

Supplementary Information

1. Supplementary Methods
 - a. Nomenclature of steatotic liver disease
 - b. PETH and AUDIT-C Classification
 - c. Estimation of Dry Body Weight
 - d. Recompensation Criteria
 - e. Integrated Diet and Exercise Program for Weight Loss
 - f. Integrated Metabolic Clinic
 - g. Integrated Alcohol Use Disorder Clinic
2. Supplementary Tables
3. Supplementary Figures

Definition of steatotic liver disease categories

Steatotic liver disease (SLD) categories were defined according to contemporary consensus nomenclature based on the presence of hepatic steatosis, cardiometabolic risk factors, and quantified alcohol intake. Hepatic steatosis was established using imaging, noninvasive biomarkers, or histology. Metabolic dysfunction–associated steatotic liver disease (MASLD) was defined by the presence of hepatic steatosis in individuals with at least one cardiometabolic risk factor, including overweight or obesity, type 2 diabetes mellitus, or other features of metabolic dysregulation, in the setting of alcohol consumption at or below established thresholds (≤ 140 g/week for women and ≤ 210 g/week for men). Metabolic dysfunction–associated alcohol-related liver disease (MetALD) was defined in individuals who fulfilled MASLD criteria but reported alcohol intake above these thresholds, reflecting combined metabolic and alcohol-related contributions to liver disease. MetALD is diagnosed when a patient meets criteria for MASLD but consumes alcohol above these thresholds (>140 g/week for women or >210 g/week for men), indicating a combined metabolic and alcohol-related etiology. Alcohol-related liver disease (ALD) was defined when hepatic steatosis and liver injury are primarily attributable to alcohol consumption, typically at similar or higher levels of intake, in the absence of required cardiometabolic risk factors (CMRF), such that alcohol is considered the dominant driver of disease. This classification framework was used to acknowledge overlapping etiologies and to categorize patients based on the relative contributions of metabolic dysfunction and alcohol exposure.(1, 2)

Patients with alcohol-associated liver disease (ALD) were excluded from the present analysis. Additional causes of hepatic steatosis, including drug-induced liver injury, monogenic disorders, viral hepatitis, malnutrition, and other secondary causes, were excluded following systematic evaluation.

PEth and AUDIT-C Classification

To improve the accuracy of SLD subclassification, alcohol intake assessment was triangulated using self-reported alcohol consumption, the Alcohol Use Disorders Identification Test–Consumption (AUDIT-C) questionnaire, and biomarker confirmation with phosphatidylethanol (PEth), with previously established cut-off for a positive PEth test >20 ng/ml. (3) AUDIT-C scores <3 Scores of 0–3 in females and <4 in males were considered low-risk, scores of 3–7 (females) or 4–7 (males) were intermediate-risk, and scores ≥ 8 were high-risk for harmful alcohol use. PEth concentrations <20 ng/ml were considered negative for recent alcohol consumption, reflecting abstinence over the preceding 2–4 weeks.(3)

PEth was measured using a commercially available competitive whole-blood enzyme immunoassay (AFG Scientific, IL, USA; Catalogue No. EK240319), the only one available in India. The test has a lower limit of detection of 0.5 ng/mL. Whole blood samples were subjected to red blood cell lysis using a hypotonic lysis buffer, followed by solubilization of erythrocyte membrane lipids with 10% methanol. The lysates were then sonicated using an ultrasonic cell disruptor with short pulses for 1 minute at 4 °C to ensure complete cellular disruption while minimising thermal degradation. Homogenates were centrifuged at 10,000G for 5 minutes, and the clarified supernatant was collected and assayed immediately according to the manufacturer's instructions. PEth concentrations were determined from an inverse standard curve generated using kit-provided standards. All samples and standards were prepared in matched solvent conditions to minimise matrix effects.

Alcohol consumption was assessed using a detailed history and the AUDIT-C questionnaire. PEth testing was performed as an objective biomarker of recent alcohol exposure and was interpreted in conjunction with clinical history and AUDIT-C results.

Disease classification was based on the overall assessment of alcohol exposure rather than on a single PEth measurement. Isolated low-level alcohol intake or transient PEth positivity below thresholds consistent with sustained alcohol use did not automatically result in reclassification from MASLD to MetALD. Repeat PEth testing and longitudinal clinical review were used when discrepancies between self-reported alcohol intake and biomarker results were identified.

Decompensated cirrhosis was defined as the appearance of one or more clinical decompensation events, i.e., ascites and/or variceal bleeding and/or hepatic encephalopathy (overt HE with West Haven Classification $\geq$ grade 2). (4)

As per the Baveno VII consensus:

- The events that define decompensation in a compensated patient are “overt ascites (or pleural effusion with increased serum ascites albumin gradient [>1.1 g/dl]), overt hepatic encephalopathy (HE; West Haven grade $\geq$ II) and variceal bleeding (VB) ”.
- Other relevant liver-related events in compensated cirrhosis are the “development of superimposed liver injury /acute-on-chronic liver failure (ACLF) and hepatocellular carcinoma (HCC)”. (5)

Definition of decompensation events

Only patients with clinically apparent ascites who had undergone paracentesis and/or required diuretics for management were eligible for the study.

Any **ascites** apparent on clinical examination, or a small amount of ascites visible on imaging, and/or requiring salt restriction and/or diuretics, was recorded as 'ascites being present' at presentation, and this was used to calculate the dry body weight. In patients with ascites at enrolment, we recorded the 'wet weight' and an estimation of dry weight was done using either the post paracentesis body weight, corroborated by POCUS, or by subtracting a percentage of weight based upon the severity of ascites (mild, 5%; moderate, 10%; severe, 15%), with an additional 5% subtracted if bilateral pedal oedema was present.(6, 7) The follow-up dry weights were confirmed by POCUS, which showed no ascites or pedal oedema.

Hepatic Encephalopathy was defined and graded according to the standard American Association for the Study of Liver Diseases (AASLD) clinical practice guidelines. Only overt HE was recorded in this study, as Minimal hepatic encephalopathy needs extensive testing and was not part of the study protocol (8)

Events such as spontaneous bacterial peritonitis and hepatorenal syndrome were defined according to standard criteria.(9)

Endoscopic Surveillance protocol

In this cohort, all patients had decompensated cirrhosis, and they were advised an esophagogastroduodenoscopy (EGD) at first diagnosis and followed up with annual visits. In patients with prior AVB, endoscopic interventions, including one or more of the following techniques, were performed: endoscopic variceal ligation (EVL), glue (N-butyl-cyanoacrylate) injection with or without coils, and argon plasma coagulation of portal hypertensive gastropathy. Repeat interventions were advised as needed for variceal eradication. The patients received dual secondary prophylaxis for AVB, consisting of both endoscopic interventions and NSBB. (2) The grading of varices was as per the AASLD guidance as 'small' <5mm or 'large' ≥ 5 mm, and the presence of cherry red spots and red wale signs was documented. (3)

Patient Follow-up

Patients who had unresolved liver-related complications or decompensation like ascites, or episodic HE, poor cardiometabolic control, recent alcohol intake or conditions like AKI, SBP or dysplastic nodules, were advised to report every 3 months to the multidisciplinary unit. After achieving medical control of decompensation and optimising CMRF, patients were generally seen every 6 months, with a window. In addition, those who developed acute illnesses were also advised to report to the Liver clinic as needed. Patients underwent clinical examination, routine tests, including AFP testing every 3-6 months, Doppler ultrasound or cross-sectional imaging of the liver for HCC and portal hypertension surveillance every 6 months.

