European Association for the Study of the Liver Congress (EASL 2025)

7th-10th May 2025

&

Digestive Disease Week (DDW 2025)

3rd-6th May 2025

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Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD/MASH)

1. MetALD Shows Higher Advanced Fibrosis and Mortality Risk Than MASLD: Global Biopsy-Proven Cohort Analysis

Background and Objectives:

- Metabolic dysfunction- and alcohol-associated liver disease (MetALD) represents an important subtype of steatotic liver disease requiring distinct clinical consideration.
- This study compared clinical profiles and outcomes between MetALD and metabolic dysfunction-associated steatotic liver disease (MASLD) patients using a large global biopsy-proven cohort.

Methods:

- 8,808 participants with biopsy-proven steatotic liver disease from over 40 countries.
- MetALD was defined by alcohol consumption of 20-50g/day (females) or 30-60g/day (males), with MASLD representing lower consumption levels.

Key Results:

Demographics and Baseline Characteristics:

- Overall cohort: Mean age 49±14 years, 50% male, BMI 33±8 kg/m^2
- MetALD represents a distinct, high-risk phenotype requiring enhanced surveillance and aggressive management compared to MASLD, with particular attention to cardiovascular comorbidities and accelerated fibrosis progression as shown in Table.

Table: Critical differences between MetALD and MASLD

Parameter	MetALD (n=170)	MASLD (n=8,638)	p-value
Age (years)	57±11	49±14	<0.01
Male (%)	68	50	<0.01
Liver Disease Severity: Histological Findings			
Advanced fibrosis (%)	57	44	<0.05
Cirrhosis (%)	16	8	<0.05
Liver Disease Severity: Non-invasive Assessment			
FIB-4 score	2.04 ±1.36	1.43 ±1.37	<0.01
VCTE liver stiffness (kPa)	13.5±10.9	10.9±8.7	<0.01
Agile-3+ score	0.645±0.292	0.522±0.315	<0.01
Mortality Outcomes			
All-cause mortality (%)	11	2	<0.0001
Cardiovascular Comorbidities			
Cardiovascular disease prevalence (%)	16	5	<0.05
Hypertension rates (%)	64	46	<0.01

FIB-4: Fibrosis-4 index; VCTE: Vibration-controlled transient elastography

- Clinical Performance: FIB-4 and VCTE showed similar diagnostic accuracy for advanced fibrosis detection in both groups (AUC = 0.82 and 0.86, respectively).

Conclusions:

- **MetALD patients exhibit significantly more severe liver disease with three-fold higher all cause mortality risk compared to MASLD.**

Younossi, Zobair, Leyla de Avila, Salvatore Petta, Atsushi Nakajima, et al.

2. Qualitative Insights into Training Needs for Primary Care Management of Metabolic Associated Steatotic Liver Disease

Background and Aims:

- Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most prevalent liver disease globally, yet often goes undetected in primary care.
- This study aimed to identify the training needs of primary care healthcare professionals (HCPs) to improve MASLD detection and management.

Methods:

- A qualitative interview study was conducted with 25 primary HCPs (GPs, nurses, pharmacists).

Results:

- Analysis identified a range of barriers and enablers to MASLD detection and management in primary care.
- Challenges were observed in distinguishing MASLD from other conditions; There was uncertainty around who is responsible for MASLD detection and escalation; HCPs were less motivated to detect MASLD due to uncertainty about subsequent management.
- Greater motivation is needed to manage MASLD when HCPs understand that early intervention can reverse the disease.

Conclusions:

- **Targeted HCP training addressing knowledge gaps, clinical skills, and disease beliefs can improve MASLD care delivery.**

Hollie Smith , Rebecca Livingston, Helen Jarvis, Yusuf Soni. et.al

3. Identifying MASLD Patients at Risk of Liver Decompensation Using a Two-Step Non-Invasive Strategy: Insights from a Multicentre Cohort

Background

- MASLD affects ~30% of adults, but only a minority develop hepatic decompensation. Early risk identification is essential for targeted care.

Methods:

- Multi-centre cohort study (16 centres: US, Europe, Asia) inlcuding 12,950 adult MASLD patients excluding those with decompensation/cancer before or within 3 months of follow-up
- Tests Used: Fibrosis-4 (FIB-4) Index (first step) and Liver stiffness measurement (LSM) by vibration-controlled transient elastography/VCTE (second step)

Results:

- Over median 47.7 months follow-up, 1.3% of patients developed hepatic decompensation.
- **Two-step risk stratification proved effective:**
- **Step 1:** Low FIB-4 safely excluded two-thirds of patients (very low annual risk <0.1%)
- **Step 2:** Among patients with elevated FIB-4, LSM by VCTE further stratified risk:
  - **LSM <10 kPa:** Low risk
  - **LSM ≥15 kPa:** High risk (>1% annually) - for younger patients, females, obese, diabetics
  - **LSM ≥12 kPa:** High risk threshold for older patients, males, non-obese, non-diabetics

Conclusions:

FIB-4 effectively rules out low-risk patients. For those with higher FIB-4, LSM helps refine risk. LSM cut-off should be adjusted by patient profile.

Terry Cheuk-Fung Yip , Jimmy Lai , Hye Won Lee , Boyu Yang, et.al

4. Long-Term Air Pollution Exposure Associated with MASLD and Fibrosis in the general population

Background

- Air pollution may contribute to liver disease. This study examined links between air pollutants, MASLD, and liver fibrosis in the general population.

Methods:

- Data from 4,185 participants in the Rotterdam Study were analyzed.
- Measurements: Liver fat detected by ultrasound, Liver stiffness measured (fibrosis = ≥8 kPa), Air pollutant levels at home addresses (PM2.5, NO2, ozone, black carbon) with exposed period of 1, 5, and 10 years
- Exclusions: Viral hepatitis, heavy alcohol use, heart failure

Results:

- MASLD prevalence: 34%; Liver fibrosis: 5.7%
- Findings showed black carbon has the strongest effects on both conditions, PM2.5 affects both but more moderately, NO2 only affects MASLD, and ozone has no significant effects on either condition (Table).

Table: Air Pollution Associations with Liver Disease

Pollutant	MASLD Risk (5 years)	Liver Fibrosis Risk (Exposure Period)
Black carbon	92% increase	131% increase (10 years)
PM2.5	12% increase	19% increase (5 years)
No_2	3% per unit	No association
Ozone	No association	No association

PM: particulate matter

Conclusions:

Long-term exposure to NO_2, PM2.5, and black carbon is linked to higher risk of MASLD and liver fibrosis. Reducing air pollution could help lower liver disease burden.

Jesse Pustjens, Bigina N.R. Ginos, Laurens A. van Kleef, Harry L.A. Janssen, et.al

5. Impact of Weekend Exercise on MASLD Mortality

Background

- Guidelines recommend ≥150 minutes/week of moderate to vigorous physical activity (MVPA) for MASLD.
- It's unclear if doing it all in 1–2 days ("weekend warrior") offers similar benefits to regular weekly activity.

Methods:

- Data from 2,490 U.S. adults with accelerometer-tracked MVPA followed up for 14.3 years.
- Classified into 3 groups:
  - Weekend warriors (≥150 min MVPA, mostly over 1–2 days)
  - Active (≥150 min MVPA, spread out)
  - Inactive (<150 min/week)
- Probable MASLD defined using U.S. Fatty Liver Index + cardiometabolic risk

Results:

Table: Physical Activity Patterns and Health Outcomes in MASLD

Group	MASLD Risk	Diabetes Risk	Obesity Risk	Death Rate (per 1,000 yrs)	Death Risk
Inactive	High (ref)	High (ref)	High (ref)	27.7	Reference
Active	↓ 52%	↓ 66%	↓ 52%	6.7	↓ 52%
Weekend Warrior	↓ 66%	↓ 57%	↓ 64%	6.7	↓ 66%

Conclusions:

- **This study supports recommendations for meeting physical activity guidelines to improve long-term outcomes in MASLD and highlights the potential to personalize training programs to fit individual schedules and lifestyles.**

James M. Paik , Shira Zelber-Sagi, Elizabeth Pekas , Dana Ivancovsky Wajcman,et.al

6. MetALD Shows Higher Rates of Heart Disease and Extrahepatic cancer Disease Types

Background and Aims

- Steatotic liver disease (SLD) is the most common chronic liver disease globally.
- While patients with metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol-related liver disease (ALD) are known to have high risks of heart problems and cancers outside the liver, little is known about the mixed type called MetALD (MASLD with increased alcohol intake).

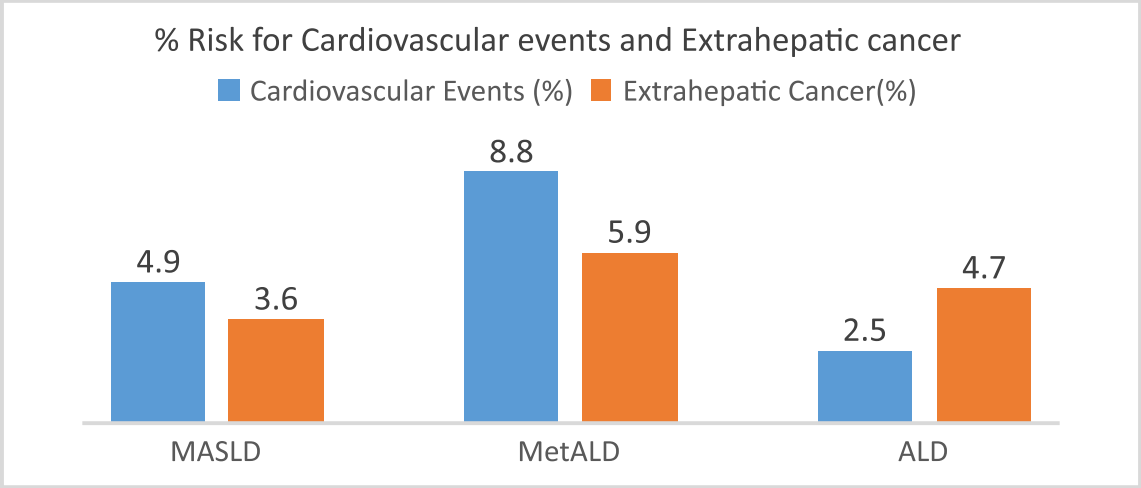
Methods:

- 726 (Mean age: 53 years, 63% male) patients with liver biopsy-confirmed SLD from one hospital over 5 years.
- Tracked new heart events (heart failure, heart attacks, strokes, blood vessel disease) and Extrahepatic cancers using medical records.
- Patient Groups: MASLD 516 patients (71%), MetALD 85 patients (12%), ALD 125 patients (17%)
- Advanced liver scarring (F3-F4): 39% of patients

Results:

- Patient Outcomes During Follow-up (Average 5 years): 64 deaths (8.8%), 44 liver complications (6.1%), 50 heart events (most common: heart attacks at 48%), 39 cancers outside liver (most common: skin 18%, prostate 13%, colorectal 13%)
- 5-year cardiovascular and cancer risk rates are shown in Figure.

Figure: 5-Year Risk Rates



- Cancer Risk Comparison (vs MASLD)
  - ALD patients: 2.4× higher cancer risk
  - MetALD patients: 2.7× higher cancer risk

Conclusions:

- **MetALD patients have a higher 5-year incidence of extrahepatic cancers and cardiovascular events compared to MASLD and ALD.**
- **Close monitoring of these patients is warranted for early detection and management of extrahepatic complications.**

Katrina Pekarska, Laura Burke Ian Rowe, Richard Parker,et.al

7. Impact of Alcohol Consumption on Liver Fibrosis in MASLD Patients

Background and Aims

- Metabolic and Alcohol-Related Liver Disease (MetALD) involves both metabolic dysfunction and moderate alcohol intake. Even low to moderate drinking in MASLD patients may increase the risk of liver fibrosis.
- This study assessed MetALD prevalence and the impact of alcohol use and abstinence on fibrosis progression and cardiovascular events.

Methods:

- Retrospective study of 482 MASLD outpatients over 66 months.
- Patients were grouped by weekly alcohol consumption: Very low-risk drinkers (VLD), Low-risk drinkers (LD), Moderate drinkers (MD), MetALD and Alcohol Related Liver Disease (ArLD) categories
- Liver fibrosis was assessed using non-invasive markers. Alcohol abstinence and cardiovascular events were tracked.

Results:

- Table shows patient distribution and key findings.

Table: Patient Distribution

Group	Definition	Percentage	Key Characteristics
VLD	0–40 g/week	77%	Lowest fibrosis risk
LD	41–90 g/week	6.75%	Intermediate risk
MD	91–140/210 g/week*	7.81%	Highest liver stiffness (47.3 KPa)
MetALD	20–50/30–60 g/day*	8.02%	Metabolic + alcohol factors
ArALD	Higher consumption	0.42%	Alcohol-related disease

- Cardiovascular Events: MD group HR = 2.3 (95% CI: 1.1–5.1)
- New Cardiovascular Risk Factors:
  - LD: HR = 1.2 (95% CI: 0.85–1.8)
  - MD: HR = 1.0 (95% CI: 0.7–1.4)
  - MetALD: HR = 1.0 (95% CI: 0.7–1.5)

Conclusions:

MetALD prevalence was consistent with other studies. Low to moderate alcohol intake in MASLD patients significantly increased liver fibrosis risk, with the highest liver stiffness seen in moderate drinkers, underscoring the importance of alcohol abstinence in slowing disease progression.

Ares Villagrasa , Anna Aguilar , Clara Sabiote , Alba Jiménez-Massip, et.al

Alcohol-Related Liver Disease

8. Binge Drinking Duration and Metabolic Risk Factors: Effects on Liver Stiffness in Steatotic Liver Disease

Background and Aims

- Current alcohol-related liver disease (ALD) screening focuses on daily/weekly alcohol intake but ignores binge duration.
- Effects of short-term binge drinking patterns and metabolic factors on liver stiffness via transient elastography were examined.

Methods:

- 2,902 participants with steatotic liver disease (SLD) defined as CAP ≥285 dB/min were analyzed.
- Inclusion criteria: age ≥18, documented liver stiffness measurements (LSM), alcohol intake responses, and metabolic risk factor data.
- Examined relationships between alcohol intake and fibrosis (LSM >8.5 kPa = any fibrosis; LSM >13.1 kPa = advanced fibrosis).

Results:

- Disease categories: MASLD: 35%, Met-ALD: 20%, ALD: 11%
- Binge frequency categories: Excessive (Every day to 4 times/week), Moderate (Twice/week to 2 times/month), Rare (Once/month or less)
- Table summarized the key odds ratios and confidence intervals.

Table: Key Findings Summary

Risk Factor	Odds Ratio (95% CI)	Significance
Metabolic Factors		
Diabetes	1.75 (1.05-2.94)	Advanced fibrosis
Hypertension	2.27 (1.56-3.31)	Advanced fibrosis
Obesity	7.36 (2.93-18.4)	Advanced fibrosis
Non-Hispanic Black	0.57 (0.33-0.96)	Protective
Binge Drinking Patterns		
Excessive (4-5 drinks/2h)	15.98 (14.49-17.47)	Any fibrosis
Excessive (4-5 drinks/2h)	17.26 (15.13-19.38)	Advanced fibrosis
≥12 drinks/day (excessive)	20.34 (16.96-23.71)	Advanced fibrosis
≥12 drinks/day (moderate)	19.08 (16.28-21.88)	Advanced fibrosis

Conclusions:

- **Both metabolic risk factors and alcohol binge duration significantly affect liver stiffness in SLD.**
- **Enhanced ALD screening should incorporate binge drinking patterns and metabolic risk stratification for improved fibrosis risk assessment.**

Liang, Lili, and Frances Lee.

9. Comorbidity Patterns in Alcohol-Related Liver Cirrhosis: A Population-Based Case-Control Study

Background

- Alcohol-related liver cirrhosis (ARLC) typically remains asymptomatic until decompensation, resulting in late-stage diagnosis with poor prognosis.
- This case-control study examined comorbidity patterns in ARLC patients versus the general population to identify potential screening opportunities.

Methods:

- Cases: 11,989 patients with first ARLC diagnosis (ICD-10: K70.3)
- Controls: 113,657 age-, sex-, and residence-matched controls (up to 10 per case)
- Comorbidity Assessment: ICD codes from specialized care contacts (1998-2020)

Results:

- ARLC patients showed significantly higher comorbidity prevalence versus controls (all $p<0.001$) as shown in Table.

Table: Comorbidity prevalence- ARLC Cases vs Controls

Comorbidity Category	ICD-10 Code	ARLC Cases (%)	Controls (%)	Prevalence Difference
Substance Use Disorders	F10-F19	48.8%	3.9%	44.9%
Other Liver Diseases	K70-K77 (excl.K70.3)	48.3%	0.3%	48.0%
Digestive System Symptoms	R10-R19	43.9%	14.5%	29.4%
Upper GI Diseases	K20-K31	33.1%	8.8%	24.3%

- All comparisons showed statistical significance ($p < 0.001$).

