 years.[5,12–14] Studies demonstrated annual incidence rates of 1.87% for HCC in HBV/HDV coinfected patients regardless of cirrhosis status, supporting surveillance for all adults with this cohort.

Caution

Several limitations warrant consideration when applying these recommendations. First, most recommendations carry low or very low certainty of evidence, highlighting the need for individualized clinical judgment. The evidence supporting treatment in the immune-tolerant phase comes largely from comparisons between antiviral strategies rather than treatment versus placebo, with a focus on virological response rather than clinical outcomes.[15,16] For horizontal transmission prevention, recommendations are based on biological plausibility rather than direct studies.[17] There are no clinical trials

supporting continuing nucleos(t)ide analogue therapy until HBsAg loss, instead, recommendation is derived from moderate risks of stopping therapy (ALT flares, 27% at 2 years; need for retreatment 42% at 5 years).[5,12]

My Practice

Not too FAST! – a simple mnemonic for providers considering factors that determine treatment for patients that fall in the "grey zone." **F**ibrosis, **A**ge, and **S**ex determine **T**reatment.

In practice, patients infrequently meet the immune active treatment thresholds. We often encounter situations that are nuanced, and until now, providers have lacked clear guidance. Given the safety profile of the "NUCs," the key decision comes down to explaining the benefits of treatment vs. monitoring, particularly for patients in the grey zone. Though guidelines provide recommendations, ultimately, there is an art as well as a science to CHB treatment.

Above all else, we do not know if we do not ask or test. For every patient that I evaluate, I ensure they have been screened for CHB at least once in their lifetime and I highly encourage vaccination for all adults even those over 60 without risk factors. This is particularly important in our pre-transplant population. Similarly, I am hesitant to discontinue therapy once started, though now with new guidance, I will be more likely to continue therapy until HBsAg loss is achieved or updated data identifies candidates in whom this strategy is appropriate. In addition, novel therapies, including bepirovirsen, are in late-stage trials to determine whether HBsAg clearance rates can be improved.

I continue to utilize resources like Transient Elastography for upfront risk stratification, and I ensure that patients have consistent 6-month follow-up visits, even when visits may be brief, to prevent gaps in care, including missed laboratory monitoring or HCC surveillance.

A final word on the CDC's Advisory Committee on Immunization Practices recent vote to end universal infant hepatitis B vaccination. This shift to individualized decision-making will undoubtedly change the landscape of CHB in the United States. However, as healthcare providers, we are still obliged to inform, advocate, and safeguard evidence-based prevention strategies to ensure our progress is not reversed.

For Future Research

Several research priorities emerge from this guideline. High-quality randomized controlled trials are needed to evaluate major liver-related outcomes (cirrhosis, HCC, mortality) with antiviral treatment in the immune-tolerant and indeterminate phases, as current evidence relies heavily on observational data with surrogate

virological endpoints. Studies examining the effectiveness of antiviral therapy in preventing horizontal transmission would strengthen recommendations currently based on indirect evidence. It would be worth examining patients specifically listed for liver transplantation as they have a heightened risk of developing HCC.[18–20] Research is needed to identify optimal biomarkers for predicting outcomes after nucleoside analogue or any other novel therapy that is discontinued beyond quantitative HBsAg, including HBV RNA and HBcrAg. Validation of HCC risk prediction models following HBsAg clearance would refine surveillance recommendations.[21] As novel therapeutic agents targeting functional cure advance through clinical development, updated guidelines incorporating these new treatment paradigms will be essential.

Reducing the burden of chronic hepatitis B will require systematic identification of infected individuals, sustained commitment to vaccination, timely antiviral treatment, and deliberate efforts to close persistent gaps in HCC surveillance and care.[22]

Social Media

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Conflict of Interest

The authors do not have conflicts of interest to disclose.

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