Liver Stiffness Measurement

Liver stiffness values were obtained at baseline and follow-up using 2D shear-wave elastography (ElastPQ) because of ascites. (Affiniti 70; **Philips Healthcare, Koninklijke Philips N.V.**, Amsterdam). During the ultrasound, after selecting the optimal acoustic window, a region of interest (ROI) is selected in the liver, positioned perpendicular to the capsule, avoiding major blood vessels and bile ducts. Studies indicate that intercostal imaging targeting liver segments 7 or 8 offers greater measurement reliability. Serial readings are taken as the patient holds their breath, and a report is generated. At least 10 measurements were performed, with at least 60% classified as “good.” The average value from these measurements was used to estimate liver stiffness. An LSM greater than 15 was associated with a predicted biopsy METAVIR score of F3/F4 or higher. (10) Additionally, a follow-up liver stiffness measurement was conducted using transient elastography (Fibroscan, Echosens, France) once ascites had resolved.

Indications for NSBB

Carvedilol was advised as the primary prophylactic agent for preventing initial episodes of acute variceal bleeding (AVB). Non-selective beta-blockers (NSBB) were indicated for patients presenting with high-risk varices (≥ 5 mm), any varices accompanied by red wale signs, Child-Pugh class C status, or the presence of gastric varices, consistent with the recommendations outlined in the AASLD guidance statement. Secondary prophylaxis of variceal bleeding was with dual NSBB plus endotherapy.(11) As most patients met criteria for NSBB per Baveno VII, with liver stiffness measurements (LSM) of ≥ 25 kPa or ≥ 20 kPa accompanied by low platelet counts or increased spleen stiffness, they received carvedilol unless contraindicated.(5)

Recompensation was defined as “no new onset of further decompensation event and if the following criteria are met. (5)

- (1) Resolution of clinical manifestations such as ascites (without the concurrent use of diuretics), episodes of HE (without the use of prophylactic medications), and absence of recurrent VB for at least a duration of 12 months.
- (2) Integrated management of cardiometabolic risk factors, medical nutrition therapy and weight loss programme with alcohol use disorder.
- (3) Improvement in synthetic liver function as determined by serum bilirubin, albumin, and INR.”

Further decompensation in cirrhosis was defined as “development of a second portal hypertension-related decompensating event (ascites, VB, overt HE). (5) Further decompensation in cirrhosis represents a prognostic stage associated with an even higher mortality than that associated with first decompensation. Specific events that define ‘*further decompensation*’ are any of the following:

- (i) Development of a second portal hypertension-driven decompensating event (ascites, variceal haemorrhage, or hepatic encephalopathy > grade 2 as per West Haven criteria) and/or jaundice.
- (ii) Development of recurrent variceal bleeding, recurrent ascites (requirement of ≥ 3 large-volume paracenteses within 1 year), recurrent encephalopathy, development of spontaneous bacterial peritonitis (SBP) and/or hepatorenal syndrome- acute kidney injury (HRS-AKI).
- (iii) In patients presenting with bleeding alone, development of ascites, encephalopathy, or jaundice after recovery from bleeding, but not if these events occur around the time of bleeding.

Integrated Metabolic and Alcohol Use Disorder Management

All patients were managed by an integrated unit for hepatology, deaddiction care, alcohol use disorder, and an endocrinology clinic, which are embedded within the Liver Clinic services, providing a single-window service.

Integrated Diet and Exercise Program for Weight Loss

An integrated metabolic clinic provided dietitian-supported outpatient nutritional therapy.(12) Dietary counselling focused on individualised, calorie-restricted, nutrient-appropriate eating

patterns to promote gradual, sustained weight reduction, with a target weight loss of approximately 10% of baseline body weight. Diet composition emphasised reducing refined carbohydrates and saturated fats while encouraging whole foods consistent with metabolically favourable, culturally appropriate dietary patterns. Patients were enrolled in a graded, supervised weight-loss and exercise programme, with adaptations based on disease severity and functional status. (13)The exercise prescription incorporated a combination of isometric and isotonic exercises to improve muscle strength, physical function, and metabolic health. Isometric exercises were used early in the programme and in individuals with reduced exercise tolerance to promote static muscle engagement and improve strength without excessive cardiovascular load. Isotonic exercises, which involve controlled dynamic movements, were progressively introduced to enhance muscle mass, endurance, and overall functional capacity. Exercise intensity and progression were individualised, with careful monitoring for fatigue, sarcopenia, and cirrhosis-related complications. (14)This integrated approach aimed to support safe, gradual weight loss, preserve lean body mass, and improve physical performance in patients with cirrhosis. This combined lifestyle intervention was delivered as standard of care and applied uniformly across the study cohort to optimise liver-related and cardiometabolic outcomes.

Medications for Diabetes, Dyslipidemia and Hypertension

Medications for diabetes included metformin, sodium glucose cotransporter 2 (SGLT2) inhibitors (empagliflozin in a dose of 25 mg qd or dapagliflozin in a dose of 10 mg qd), (15)dipeptidyl peptidase 4 (DPP-4) inhibitors [(linagliptin in a dose of 10 mg qd) and sitagliptin (in a dose of 50 mg qd)], voglibose, and insulin, used alone or in combination.(16) Since the protocol began in 2019, we have had only 5 patients on oral semaglutide (GLP-1 receptor agonist) due to cost constraints. All patients underwent self-monitoring of blood glucose as per the institution's protocol.

Statins, including simvastatin in a dose of 20 mg per day or atorvastatin in a dose of 10 mg/day, were prescribed for hypercholesterolemia and/or fenofibrate in a dose of 140 mg per day for hypertriglyceridemia, as part of a treatment regimen for dyslipidemia.(17)

Besides carvedilol, which was given for portal hypertension, and diuretics for ascites, patients were prescribed telmisartan or amlodipine to manage hypertension. All patients maintained ambulatory blood pressure records at regular intervals.

Management of Alcohol Use Disorder

In participants classified as having metabolic dysfunction–associated alcohol-related liver disease (MetALD), management of alcohol use disorder (AUD) was incorporated as a core component of care. All individuals underwent a structured assessment of alcohol consumption and received brief interventions focused on education, motivational enhancement, and goal setting aimed at reducing or achieving abstinence from alcohol. Where indicated, patients were referred for cognitive behavioural therapy (CBT) to address maladaptive drinking behaviours, enhance coping strategies, and support sustained behaviour change.(18) Pharmacotherapy for AUD was offered when clinically appropriate, including the use of baclofen, particularly in patients with advanced liver disease, and naltrexone in those without contraindications, to reduce alcohol craving and consumption. Those with recent binges received brief supervised courses of lorazepam for alcohol withdrawal.(19)

These interventions were delivered in conjunction with metabolic risk factor management to address the dual etiologic drivers of liver disease in MetALD.

Supplementary Table S1. Cohort characteristics at baseline, including liver fibrosis and severity indices, decompensation events, and laboratory parameters stratified by aetiology (MASLD vs MetALD).