Conclusions:

- **Nearly 50% of ARLC patients had prior substance abuse diagnoses, suggesting alcohol use disorder centers could serve as screening sites for pre-cirrhotic disease.**
- **These comorbidity patterns may facilitate early identification of at-risk patients.**

Jakobsson, Gustav, Ying Shang, Linnea Widman, and Hannes Hagström.

10. Impact of Diabetes on Mortality in Alcohol-Related Acute-on-Chronic Liver Failure

Background

- Acute-on-Chronic Liver Failure (ACLF) causes high death rates due to multiple organ failure in patients with chronic liver disease (CLD).
- Alcohol is the main cause of ACLF globally. While diabetes increases risk in chronic liver disease, its effect on death rates in alcohol-related ACLF is unclear.
- This study determined if diabetes affects 90-day mortality in patients with alcohol-related ACLF.

Methods:

- Data of patients with alcohol-related ACLF (alcohol caused both chronic liver disease and acute episode) was analyzed
- Patients were divided into diabetic and non-diabetic groups. 90-day death rates using clinical scores and lab tests were measured.

Results:

- 2,150 patients were included; Patients characteristics are summarized in Table.

Table: Patient Characteristics

Group	Number	Medican age	Male (%)	MELD-Na Score	CTP Score
Diabetic	121	45 years	91.7%	31.1 (27.0-36.0)	12.0 (IQR
Non-diabetic	2,029	42 years	90.0%		11.0–12.0)

MELD-Na:Model for End-Stage Liver Disease - Sodium; CTP: Child-Turcotte-Pugh

- 90-Day Outcomes
  - Overall deaths: 986 patients (46%)
  - Liver transplants: 110 patients (5%)
  - Post-transplant deaths: 12 patients
- Diabetes increased the risk of death by 22.7 percentage points (68.1% vs 45.4%) in alcohol-related ACLF patients.

Conclusions:

Diabetes mellitus substantially worsens the 90-day mortality in alcohol-related ACLF.

Ashish Kumar , Shiv Kumar Sarin , Rakhi Maiwall , Ashok Choudhury, et.al

11. Alcohol Use Disorder Misclassification in MASLD and MetALD: Prevalence and Clinical Impact

Background and Aims

- Metabolic and Alcohol-Related Liver Disease (MetALD) overlaps conceptually with MASLD (Metabolic dysfunction-Associated Steatotic Liver Disease) and Alcohol-Related Liver Disease (ALD), but Alcohol Use Disorder (AUD) is often misclassified in these diagnoses.
- This study assessed the prevalence and clinical impact of misclassified AUD among MASLD and MetALD patients.

Methods:

- 3,362,552 individuals (average follow-up: 9.8 years)
- Steatosis was defined via Hepatic Steatosis Index ≥36.
- AUD was determined by medical records of alcohol-related conditions.

Results:

- MASLD and MetALD prevalence were 23.8% and 1.9%, respectively. Among them, 1.1% of MASLD and 4.7% of MetALD patients had AUD but were misclassified.
- These misclassified groups showed significantly higher all-cause and liver-related mortality. Adjusted hazard ratios (aHRs) for liver mortality were 6.53 (MASLD-AUD) and 6.98 (MetALD-AUD), and aHRs for extrahepatic cancer mortality were 1.33 and 1.44, respectively.

Conclusions:

A notable portion of patients with AUD are misclassified as MASLD or MetALD, and these individuals have worse liver and cancer outcomes, emphasizing the need for more accurate alcohol history assessment in liver disease classification.

Hyo Young Lee, Eileen Yoon, Jihyun An, Ha Il Kim, et.al

Semaglutide

12. Semaglutide Treatment Shows Superior Non-Invasive Test Improvements in ESSENCE Phase 3 Trial

Background and Aims

- Patients with metabolic dysfunction-associated steatohepatitis (MASH) may not be fully assessed by histology alone.
- This secondary analysis examined whether semaglutide 2.4 mg treatment improves non-invasive test (NIT) outcomes compared to placebo.

Methods:

- 801 participants with biopsy-confirmed MASH and liver fibrosis stage 2-3.
- Participants received semaglutide 2.4 mg or placebo for 72 weeks.
- Non-invasive assessments included: Alanine aminotransferase (ALT) levels, FibroScan-aspartate aminotransferase (FAST) score, Enhanced liver fibrosis (ELF) score, Liver stiffness by vibration-controlled transient elastography (VCTE LSM)
- Treatment response was defined as resolution of steatohepatitis (no worsening of liver fibrosis + ≥2-point decrease in NIT levels) and improvement in liver fibrosis (≥1 stage improvement + no worsening of steatohepatitis).

Results:

- The key response rates comparing semaglutide to placebo across different parameters has been shown in Table.

Table: Key Response Rates Comparison

Parameter	Semaglutide 2.4 mg	Placebo
Steatohepatitis Resolution		
Any two measures	75.1%	30.4%
ALT+FAST response	62.5%	20.0%
Complete response (ALT+FAST+histology)	45.7%	10.4%
Liver Fibrosis Improvement		
All fibrosis criteria met	16.0%	5.6%
Any two measures	19.2%	10.5%
ELF+VCTE LSM overlap	37.7%	10.5%
LSM-VCTE response	53.6%	30.9%

Conclusions:

- **Semaglutide 2.4 mg demonstrated significantly higher concordance in non-invasive test improvement compared to placebo.**
- **More participants experienced improvements in NITs beyond those captured by histology alone, suggesting semaglutide provides broader therapeutic benefits for MASH patients than traditional histological assessment might indicate.**

Rinella, Mary E., Manal F. Abdelmalek, Elisabetta Bugianesi, et al.

Drug-Induced Liver Injury (DILI)

13. Circulating Immune Checkpoint Levels in Drug-Induced Liver Injury and Metabolic Dysfunction-Associated Steatotic Liver Disease

Background

- The adaptive immune system contributes significantly to drug-induced liver injury (DILI) and metabolic dysfunction-associated steatotic liver disease (MASLD) pathogenesis. Immune checkpoints regulate T-lymphocyte activation and maintain hepatic immune tolerance.
- This study examined serum immune checkpoint levels across different liver disease states.

Methods:

- Blood samples were collected from DILI patients within one week of symptom onset (n=14), MASLD patients (n=38), and healthy controls (n=28).
- MASLD patients were stratified by fibrosis severity using transient elastography: minimal fibrosis (F≤2, n=19) and significant fibrosis (F>2, n=19).
- Seven immune checkpoint proteins were quantified.

Results:

- DILI and MASLD F>2 patients exhibited similar immune checkpoint profiles without significant differences as shown in the Table.

Table: Key Immune Checkpoint Findings

Marker	Controls	MASLD F≤2	DILI	MASLD F>2
BTLA	121±20	139±33	312±59*	250±24*
CTLA4	31±2	29±4	46±4*	51±3*
CD28	101±9	91±9	142±11*	138±10*
CD80	40±4	44±4	84±10*	64±4*
PD-1	9±1	7±1	24±4*	17±2*
PD-L1	0.1±0.1	0.6±0.3	0.7±0.1	1.4±0.4†
PD-L2	639±49	828±87	1072±102*	1140±65*

*Significantly higher than controls and MASLD F≤2; †Significantly higher than all other groups
BTLA - B and T Lymphocyte Attenuator; CTLA4 - Cytotoxic T-Lymphocyte Associated Protein 4; CD28 - Cluster of Differentiation 28; CD80 - Cluster of Differentiation 80 (also known as B7-1); PD-1 - Programmed Cell Death Protein 1; PD-L1 - Programmed Death-Ligand 1; PD-L2 - Programmed Death-Ligand 2

Conclusions:

- **Immune checkpoint proteins effectively distinguish MASLD patients with and without significant fibrosis.**
- **However, these markers cannot differentiate between chronic liver disease (MASLD with significant fibrosis) and acute liver disease (DILI), suggesting shared immune tolerance mechanisms in both conditions.**
- **PD-L1 emerges as a potential specific biomarker for advanced MASLD fibrosis.**

Toro Ortiz, Juan Pedro, Jose Pinazo Bandera, Alberto García-García, et al.

14. Prognostic Impact of Markedly Elevated ALT with Normal Bilirubin in Idiosyncratic Drug-Induced Liver Injury

Background

- While high aminotransferase with jaundice predicts poor outcomes in drug-induced liver injury (DILI), the prognostic significance of markedly elevated ALT without jaundice remains unclear.

Methods:

- 964 DILI patients from US DILIN (n=692) and Spanish DILI Registry (n=272); stratified into five groups based on peak ALT (U/L) and total bilirubin (TBL, mg/dL).
- Primary outcome: Development of Hy's law criteria (ALT >150 U/L + TBL >2.5 mg/dL). Secondary outcome: liver-related death or transplantation.

Results:

- Table clearly shows the patient distribution and outcomes across all five groups.

Table: Patient Characteristics and Outcomes by ALT/Bilirubin Groups

Group	ALT Range (U/L)	TBL Range (mg/dL)	DILIN (n)	Spanish (n)	Hy's Law (%) DILIN/Spanish	Death/Transplant (%) DILIN/Spanish
A	<500	≤1.0	210	147	3.3/2.0	0.5/0.0
B	500-1000	≤1.0	157	40	4.5/5.0	0.0/2.5
C	500-1000	1.1-2.5	121	32	24.0/22.0	3.3/0.0
D	>1000	≤1.0	67	24	10.4/25.0	1.5/8.4
E	>1000	1.1-2.5	137	29	28.5/24.0	1.5/3.5

Note: Hy's Law is a clinical rule used to identify cases of drug-induced liver injury (DILI) that have a high risk of progressing to acute liver failure and death.

Risk Stratification Based on ALT and Bilirubin Levels:

- **Low Risk:** Very high ALT (500-1000 U/L) with normal bilirubin (≤1.0 mg/dL); Hy's law incidence: 4.5-5.0%; Mortality/transplant: 0-2.5%
- **Moderate Risk:** Towering ALT (>1000 U/L) with normal bilirubin; Variable outcomes between cohorts; Requires careful monitoring
- **High Risk:** Any elevated ALT with mild bilirubin elevation (1.1-2.5 mg/dL); Hy's law incidence: 22-28.5%; Significantly increased adverse outcomes

Conclusions:

- **Very high ALT (500-1000 U/L) predicts poor outcomes only with concurrent minimal bilirubin elevation, while towering ALT (>1000 U/L) indicates poor prognosis regardless of bilirubin levels.**
- **These findings enable better risk stratification in DILI patients with markedly elevated ALT but without overt jaundice.**

Chalasani, Naga, Ismael Alvarez-Alvarez, Paul Hayashi, Raj Vuppalanchi, et al.

Acute Liver Failure

15. Comparative Outcomes of CRRT versus Plasma Exchange in Acute Liver Failure: A Retrospective Analysis

Background

- Continuous renal replacement therapy (CRRT) and plasma exchange (PLEX) serve as bridging therapies in acute liver failure (ALF) patients awaiting transplantation.
- This study compared therapeutic outcomes between these modalities and standard medical therapy (SMT).

Methods:

- Retrospective analysis of 50 ALF patients (≥18 years).
- Primary outcomes included hepatic encephalopathy (HE) grade improvement, organ function changes, and 28-day transplant-free survival.

Results:

- Patient characteristics: n= 50, mean age 31.0±13.2 years, 62% female, MELD score 31.4±6.9, with hepatitis A virus predominating (34%).
- Treatment distribution and key outcomes are shown in Table.

Table: Primary Outcomes Comparison

Outcome Measure	CRRT (n=18)	PLEX (n=18)	SMT (n=14)	p-value
HE Grade Improvement	Superior	Moderate	Baseline	CRRTvs SMT: 0.014
Ammonia Reduction (µmol/L)	172→136.4*	132→105	86→75	0.01
Organ Function Improvement	Significant	Non-significant	Baseline	CRRT: 0.007, PLEX: 0.32
28-day Survival (%)	33.0	61.1	21.4	PLEX vs CRRT:0.09

*Statistically significant reduction

Conclusions:

- **Both CRRT and PLEX improved outcomes compared to SMT alone.**
- **PLEX demonstrated superior survival rates while CRRT showed better biochemical and encephalopathy improvements.**

Das, Anshuman, Vivekanand Balijepalli, Sairam Reddy, Anand Gupta, et al.

16. Universal Early Antimicrobial Therapy in Acute Liver Failure: Clinical Outcomes at a UK Transplant Center

Background

- This study evaluated clinical outcomes of universal early antimicrobial therapy in critically ill acute liver failure (ALF) patients at a tertiary liver ICU.

Methods:

- Retrospective analysis of 37 ALF patients.
- Data included infection markers, systemic inflammatory response syndrome (SIRS), non-neurologic sequential organ failure (SOFA) scores, antimicrobial prescriptions, and resistance patterns.

Results:

Patient Demographics and Outcomes

- Admission Infections: 10 (27%)- Radiologic evidence (9), Culture positive (1)
- Antimicrobial Escalation: 18 (49%); Resistant Organisms: 2 (5%)
- Mortality: 6 (16%); Transplantation: 19 (51%)

Antimicrobial Regimens

- Universal Treatment (100%): Fluconazole 37/37 (100%), Piperacillin/Tazobactam 35/37 (94.6%), Meropenem 2/37 (5.4%)
- Antibiotic-free days: 0% (0-26.5) of ICU stay
- All the comparative key findings are summarized in Table.

Table: Infected vs Non-infected Patients

Parameter	Infected (n=10)	Non-infected (n=27)	p-value
SOFA score	12 (8.5-14)	8 (7-10)	<0.05*
CRP (mg/L)	11 (6-25)	11 (3-14)	NS
WCC ($\times 10^9$/L)	14.5 (9.5-19.5)	11.5 (7.5-15)	NS
SIRS score	2 (1-2)	1 (1-2)	NS
Blood cultures taken	2/10 (20%)	8/27 (30%)	-

*Significant difference; NS = Not significant; Values: median (IQR) or n (%)

Conclusions:

Universal antimicrobial therapy resulted in minimal antibiotic-free days, frequent escalation, and resistance development, highlighting potential overtreatment risks. Better ALF-specific infection biomarkers are needed.

Thomas, Gladson, Manan Bajaj, Rosemary Worrall, Nicholas Murphy, et al.

17. Non-transplant Therapies for Acute Liver Failure from Infectious Causes: Efficacy and Safety Analysis

Background

- Acute liver failure (ALF) in India predominantly results from infectious etiologies, unlike Western drug-induced cases.
- This study evaluates non-transplant rescue therapies—plasma exchange (PLEX) and continuous veno-venous hemofiltration (CVVH)—given high mortality and limited transplant availability in resource-constrained settings.

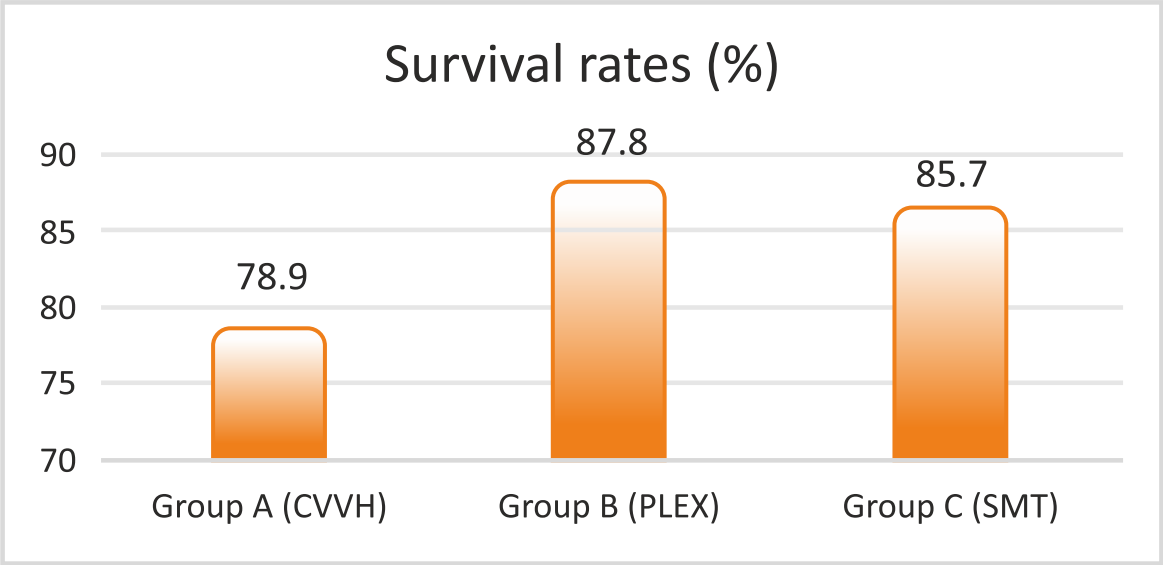
Methods:

- Retrospective analysis of 76 ALF patients categorized into: Group A (CVVH only), Group B (PLEX: B1 without CVVH, B2 with CVVH), Group C (standard medical treatment).
- Primary endpoint was transplant-free survival at discharge/day 21.
- Severity scores Model for End-Stage Liver Disease (MELD), Sequential Organ Failure Assessment (SOFA), Acute Physiology and Chronic Health Evaluation (APACHE), Assessment of Liver Failure (ALFA) Score, and Acute Liver Failure Study Group (ALFSG) index - were used to develop predictive models.