Parameter	TOTAL N=344	MASLD N=158	Met ALD N=186	p value
Measurement of Liver Fibrosis				
APRI	2.3 ±0.5	2.4±0.4	2.3±0.5	0.462
Fib-4	4.8 ±1.2	4.6±1.2	5±1.1	0.003
Decompensation events at Enrolment				
Number of decompensation events at enrolment				<0.001
1	107(31.1)	69(43.7)	38(20.4)	
2	167(48.5)	67(42.4)	100(53.8)	
≥3	70(20.3)	22(13.9)	48(25.8)	
Presence of ascites	344(100%)	158(100%)	186(100%)	-
Current Ascites	297(86.3%)	136 (86.1%)	161 (86.6%)	0.897
Grade of ascites based on 1 st Imaging at enrolment. ¶				0.010
No Ascites	47(13.7%)	22(13.9%)	25(34.5%)	
Grade 1	143(41.6%)	78(49.4%)	65(34.9%)	
Grade 2	131(38.1%)	53(33.5%)	78(41.9%)	
Grade 3	23(6.7%)	5(3.2%)	18(9.7%)	
Hepatic Encephalopathy at enrolment	127(36.9%)	38 (24.1%)	89 (47.8%)	<0.001
				0.325
Grade 1	59(46.5%)	20 (52.6%)	39(43.8%)	
Grade 2	56(44.1%)	14(36.8%)	42(47.2%)	
Grade 3	11(8.7%)	3(7.9%)	8(9%)	
Grade 4	1(0.8%)	1(2.6%)	0	
Cardiometabolic factors				
Number of CMRF at enrolment				0.251
1	117(34)	48(30.4)	69(37.1)	
2	188(54.7)	94(59.5)	94(50.5)	
≥ 3	39(11.3)	16(10.1)	23(12.4)	
Laboratory Parameters				
Hemoglobin (g/dl)	10.1±2.7	10.8 ± 2.7	9.4±2.6	<0.001
Total leucocyte Count (x10 ⁹ /l) *	7132.9(6251.1-8014.8)	6794.6(5990.2-7599.3)	7419.5(5933-8906)	0.488
Platelet Count (x10 ⁹ /l) *	121.4(111.9-131)	123.1(65.5-130.1)	119.4(70.7-135.3)	0.664
Total Bilirubin(mg/dl)	5.1(4.2-5.9)	4.5(3.3-5.8)	5.4(4.2-6.7)	0.328
AST(U/L) *	101.9(84.9-118.8)	101.4(67.4-135.4)	102.2(89.3-115.1)	0.964
ALT (U/L) *	50.9(43.6-58.3)	69.6 (50.3-88.9)	52.5 (45.6-59.4)	0.081
Creatinine(mg/dl) *	1.1(1-1.2)	1.2(1-1.3)	1 (0.9-1.1)	0.112
Sodium(mmol/L) *	135.9(135.3-136.5)	136.8(136-137.6)	135.1(134.2-136)	0.009
Albumin(g/dl) *	3.4(3.1-3.7)	3.8(3.3-4.4)	3(2.9-3.2)	0.003
INR *	2(1.6-2.5)	2.4(1.04-3.3)	1.8(1.5-2)	0.222

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; APRI, AST to platelet ratio index; Fib-4, fibrosis-4 index. * Median with interquartile range. ** p-value in bold indicates significance at <0.05.

¶ Dry weight was defined as measured weight with subtraction based on the severity of ascites: 5%, 10%, and 15% for mild, moderate, and severe ascites, respectively. An additional 5% was subtracted if there was bilateral pedal edema. Weight is reported as 'dry' unless otherwise specified. Dry body weight was confirmed by point-of-care ultrasound (POCUS) to determine the status of any ascites and minimal or absent subcutaneous oedema, as per established criteria.

Supplementary Table S2. Cohort at 12 months from enrolment, including liver fibrosis and severity indices, decompensation events, laboratory parameters, and changes in modifiable cardiometabolic risk factors, stratified by etiology (MASLD vs MetALD).

Parameter	TOTAL N=344	MASLD N=158	Met ALD N=186	p value**
Measurement of Liver Fibrosis				
APRI 12 months	1.4 ±0.4	1.4±0.3	1.4±0.4	0.595
Fib-4 12 months	3.3 ±1.2	3.1±1.2	3.5±1.1	0.003
Decompensation events at follow-up				
Ascites (Follow-up)	131(38.1%)	75(47.5%)	56(30.1%)	0.001
Hepatic Encephalopathy event (Follow-up)	23(6.7%)	11(7%)	12(6.5%)	0.956
Laboratory Parameters				
Platelet Count (x10 ⁹ /l) at 12 m*	124.4(90.9-134)	125(76.5-133)	120.4(84-140)	0.774
Total Bilirubin(mg/dl) 12 months	3.4(3.1-3.7)	2.9(2.2-3.2)	3.8(3.4-4.3)	<0.001
AST(U/L) * 12 m	74.6(65.9-83.2)	66.2(51.8-80.6)	82.1(72-92.3)	0.964
ALT (U/L) * 12m	50.9(43.6-58.3)	57.7 (43.4-72)	44.8(39.4-50.3)	0.072
Creatinine (mg/dl) *at 12m	1(0.9-1.2)	1.1(1-1.2)	1(0.8-1.1)	0.344
Sodium (mmol/L) at 12m*	135.2(134.7-135.8)	135.2(134.5-136)	135.2(133.4-136)	0.928
Albumin(g/dl) at 12m*	3.9(3.1-4.7)	3.7(2.9-4.5)	4(2.7-5.3)	0.004
INR at 12m*	1.5(1.7-2.2)	1.5(1.3-1.8)	1.6(1.4-1.8)	0.038
HbA1c (g/dL) *	6(5.8-6.3)	6.1(5.7-6.5)	6(5.6-6.4)	0.670
HbA1c (g/dL) at 6 m *	5.1(5-5.2)	5.1(5-5.3)	5.1(4.9-5.3)	0.581
HbA1c (g/dL) at 12 m	4.8(4.7-4.9)	4.8(4.6-5)	4.8(4.6-5)	0.930
HbA1c (g/dL) at 18 m	4.8(4.7-5)	4.9 (4.7-5)	4.7(4.6-4.8)	0.971
Total Cholesterol (mg/dL) *	157.9(150-165)	172(161-182)	146(137-155)	<0.001
Total Cholesterol (mg/dL) at 6 m*	137(131-144)	148(138-158)	128(120-137)	0.003
Total Cholesterol (mg/dL) at 12 m*	139(133-146)	145(135-155)	135(125-144)	0.133
Total Cholesterol (mg/dL) at 18 m*	127 (110-149)	130(117-135)	119(109-126)	0.175
HDL Cholesterol (mg/dL) *	38.7(37-41)	43(39-46)	35(32-38)	<0.001
HDL Cholesterol (mg/dL) at 6 m*	38(34-41)	42(40-47)	33(28-38)	0.004
HDL Cholesterol (mg/dL) at 12 m*	51.7(49-55)	56(52-59)	48(43-52)	0.010
HDL Cholesterol (mg/dL) at 18 m*	62(49-79)	63(61-70)	59(55-65)	0.002
LDL Cholesterol (mg/dL) *	55(41-85)	58.4 (42-87.4)	53(35.6-75)	0.003
LDL Cholesterol (mg/dL) at 6 m*	54(40-77)	60(43-87)	47(34-67)	0.006
LDL Cholesterol (mg/dL) at 12 m*	61(37-90)	70(45-102)	56(34-80)	0.001
LDL Cholesterol (mg/dL) at 18 m*	66(56-76)	70(62-77)	52(45-56)	<0.001
Triglycerides (mg/dL) *	95.7(87.9-103.5)	98.6(86.1-111)	89.5(81.4-97.7)	0.490
Triglycerides (mg/dL) at 6 m*	88(82.2-93.7)	91.3(83-99.6)	86.2(78-94.4)	0.425
Triglycerides (mg/dL) at 12 m*	88.6(83.7-93.4)	88.8(82.1-95.4)	87.5(80.3-94.6)	0.949
Triglycerides (mg/dL) at 18 m*	83(75-98)	88(66-98)	78(69-92)	0.098

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; APRI, AST to platelet ratio index; HDL, high density lipoprotein; LDL, low density lipoprotein; Fib-4, fibrosis-4 index. * Median with interquartile range.