Results:

- Groups showed similar demographics except creatinine levels (Group A: 3.1 vs. Groups B/C: 1.4, p=0.001).
- Group C had significantly lower bilirubin, ammonia, INR, and lactate.
- Survival rates are shown in Survival Rates Bar Chart. (Figure)

Figure: Treatment Group Survival Rates



- Clinical improvement: 45% (A) vs. 71% (B: 81% B2, 56% B1) vs. 86% © (p=0.031).
- Predictive Models: Developed using MELD, SOFA, APACHE, ALFA, and ALFSG scores, achieving 90.9% accuracy for treatment selection with 90% sensitivity and 72% accuracy on external validation.
- Patients with creatinine >1.5 and unstable SOFA/ALFSG benefited most from CVVH; high ammonia levels responded best to PLEX.

Conclusions:

- **PLEX is optimal for unstable infectious ALF patients, while CVVH effectively manages acute kidney injury.**
- **The validated predictive models demonstrate high accuracy for individualized treatment selection in resource-limited settings.**

Mahajan, Ramit, Saurabh Singhal, Ajit Sood, Parshotam Gautam, et al.

UDCA

18. Nationwide Assessment of UDCA Response in Primary Biliary Cholangitis: Biochemical Predictors and Long-term Outcomes

Background and Objectives:

- Alkaline phosphatase (ALP) and total bilirubin (TB) evaluation after 1-year UDCA therapy guides second-line treatment decisions in primary biliary cholangitis (PBC).
- This study assessed ALP and TB responses after one year of UDCA and their association with long-term clinical outcomes.

Methods:

- PBC Patients with available biochemistry after one year of UDCA monotherapy were analyzed. Laboratory values are expressed as upper limits of normal (ULN).
- Liver transplant (LT)-free survival was assessed according to ALP and TB thresholds.

Results:

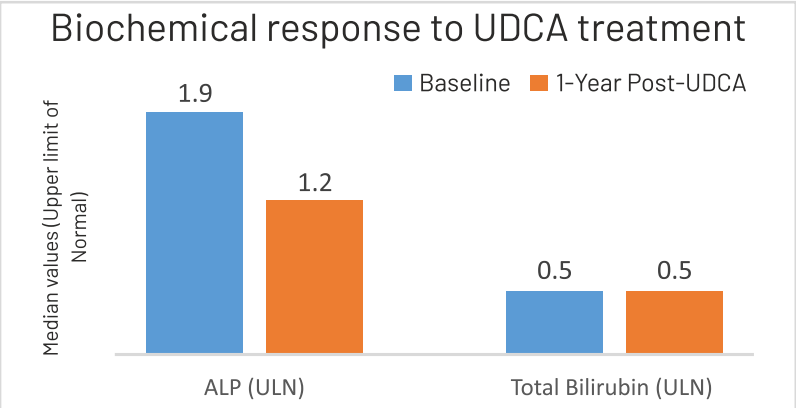
- Key Survival Outcomes are shown in Table.

Table: Patient Outcomes by Biochemical Response Categories

Response Category	ALP (ULN)	TB (ULN)	N (%)	10-year LTFS 11-(95% CI)
Deep Response	≤1.0	≤0.6	642 (23.3%)	91.0% (88.2-93.9)
Standard Response	≤1.5	Normal	1,781 (64.6%)	88.7% (86.8-90.6)
ALP-based Poor Response	>2.0	Any	489 (15.8%)	77.4% (73.2-81.8)
TB-based Poor Response	Any	>1.0	267 (8.6%)	56.8% (50.5-63.9)

- Baseline vs 1-Year Post-UDCA Biochemistry is shown in Figure.

Figure: Baseline vs 1-Year Post-UDCA Biochemistry



- During 8.3-year median follow-up, 74 patients (2.4%) underwent LT and 522 (16.9%) died. Both log ALP (aHR 1.8, 95% CI 1.5-2.1, p<0.001) and log TB (aHR 3.0, 95% CI 2.5-3.6, p<0.001) independently predicted LT or death.

Conclusions:

- **One-year post-UDCA ALP and TB levels independently predicted long-term clinical outcomes.**
- **Nearly one-quarter of patients achieved deep biochemical response to UDCA monotherapy, associated with excellent transplant-free survival.**

Werner, Ellen, Gemma Weijsters, Maria C. van Hooff, et al.

19. Real-world Misclassification of UDCA Response in Primary Biliary Cholangitis Patients

Background

- Primary biliary cholangitis (PBC) patients receive ursodeoxycholic acid (UDCA) treatment with response classified by Paris II criteria after 12 months (alkaline phosphatase [ALP] and aspartate-aminotransferase [AST] ≤1.5× upper limit of normal [ULN], bilirubin <1 mg/dL).
- This study examined alignment between clinical judgment and formal Paris II criteria in the German PBC registry.

Methods:

- Clinical assessment of UDCA response was compared to formal Paris II criteria evaluation.

Results:

- Clinical judgement differed from formal criteria in 48/383 cases (12.5%).
- Misclassification rates are shown in Table according to Centers.

Table: Misclassification rates in Centers

Center Type	Misclassification Rate	Main Discriminating Factor
Non-academic	26% (22/85)	ALP levels (baseline & 12-month)
Academic	13% (22/168)	AST and bilirubin levels

- The table shows the significant differences in laboratory values that contributed to misclassification patterns.

Table: Laboratory Parameters in Misclassified Cases

Center Type	Parameter	Time point	Incorrectly Classified	Correctly Classified	p-value
Non-academic	ALP (×ULN)	Baseline	3.6±3.0	1.7±0.9	<0.001
	ALP (×ULN)	12-month	2.3±1.2	0.9±0.3	<0.001
Academic	AST (×ULN)	Baseline	5.1±9.2	2.4±5.9	0.008
	AST (×ULN)	12-month	1.2±0.7	0.8±0.2	0.001
	Bilirubin (×ULN)	Baseline	1.8±3.3	0.9±2.7	<0.001
	Bilirubin (×ULN)	12-month	1.2±1.8	0.4±0.2	<0.001

- Paris II Criteria Violations in Misclassified "Adequate" Responders: ALP >1.5×ULN (57% of cases), AST >1.5×ULN (23% of cases), Bilirubin >1 mg/dL (28% of cases)

Conclusions:

- **Clinical judgement and Paris II criteria disagreed in 12.5% of cases, particularly at non-academic centers.**
- **Higher baseline ALP levels may influence clinical perception of adequate response despite not meeting formal criteria.**

Wiegand, Johannes, Annegret Franke, Tobias Müller, Kerstin Stein, et al.

20. POISE Criteria Validation as Surrogate Endpoint in PBC Patients Receiving UDCA-PPAR Agonist Combination Therapy: A Japanese Real-World Retrospective Study

Background

- POISE criteria (alkaline phosphatase <1.67× upper limit of normal with ≥15% reduction from baseline, plus normal bilirubin at one year) serve as primary endpoints in PPAR agonist trials for primary biliary cholangitis (PBC) patients with incomplete ursodeoxycholic acid (UDCA) response.
- However, these criteria were originally validated for UDCA monotherapy, raising questions about their prognostic value in UDCA-PPAR agonist combination therapy.
- Study evaluated whether POISE criteria predict long-term outcomes in PBC patients treated with UDCA plus bezafibrate (BZF)

Methods:

- 2,051 patients: BZF add-on therapy to UDCA, alkaline phosphatase ≥1.5× upper limit of normal at BZF initiation, ≥1-year follow-up, and complete treatment/prognosis data.
- Exclusion criteria: concurrent hepatitis B/C or autoimmune hepatitis. Patients were stratified by POISE criteria achievement at one year post-BZF initiation.

Results:

- Of 226 eligible patients (46 male, 180 female; mean age 57.7±12.8 years; mean follow-up 8.7±5.0 years), 92 achieved POISE criteria (POISE-in) and 134 did not (POISE-out).
- Primary outcomes showed significant differences: Liver transplantation/all-cause mortality- 4 POISE-in vs 16 POISE-out patients (5.76 vs 9.81 per 10,000 person-years)
- Composite endpoint (including decompensated events and hepatocellular carcinoma): 5 POISE-in vs 32 POISE-out patients (4.9 vs 28.6 per 10,000 person-years)

Conclusions:

POISE criteria achievement significantly correlates with improved long-term prognosis in PBC patients receiving UDCA-BZF combination therapy, validating POISE as an appropriate surrogate endpoint for UDCA-PPAR agonist clinical trials.

Miura, Ryo, Katsunori Yoshida, Masanori Abe, Tadashi Namisaki, et al.

Others

21. Diabetes Mellitus Increases Hepatocellular Carcinoma Risk in Chronic Hepatitis B Patients with Low-Level Viremia: Supporting WHO 2024 Treatment Guidelines

Background and Aims:

- The WHO 2024 guidelines recommend antiviral therapy for chronic hepatitis B (CHB) patients with diabetes mellitus regardless of HBV DNA levels, fibrosis status, or ALT levels.
- To validate these recommendations by assessing hepatocellular carcinoma (HCC) risk in CHB patients with concomitant diabetes.

Methods:

- 38,979 CHB patients were identified via hepatitis B surface antigen positivity or ICD-9 coding. Primary outcome was incident HCC development.

Results:

- Patient Characteristics: Mean age 47.5±15.4 years; Male 41.9%; Antiviral therapy 43.3% (median 5.2 years); Newly diagnosed diabetes 24.3%
- Table shows risk analysis with hazard ratios.

Table: HCC Risk in CHB Patients with Diabetes

Patient Group	Adjusted HR (aHR)	95% CI	Risk Level
Overall Diabetes Effect	1.53	1.29-1.82	High
Untreated Patients	1.50	1.07-2.10	High
Low Viremia (<2000 IU/mL)	1.53	1.09-2.14	High
Non-advanced Fibrosis	1.24	1.24-3.04	Highest

Treatment Benefits:

- Antiviral therapy reduced HCC risk in CHB-diabetes patients (aHR 0.76, 95% CI 0.68-0.84)
- Greater benefit in patients <65 years (aHR 0.64, 95% CI 0.56-0.74) vs ≥65 years (aHR 0.91, 95% CI 0.78-1.07) (P<0.001)

Conclusions:

- **Diabetes is a significant HCC risk factor in CHB patients regardless of viral load or fibrosis status, supporting WHO 2024 guidelines for treatment expansion.**
- **Antiviral therapy provides greater protection in younger patients.**

Hui, Rex Wan-Hin, Xianhua Mao, Matthew Shing Hin Chung, et al.

22. Bayesian Recalibration of MELD 3.0 for Contemporary Liver Transplant Allocation

Background:

- The Model for End-Stage Liver Disease (MELD) score guides liver transplant allocation, with MELD 3.0 representing the latest iteration.
- Changing disease patterns and clinical practices require continuous model updates to maintain predictive accuracy.

Methods:

- A retrospective cohort study of 13,764 US adult liver transplant candidates (41.1% female).
- Using a two-thirds training and one-third validation split, Bayesian proportional hazards modeling with MELD 3.0 coefficients as informative priors to develop MELD 3.1 was applied.

Results:

- MELD 3.1 improved 90-day mortality prediction (C-statistic: 0.7195 vs 0.7152, p=0.036)
- Reclassification: 5.9% upcategorized, 2.8% downcategorized patients
- Net gain of 3.1% among decedents, exclusively in female candidates
- Improvements reflected higher female sex coefficient and lower creatinine coefficient.

Conclusions:

- **Bayesian recalibration of MELD using contemporary data improves predictive accuracy.**
- **An iterative MELD 3.i framework could enable adaptive updates to maintain optimal transplant allocation as demographics and practices evolve.**

Tomohiro Tanaka, David Axelrod, Jennifer Lai, Daniel Sewell

23. Genetic Testing in Adult Cholestatic Liver Disease: A Review

Background:

- Many adult cholestatic liver disease cases remain unexplained after ruling out common causes like PBC and PSC.
- Genetic mutations (e.g. ABCB4, ABCB11, ATP8B1) may help explain these cases.

Methods:

- Retrospective review of 166 patients (2016–2024)
- Genetic panel screened 77 genes (e.g. via Prevention Genetics, Eurofins)
- Clinical and imaging data also reviewed

Results:

- 82 patients (49.4%) were found to have genetic variants likely associated with their cholestatic liver disease.
- Genetic Variants Identified:

- ABCB4 (ATP-binding cassette sub-family B member 4)- 13.9%, CFTR (Cystic Fibrosis Transmembrane Conductance Regulator)- 12.7%, PKHD1 (Polycystic Kidney and Hepatic Disease 1)- 4.8%, ATP8B1 (ATPase phospholipid transporting 8B1)- 2.4%, HNF1B (Hepatocyte Nuclear Factor 1 Beta)- 1.8%, NOTCH (Notch receptor genes)- 1.2%, ABCB11 (ATP-binding cassette sub-family B member 11)- 0.6%

- Clinical Context (n = 82 with variants, mean age 41.6 years): 35.4% with Unexplained cholestasis after excluding PBC/PSC; 54.3% females; 18.3% with Sclerosing cholangitis seen on MRI; 19.5% with family history of liver disease

Table: Treatment and Imaging Findings

Treatment / Finding	% (n)
Treated with Ursodeoxycholic Acid (UDCA)	**59.8% (49)**
Required anti-pruritic treatment	23% (19)
Sclerosing cholangitis on MRI	23% (19)
Underwent cholecystectomy	31.7% (26)
Positive autoimmune serology (ANA/SMA)	49% (40)

Conclusions:

Genetic testing in adults with cholestatic liver disease shows a high yield (~50%). Sclerosing cholangitis on imaging does not rule out genetic causes, especially without inflammatory bowel disease.

Chloe Nguyen, Shani Nagler , Kristel Leung , Aliya Gulamhusein, et.al.

24. Nutritional Therapy Reduces Hepatic Encephalopathy After TIPS: A Randomized Trial

Background:

- Hepatic Encephalopathy (HE) is a major complication after Transjugular Intrahepatic Portosystemic Shunt (TIPS) in cirrhotic patients.
- Poor nutritional status and sarcopenia (muscle loss) increase the risk.
- This study evaluated evaluate whether structured nutritional therapy can prevent first episode of OHE after TIPS.

Methods:

78 patients with cirrhosis post-TIPS were randomized into:

- **Group 1:** 35 kcal/kg/day diet, protein increased rapidly to 1.2–1.5 g/kg/day,
- **Group 2:** Same calories, slower protein increase,
- **Group 3:** No dietary change (control); followed up for 24 weeks

- No use of rifaximin or lactulose (common HE medications)

Outcomes:

- **Primary:** Incidence of OHE (West Haven grade II or higher)
- **Secondary:** Minimal HE (MHE) measured by Number Connection Test-A (NCT-A) and Line-Tracing Test (LTT), Sarcopenia measured by skeletal muscle index (SMI) at L3 vertebral level on CT scan (L3-SMI)

Results:

- OHE incidence: Group 1 (18.5%); Group 2 (34.6%), Group 3 (48.0%) (Group 1 significantly lower than Group 3, $p = 0.034$)
- Group 1 showed improved MHE scores (NCT-A, LTT).
- Muscle mass (L3-SMI) increased in all groups
- No difference in other complications between groups.

Conclusions:

- **Early nutritional therapy (35 kcal/kg/day and 1.2–1.5 g/kg protein) significantly reduces OHE and improves cognitive function in cirrhotic patients after TIPS.**
- **Nutritional support should be started as early as possible post-TIPS.**

Ying Li , Xin Quan , Ou Luo , Bo Wei , et.al.

Functional Dyspepsia and Belching

1. New GastroPanel Quick Test for Non-Invasive Dyspepsia Diagnosis in Primary Care

Background and Objectives:

- GastroPanel is a non-invasive serological test for evaluating gastric mucosal health and detecting H. pylori or atrophic gastritis , In cases of dyspepsia and other stomach disorders standard testing requires rapid lab processing due to gastrin-17 instability. This study aimed to assess the clinical utility of the new GastroPanel Quick Test (GPQT) in dyspeptic patients in primary care, using gastroscopy and biopsy as reference standards.