Supplementary Table S3. Alcohol exposure, as assessed by self-reported intake, the AUDIT-C questionnaire, and phosphatidylethanol (PEth) testing in the overall cohort and stratified by disease etiology.

Parameter	Total	MASLD	Met ALD	p-value**
	N=344	N=158	N=186	
Any Alcohol intake (n, %)	186(54.1)	13 (8.2)	173(93)	0.001
Smoking (n, %)	27(7.8)	2(1.3)	25(13.4)	0.001
Complementary and Alternative Medication (n, %)	34(9.9)	0	34(18.3)	0.015
AUDIT C score (Median, IQR)	3.9(3.7-4.1)	3(2.9-3.1)	4.7(4.4-5.1)	0.001
AUDIT C scores				<0.001
<i>Low</i>	207(60.2)	155(98.1)	52(28)	
<i>Intermediate</i>	100(29.1)	3(1.9)	97(52.2)	
<i>High</i>	37(10.8)	0	37(19.9)	
Self-reported alcohol intake				0.001
<i>Never consumed alcohol</i>	143(41.5)	143(90.5)	0	
<i>Quit Alcohol after a diagnosis of cirrhosis</i>	175(50.9)	2(1.3)	173(93)	
<i>Did not quit, consumed intermittently</i>	26(7.6)	13(8.2)	13(7)	
Type of Alcohol Consumed (>1 type possible per patient)				0.001
<i>Country Liquor</i>	96(51.6)	0	96(55.5)	
<i>Whisky</i>	65(34.1)	11(84.6)	54 (31.2)	
<i>Beer</i>	6(3.2)	2(15.4)	4(2.3)	
<i>Spirits</i>	30(16.1)	0	30(17.3)	
PEth Baseline				0.418
<20ng/ml	213(61.9)	156(98.7)	57(30.6)	
20-79ngm/ml	102(29.6)	2(1.3)†	100(53.8)	
80-199ng/ml	20(5.8)	0	20(10.8)	
>200ngm/ml	9(2.6)	0	9(4.8)	
PEth at 12 m(Follow-up) ¶				0.324
<20ng/ml	318(92.4)	152(96.2)	166(89.2)	
20-79ngm/ml	25(7.3)	6(3.8)	19(10.2)	
80-199ng/ml	1(0.3)	0	1(0.5)	
Positive PEth at enrolment	129(37.5)	0	129(69.4)	0.001
Positive PEth at 12 m(Follow-up)	26(7.6)	6(3.8)	20(10.8)	0.017

Abbreviations: AUDIT-C, alcohol use disorder identification test-consumption; PEth, phosphatidylethanol

† Reported only a recent social drinking episode within 1-2 weeks prior to the random PEth test and subsequently tested negative.

¶ Performed at 12 months from enrolment with a window of 1 month, and repeated at random as needed or as per AUDIT-C.

** p-value in bold indicates significance at <0.05.

Supplementary Table S4: Baseline characteristics (demographic, clinical, liver disease severity, decompensation events, and therapeutics) of patients stratified by subsequent attainment of recompensation.

Parameter	Total N=344	Recompensated N=64	Did not Recompensate N=280	p value**
Age (years)	46.9±11.7	46.7±11	46.4±11.8	0.174
Men n (%)	286(83.1)	52(81.3)	234(83.6)	0.711
Diagnosis				0.781
MASLD	158(45.9)	28(43.8)	130(46.4)	
MetALD	186(54.1)	36(56.3)	150(53.6)	
Diabetes mellitus, n (%)	95(27.6)	26(40.6)	69(24.6)	0.013
Hypertension, n (%)	73(21.2)	13(20.3)	62(22.1)	0.844
Coronary artery disease n (%)	3(0.9)	0	3(1.1)	0.406
Hepatitis C virus n (%)	47(13.6)	12(18.7)	35(12.5)	0.189
Hepatitis B virus n (%)	10(2.9)	3(4.6)	7(2.5)	0.347
Details of Alcohol Use				
Alcohol intake	186(54.1)	36(56.3)	150(53.6)	0.698
Quit Alcohol entirely	175(94)	34(94.4)	141(94)	0.903
Alcohol intake in g/week*	180.6(161.5-199.7)	178(132.4-223.5)	181.2(159.9-202.5)	0.895
AUDIT-C at enrolment				0.440
<i>Low</i>	207(60.2)	43(67.2)	164(58.6)	
<i>Intermediate</i>	100(29.1)	15(23.4)	85(30.4)	
<i>High</i>	37(10.8)	6(9.4)	31(11.1)	
PEth level at enrolment (ng/mL) *	28.8(24-33.6)	23(15.1-30.9)	30.1(24.5-35.7)	0.257
PEth baseline				0.418
<20ng/mL	213(61.9)	39(60.9)	174(62.1)	
20-79ngm/mL	102(29.7)	22(34.4)	80(28.6)	
80-199ng/mL	20(5.8)	3(4.7)	17(6.1)	
>200ngm/mL	9(2.6)	0	9(3.2)	
Control of CMRF				
Number of CMRF at enrolment				0.097
1	117 (34.0%)	29 (45.3%)	88 (31.4%)	
2	188 (54.7%)	28 (43.8%)	160 (57.1%)	
≥3	39 (11.3%)	7 (10.9%)	32 (11.4%)	
Dry Weight Loss				<0.001
>10%	50(14.5)	20(31.3)	30(10.7)	
7-10%	171(49.7)	37(57.8)	134(47.9)	
<7%	123(35.8)	7(10.9)	116(41.4)	
BMI (kg/m ²) *	24(23.5-24.5)	23.7(22.5-24.9)	24.1(23.5-24.6)	0.613
Severity scores				
CTP at enrolment	9.2±1.9	9±1.8	9.2±1.9	0.372
MELD-Na at enrolment	14.7±3.6	14.3±3	14.8±3.6	0.288
CTP Class at enrolment				0.365
A	47(13.7)	8(12.5)	39(13.9)	
B	119(34.6)	27(42.2)	92(32.9)	
C	178(51.7)	29(45.3)	149(53.2)	
Decompensation events				0.022
1	107 (31.1%)	23 (35.9%)	84 (30.0%)	
2	167 (48.5%)	36 (56.3%)	131 (46.8%)	
≥3	70 (20.3%)	5 (7.8%)	65 (23.2%)	
Clinical Ascites at enrolment	344 (100)	64 (100)	280 (100)	
Ascites at first imaging	297(86.3)	51(79.7)	246(87.9)	0.086

Episode of SBP at or prior to enrolment	94(27.3)	25(39)	69(24.6)	<0.001
Hepatic Encephalopathy	127(36.9)	15(23.4)	112(40)	0.013
Acute Variceal Bleed	197(57.3)	40(62.5)	157(56.1)	0.348
Variceal Status at Enrolment				0.099
<i>Small Varices ± PHG</i>	176(51.2)	30(46.9)	146(52.2)	
<i>Large Varices ± PHG</i>	93(27)	25(39.1)	68(24.3)	
<i>Gastric varices ± EV ± PHG</i>	45(13.1)	4(6.3)	41(14.6)	
<i>PHG alone</i>	20(5.8)	4(6.3)	41(14.6)	
<i>No Varices</i>	10(2.9)	1(1.6)	9(3.2)	
Liver Stiffness Measurement (LSM)				
LSM, 2D-SWE (kPa)†	27.8±11.5	28.1±11.1	27.8±11.5	0.861
Treatment				
Lactulose	281(81.7)	64 (100)	217(77.5)	<0.001
Stopped Lactulose	207/281(73.7)	64(100)	143/217(65.9)	0.394
Rifaximin	164(47.7)	24(37.5)	140(50%)	0.073
Stopped rifaximin	108/164(65.9)	24/24(100)	84/140(60)	0.591
Diuretic	302(87.8)	58(90.6)	244(87.1)	0.503
Stopped diuretic	140(46.4)	58/58(100)	82/244(33.6)	0.905
Carvedilol	328(95.3)	64(100)	264(94.3)	0.050
Metformin	89(25.9)	24(37.5)	65(23.2)	0.026
Gliptin	42(12.2)	14(21.9)	28(10)	0.018
Empagliflozin	23(6.7)	8(12.5)	15(5.4)	0.051
Dapagliflozin	7(2)	1(1.6)	6(2.1)	0.615
Oral Semaglutide	2 (0.6)	1(1.5)	1 (0.4)	0.977
Statin	45(13.1)	10(15.6)	35(12.5)	0.538
Fenofibrate	15(4.4)	2(3.1)	13(4.6)	0.746

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; APRI, AST to platelet ratio index; HDL, high density lipoprotein; LDL, low density lipoprotein; Fib-4, fibrosis-4 index; 2D SWE, 2-dimensional shear wave elastography * Median with interquartile range.

† LSM was measured by ElastPQ 2D shear wave elastography in patients at baseline and at follow-up. (Philips Affiniti 70) Follow-up LSM was also measured using transient elastography (Fibroscan, Echosens) and reported separately.

** *p*-value in bold indicates significance at <0.05.

Supplementary Table S5. Changes in biochemical reports concerning cardiometabolic risk, including dyslipidemia, glycemic control, liver biochemistry, and non-invasive fibrosis assessment, stratified by subsequent attainment of recompensation.

Parameter	TOTAL	Recompensated	Did not Recompensate	p value **
	N=344	N=64	N=280	
HbA1c (g/dL)				
<i>Enrolment</i>	6.5 ± 2	6.4 ± 2.1	6.5 ± 2	0.003
<i>6 months</i>	5.3 ± 0.9	5.3 ± 1	5.3 ± 0.8	0.950
<i>12 months</i>	5.2 ± 0.9	5.1 ± 0.8	5.3 ± 0.9	0.008
<i>18 months</i>	5.8 ± 0.9	5.6 ± 0.9	5.9 ± 0.8	0.003
<i>Dyslipidemia evaluation</i>				
Total Cholesterol (mg/dl)*				
<i>Enrolment</i>	158(151-165)	161(143-178)	157(150-165)	0.707
<i>6 months</i>	138(131-144)	137(120-154)	138(131-145)	0.896
<i>12 months</i>	140(133-146)	127(110-144)	143(135-150)	0.067
<i>18 months</i>	127 (110-149)	131(105-148)	124 (117-132)	0.107
HDL Cholesterol (mg/dl)*				
<i>Enrolment</i>	39(36-41)	44(39-48)	38(35-40)	0.033
<i>6 months</i>	38(34-41)	40(31-48)	37(33-41)	0.658
<i>12 months</i>	52(49-55)	57(52-62)	50(47-54)	0.092
<i>18 months</i>	62(49-79)	62(54-78)	60(45-77)	0.177
Cholesterol LDL (mg/dl)*				
<i>Enrolment</i>	65(59-70)	74(61-86)	63(57-69)	0.150
<i>6 months</i>	58(51-65)	58(45-70)	57(50-66)	0.964
<i>12 months</i>	77(71-82)	86(73-98)	75(69-81)	0.145
<i>18 months</i>	66(56-76)	59(55-70)	70(62-78)	0.072
Triglycerides (mg/dl)*				
<i>Enrolment</i>	98(90-105)	100(80-120)	97(88-106)	0.766
<i>6 months</i>	93(87-99)	80(70-91)	96(89-103)	0.041
<i>12 months</i>	95(90-101)	88(77-100)	97(91-103)	0.188
<i>18 months</i>	83(75-98)	73 (58-90)	88(72-105)	0.017
<i>Liver biochemistry</i>				
Bilirubin (mg/dL)*	5.1(4.2-6)	4(2.3-5.6)	5.3(4.3-6.4)	0.246
Bilirubin at 12 m (mg/dL)*	3.4(3.1-3.7)	2.5(1.9-3)	3.6(3.3-4)	0.002
INR *	2.1(1.6-2.6)	1.4(1.3-1.5)	2.3(1.7-2.8)	0.152
INR at 12 m*	1.5(1.7-2.2)	1.2(1.2-1.3)	1.7(1.4-2.5)	0.005
Albumin(g/dl) *	3.4(3.1-3.7)	3.4(3.1-3.6)	3.5(3.2-3.8)	0.746
Albumin(g/dl) at 12m*	3.9(3.1-4.7)	4.3(2.9-4.7)	3.2(2.8-3.6)	0.048

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; APRI, AST to platelet ratio index; HDL, high density lipoprotein; LDL, low density lipoprotein; Fib-4, fibrosis-4 index. * Median with interquartile range. ** p-value in bold indicates significance at <0.05.

Supplementary Table S6: Characteristics at follow-up after 12 months of therapy of patients stratified by subsequent attainment of recompensation.