Methods:

- A total of 127 dyspeptic patients (mean age 48.4) were enrolled in primary care, all of whom underwent endoscopy and the new point-of-care test (POCT).
- GastroPanelÂ® quick test (Biohit Finland), is a rapid lateral flow immunochromatographic POCT.
- GastroPanel Quick Test uses fingerstick or venous blood, which measured four biomarkers—H. pylori IgG, Gastrin-17, Pepsinogen I, and Pepsinogen II—with results available in approximately 15 minutes via the GP Reader NT device.

Results:

- Diagnoses included: Functional Dyspepsia (51), GERD (27), GERD on PPIs (19), Non-atrophic Gastritis with Hp (22), Atrophic Gastritis (8).
- Serological diagnoses matched endoscopic findings in all cases except 4.

Conclusions:

- **The GPQT is a reliable and rapid tool for diagnosing dyspepsia in primary care.**
- **It can guide early, appropriate treatment without immediate endoscopy.**

Crafa P, Franzoni L, Franceschi M, Rodriguez Castro KII,et.al.

2. Duodenal Mucosal Microbiota and Its Association with Mucosal and Peripheral Immune Homeostasis in Functional Dyspepsia

Background and Objectives:

- People with Functional Dyspepsia (FD) may have changes in the bacteria that live on the lining of their duodenum (upper small intestine), these differences may reflect alterations in host-microbiome homeostasis. These changes could be linked to problems with the immune system. This study looked at whether the gut bacteria in FD patients are related to immune system changes in the gut and blood.

Methods:

- 17 patients with functional dyspepsia (FD, average age 46) and 11 healthy controls (average age 58) provided duodenal tissue and blood samples for analysis of bacteria (via 16S rRNA sequencing), immune cells (CD4/CD8 T cells via flow cytometry), and other cell markers.

Results:

- Initial analysis showed FD patients had fewer villous goblet cells (P<0.05) and higher levels of Lymphocytes from Peripheral Blood Mononuclear Cells (LPMC) CD4+ Central Memory (P<0.01), LPMC CD8+ (P<0.05), and Peripheral Blood Mononuclear Cells (PBMC) CD4+ Central Memory Th17 cells (P<0.05) vs. controls.
- In controls, goblet cells correlated positively with *Massilia* and negatively with *Exiguobacterium*; LPMC CD4+ Central Memory T cells negatively with *Veillonella*.
- FD patients demonstrated a significant negative correlation between LPMC CD8 and *Sulfophobococcus*, and a positive correlation between PBMC CD4+ Central Memory Th17 and both *Gemella* and *Fusobacterium*.

Conclusions:

Study reports that FD patients have distinct alterations in duodenal mucosa-associated microbiota and immune profiles compared to healthy people. The normal relationship between bacteria and the immune system seems to be disrupted in FD, which might play a role in causing the condition.

Hoedt EC, Burns GL, Kang S, Bruce JK, et al.

3. Effects of Club Soda on Belching in Healthy Individuals vs. Functional Dyspepsia Patients: A Comparative Study

Background and Objectives:

- Belching, triggered by gastric distension, may differ in patients with Functional Dyspepsia (FD) compared to healthy individuals. Carbonated beverages like club soda can induce belching and related symptoms, providing a model to study gastric sensory responses. This study helps to compare belching patterns and upper gastrointestinal symptom responses to club soda between healthy volunteers (HV) and FD patients.

Methods:

- 29 FD patients (Rome IV criteria) and 30 HV consumed 250 mL of Singha™ club soda in 50 mL increments over 5 minutes.
- Belching characteristics (onset, frequency, size), and symptoms (gas sensation, discomfort, pain) were recorded during consumption and at 10, 30, and 120 minutes post-drinking.

Results:

- In this study, FD patients (n=29; 18 postprandial distress syndrome (PDS), 11 epigastric pain syndrome (EPS)) had a lower belch threshold (100 mL vs. 200 mL in healthy volunteers) and shorter desire-to-belch duration; All HV began belching within 10 minutes while one FD patient did not belch even after 120 minutes.

- After consuming 250 mL soda in 5 minutes, 58.6% FD and 70% HV reported increased gas sensation, 51.7% FD and 56.7% HV experienced more abdominal discomfort and 34.5% FD and 23.3% HV reported more abdominal pain.
- Symptoms improved faster in HV, with minimal symptoms by 120 minutes. FD patients showed delayed recovery, but by 120 minutes, 34.5% reported reduced gas, 31.0% less discomfort, and 24.1% less pain.
- Notably, symptom improvement in FD was linked to higher belching frequency.

Conclusions:

- **The carbonated drink test showed that FD patients had a lower threshold for belching and shorter belch urge duration than healthy volunteers. While both groups developed symptoms after soda intake, FD patients had more prolonged discomfort, highlighting altered belching and symptom responses in FD.**

Siriwong N, Prompongsa K, Pitisuttithum P, Yunuch S, et al.

4. Prevalence of Subjective Poor Sleep Quality in Functional Dyspepsia: A Systematic Review and Meta-Analysis

Background and Objectives:

- Functional dyspepsia (FD) is a common Functional Gastrointestinal Disorder (FGID) with symptoms like fullness and epigastric pain. Poor sleep quality (PSQ) is often linked to FGIDs, but data in FD are limited. This systematic review and meta-analysis aimed to determine the pooled prevalence of PSQ in FD patients.

Methods:

- A systematic review of studies using the Pittsburgh Sleep Quality Index (PSQI) assessed poor sleep quality (PSQ) in functional dyspepsia (FD) patients diagnosed by Rome III/IV criteria (developed by the Rome Foundation for Functional Gastrointestinal Disorders) exhibit upper GI symptoms like early satiety, postprandial fullness, or epigastric pain without structural abnormalities).

Results:

- Seven studies with 2,138 FD patients from Asia and Europe found a pooled poor sleep quality (PSQ) prevalence of 57.2%. FD patients had significantly higher odds of PSQ than controls (OR = 2.39; $p \leq 0.001$). PSQ rates were higher with interview-based data, Rome IV criteria, and PSQI cut-off ≥8. Larger sample sizes correlated with higher prevalence.

Conclusions:

- **This is the first study to estimate pooled prevalence of poor sleep quality (PSQ) in functional dyspepsia (FD), showing over half of FD patients are affected. Findings highlight the need to assess and manage sleep issues in FD care. Future research should explore causal links and develop targeted sleep interventions.**

Marsool MDM, Hasan F, Prajjwal P, Netyam R, et al.

Nausea, Vomiting, and Motility Disorders

5. Impact of Herbal Medicine for Postoperative Nausea and Vomiting After Laparoscopic Surgery: A Meta-Analysis

Background and Objectives:

- Herbal medicines have traditionally been used to relieve nausea and vomiting. However, clinical evidence on their effectiveness in treating postoperative nausea and vomiting (PONV), especially after laparoscopic surgery, remains limited. Objective of this study was to assess the efficacy and safety of herbal medicine in preventing and managing postoperative nausea and vomiting compared to no treatment, placebo, and conventional (Western) medicine.

Methods:

- A systematic review and meta-analysis was conducted using 19 randomized controlled trials (RCTs) with 2,726 participants were identified.
- Primary outcome was incidence of postoperative nausea and vomiting (PONV).
- Secondary outcomes included symptom severity and frequency and intensity of PONV, symptom improvement time, antiemetic requirement frequency, and incidence of adverse events.

Results:

Compared to no treatment, herbal medicine significantly reduced vomiting incidence (Risk Ratio = 0.43, 95% Confidence Interval [CI]: 0.32–0.57, P < .00001).
Compared to placebo, it significantly reduced nausea severity at 12 hours post-surgery (Standardized Mean Difference = –2.04, 95% CI: –3.67 to –0.41, P = .01).
Herbal medicine showed similar effectiveness as Western medicine in reducing nausea (Risk Ratio = 0.94, P = .77) and vomiting (Risk Ratio = 0.68, P = .45).
Adverse events were lower in the herbal medicine group (Risk Ratio = 0.45, P = .001).

Conclusions:

- **Herbal medicine is a potentially effective and safe treatment for postoperative nausea and vomiting following laparoscopic surgery.**

Kim J, Ha N-Y, Jeong H, Jeong D, et al.

6. Effect of GLP-1 Therapy on GI Symptoms in Motility Disorders

Background and Objectives:

- Glucagon-like peptide-1 receptor agonists (GLP-1 agonists) are widely used for type 2 diabetes and weight loss, but their impact on gastrointestinal (GI) symptoms in patients with GI motility disorders is unclear. Objective of this study was to evaluate the effects of GLP-1 agonists on GI symptoms in patients with motility disorders.

Methods:

- From January to August 2024, 1,041 patients at a GI Motility Center were screened. Among 115 with GLP-1 agonist use, symptom changes before, during, and after use were recorded.

Results:

- 52.2% reported worsening GI symptoms, 47.0% no change, and 0.9% noticed improvement with GLP-1 agonist use.
- Of 115 patients, 41 were current and 74 were past GLP-1 agonist users. Among past users, 39.2% reported symptom improvement after stopping, while 43.2% had persistent symptoms.
- Gastroparesis (Gp) patients had the highest symptom worsening (68%) compared to GERD (54.5%) and constipation (9.1%) (p=0.0077).
- Improvement after stopping was seen in 43.2% of Gp, 40% of GERD, and 16.7% of constipation patients.
- Symptom worsening was most common in those using GLP-1 for both diabetes and weight loss (60%), and improvement after stopping was highest in the weight loss group (45.5%).

Conclusions:

- **Among 115 GLP-1 agonist users, 52.2% reported GI symptom worsening, 47.0% had no change, and 0.9% saw improvement.**
- **GLP-1 agonists may worsen GI symptoms in over half of patients with motility disorders, especially in those with gastroparesis. Symptom improvement is common after discontinuation.**

Reddy R, Strauch E, Kim SA, Yu D, et al.

7. Exploring The Complex Relationship Between Chronic Nausea, Fatigue, Sleep Disturbance, Anxiety, And Depression

Background and Objectives:

- Chronic nausea is a common and distressing symptom. This study explored how it relates to fatigue, sleep disturbance, anxiety, and depression.

Methods:

- Adults (18+) with chronic nausea (>6 months) enrolled in an open-label study of the wearable Transcutaneous Electrical Nerve Stimulation (TENS) device Emeterm® completed baseline surveys on nausea, fatigue, sleep, and mood.
- Nausea frequency (daily episodes) and duration (from <30 minutes to >4 hours) were recorded, and a total nausea score was calculated by combining intensity, frequency, and duration.
- Fatigue and sleep were assessed using standardized scales (no fatigue (0-6) to severe fatigue (19-25)), with higher scores indicating greater severity.

Results:

- Among 51 mostly female participants (mean age 40), 80% had moderate or severe nausea. Nausea was positively correlated with depression and negatively correlated with sleep quality. No strong link was found with anxiety or fatigue. Sleep disturbance was the strongest predictor of moderate to severe nausea.

Conclusions:

- **Study findings highlight the complex relationship between chronic nausea, sleep disturbance, fatigue, and depression. A holistic approach is needed to address sleep issues, managing depression, and investigating the underlying causes of fatigue—may benefit patients with chronic nausea.**

Stuart K, Mudhar A, Chakraborty S, et al.

8. Do Symptoms Differentiate Delayed Regional vs. Generalized GI Transit? More Than Just a Feeling?

Background and Objectives:

- Gastrointestinal (GI) dysmotility often affects multiple regions, but it's unclear if symptoms can distinguish isolated from generalized transit delays. This study assessed whether symptom profiles reflect regional vs. widespread GI transit abnormalities.

Methods:

- Patients with suspected dysmotility underwent wireless motility capsule (WMC) testing using the Atmo Gas Capsule. Delayed transit was defined by region-specific thresholds. Patients were grouped by no delay, isolated delay, or generalized delay. Symptoms were evaluated using Patient Assessment of Gastrointestinal Disorders - Symptoms (PAGI-SYM) and Patient Assessment of Constipation Symptoms (PAC-SYM) questionnaires.

Results:

- Of 157 analyzable participants, 57% had delayed GI transit—65% isolated and 35% generalized.
- Delays occurred in the stomach (n=40) and colon (n=54), with similar isolated vs. generalized patterns.
- Symptom scores (PAGI-SYM, PAC-SYM) did not differ across no delay, isolated, or generalized delay groups, nor between isolated and generalized delays in gastric or colonic regions ($p>0.05$).

Conclusions:

- **WMC measurements using the Atmo Gas Capsule showed that delayed transit affecting multiple GI regions was common. However, symptom profiles did not differentiate between isolated and generalized delays, indicating that symptoms alone are unreliable indicators of GI transit abnormalities.**

Kuo B, Lee A, Abell T, Attaluri A, et al.

9. Evaluation of Dietary Patterns and Nutrient Intake in Cyclic Vomiting Syndrome Patients Using a Food Frequency Questionnaire

Background and Objectives:

- Cyclic vomiting syndrome (CVS) involves recurrent severe vomiting, potentially affecting nutrition, yet data on dietary intake are limited. This study aimed to assess malnutrition risk, describe dietary patterns using the Healthy Eating Index (HEI), and compare nutrient intake in CVS patients to historical controls.

Methods:

- This cross-sectional study of CVS patients used Rome IV criteria (developed by the Rome Foundation for Functional Gastrointestinal Disorders) exhibit upper GI symptoms like early satiety, postprandial fullness, or epigastric pain without structural abnormalities)and included electronic assessments with the malnutrition screening tool (MST), food security questionnaire (FSQ), and Vioscreen® food frequency questionnaire (FFQ) during symptom-free periods. The FFQ measured nutrient intake and dietary patterns using the Healthy Eating Index (HEI). Demographics and clinical data were collected via intake questionnaires.

Results:

- Among 44 CVS patients (mean age 39±16 years; 70% female; 82% White), 86% had moderate to severe disease. Over half (52%) were at risk for malnutrition (MST≥2), and 16% were food insecure. HEI scores were lower in CVS patients than controls (55±11 vs. 65±12; $p<0.0001$), with 41% classified as having a "poor" diet, 57% needing improvement, and only one with a "good" diet. Caloric and macronutrient intake did not differ from controls ($p>0.05$). Based on BMI, 68% were overweight/obese, 25% had normal BMI, and 7% were underweight. BMI was not significantly associated with disease severity, cannabis use, HEI score, or food insecurity.

Conclusions:

- **CVS patients have poorer diet quality than controls, with most being overweight or obese—independent of disease severity, cannabis use, or food security. BMI is not a reliable marker of nutrition status, and further research is needed to understand the drivers of poor diet and obesity in CVS.**

Venkatesan T, Goday PS, Subramaniam S, Arumugam S, et al.

Gastroparesis

10. Predominant Symptom in Gastroparesis: Associations with Quality of Life, Treatment Response, and Outcomes

Background and Objectives:

- Gastroparesis (Gp) treatment is challenging due to unclear causes of dominant symptoms, making symptom-based therapy essential. This study aimed to: 1) classify patients by predominant symptom (PdS), 2) compare symptoms, gastric emptying, quality of life, and treatments across PdS groups, and 3) assess PdS and overall symptom improvement over 48 weeks.

Methods:

- A total of 1,013 patients were enrolled in a multicenter registry and followed for 48 weeks.
- At baseline, the predominant symptoms were nausea (N=315), vomiting (N=205), abdominal pain (N=200), bloating (N=96), fullness (N=45), GERD (N=45), constipation (N=29).
- Predominant symptom (PdS) and symptoms were evaluated using the Patient Assessment of Upper Gastrointestinal Symptoms (PAGI-SYM) and Gastroparesis Cardinal Symptom Index (GCSI). QOL was assessed using the 36-Item Short Form Survey (SF-36) and Patient Assessment of Upper Gastrointestinal Disorders–Quality of Life (PAGI-QOL).

Results:

- Vomiting was more common in diabetic Gp, while abdominal pain was more frequent in idiopathic Gp (P=0.009). GCSI scores and gastric emptying were similar across PdS groups, but quality of life was lower in those with abdominal pain and constipation. Treatment varied by PdS. Over 48 weeks, PdS changed in 62% of patients. GCSI improved ≥1 point in 26%, most often in those with initial nausea (32%) or bloating (35%), and least with fullness (13%) or pain (15%) (P=0.01).

Conclusions:

- **In gastroparesis patients, the most common predominant symptoms (PdS) were nausea, vomiting, abdominal pain, and bloating. While PdS frequently changes over time, the initial PdS is linked to quality of life, treatment choices, and outcomes. Ongoing analysis aims to assess whether the PdS at 48 weeks, if different from baseline, has a similar influence on these factors during continued follow-up.**

Parkman HP, Wilson L, McCallum RW, Hasler WL, et al.

11. Risk Of Development Of Gastroparesis in 3 Years Of The Diagnosis following Chronic Pancreatitis: A Large Population-Based Study

Background and Objectives:

- Idiopathic gastroparesis (GP) is frequently observed, and inflammation may play a role in its development. This study assessed the risk of GP in patients with chronic pancreatitis (CP), with or without diabetes mellitus (DM), using propensity score-matched cohorts.

Methods:

- Retrospective cohort study was done using the TriNetX database (2019–2021) to assess gastroparesis risk in chronic pancreatitis (CP) patients. CP cases were 1:1 propensity score–matched to controls based on demographics, comorbidities, medications, and other factors affecting gastric motility. Adjusted odds ratios (aOR) with 95% confidence intervals (CI) were calculated for gastroparesis at 1, 2, and 3 years post-CP diagnosis. Significance was set at $P < 0.05$.

Results:

- After propensity score matching, 28,182 patients were included in each cohort. CP was associated with a significantly higher risk of gastroparesis at all time points. Patients aged 18–64 had greater risk than those ≥65. Both sexes showed increased risk, slightly higher in females. No racial differences were observed. CP patients with diabetes had the highest risk, especially at 3 years (aOR 3.62; $p < 0.001$). Similar trends were noted at 2 years across all analyses.

Conclusions:

- **This large database study shows that patients with chronic pancreatitis (CP) are at increased risk of developing gastroparesis (GP), particularly those under 65 years of age and females.**

Alchirazi KA, Albuni MK, Baliss MS, Telbany A, et al.

12. A Noninvasive "3-in-1" Test to Characterize Pathophysiology in Gastroparesis Patients

Background and Objectives:

- Gastroparesis (Gp), especially diabetic gastroparesis, is characterized by impaired gastric motility, gastric accommodation, and frequently autonomic nervous system dysfunction. Current diagnostic tests for these functions are often invasive and not feasible for routine clinical use. A noninvasive "3-in-1" test was developed to assess all three key physiological components simultaneously.

Methods:

- In this study, 21 patients with diabetic gastroparesis and 16 age- and sex-matched healthy controls underwent a 3-in-1 assessment combining gastric accommodation (measured by Maximum Tolerable Volume [MTV]), gastric motility (assessed by the percentage of Normal Slow Waves [NSW%] via electrogastrogram [EGG]), and autonomic function (evaluated through Heart Rate Variability [HRV], specifically high frequency [HF] and low frequency/high frequency [LF/HF] ratio from electrocardiogram [ECG]); symptoms such as nausea, fullness, satiety, bloating, and abdominal pain were recorded before and after a standardized water-load test.

Results:

Compared to healthy controls, diabetic gastroparesis patients showed

- Decreased vagal activity and rise in sympathovagal ratio (LF/HF);
- Decreased percentage of normal slow waves in channel 3 (corresponding to the gastric antrum) of the EGG, suggesting impaired gastric motility/emptying;
- Decreased MTV, suggesting reduced gastric accommodation;

- Severe symptoms of nausea, fullness, satiety, bloating and abdominal pain during the 30-min post drinking period.
- Symptoms in controls resolved faster, suggesting the water load test may serve as a useful provocative ztool. The noninvasive "3-in-1" test was well tolerated by all participants.

Conclusions:

The noninvasive "3-in-1" test is a safe, well-tolerated, and clinically useful method for evaluating autonomic function, gastric motility, and accommodation in diabetic gastroparesis. It shows promise as a practical diagnostic tool to guide personalized treatment strategies for gastroparesis.

Nojkov B, Li F, Daassa O, Hang B, et al.

13. Uncovering the Link Between Gastroparesis and GERD: The Role of Supine Acid Exposure

Background and Objectives:

- The relationship between gastroparesis and GERD is unclear. Delayed gastric emptying (GET) may increase reflux, but its effect on acid exposure time (AET) is uncertain.

Methods:

- Adults who had both Multichannel Intraluminal Impedance and pH monitoring (MII-pH) and gastric emptying studies (GES) between Jan 2022 and Sep 2024 were included. Patients were grouped by GET: normal (<10%), mild/moderate (10–30%), and severe (>30%). GERD was defined using Lyon 2.0 criteria.

Results:

- Among 286 patients (mean age 58, 60% female), no significant association was found between GET and AET (total, supine, or postprandial). Severe delay group had highest PPI use (83%) but similar reflux profiles. Adjusted models also showed no link between GET and GERD diagnosis.

Conclusions:

Delayed gastric emptying was not associated with increased acid exposure or GERD diagnosis. These findings challenge the theory that gastroparesis directly contributes to GERD and highlight a more complex interplay.

El Halabi M, Aponte-Rolón VS, Corradini GM, Kuo B, et al.

Irritable Bowel Syndrome (IBS)

14. GLP-1 Agonist Use Is Linked to Symptom Improvement in Patients with IBS-D and Obesity: A National Database Study

Background and Objectives:

- Approximately 30% of patients with irritable bowel syndrome (IBS) are overweight or obese. GLP-1 receptor agonists (GLP-1 RAs), used for diabetes and obesity, have shown potential in easing IBS symptoms like pain and stress-related defecation. This study aimed to assess outcomes in patients with IBS-D and obesity using GLP-1 RAs.

Methods:

- A retrospective cohort study using TriNetX data (2015–2024) assessed adults with obesity (BMI ≥30) and IBS-D who received GLP-1 receptor agonists. Patients were matched 1:1 with non-users by age, demographics, comorbidities, and medications. Outcomes included GI symptoms, Gastroesophageal Reflux Disease (GERD), mental health conditions, and female pelvic disorders. Odds ratios were calculated using logistic regression.

Results:

- Among 8,736 IBS-D patients with obesity, 929 used GLP-1 receptor agonists. After matching, GLP-1 RA users showed significantly lower odds of GERD, abdominal pain, bloating, nausea, diarrhea, depression, anxiety, and chronic fatigue syndrome compared to non-users. No differences were seen in fecal urgency, pelvic disorders, or fibromyalgia.

Conclusions:

- **GLP-1 RA use in IBS-D with obesity is linked to fewer GI and mental health symptoms, with no change in pelvic disorder rates.**

Nieto LM, Narvaez S, Villa N, Kim DH, et al.

15. DOMINO Diet Application Significantly Improves Symptoms in Tertiary Care IBS Patients

Background and Objectives:

- The low FODMAP - Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols (FODMAP)diet helps manage IBS symptoms but is complex and restrictive. A simplified self-guided approach using the DOMINO app showed positive results in primary care, but its effect in tertiary care is unknown. Aim was to assess the effectiveness of the DOMINO app in improving IBS symptoms, nutrition, and mental health in tertiary care patients.

Methods:

- IBS patients followed the DOMINO diet for 8 weeks using an app after a two-week baseline. symptom diary, including the Bristol stool scale (BSS), was filled out daily. Questionnaires to assess IBS symptom severity (IBS-SSS) and psychosomatic comorbidities (PHQ and GAD-7) were completed at baseline and after the diet. Seven-day food diaries were collected during regular food intake and during the diet period. Data are reported as meanÂ±SD or median(IQR).

Results:

- Data from 40 IBS patients on the DOMINO diet app showed an 80% overall response rate (≥50-point IBS-SSS improvement). IBS severity scores significantly decreased. Abdominal pain, bloating, flatulence, and life impact all improved, though stool frequency remained stable. Soft stools and urgency episodes decreased, while normal stool consistency increased. Nutrient intake and body weight remained unchanged. FODMAP intake dropped significantly, particularly sorbitol, fructans, and galacto-oligosaccharides. Psychological symptoms also improved, including reductions in extra-intestinal symptoms, depression, and anxiety.

Conclusions:

- **The DOMINO diet app is a safe, effective, and user-friendly dietary tool for managing IBS in tertiary care, offering symptom relief without affecting nutrition.**

Routhiaux K, Waegemans L, Schaar L, Warnant M, et al.

GERD and Acid-Related Disorders

16. Erythromycin and the Clock: Timing Erythromycin for Better Endoscopy Results in Upper GI Bleeding

Background and Objectives:

- Erythromycin, a motilin receptor agonist, improves gastric emptying and mucosal visibility during endoscopy. Despite its benefits, it is not routinely used before procedures. This study evaluated the timing of erythromycin administration and its effect on endoscopic outcomes in upper gastrointestinal bleeding.

Methods:

- A total of 110 patients undergoing endoscopy for upper GI bleeding were evaluated. 63 received erythromycin, with comparisons made between those given the drug two hours before the procedure versus less than two hours. Key outcomes included mucosal visibility, need for repeat endoscopy, procedure duration, and hospital stay.This analysis helped assess the impact of erythromycin timing on endoscopic visibility and patient recover.

Results:

- In this study of 63 patients with upper GI bleeding, those given erythromycin two hours before endoscopy had better mucosal visibility, fewer repeat procedures, shorter hospital stays (3 vs. 7 days), and reduced procedure time (25 vs. 37 minutes), highlighting the benefit of earlier erythromycin administration.

Conclusions:

- **Administering erythromycin two hours before endoscopy significantly improves procedural quality and patient recovery in upper GI bleeding, supporting its inclusion in pre-endoscopy protocols.**

Rammohan R, Magam SR, Patel A, Natt D, et al.

17. GERD Treatment Biases Across GI and Surgical Guidelines

Background and Objectives:

- Gastroesophageal Reflux Disease (GERD) is a common gastrointestinal disorder. Management guidelines differ between Gastroenterology and Surgical societies, potentially impacting patient care.

Methods:

- This study analyzed guidelines from the American College of Gastroenterology (ACG), American Gastroenterological Association (AGA), and Surgical Multi-Society/American Society for Gastrointestinal Endoscopy (ASGE). Key comparisons included Proton Pump Inhibitor (PPI) duration, criteria for escalation, surgical indications, and refractory GERD management.

Results:

- ACG and AGA recommend up to 8 weeks of empiric PPI therapy before further steps (Figure below).
- Surgical guidelines do not specify PPI duration and favor early Anti-Reflux Surgery (ARS) over long-term
- PPI use for refractory GERD. Most recommendations aligned with the authors' specialties.

Figure: Guideline Comparison: PPI Use and Severe Esophagitis Treatment

	ACG	AGA	Multi-Society Consensu
Recommended length of PPI trial in patients without alarm features	8 weeks (strong recommendation, moderate level of evidence)	4-8 weeks (best practice advice)	No recommendation on PPI length
Treatment of LA C or D esophagitis	Maintenance PPI therapy indefinitely or anti-reflux surgery (Strong recommendation, moderate level of evidence)	Indefinite long-term PPI therapy and/or an invasive anti-reflux procedure (best practice advice)	MSA is superior to continued PPI use (conditional recommendation, moderate certainty evidence)

Abbrevations: ACG – **MSA** – Magnetic Sphincter Augmentation, **PPI** – Proton Pump Inhibitor, **LA C or D esophagitis** – Los Angeles Classification Grade C or D Esophagitis

Conclusions:

There are clear specialty-driven differences in GERD management. Collaborative, multidisciplinary guidelines could reduce bias and improve consistency in clinical decision-making.

Jafri FI, Ahuja R, Saleem F, Buckley FP, et al.

18. Pharmacogenetic Testing To Optimize PPI Therapy: A Quality Improvement Study At Phoenix VA

Background and Objectives:

- Gastroesophageal reflux disease (GERD) often shows poor response to standard proton pump inhibitor (PPI) therapy in ~50% of patients. Since most PPIs are metabolized by the liver enzyme CYP2C19, individuals with rapid/ultrarapid metabolizer genotypes (CYP2C19*17) may need higher doses. This quality improvement (QI) project at the Phoenix VA Medical Center evaluated the role of pharmacogenetic (PGx) testing in guiding PPI dose adjustments for better symptom control.

Methods:

- From November 2020 to June 2024, 156 patients with GERD or related conditions underwent PPI PGx testing via Sanford Health. CYP2C19 genotypes were reviewed, and patients with rapid/ultrarapid metabolism were followed by a GI pharmacist for PPI dose adjustment (often increased to 80 mg twice daily). Symptom response was assessed retrospectively.

Results:

- **47/156 patients (30.1%)** had rapid/ultrarapid metabolizers (RM/UM) CYP2C19 genotypes.
- 41 completed follow-up after PPI dose increase.

Response rates:

- ✓ Good: 80.5% (33 patients)
- ✓ Partial: 4.9% (2 patients)
- ✓ Poor: 14.6% (6 patients)

Conclusions:

- **PGx-guided PPI dosing led to symptomatic improvement in most GERD patients. Routine PGx testing at the Phoenix VA may enhance personalized care and treatment success in refractory GERD.**

Ma SD, Li XJ, Powell A, Kupferer K, et al.

19. Reducing Inappropriate Proton Pump Inhibitor (PPI) Use in the Intensive Care Unit (ICU): A Quality Improvement (QI) Initiative

Background and Objectives:

Proton Pump Inhibitors (PPIs) are used in the Intensive Care Unit (ICU) to prevent stress-related gastrointestinal (GI) bleeding. However, overuse can lead to unnecessary risks. This Quality Improvement (QI) project aimed to reduce inappropriate PPI use based on Society of Critical Care Medicine (SCCM) and American Society of Health-System Pharmacists (ASHP) guidelines.

Methods:

Using the Plan–Do–Study–Act (PDSA) model, a quality improvement initiative was implemented. Pre-intervention data from March 2024 included 139 ICU patients. Variables assessed included demographics, PPI indications, and ICU stay duration. A presentation on SCCM guidelines was delivered to the ICU team, and pocket cards summarizing appropriate PPI use were distributed to critical care physicians and computer stations. Post-intervention data from August 2024 included 141 ICU patients, with 13 excluded for hospitalist care. The same variables were analyzed through daily chart reviews.

Results:

A total of 280 patients were evaluated—139 before and 141 after the intervention. Prior to the intervention, PPI overuse in the ICU was observed in 23.08% of cases based on guideline criteria. Following the clinical education initiative, inappropriate PPI use decreased by 30%, reducing the overuse rate to 15.08%.

Conclusions:

- **Targeted clinical education significantly improved appropriate PPI prescribing in ICU settings, enhancing adherence to best-practice guidelines.**

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20. Continuous IV PPI Therapy Improves Outcomes In Critically Ill Patients With Upper GI Bleed

Background and Objectives:

- Upper GI bleeding (UGIB) causes significant ICU burden. PPI therapy is essential, but the impact of continuous vs intermittent IV administration in ICU settings is unclear.

Methods:

- A retrospective cohort study using the Medical Information Mart for Intensive Care IV (MIMIC-IV) database analyzed Intensive Care Unit (ICU) patients with Upper Gastrointestinal Bleeding (UGIB) who received either continuous or intermittent intravenous (IV) Proton Pump Inhibitor (PPI) therapy. Outcomes assessed included mortality and ICU Length of Stay (LOS).

Results:

- After matching, the continuous IV PPI group had lower mortality (15.66% vs 22.29%) and shorter ICU LOS (1.96 vs 3.41 days). Multivariate analysis showed reduced mortality risk (HR 0.57, $p < 0.0001$). Kaplan-Meier curves confirmed better 100-day survival with continuous PPI therapy.

Conclusions:

- **In ICU patients with severe upper GI bleeding, continuous IV PPI therapy led to better outcomes-lower mortality, shorter ICU stay, and improved survival-compared to intermittent dosing.**

Patel AH, Bussetty A, Shen J, Chen C, et al.

21. Factors Driving Long-Term Proton Pump Inhibitor Use, Associated Clinical Outcomes, and Healthcare Cost Impact

Background and Objectives:

- Proton Pump Inhibitor (PPIs) are commonly used for acid-related conditions, but long-term use may lead to adverse effects and increased healthcare costs. Identifying contributing factors and outcomes is crucial.

Methods:

- A retrospective National Institutes of Health (NIH) database study (2010–2020) analyzed adults on PPI therapy. Key variables included age, comorbidities, therapy duration, adverse outcomes, and healthcare costs. Logistic regression identified predictors.

Results:

- Among 1 million patients, 25% used PPIs long-term (≥1 year). Predictors included age ≥65 (OR 1.5), Gastroesophageal Reflux Disease (GERD) (OR 2.0), and Nonsteroidal Anti-Inflammatory Drug (NSAID) use (OR 1.3). Long-term users had more hip fractures (3% vs 1%) and C. difficile infections (2% vs 0.5%). Annual costs were 43% higher in long-term users ($10,000 vs $7,000).