Parameter	Total N=344	Recompensated N=64	Did not Recompensate N=280	p value**
PEth level at 12 m (ng/mL) † *	5.2(3.9-6.5)	3(1.9-4.2)	5.7(4.1-7.2)	0.125
PEth at follow-up				0.324
<20ng/mL	318(92.4)	62(96.9)	256(91.4)	
20-79ngm/mL	25(7.3)	2(3.1)	23(8.2)	
80-199ng/mL	1(0.3)	0	1 (0.4)	
PETH and AUDIT-C corroborated Abstinence in the cohort at 12 months	318/344 (92.4)	62/64 (96.9)	256/ 280 (91.4)	0.137
Optimisation of CMRF				
Dry Weight Loss				<0.001
>10%	50(14.5)	20(31.3)	30(10.7)	
7-10%	171(49.7)	37(57.8)	134(47.9)	
<7%	123(35.8)	7(10.9)	116(41.4)	
BMI (Follow-up)	22.3±4.6	22±4.7	22.3±4.6	0.626
% Dry weight loss at 12 months*	-7.8(-8to7.6)	-8.7(-9.1to -8.2)	-7.6(-7.8to 7.4)	<0.001
Achievement of Glycemic Control in patients with DM (n=95) at 12 months	76/95 (80)	21/26(80.8)	55/69(79.7)	0.908
Achievement of Glycemic Control in patients with DM (n=91) at 18 months	80/91 (87.9)	25/26(96.2)	51/65(78.4)	0.039
CMRF control: Achievement of weight loss>7% at 12 m	221 (64.2)	57 (89)	164 (58.6)	<0.001
Severity scores				
CTP score at follow-up at 12 months	7.3±1.5	6.5±0.8	7.5±1.6	<0.001
MELD-Na at 12m	13±4.9	9.8±2.2	13.8±5	<0.001
CTP Class at Follow-Up at 12 m				<0.001
A (Follow Up)	169(49.1)	63(98.4)	106(37.9)	
B (Follow Up)	151(43.9)	1(1.6)	150(53.6)	
C (Follow Up)	24(7)	0	24(8.6)	
Decompensation events				0.022
1	107 (31.1%)	23 (35.9%)	84 (30.0%)	
2	167 (48.5%)	36 (56.3%)	131 (46.8%)	
≥3	70 (20.3%)	5 (7.8%)	65 (23.2%)	
Ascites (Follow-up)	126(36.6)	1(1.6) ±	125(44.6)	<0.001
Episode of SBP (Follow-up)	18(5.2)	0	18(6.4)	-
Hepatic Encephalopathy (Follow-up)	23(6.7)	0	23(8.2)	-
Acute Variceal Bleed (Follow-up)	18(5.2)	1(1.6) ±	17(6.1)	0.143
Variceal Status at 12 follow-ups				0.573
Small Varices± PHG	111(32.3)	23(35.9)	88(31.4)	
Eradicated varices ± PHG	175(50.9)	33(51.6)	142(50.7)	
PHG alone	20(5.8)	4(6.3)	16(5.7)	
No Varices	38(11)	4(6.3)	34(12.1)	

Abbreviations: BMI, body mass index; CMRF, cardiometabolic risk factor; PEth, phosphatidylethanol; PHG, portal hypertensive gastropathy; SBP, spontaneous bacterial peritonitis.

** Median (Interquartile range)*

† PEth tests were conducted at enrolment and at 12 months in all patients. Additional PEth tests were performed at the physician's discretion. These tests were conducted free of charge under the protocol

‡ A single patient had a recurrence of variceal bleed at 6 months from enrolment with transient self-resolving ascites but recompensated by 17 months.

*** p-value in bold indicates significance at <0.05.*

Supplementary Table S7. Characteristics of patients who attained Child-Turcotte-Pugh (CTP) class A at 12 months of follow-up.

Parameter	TOTAL	Attained CTP A	Did not attain CTP A	<i>p</i> value**
	N=344	N=169	N=175	
Age (years)	46.9±11.7	48.3±11.3	45.4±11.9	0.023
Sex (Male)	286 (83.1)	141(83.4)	145(82.9)	0.887
Diagnosis				0.224
MASLD	158(45.9)	72(42.9)	86(49.1)	
MetALD	186(54.1)	97(57.4)	89(50.9)	
Co-morbid ailments				
Diabetes mellitus, n (%)	95(27.6)	55(32.5)	40(32.5)	0.045
Hypertension, n (%)	73(21.2)	38(22.5)	35(20)	0.573
Hepatitis C virus infection (post-SVR for 3 years)	47(15.3)	24(17.1)	23(13.7)	0.775
Hepatitis B virus (on antivirals with HBV DNA negative for 3 years)	10(3.2)	8(5.7)	2(1.2)	0.047
Alcohol intake	186(54.1)	97(57.4)	89(50.9)	0.224
AUDIT C score	3.9(3.7-4.1)	3.8(3.5-4)	4(3.7-4.3)	0.185
AUDIT C Score Category				0.094
<i>Low</i>	207(60.2)	101(59.8)	106(59.8)	
<i>Intermediate</i>	100(29.1)	44(26)	56(32%)	
<i>High</i>	37(10.8)	24(14.2)	13(7.4)	
PEth Baseline±				0.490
<20ng/ml	213(61.9)	101(59.8)	112(64)	
20-79ngm/ml	102(29.7)	53(31.4)	49(28)	
80-199ng/ml	20(5.8)	12(7.1)	8(4.6)	
>200ngm/ml	9(2.6)	3(1.8)	6(3.4)	
PEth (Follow-up)±				0.020
<20ng/ml	318(92.4)	163(96.4)	155(88.6)	
20-79ngm/ml	25(7.3)	6(3.6)	19(10.9)	
80-199ng/ml	1(0.3)	0	1(0.6)	
Positive Peth >20 ng/ml	129(37.5)	67(39.6)	62(35.4)	0.419
Positive PEth (Follow-up) >20 ng/ml	26(7.6)	6(3.6)	20(11.4)	0.006
Waist Circumference(cm)	38.4(37.5-39.4)	38.1(36.5-39.7)	38.6(37.4-39.8)	0.686
% Weight loss at 12 months	-7.8(-7.9to-7.6)	-7.9(-8.2to-7.7)	-7.6(-7.8to-7.4)	0.088
Weight Loss				0.060
>10%	50(14.5)	30(17.8)	20(11.4)	
7-10%	171(49.7)	88(52.1)	83(47.4)	
<7%	123(35.8)	51(30.2)	72(41.1)	
BMI (kg/m ²)	24±4.6	23.9±4.4	24.1±4.9	0.676
BMI (Follow-up at 12 months) (kg/m ²)	22.2±4.6	22.1±4.3	24.1±4.8	0.655

Decompensation events at Enrolment				
Ascites	297(86.3)	141(83.4)	156(89.1)	0.123
Episode of Ascites (Follow-up)	125(36.3)	40(23.7)	85(48.6)	<0.001
Hepatic Encephalopathy	127(36.9)	46(27.2)	81(46.3)	<0.001
Episode of Hepatic Encephalopathy (Follow-up)	23(6.7)	8(4.7)	15(8.6)	0.154
Portal Hypertension Surveillance				
Acute Variceal Bleed	197(57.3)	104(61.5)	93(53.1)	0.116
AVB follow-up	18(5.2)	3(1.8)	15(8.6)	0.005
Severity scores				
MELD Na*	14.7±3.6	13.1±2.7	16.2±3.6	<0.001
MELD Na 12m	13±4.9	11±3	15±5.5	0.545
Liver Stiffness Measurement 2D SWE (Kpa) †	27.8 ±11.4	28.3±11.4	27.3±11.4	0.458
Liver Stiffness Measurement 2D SWE (Follow Up; Kpa) †	16.9 ±11.5	17.3±11.4	16.5±11.5	0.555
LSM at follow-up based on Fibroscan.†	23.5 ±10	21.5 ±12	24.5 ±12	0.766
Outcomes				
Recompensation as per Baveno VII	64(18.6)	63(37.3)	1(0.6)	<0.001
Deaths	61(17.7)	12(7.1)	49(28)	<0.001
TIPS	8(2.3)	4(2.4)	4(2.3)	0.960
Liver Transplant	11(3.2)	6(3.6)	5(2.9)	0.715
Hepatocellular Carcinoma	5(1.5)	1(0.6)	4(2.3)	0.189
Laboratory Parameters				
Total Bilirubin(mg/dl)	5.1(4.2-5.9)	3.8(2.8-4.8)	6.2(4.7-7.7)	0.009
Total Bilirubin(mg/dl) 12 months	3.4(3.1-3.7)	2.9(2.5-3.3)	3.9(3.5-4.3)	0.001
Albumin(g/dl)	2.9(2.8-3)	3.1(2.8-3.3)	2.8(2.6-3)	0.067
Albumin(g/dl) 12m	3.4(3.1-3.7)	3.7(3.2-4.2)	3.2(3-3.3)	0.043
INR	2(1.6-2.5)	1.7(1.2-2.3)	2.4(1.6-3.1)	0.174
INR 12m	1.9(1.7-2.2)	1.4(1.1-1.8)	2.1(1.7-2.5)	0.182

Abbreviations: AUDIT-C, alcohol use disorder identification test-consumption; BMI, dry body mass index; SVR- sustained virological response; PEth, phosphatidylethanol; TIPS, transjugular intrahepatic portosystemic shunt.