Conclusions:

- **Extended PPI use is associated with adverse health and economic outcomes. Regular review of therapy necessity is recommended to reduce risks and costs.**

Aregbesola E, Oshobu I, Elendu C, Omeludike EK, et al.

22. Simethicone With Polyethylene Glycol Improves Bowel Prep Quality: A Meta-Analysis

Background and Objectives:

Simethicone is an anti-foaming agent used during endoscopy to reduce bubbles. This meta-analysis evaluated whether adding simethicone to Polyethylene Glycol (PEG)-based bowel prep improves bowel cleansing, measured by the Boston Bowel Preparation Score (BBPS).

Methods:

These compared PEG-based regimens with and without simethicone. Effect sizes were calculated using a random-effects model.

Results:

Simethicone significantly improved BBPS scores (mean effect size: 0.266; p = 0.004). Subgroup analysis showed benefits in both oral sulfate tablet (OST) and PEG regimens, with effect sizes of 0.161 and 0.286, respectively.

Conclusions:

- **Simethicone modestly but significantly enhances bowel prep quality in both OST and PEG regimens.**

Nageswaran GA, Nagesh VK, Abosheaishaa H, Rego RF.

23. Obesity and Esophageal Clearance Impairment: Insights from PSPW Index

Background and Objectives:

Obesity is linked to GERD, but its impact on specific reflux mechanisms is unclear. The Post-reflux Swallow-induced Peristaltic Wave (PSPW) index, measured via impedance-pH monitoring, reflects esophageal chemical clearance. This study evaluated the association between BMI and PSPW index in patients with reflux symptoms.

Methods:

A retrospective study of 273 adults who underwent high-resolution impedance manometry (HRiM) and impedance-pH monitoring off PPI therapy. Patients were grouped by BMI: normal (<25), overweight (25–30), and obese (>30). Statistical analyses included Spearman's correlation and multivariable regression adjusting for confounders.

Results:

- Higher BMI correlated with lower PSPW index and increased acid exposure time (AET), reflux episodes, and symptom intensity. On multivariable analysis, obesity was independently associated with a reduced PSPW index (β = -0.085, p = 0.021), indicating impaired esophageal chemical clearance.

Conclusions:

- **Obesity is independently linked to impaired esophageal chemical clearance, as shown by reduced PSPW index. This may explain increased reflux burden in obese patients and highlights the value of esophageal function testing for personalized GERD management.**

Smith N, Algara M, Nadella P, Fernandez AM, et al.

24. Exploring the Link Between Gastroesophageal Reflux Disease and Chronic Kidney Disease: A Meta-Analysis of Over 4 Million Patients

Background and Objectives:

- Gastroesophageal reflux disease (GERD) affects around 20% of adults in Western countries and is linked to serious complications like Barrett's esophagus and esophageal cancer. Emerging evidence suggests a higher incidence of GERD in patients with chronic kidney disease (CKD), which affects about 10% of the global population. CKD-related factors such as inflammation, uremic toxins, and impaired GI motility may contribute, though the exact mechanisms remain unclear. Study aims to perform a systematic review and meta-analysis evaluating the prevalence of GERD in CKD patients and the strength of their association.

Methods:

- A comprehensive search was conducted across major databases up to November 2024 for studies reporting GERD prevalence or its association with CKD. Two independent reviewers extracted data; discrepancies were resolved by a third.

Results:

- 9 studies with 4.65 million participants (55.6% female) were included. The pooled odds ratio (OR) for GERD in CKD was 1.98, and pooled prevalence was 18%. GERD prevalence was higher in U.S. studies (23.5%) versus Asian studies (14.6%). Advanced CKD stages, particularly ESRD, showed higher GERD rates (up to 28%).

Conclusions:

- **GERD is significantly more common in CKD patients, with nearly 1 in 5 affected. This underexplored link highlights the need for further research into shared mechanisms and tailored management strategies to improve care in this high-risk group.**

Chaponan-Lavalle A, Godoy A, Estrada-Grossman JM, Alarcon-Braga EA,et.al

25. Fexuprazan vs Esomeprazole for Nocturnal Acid Breakthrough: A Comparative Study

Background and Objectives:

- Nocturnal acid breakthrough (NAB) in GERD reduces quality of life. Proton pump inhibitors (PPIs) often fail to fully control NAB. This study compares the efficacy of fexuprazan, a potassium-competitive acid blocker, with esomeprazole in managing NAB.

Methods:

- A prospective crossover study was conducted in 39 patients. Each received fexuprazan 40 mg or esomeprazole 40 mg for 4 weeks, followed by a 4-week on-demand period, then crossed over to the alternate drug. NAB severity Visual Analogue Scale ((VAS), frequency, and sleep disturbances were assessed.

Results:

- Fexuprazan reduced NAB severity by 81.3% vs. 63.5% with esomeprazole ($p = 0.019$). Frequency and sleep disturbance also improved more with fexuprazan, though not significantly. During on-demand periods, symptoms remained improved. After crossover, fexuprazan showed greater NAB severity reduction (87.2% vs. 52.5%, $p = 0.001$).

Conclusions:

Fexuprazan is more effective than esomeprazole in controlling NAB severity and may offer better symptom relief in GERD patients with NAB.

Oh DJ, Lim YJ.

26. Tegoprazan Offers Early Symptom Relief and QoL Gains in Mexican GERD Patients: Interim Results from TOP-GERD Study

Background and Objectives:

- Tegoprazan, a potassium-competitive acid blocker, has shown superior efficacy over PPIs in Asian populations. Its effectiveness in non-Asian populations, particularly in terms of rapid symptom relief and quality-of-life (QoL) improvement, remains underexplored. Aim is To compare the efficacy of tegoprazan 50 mg vs. pantoprazole 40 mg in symptom control, QoL, and healing in Mexican GERD patients over 4 weeks.

Methods:

- In this randomized, double-blind trial, 37 Mexican GERD patients (29 erosive, 8 NERD) received either tegoprazan or pantoprazole daily. GERD-Q and GERD-HRQL assessed symptom severity and QoL at days 7, 14, and 28. Endoscopic healing was evaluated at day 28.

Results:

- Tegoprazan showed faster symptom relief: by day 1, significantly more patients were symptom-free ($p<0.01$). By day 7, 63% of tegoprazan patients were asymptomatic vs. 21% with pantoprazole ($p<0.01$). QoL

improved more in the tegoprazan group (21.38 vs. 13 points, p=0.04). Healing rates were higher at week 4 (90.9% vs. 72.7%, p=0.027).

Conclusions:

- **Tegoprazan delivers faster and more effective symptom relief, better QoL outcomes, and higher healing rates than pantoprazole in Mexican GERD patients.**

Remes-Troche JM, Valdovinos-Garcia LR, Valdovinos MA, Vargas Basurto JL, et al.

27. Impact of New GERD Guidelines on Primary Care Prescriptions and Engagement with Point-of-Care Alerts

Background and Objectives:

- In March 2023, Germany updated its GERD guidelines, recommending limiting PPI use to 4–8 weeks unless long-term indications exist. Study helps to evaluate the impact of the new guidelines and point-of-prescription educational alerts on PPI prescribing in primary care.

Methods:

- A 12-month real-world study involving 2,400 German primary care practices used Clinical Decision Support System (CDSS) alerts based on International Classification of Diseases (ICD) codes and prior Proton Pump Inhibitor (PPI) use. Provider engagement (measured by click rates) and changes in prescribing patterns were evaluated for patients with Uncomplicated Reflux (UR), diagnosed Gastroesophageal Reflux Disease (dGERD), and Non-Erosive Reflux Disease (NERD).

Results:

- In 2023, 31,629 Clinical Decision Support System (CDSS) messages were triggered for an average of 867 General Practitioners (GPs). CDSS alerts had minimal impact on Proton Pump Inhibitor (PPI) prescribing, with 99.5% of prescriptions exceeding the recommended 8-week duration. For diagnosed Gastroesophageal Reflux Disease (dGERD), Non-Erosive Reflux Disease (dNERD), and Uncomplicated Reflux (UR), 100% of prescriptions surpassed 8 weeks. Among GPs alerted for dGERD, 47 more prescribed PPIs without an indicated diagnosis (95% CI: 19.7–74.3; P<0.0017), and for UR, 15 more did so (95% CI: 9.7–20.1; P<0.001).

Conclusions:

- **CDSS alerts had minimal impact on prescribing behavior, underscoring poor guideline adoption and coding practices.**

De Grey-Warter F, Horvath E, Aluko P, Wray J, et al.

28. Comparative Safety and Effectiveness of Proton Pump Inhibitors on Cardiovascular Outcomes in Clopidogrel-Treated Patients: A Multinational Retrospective Cohort Study

Background and Objectives:

- PPIs may interfere with clopidogrel's antiplatelet effect, potentially increasing cardiovascular risk. This study compared cardiovascular outcomes between strong (omeprazole, esomeprazole) and weak CYP2C19-inhibiting PPIs in clopidogrel users.

Methods:

- A multinational, retrospective cohort study using Observational Medical Outcomes Partnership–Common Data Model (OMOP-CDM)databases from the U.S., South Korea, and Taiwan (1985–2023). Adults on clopidogrel + PPI were matched 1:1 via propensity scores. The primary outcome was major adverse cardiovascular events(MACE)within 1year. Cox models and random-effects meta-analysis were used.

Results:

- Among 166,005 matched pairs, MACE occurred in 2,822(strong inhibitors)vs. 2,696(weak inhibitors); HR: 1.00(95% CI: 0.79–1.26). No significant differences in secondary outcomes: CV mortality(HR: 1.10), MI(HR: 0.98), stroke(HR: 1.05), all-cause mortality(HR: 1.18).

Conclusions:

- **This large-scale OMOP-CDM study found no clinically significant interaction between clopidogrel and strongly competitive proton pump inhibitors.**

Seo SI, Kim S, Park J, You SC, et al.

Liver and Metabolic Disorders (MASLD, MASH, Cirrhosis, etc.)

29. Non-Invasive Tests: A Cost-Effective Strategy to Detect Hepatocellular Carcinoma Early

Background and Objectives:

- Fibrosis-4 Index (FIB-4) and vibration-controlled transient elastography (VCTE) are non-invasive tests (NITs) used to identify metabolic dysfunction-associated steatotic liver disease (MASLD) patients at risk for hepatocellular carcinoma(HCC).
- This study assessed their cost-effectiveness in guiding HCC surveillance.

Methods:

- A Markov model compared no testing with three non-invasive test (NIT) strategies—FIB-4/VCTE, FIB-4 alone, and VCTE alone—to identify advanced fibrosis and guide HCC surveillance in four MASLD populations. The analysis, conducted in both Thailand and the US, showed that using NITs improved early HCC detection and patient outcomes. Cost-effectiveness was assessed using Incremental cost-effectiveness ratio (ICER) and deemed acceptable at $4,665/QALY in Thailand and $50,000/QALY in the US.

Results:

- In both Thailand and the US, FIB-4/VCTE was the most cost-effective strategy across all MASLD groups, showing the lowest ICER.
- In Thailand, it was the only cost-effective option for general MASLD and those with BMI >30, while FIB-4 alone was also cost-effective in patients with diabetes or 3 metabolic traits. VCTE alone was not cost-effective in any Thai group.
- In the US, both FIB-4/VCTE and FIB-4 alone were cost-effective for all MASLD populations, with VCTE alone only cost-effective in high-risk subgroups. Sensitivity analysis in Thailand showed FIB-4/VCTE remained cost-effective if HCC incidence exceeded 0.01% and test specificity stayed above 69% (FIB-4) and 89% (VCTE).
- In the US, results were stable across sensitivity ranges. Probabilistic analysis confirmed FIB-4/VCTE as the most likely cost-effective strategy at the defined thresholds.

Conclusions:

FIB-4 with VCTE is a cost-effective way to start HCC surveillance in MASLD patients. If VCTE is unavailable, FIB-4 alone is a suitable alternative for those with diabetes or multiple metabolic risks.

Decharatanachart P, Poovorawan K, Tangkijvanich P, Charatcharoenwitthaya P, et al.

30. Metabolic Overlap: The Influence of MASLD on GERD Outcomes

Background and Objectives:

- Metabolic dysfunction-associated steatotic liver disease (MASLD) is a known risk factor for gastroesophageal reflux disease (GERD), but its link to GERD-related complications remains unclear.

Methods:

- Using the 2016–2020 National Inpatient Sample, the study analyzed adult GERD patients with and without MASLD. Outcomes included esophagitis, esophageal stricture, Barrett's esophagus, and esophageal cancer. Multivariable regression adjusted for demographics, metabolic and substance use factors.

Results:

- Among 27.2 million GERD patients, 956,640 had MASLD. MASLD was associated with higher rates of esophagitis (4.7% vs 3.2%), esophageal strictures (0.8% vs 0.7%), and Barrett's esophagus (1.7% vs 1.2%), all $p<0.001$. Adjusted odds confirmed significant associations, except for esophageal cancer (aOR 0.97, $p=0.44$).

Conclusions:

- **This study shows that MASLD patients have a higher risk of GERD complications, independent of other risk factors. This may be due to inflammation from fat-induced liver injury, which can reduce lower esophageal sphincter (LES) tone and increase susceptibility to esophagitis, strictures, and Barrett's esophagus.**

Patel A, Sandhu D, Sohal A, Kumar V,et.al

31. Risk of De Novo Obesity-Related Cancers in Patients with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Background and Objectives:

- Obesity, MASLD, and MASH are associated with increased cancer risk. Weight loss interventions, including GLP-1 agonists and bariatric surgery, may reduce this risk. This study compared the incidence of obesity-related cancers in patients treated with GLP-1 agonists versus bariatric surgery.

Methods:

- A global retrospective cohort study using the TriNetX database identified adults with BMI ≥30kg/m^2, type 2 diabetes, and MASLD/MASH. Patients on GLP-1 agonists were 1:1 matched to those who underwent bariatric surgery. Prior cancer cases were excluded. New cancer incidence was assessed from one year post-treatment, with follow-up up to 10 years.

Results:

- A total of 1,498 patients were included in each matched group. Over 10 years, the cumulative incidence of de novo obesity-related cancers was 3.2% (48 patients) in the bariatric surgery group and 4.0% (60 patients) in the GLP-1 group (HR 0.696, 95% CI 0.476–1.019; p=0.061). Rates of specific cancers—breast, ovarian, colorectal, endometrial, and thyroid—were similar between groups.

Conclusions:

- **GLP-1 agonists may offer a comparable reduction in obesity-related cancer risk to bariatric surgery. These findings suggest that both treatments, through their ability to achieve weight loss and metabolic improvement, may mitigate the cancer-promoting effects of obesity.**

Naseem Z, Aitharaju V, Muhammad A, Chatterjee A.,et.al

32. Link Between Wrist Circumference and MASLD in KADEM Cohort

Background and Objectives:

- Metabolic dysfunction-associated fatty liver disease (MAFLD) is linked to metabolic risk and cardiovascular disease. This study assessed wrist circumference as a non-invasive marker for MAFLD in the Kuwait Adult Diabetes and Epidemiological Multidisciplinary (KADEM) program.

Methods:

- This study included 449 participants, with MAFLD assessment performed using FibroScan®. Routine clinical blood tests, along with measurements of Body Mass Index and wrist circumference, were also conducted. The Controlled Attenuation Parameter (CAP) score was used to stage MAFLD, categorizing participants into four groups: normal (<238 dB/m), S1 (238–260 dB/m), S2 (261–290 dB/m), and S3 (>290 dB/m).

Results:

- In a cohort of 449 participants, MAFLD severity based on CAP score was linked to increasing wrist circumference: 16 cm (normal), 17cm (S1/S2), and 17.2cm (S3) ($p<0.001$). Wrist circumference correlated with MAFLD ($r=0.328$, $p<0.001$) and was positively associated with Triglycerides (TG), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), and negatively associated with High-Density Lipoprotein (HDL) levels. ($p<0.05$). Gender, wrist circumference, ALT, and TG were significant predictors of high CAP scores. A logistic regression model using these factors correctly identified 76.3% of high CAP cases, with 69.4% sensitivity and 73.4% specificity.

Conclusions:

- **Wrist circumference is a simple and safe, non-invasive marker that may help identify individuals at high risk for MAFLD in outpatient settings.**

Shehab M, Ali Z, AL-Enezi A, Alturki M, et al.

33. Vitamin D Deficiency in Patients with Cirrhosis: Prevalence and Insights

Background and Objectives:

- Vitamin D is essential for bone health and immune regulation. Cirrhotic patients are at high risk for deficiency. This study aimed to determine the prevalence of vitamin D deficiency and its association with cirrhosis severity.

Methods:

- A descriptive, cross-sectional study was conducted in cirrhotic patients by measuring 25-OH vitamin D levels. Patients were classified into compensated (no ascites, GI bleeding, or encephalopathy) and decompensated (presence of any of these). Vitamin D deficiency was defined as <20 ng/mL, insufficiency as 21–30 ng/mL, and optimal levels as 30–100 ng/mL.

Results:

- Among 64 cirrhotic patients, 39 had compensated and 25 had decompensated cirrhosis. Overall, 67.2% had vitamin D deficiency and 23.4% had insufficiency. In the compensated group, 51.3% were deficient and 35.9% insufficient. In the decompensated group, 92% had deficiency and only 4% had insufficiency or sufficiency (p=0.0029).

Conclusions:

- **This study found a high prevalence of Vitamin D deficiency and insufficiency among cirrhotic patients, with deficiency significantly more common in those with decompensated cirrhosis. It was also associated with higher Child-Pugh and MELD-Na scores.**
- **However, Vitamin D levels were less effective than these scores in predicting decompensation. As the first study of its kind, findings highlight the potential importance of early Vitamin D assessment and intervention to help prevent adverse outcomes in cirrhotic patients.**

Pacheco J, Melendez N, Sanchez A, Chocó-Cedillos A, et al.

34. Antioxidant Levels and Their Association with NAFLD, MAFLD, MASLD, and Fibrosis

Objectives:

- This study evaluated the association of antioxidant vitamins (A, C, D, E) and carotenoids with NAFLD, MAFLD, MASLD, and liver fibrosis using U.S. NHANES 2017–2018 data.

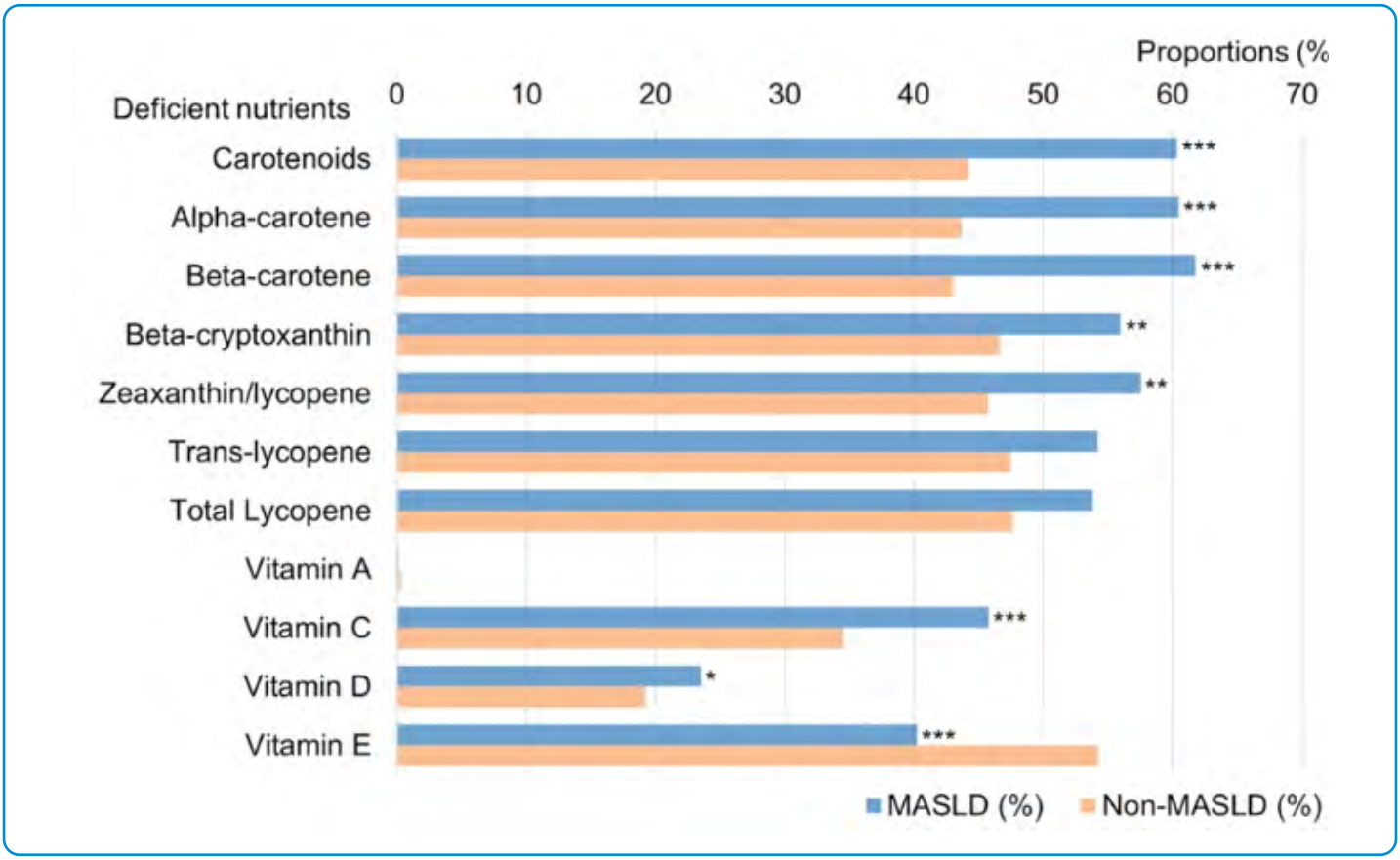
Methods:

- Hepatic steatosis and fibrosis were assessed using transient elastography. Logistic regression and spline models analyzedcorrelations between serum antioxidant levels and liver disease.

Results:

- Higher levels of total carotenoids, α-carotene, β-carotene, and 25-hydroxyvitamin D were inversely associated with NAFLD, MAFLD, MASLD, and significant fibrosis (Figure below). Vitamin E showed a positive correlation with MASLD at lower steatosis thresholds. Vitamin A was linked to higher MASLD risk in underweight individuals.

Figure: The comparison of nutrient deficiency proportions between patients with MASLD and those without MASLD ***p <0.01. *p <0.05



Conclusions:

Serum carotenoids and vitamin D appear protective against fatty liver disease and fibrosis. Antioxidant vitamin associations with MASLD vary by type and patient subgroup.

Tuo X, Deng J, Zhang P, Shi A, et al.

35. Gut Microbiota Predicts Empagliflozin Response in Non-Diabetic MASLD Patients

Background and Objectives:

- Empagliflozin reduces liver fat in non-diabetic MASLD patients. This study evaluated if baseline gut microbiota can predict treatment response.

Methods:

- 45 non-diabetic MASLD patients received empagliflozin 10 mg daily for 52 weeks. Response was defined as ≥30% reduction in Magnetic Resonance Imaging–Proton Density Fat Fraction (MRI-PDFF). Baseline stool samples were analyzed using shotgun metagenomics.

Results:

- In a cohort of 45 MASLD patients, 48.9% showed treatment response at end of treatment (EOT).
- Baseline gut microbiome diversity differed between responders and non-responders.
- Three bacterial species-*Lachnospira pectinoschiza, Anaerostipes hadrus, and Agathobaculum butyriciproducens*-were significantly enriched in responders and independently associated with treatment response (aORs: 22.3–35.0).
- Combined, these species distinguished responders with an AUROC of 0.89. *A. hadrus and A. butyriciproducens* correlated with pathways involved in beneficial metabolite production, though their relative abundance remained unchanged at EOT.

Conclusions:

Baseline gut microbiota composition, particularly *A. hadrus, L. pectinoschiza,* and *A. butyriciproducens,* may predict empagliflozin response in MASLD patients without diabetes.

Cheung KS, Ng HY, Zhang L, Tan JT, et al.

36. GLP-1 Receptor Agonists and Risk of Alcohol-Related Cirrhosis in T2DM with Alcohol Use Disorder.

Background and Objectives:

- GLP-1 receptor agonists (GLP1-RAs) may reduce alcohol cravings and liver inflammation. This study assessed whether GLP1-RAs lower the risk of alcohol-associated cirrhosis (AC) and hepatic decompensation in patients with type 2 diabetes mellitus (T2DM) and alcohol use disorder (AUD).

Methods:

- This study analyzed patients with Alcohol Use Disorder (AUD) and Type 2 Diabetes Mellitus (T2DM) from the TriNetX database. Outcomes were compared between GLP-1 receptor agonist (GLP1-RA) users and those on metformin, DPP-4 inhibitors, SGLT-2 inhibitors, sulfonylureas, or thiazolidinediones (TZDs). A total of 2,912 patients were matched in the GLP-1RA vs. insulin group, 2,922 in the GLP-1RA vs. metformin group, 4,070 in the GLP-1RA vs. DPP-4 inhibitor group, 3,251 in the GLP-1RA vs. SGLT-2 inhibitor group, 4,127 in the GLP-1RA vs. sulfonylurea group, and 1,456 in the GLP-1RA vs. TZD group.

- AC and its complications (ascites, encephalopathy, peritonitis, varices, and hepatocellular carcinoma [HCC]) were assessed using ICD-10 codes. A propensity score model adjusted for demographics, comorbidities, BMI, HbA1c, liver enzymes, and AUD treatments. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.

Results:

- The odds of acute-on-chronic liver disease (AC) were significantly lower in the GLP-1RA group compared to SGLT-2 inhibitors and DPP-4 inhibitors, with no significant difference compared to insulin or metformin.
- For hepatic decompensation, GLP-1RA use was associated with lower odds compared to insulin (OR=0.46; 95% CI: 0.28–0.78), SGLT-2 inhibitors , and DPP-4 inhibitors.

Conclusions:

- **GLP1-RAs may reduce the risk of alcohol-associated cirrhosis and decompensation in patients with T2DM and AUD.**

Hwang SY, Hsieh P, Schaefer E, Luther J, et al.

37. Clinical Outcomes in Patients with Metabolic Dysfunction–Associated and Alcohol-Related Liver Disease Compared to Alcohol-Associated Liver Disease Undergoing Liver Transplant Evaluation

Background and Objectives:

- Metabolic dysfunction and alcohol-related liver disease (MetALD) combines alcohol use with metabolic risk. This study compared liver transplant (LT) outcomes, survival, and recompensation in MetALD vs. alcohol-associated liver disease (ALD) patients.

Methods:

- In this retrospective cohort (Oct 2021–Aug 2023), 158 patients referred for LT at Baylor College of Medicine were evaluated. Clinical outcomes, Model for End-Stage Liver Disease–Sodium (MELD-Na) scores, and recompensation (MELD <15 without complications) were assessed at multiple time points.

Results:

- In this study of 158 patients were listed for LT, 48 (30.8%) underwent LT, and 46 (29.5%) died post-evaluation. Compared to ALD, MetALD patients had higher BMI (31 vs. 24.3, p=0.001) and more CKD (24.0% vs. 9.1%, p=0.023). Transplantation was more frequent in MetALD at 6 months. Time to listing was shorter in MetALD (56.9 vs. 66.8 days, p=0.054). MELD-Na was higher in MetALD at 12 months . Recompensation rates were significantly lower in MetALD at 6 months (2.3% vs. 28%,) and 12 months (15.0% vs. 76.2%).

Conclusions:

- **MetALD patients had worse pre-transplant outcomes and lower recompensation rates compared to ALD, despite similar transplant listing rates.**

Ibrahim MA, Ramadan N, Mohamed IB, Ankoma-Sey C, et al.

38. SGLT-2 Inhibitors in Alcoholic Cirrhosis with T2DM: A Multinational Survival Analysis

Background and Objectives:

- Alcoholic liver disease (ALD) can progress to cirrhosis. SGLT-2 inhibitors have shown liver and cardiovascular benefits in MASLD with T2DM, but their role in alcoholic cirrhosis is unclear. This study evaluated their impact on mortality and clinical outcomes in patients with alcoholic cirrhosis and T2DM.

Methods:

- A retrospective cohort study using TriNetX data identified adults with alcoholic cirrhosis and T2DM. Patients prescribed SGLT-2 inhibitors were matched 1:1 with non-users using propensity scores. Outcomes assessed: all-cause mortality, hepatic decompensation, Hepatocellular Carcinoma (HCC), Acute Kidney Injury (AKI), Chronic Kidney Disease (CKD), and Major Adverse Cardiovascular Events (MACE).

Results:

- In this study, 793 patients with alcoholic cirrhosis and type 2 diabetes mellitus who were taking SGLT-2 inhibitors were matched with 793 similar patients not on SGLT-2 inhibitors. The SGLT-2 group had a significantly lower risk of all-cause mortality (HR 0.52; 95% CI: 0.41–0.66). For other outcomes—including hepatocellular carcinoma (HCC), hepatic decompensation, acute kidney injury, chronic kidney disease, and major adverse cardiovascular events (MACE)—no statistically significant differences were observed between the two groups.

Conclusions:

- **SGLT-2 inhibitors were linked to reduced mortality in patients with alcoholic cirrhosis and T2DM, although no significant differences were noted in liver or cardiovascular events. These findings support their potential as adjunctive therapy in this population.**

Kim DH, Ko D, Porres JA, Basegoda WS, et al.

39. GLP-1 RAs Reverse the Adverse Impact of Body Weight Variability on Cardiovascular Outcomes Across Diverse Metabolic Profiles

Background and Objectives:

- BMI variability is associated with increased cardiovascular (CVD) risk. This study assessed whether GLP-1 receptor agonists (GLP-1 RAs) can counteract this effect in patients with T2DM, obesity, and MASLD.

Methods:

- Study analyzed adults from the All of Us database (2016–2022) who used GLP-1 RAs for ≥3 months. BMI variability was measured using the Coefficient of Variation and categorized into quartiles. CVD outcomes (stroke/MI) were assessed using multivariable Cox models, adjusting for demographics, comorbidities, and medications. Subgroup analyses included T2DM, obesity, and MASLD populations.

Results:

- In a cohort of 4,524 patients, higher BMI variability was linked to reduced CVD risk among GLP-1RA users. Compared to Quartile 1, Quartiles 2–4 showed significantly lower adjusted hazard ratios (Q2: 0.31, Q3: 0.42, Q4: 0.33; all $p<0.05$). In T2DM patients, Quartile 4 had aHR=0.31 ($p=0.006$), while in obese patients, it was even stronger (aHR=0.28, $p<0.001$). No significant association was found in MASLD patients.

Conclusions:

- **GLP-1 RAs reverse the harmful impact of BMI variability on cardiovascular outcomes, particularly in patients with T2DM and obesity, highlighting their role in long-term metabolic and cardiovascular management.**

Boateng S, Issaka Y, Njei B.

40. Retrospective Study of Vitamin and Trace Element Deficiencies in Advanced Liver Disease at Veterans Affairs (VA) Center

Background and Objectives:

- Vitamin and trace element deficiencies are common in cirrhosis and linked to worse outcomes. As per 2021 AASLD guidelines, regular screening is recommended. This study assessed the prevalence of micronutrient deficiencies in Veterans with advanced liver disease (ALD) to identify targets for intervention.

Methods:

- A retrospective review was conducted at the Atlanta Veterans Affairs (VA) Liver Clinics. Veterans ≥18 years with cirrhosis or advanced fibrosis and ≥3 micronutrient labs were included. Data collected: demographics, liver etiology, MELD 3.0, and decompensation history. Nutrients analyzed: vitamins A, D, E, K, B1, B6, B9, B12, C; zinc, selenium, copper, and iron.

Results:

- In a cohort of 100 patients with alcohol-associated liver disease (ALD), average age 64 and 95% male, 82% had at least one vitamin or trace element deficiency. The most common deficiencies were vitamin D (43%), vitamin A (40%), zinc (25%), vitamin C (21%), vitamin B1 (18%), and iron (16%). Metabolic dysfunction-associated steatohepatitis (MASH) was the leading etiology (26%).

Conclusions:

- **Micronutrient deficiencies—especially vitamins A and D—are highly prevalent in Veterans with ALD. These findings support routine screening and potential supplementation as per AASLD guidance.**

Sharif N, Hang T-V.

41. Gut Microbiome Associations with Noninvasive Risk Scores in Steatotic Liver Disease: A Cross-Sectional Microbiome And Insulin Longitudinal (MILES) Analysis

Background and Objectives:

- Metabolic dysfunction-associated steatotic liver disease (MASLD) is linked to gut microbiota alterations. Noninvasive indices like the Fatty Liver Index (FLI), Hepatic Steatosis Index (HSI), and NAFLD Liver Fat Score (NLFS) are used to detect steatosis, but their ability to reflect gut–liver axis changes is unclear.