† LSM was measured by Philips ElastPQ 2D shear wave elastography at baseline in patients with ascites, and a repeat assessment was performed with the same technique at follow-up.

At follow-up, another LSM assessment was performed with Fibroscan (Echosens, France), which is reported separately.

‡ Peth tests were conducted at enrolment and at 12 months in all patients. Additional Peth tests were performed at the physician's discretion. These tests were conducted free of charge in accordance with the protocol.

**** p-value in bold indicates significance at <0.05.**

Supplementary Table S8 Baseline demographic and liver disease severity characteristics, with changes on follow-up, stratified by baseline MELD-Na category (<15, 16–20, and ≥21).

Indicator	Total (n=344)	MELD 10- 15(n=231)	MELD 16- 20(n=85)	MELD ≥21 (n=28)	p value**
Age(years)	46.9±11.7	47.8±11.1	45.1±12.8	44.2±12.4	0.080
Male (%)	286(83.1%)	183(79.2%)	77(90.6%)	26(92.9%)	0.020
BMI	24±4.6	24.5±4.5	23.6±4.7	22.4±4.4	0.016
BMI (Follow-up)	22.2±4.6	22.7±4.5	21.5±4.7	20.6±4.3	0.017
BMI>23	202(58.7%)	144(62.3%)	37(43.5%)	18(64.3%)	0.023
BMI>27	87(25.3%)	65(28.1%)	18(21.2%)	4(14.3%)	0.170
Diagnosis					0.016
MASLD	158(45.9%)	117(50.6%)	34(40%)	7(25%)	
MetALD	186(54.1%)	114(49.4%)	51(60%)	21(75%)	
Diabetes mellitus, n (%)	95(27.6%)	71(30.7%)	21(24.7%)	3(10.7%)	0.064
Hypertension, n (%)	73(21.2%)	50(21.6%)	19(22.4%)	4(14.3%)	0.639
Alcohol	189(54.9%)	116(50.2%)	52(61.2%)	21(75%)	0.019
Smoking	27(7.8%)	14(6.1%)	9(10.6%)	4(14.3%)	<0.001
Positive PETH Baseline >20ng/ml	28.8(24-33.6)	26.3(20.8-31.9)	37.1(25.2-49)	23.7914.9-32.6)	0.141
Positive PETH (Follow-up) >20ng/ml *	5.2(3.9-6.5)	3.8(2.7-4.8)	8.6(4.4-12.9)	6.3(1.6-10.9)	0.006
AUDIT-C score	3.9±1.8	3.9±1.8	3.8±1.7	4.3±2.4	0.435
Decompensation Event					
Ascites (%)	297(86.3%)	198(85.7%)	77(90.6%)	22(78.6%)	0.245
Variceal Bleed (%)	197(57.3%)	120(51.9%)	55(64.7%)	22(78.6%)	0.007
HE (%)	127(36.9%)	59(25.5%)	51(60%)	17(60.7%)	<0.001
Further Decompensation					
Variceal Bleeding (Follow-up)	18(5.2%)	14(6.1%)	3(3.5%)	1(3.6%)	0.615
Spontaneous Bacterial Peritonitis (Follow-up)	19(5.5%)	9(3.9%)	6(7.1%)	4(14.3%)	0.059
Ascites (Follow-up)	125(36.3%)	82(35.3%)	30(35.3%)	13(46.4%)	0.511
Hepatic Encephalopathy (Follow-up)	23(6.7%)	16(6.9%)	5(5.9%)	2(7.1%)	0.942
Variceal Status*					0.001
Small Varices ± PHG	176(51.2%)	143(61.9%)	24(28.2%)	9(31.1%)	
Large Varices ± PHG	93(27%)	57(24.7%)	25(29.4%)	11(39.3%)	
Gastric varices ± EV ± PHG	45(13.1%)	23(10%)	16(18.8%)	6(21.4%)	
Portal Hypertensive Gastropathy only	20(5.8%)	4(1.7%)	16(18.8%)	0	
No Varices	10(2.9%)	4(1.7%)	4(4.7%)	2(7.1%)	
Severity scores					
Child Turcotte Pugh (CTP) score	9.2± 1.9	8.6 ±1.8	10.7 ± 1.4	10.5 ± 1.5	<0.001
CTP score at 12 months12m	7.3±1.5	7±1.6	7.8±1.2	7.9±1.4	0.001
Liver Stiffness Measurement (LSM 2D SWE) †	27.8 ±11.4	29.6±11.9	24.1±9.8	25.2±8.4	<0.001
LSM (2D SWE) at follow-up†	16.9 ±11.5	18.6±12	13.2±9.7	14.1±8.6	<0.001
Liver Stiffness Measurement (Follow-Up; kPa, Fibroscan) ‡	23.5 ±10	20.5 ±11	22. 2±11.5	26.5 ±12	0.010

APRI	2.3 ±0.5	2.4±0.5	2.3±0.6	2.2±0.4	0.541
APRI at 12 months	1.4 ±0.4	1.4±0.3	1.4±0.4	1.4±.3	0.567
Fib-4	4.8 ±1.2	4.8±1.3	4.9±0.9	4.8±1.2	0.761
Fib-4 12 months	3.3 ±1.2	3.3±1.2	3.4±0.9	3.3±0.8	0.761
Laboratory parameters					
HDL Cholesterol (mg/dL) *	40(37-43)	43.5(40.1-47)	29.4(22.6-36.2)	29.5(18.4-40.5)	< 0.001
HDL Cholesterol (mg/dL) at 6 m*	34.8(30.6-39.1)	36.4(31.3-41.4)	34.3(23.4-45.3)	23.4(10.6-36.1)	0.235
HDL Cholesterol (mg/dL) at 12 m*	51.6(48.6-54.7)	55.2(51.8-58.6)	41(34.4-47.7)	41.5(30.4-52.5)	< 0.001
LDL Cholesterol (mg/dL) *	64.7(59.3-70.2)	70.3(64-76.7)	46.7(35.9-57.4)	50.2(27.8-72.7)	< 0.001
LDL Cholesterol (mg/dL) at 6 m*	63.6(54.9-72.2)	67.8(57.2-78.3)	56.4(37.3-75.6)	44.2(13.6-74.9)	0.263
LDL Cholesterol (mg/dL) at 12 m*	137.5(17.7-257.3)	163.2(4.6-321.9)	57.2(46.2-68.3)	58.8(35.5-82.2)	0.758
Triglycerides (mg/dL) *	93.8(86.5-101)	97.9(87.9-107.9)	86.6(76.5-96.8)	83.6(62.1-101)	0.295
Triglycerides (mg/dL) at 6 m*	88.6(82.8-94.4)	91.16(84.1-98.1)	88.6(75.6-101.6)	71.4(56.6-86.2)	0.169
Triglycerides (mg/dL) at 12 m*	88.1(83.2-93)	86.4(80-92.9)	91.9(83.7-100.2)	87.4(70.1-104.7)	0.609
HbA1c (g/dL) *	6(5.8-6.3)	6.2(5.9-6.6)	5.8(5.3-6.3)	5.3(4.6-6)	0.101
HbA1c (g/dL) at 6 m *	5.1(5-5.2)	5.2(5-5.3)	4.9(4.7-5.1)	5.2(4.4-5.9)	0.147
HbA1c (g/dL) at 12 m	5(4.8-5.1)	5(4.9-5.1)	4.9(4.7-5.1)	4.8(4.3-5.2)	0.292
Outcomes					
Recompensated	64(18.6%)	47(20.3%)	14(16.5%)	3(10.7%)	0.393
TIPS	8(2.3%)	6(2.6%)	2(2.4%)	0	0.690
Liver transplant	11(3.2%)	9(3.9%)	1(1.2%)	1(3.6%)	0.473
Death	61(17.7%)	32(13.9%)	21(24.7%)	8(28.6%)	0.024