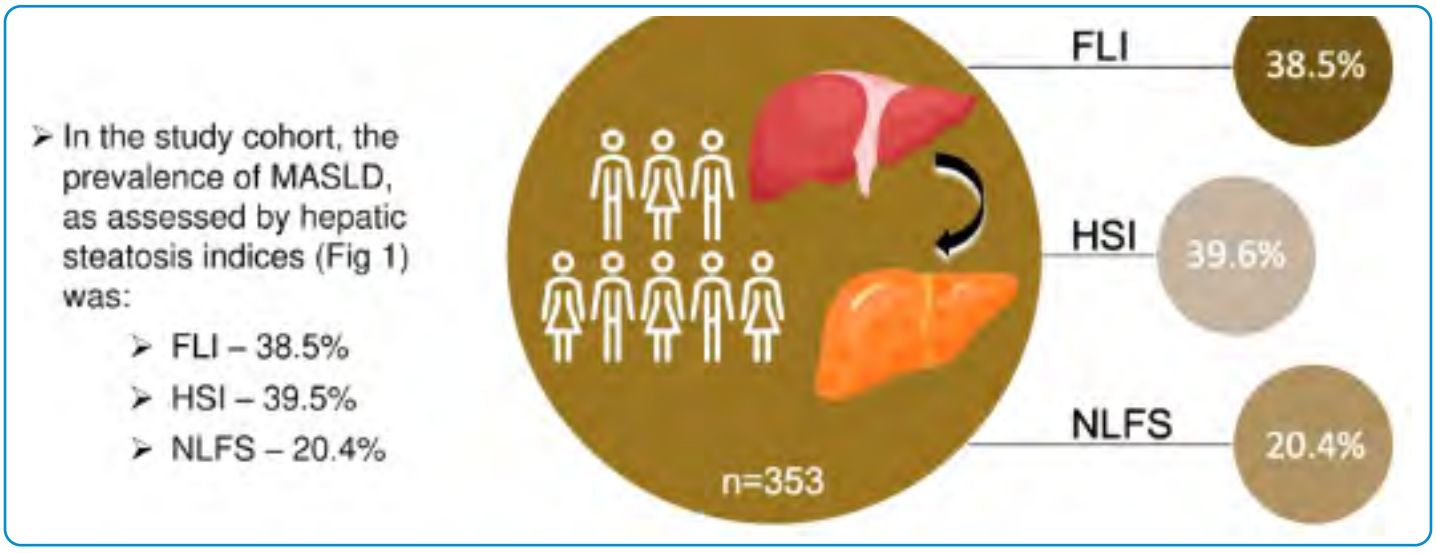
Methods:

- Cross-sectional analysis of 353 adults from the Microbiome and Insulin Longitudinal Evaluation Study (MILES). MASLD was diagnosed using FLI ≥60, HSI ≥36, or NLFS ≥ -0.640 with cardiometabolic risk factors. Gut microbiome was analyzed by shotgun metagenomic sequencing. Diversity and species-level changes were assessed.

Results:

- MASLD prevalence was 38.5% (FLI), 39.6% (HSI), and 20.4% (NLFS) (Figure below). Lower alpha diversity was seen with FLI-defined MASLD (p=.004), but not with HSI or NLFS. Beta diversity differed significantly with FLI (p=.0002) and NLFS (p=.006). Prevotella copri was enriched, while Methanobrevibacter smithii and Roseburia sp. were reduced in FLI-defined MASLD.

Figure: Prevalence of MASLD by Hepatic Steatosis Indices (FLI, HSI, NLFS)



Conclusions:

FLI and NLFS are more strongly associated with gut microbiome alterations than HSI in MASLD. Inclusion of metabolic markers like gamma-glutamyl transferase (GGT) in FLI may enhance its ability to detect gut–liver interactions and early liver disease.

Cundra LB, Maffei VJ, Bonkovsky HL, Weinberg RB, et al.

42. Cognitive Impact of MASLD, MASH, and Metabolic Risk Factors

Background and Objectives:

- Metabolic dysfunction-associated steatotic liver disease (MASLD) and steatohepatitis (MASH) are linked to inflammation and cognitive decline. This study assessed their impact on long-term cognitive outcomes.

Methods:

- A retrospective cohort analysis using the TriNetX US database included patients >50 years with metabolic risk factors (e.g., Type 2 diabetes mellitus [T2DM], obesity, hypertension). Patients were divided into:

Group 1: Healthy controls

Group 2: Metabolic risk factors without MASLD/MASH

Group 3: Metabolic risk factors with MASLD/MASH

- Cognitive outcomes (dementia, mild cognitive impairment, Alzheimer's disease) were assessed at <5 and >5 years.

Results:

- A total of 1,662,729 patients in Group 1 were matched with Group 2.
- Group 2 had higher odds of overall dementia at <5 years (OR=1.985, 95% CI: 1.920–2.053) and >5 years (OR=2.097, 95% CI: 2.032–2.163); mild cognitive disorder at <5 years (OR=1.469) and >5 years (OR=1.543); but lower odds of Alzheimer's at <5 years (OR=0.846) and >5 years (OR=0.863).
- In a second comparison, 498,734 patients in Group 3 were matched with Group 2. Group 3 had lower odds of overall dementia at <5 years (OR=0.859) and >5 years (OR=0.910); similar odds of mild cognitive disorder at <5 years (OR=1.447) and >5 years (OR=1.444); and reduced Alzheimer's risk at <5 years (OR=0.676), but not significant at >5 years (OR=0.874).

Conclusions:

Study findings offer real-world evidence that MASLD/MASH with metabolic risk factors influences cognitive outcomes in distinct ways. This highlights a complex relationship between liver disease and brain health, underscoring the need for prospective studies to explore underlying mechanisms and clinical significance.

Nasir AB, Zouridis S, Brotherton P, Kilani Y, et al.

43. Characteristics of T2DM Patients with MASH Treated with Resmetirom

Background and Objectives:

- Resmetirom is FDA-approved for non-cirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with F2–F3 fibrosis. This study assessed real-world characteristics of patients with Type 2 diabetes mellitus (T2DM) prescribed resmetirom.

Methods:

- Data from 227 T2DM patients with metabolic dysfunction-associated steatotic liver disease (MASLD) across six U.S. centers (Mar–Nov 2024) were analyzed.

Results:

- Advanced fibrosis (F2–F3) was seen in 86.8% (median LSM 11.6 kPa). Enhanced Liver Fibrosis (ELF) testing was done in 12.3%, with 73.2% scoring 9.2–11.3. Only 24.2% had liver biopsy. Common comorbidities included statin use (50.2%), metformin (56.4%), and GLP-1RA (29.5%). Patients had 1–4 additional cardiometabolic risk factors. Most received resmetirom at 80 mg (50.9%) or 100 mg (47.2%).

Conclusions:

- **In this real-world cohort of MASH patients with T2D on resmetirom, obesity and multiple cardiometabolic comorbidities were common. Noninvasive tools like transient elastography and ELF were widely used, reflecting a shift from biopsy-based diagnosis. Findings highlight the need for holistic cardiometabolic care and support resmetirom as a potential therapy for high-risk T2D patients with MASH.**

Alkhouri T, Singal AK, Asaad I, Dinani A, et al.

44. Long-Term Aspirin Use and Outcomes in MASLD: Nationwide Inpatient Insights

Background and Objectives:

- Metabolic dysfunction–associated steatotic liver disease (MASLD) affects over 30% of U.S. adults. Aspirin may reduce disease severity and prevent progression to hepatocellular carcinoma (HCC).

Methods:

- This retrospective cohort study used 2016–2021 NIS data to identify MASLD patients via ICD-10 codes, stratified by long-term aspirin use. Demographics, comorbidities, hospital data, and outcomes (mortality, ICU stay, shock, sepsis, peritonitis, Acute Kidney Injury (AKI), Length of Stay (LOS) were analyzed. Multivariable logistic regression adjusted for key confounders assessed the impact of aspirin use on outcomes.

Results:

- Among 2,883,584 MASLD patients, 11.6% were on long-term aspirin. Aspirin users were older, mostly male, White, and more likely to have Medicare. Aspirin use was linked to lower odds of in-hospital mortality (aOR 0.46), ICU admission (aOR 0.59), shock (aOR 0.54), sepsis (aOR 0.71), peritonitis (aOR 0.59), and AKI (aOR 0.81), all $p<0.001$. It also reduced length of stay (4.7 vs. 5.2 days).

Conclusions:

- **Long-term aspirin use in MASLD patients is linked to significantly better clinical outcomes.**

Oum M, Aloum K, Iqbal H, Narendra N.

45. Enhancing MASH Risk Stratification Using FAST Score: A Multicenter Analysis.

Background and Objectives:

- Metabolic dysfunction-associated steatohepatitis (MASH) patients are often diagnosed using noninvasive tests. The FibroScan-Aspartate Aminotransferase (FAST) score may improve upon liver stiffness measurement (LSM) alone in identifying treatment candidates.

Methods:

- In a real-world cohort of 424 metabolic dysfunction-associated steatotic liver disease (MASLD) patients on resmetirom, 303 had LSM 8–20 kPa (per American Association for the Study of Liver Diseases (AASLD) guidance). FAST scores were used to stratify risk.

Results:

- The study included 424 patients (median age 58; IQR 49–67), with 42.0% male. Liver biopsy was performed in 20.8%, revealing F2 fibrosis in 45.5% and F3 in 46.6%.
- Transient elastography was available in 88.9%, with 69.8% showing LSM values within the AASLD range (8–20 kPa).
- ELF testing was done in 13.2%, with 73.2% between 9.2–11.3.
- Of the 303 patients meeting LSM criteria, FAST Score categorized 28.2% as low risk, 45.8% as intermediate, and 25.9% as high risk.

Conclusions:

This real-world study highlights that relying solely on LSM, as per AASLD guidelines, may lead to overtreatment, as nearly one-third with low FAST scores (<0.35) likely had low risk for at-risk MASH. Using composite scores like FAST may improve risk stratification and guide more precise treatment decisions, supporting the need for updated clinical guidance.

Dunn W, Singal AK, Asaad I, Mena E, et al.

46. Valproate Linked to Worse Outcomes in MASLD/MASH: Multinational Study

Background and Objectives:

- Valproate, a common anti-seizure medication, disrupts mitochondrial fatty acid metabolism and may worsen metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH). This study assessed the impact of long-term valproate use on liver-related and cardiovascular outcomes.

Methods:

- Using the TriNetX database (2014–2024), MASLD/MASH patients with epilepsy on valproate were matched 1:1 to similar patients not on anti-epileptic drugs. Outcomes included all-cause mortality, hepatic decompensation, hepatocellular carcinoma (HCC), and major adverse cardiovascular events (MACE).

Results:

- Among 1,325,246 MASLD/MASH patients, 8,976 were on valproate and matched with 8,975 non-AED users. Valproate users had higher risks of hepatic decompensation (306 vs. 182 events), all-cause mortality (889 vs. 587 deaths), and MACE (653 vs. 525 events). No significant difference in HCC risk was seen (86 vs. 101 events).

Conclusions:

- **Chronic valproate use in MASLD/MASH patients is associated with increased risks of mortality, hepatic decompensation, and cardiovascular events. These findings highlight the need for caution when prescribing valproate to patients with steatotic liver disease.**

Ko D, Kim DH, Basegoda WS, Porres JA, et al.

47. Evaluating Early Real-World Response to Resmetirom: Single-Center Experience

Background and Objectives:

- Metabolic dysfunction-associated steatohepatitis (MASH) is a leading cause of cirrhosis. Resmetirom, approved in March 2024, is the first drug shown to improve fibrosis. While current guidance recommends response assessment at 12 months, this study evaluates whether meaningful changes are detectable at 3 months.

Methods:

- A single-center cohort of 36 patients with F2/F3 fibrosis initiated on resmetirom was studied. Data from 19 patients with 3-month follow-up were analyzed. Liver stiffness measurement (LSM), lipids, HbA1c, Body Mass Index (BMI), and liver enzymes were tracked. Pre- and post-treatment values were compared using Wilcoxon signed-rank tests.

Results:

- Mean LSM dropped significantly from 10.9 to 8.2 kPa ($p=0.02$) after 3 months.
- Controlled Attenuation Parameter (CAP) showed a non-significant improvement (−21.2 dB/m, $p=0.06$).
- 52% of patients had ≥25% LSM reduction
- No significant change in BMI, HbA1c, or liver enzymes
- GLP-1 RA use did not affect LSM change.

Conclusions:

- **Resmetirom therapy shows measurable improvement in LSM at 3 months, independent of metabolic or enzyme changes. Early response assessment may be feasible, aiding clinical decisions.**

Saggese A, Buckholz A, Schwartz RE, Krisko T, et al.

48. Predicting Fibrosis in MASLD Using Non-Invasive Biomarkers: Ontario Prospective Study

Background and Objectives:

- Metabolic dysfunction-associated steatotic liver disease (MASLD) is a major global health burden with variable progression to advanced fibrosis. Identifying early predictors of disease severity is key to targeted intervention.

Methods:

- A prospective chart review conducted from September 2021 to April 2023 included patients with Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD). Clinical, lifestyle, laboratory, and elastography data were collected. Liver Stiffness Measurement (LSM) and Controlled Attenuation Parameter (CAP) were used to evaluate liver fibrosis and steatosis, respectively. Correlation analyses were performed using Statistical Package for the Social Sciences (SPSS).

Results:

- Among 116 encounters:
  - **Higher HbA1c** correlated with increased LSM ($r=0.28$, $p<0.05$)
  - **Longer disease duration** also predicted higher LSM ($r=0.23$, $p<0.05$)
  - **Lower platelets** correlated with higher LSM ($r=-0.28$, $p<0.05$)
- Alcohol and cannabis use were not significantly associated with CAP or LSM
- InBody trunk reactance (250kHz) showed a strong correlation with LSM ($r=0.59$, $p<0.05$), though only 15 patients were assessed.

Conclusions:

HbA1c, platelet count, and disease duration are simple, non-invasive predictors of advanced fibrosis in MASLD. Bioimpedance may be a promising adjunct tool. These findings support developing primary-care–friendly risk stratification models to reduce reliance on biopsy or FibroScan.

Song YN, Mortuza R, Arab JP, Khan Q.

H. pylori and Pancreatic Disorders

49. Elevated Risk Of Acute Pancreatitis In Patients With H. Pylori: A Multicenter 10-Year Analysis

Background and Objectives:

- Helicobacter pylori (H. pylori) is a common bacterial infection of the gastroduodenal tract. Emerging evidence suggests a potential link between H. pylori and pancreatic disorders. This study investigates the association between H. pylori infection and the risk of acute pancreatitis (AP) in patients undergoing esophagogastroduodenoscopy(EGD).

Methods:

- A retrospective cohort study using the TriNetX platform included patients from 2010 to 2024 who underwent EGD prior to H. pylori diagnosis. Two matched cohorts—H. pylori positive and negative—were compared. Exclusions included AP due to alcohol, biliary disease, or chronic pancreatitis. Propensity score matching (PSM) adjusted for demographics, comorbidities, and medication use. Kaplan-Meier survival analysis and hazard ratios (HRs) with 95% confidence intervals (CIs) were used to assess outcomes.

Results:

- After matching, 30,357 patients were included in each group. H. pylori infection was significantly associated with an increased risk of acute pancreatitis within 1 year (HR 2.31; 95% CI: 1.05–5.08), and this trend persisted at 3, 5, and 10 years. No significant difference was found in the incidence of pancreatic cancer(PC)between groups(HR 0.85; 95% CI: 0.62–1.16).

Conclusions:

- **H. pylori infection is associated with a higher risk of developing acute pancreatitis, suggesting it may serve as a co-risk factor. No link was found between H. pylori and pancreatic cancer.**

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50. 10-Day Vonoprazan-Amoxicillin Dual Therapy vs. 14-Day PPI-Based Regimen for Helicobacter pylori Eradication: A Meta-Analysis of Randomized Controlled Trials

Background and Objectives:

- H. pylori is a major cause of gastric diseases. Standard eradication therapies are less effective due to antibiotic resistance and limited acid suppression from PPIs. Vonoprazan, a stronger acid blocker, may improve outcomes. This meta-analysis compared 10-day vonoprazan-amoxicillin (VPZ-Amox-10) dual therapy with 14-day PPI-based quadruple therapy(PPI-Q-14).

Methods:

- A systematic search was conducted through October 2024 for Randomized controlled trials (RTCs) comparing VPZ-Amox-10 vs PPI-Q-14 in adults with H. pylori. Primary outcomes were eradication rates and adverse events. Pooled odds ratios (ORs) were calculated using random-effects models.

Results:

- Four RCTs (1,545 patients) were included. Eradication rates were similar between VPZ-Amox-10 and PPI-Q-14 (OR = 1.08, p = 0.84). However, VPZ-Amox-10 had significantly fewer adverse events (OR = 0.35, p < 0.01).

Conclusions:

- **VPZ-Amox-10 is not more effective for eradication but has fewer side effects. It may be a safer alternative to standard quadruple therapy for H. pylori treatment.**

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