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; APRI, AST to platelet ratio index; HDL, high density lipoprotein; LDL, low density lipoprotein; Fib-4, fibrosis-4 index. * Median with interquartile range.

† LSM was measured by ElastQ 2D shear wave elastography in patients at baseline and follow-up

At follow-up at about 12 m, LSM was also measured with transient elastography (Echosens) and reported separately.

** *p*-value in bold indicates significance at <0.05.

Supplementary Table S9: Landmark analysis of treatment-response variables at 12 months associated with subsequent recompensation, using Fine–Gray competing-risk regression adjusted for baseline MELD-Na. *

Variable (12-month predictors)	Adjusted sHR§	95% CI	p value**
Follow-up LSM (2D SWE)†	0.997	0.975-1.020	0.808
‡ Dry Weight loss <7% at 12 months	Reference		
Weight Loss 7-10%	4.057	1.835-8.967	0.001
Weight Loss ≥10%	7.419	3.151-17.467	<0.001
PEth <20 ng/mL at 12 months (vs ≥20 ng/mL)	1.87	1.29–3.32	0.003
Good glycemic control vs poor control¶	1.431	1.032-2.79	0.038

Abbreviations: sHR, subdistribution hazard ratio; LSM, liver stiffness measurement; MELD-Na, Model for End-stage Liver Disease-sodium; PEth, phosphatidylethanol; 2D SWE, two-dimensional shear wave elastography.

*Of 344 enrolled patients, 329 were alive and transplant-free at the 12-month landmark and were eligible for analysis. Complete data were available for weight-loss category, PEth testing, and glycemic control assessment in all eligible patients. Follow-up liver stiffness measurements were available in 304 patients (92.4%). No imputation of missing values was performed.

† LSM was measured by ElastPQ 2D shear wave elastography at the 12-month follow-up visit.

‡ Weight-loss categories were based on percentage dry-weight loss from enrolment to 12 months: <7%, 7–10%, and ≥10%.

§ Fine–Gray competing-risk regression was performed among patients alive and transplant-free at the 12-month landmark. Follow-up commenced at the landmark time point. Death and liver transplantation were treated as competing events. All models were adjusted for baseline MELD-Na.

¶ Good glycemic control was defined according to the prespecified study definition and assessed at the 12-month follow-up visit.

** p-value in bold indicates significance at <0.05.

Supplementary Table S10. Exploratory analysis of achievement of alcohol abstinence and metabolic targets at 12 months. Patients with MASLD and MetALD achieved comparable numbers of prespecified etiologic-control targets at 12 months.

Number of etiologic-control targets achieved*	MASLD (n=154)	MetALD (n=175)	p value
0-1 target	19 (12.3)	19 (10.9)	
2 targets	62 (40.3)	71 (40.6)	
3 targets	73 (47.4)	85 (48.6)	0.750

*Targets included PEth-confirmed alcohol abstinence (PEth <20 ng/mL), good glycemic control, and ≥7% dry-weight loss at 12 months.

Supplementary Table S11: Exploratory analysis of recompensation according to the number of prespecified etiologic-control targets achieved at the 12-month landmark.

Number of etiologic-control targets achieved*	Overall Recompensation n/N (%)	MASLD Recompensation n/N (%) (n=154)	MetALD Recompensation n/N (%) (n=175)
0–1 target	0/38 (0%)	0/19 (0.0)	0/19 (0.0)
2 targets	19/133 (14.3%)	7/62 (11.3)	12/71 (16.9)
3 targets	45/158 (28.5%)	21/73 (28.8)	24/85 (28.2)
p-value for trend**	<0.001	<0.001	<0.001

Of the 344 enrolled patients, 329 were alive and transplant-free at the 12-month landmark and were eligible for this exploratory analysis. Complete data were available for weight-loss category, PEth testing, and glycemic-control assessment in all eligible patients.

*Prespecified targets included PEth-confirmed alcohol abstinence (PEth <20 ng/mL), good glycemic control, and ≥7% dry-weight loss at 12 months.

** *p-value in bold indicates significance at <0.05.*

Supplementary Table S12: Exploratory subgroup analysis among patients with diabetes mellitus (n=95): association of glycemic control at enrolment and at 12 months with recompensation using Fine–Gray competing-risk regression adjusted for baseline MELD-Na.

<i>Multivariable Fine-Gray Model 2§ in subgroup of patients with diabetes (n=95)</i>	Adjusted sHR	95% CI	p value
Controlled Diabetes at enrolment	1.228	0.574-2.625	0.597
Controlled Diabetes at 12 months	4.413	1.937-7.191	<0.001
Baseline MELD-Na	0.927	0.812–1.057	0.258

§ Fine–Gray competing-risk regression performed in the subgroup of patients with diabetes mellitus (n=95), adjusted for baseline MELD-Na. Glycemic control at enrolment and at 12 months was defined according to prespecified maintained HbA1c target <7mg/dl. Death and liver transplantation were treated as competing events.

Supplementary Table S13: Causes of Death in the study cohort.

	Total	MASLD	MetALD	<i>p</i> value
Deaths	61(17.7)	19(12)	42(22.6)	0.011
Cause of Death (Liver-Related)	57(93.4)	18(94.7)	39(92.8)	0.794
<i>Sepsis event</i>	22(38.5)	6(33.3)	16(41)	
<i>Progressive Liver Failure</i>	22(38.5)	7(38.8)	15(38.4)	
<i>Refractory bleed</i>	9(15.7)	3(16.6)	6(15.3)	
<i>Portal vein thrombosis</i>	4 (7)	1(5)	3(7.6)	
<i>Hepatocellular carcinoma</i>	4 (7)	1(5)	3(7.6)	
Cause of Death (Cardiac Arrest)	4 (7)	1(5.5)	3(7.6)	0.783

Supplementary Table S14. Competing-risk regression analysis for mortality. Subdistribution hazard ratios (sHRs) for death were estimated using Fine–Gray regression models, with liver transplantation treated as a competing event and adjustment for baseline MELD-Na.

Recompensation was modelled as a time-dependent covariate, and mortality was analysed using **cause-specific Cox proportional hazards regression**, treating liver transplantation as a competing event.

Exposure	Comparison	sHR	95% CI	P value
Recompensation *	Not recompensated vs recompensated	No deaths occurred	—	
Etiology†	MetALD vs MASLD	1.87	1.09–3.22	0.023
Weight loss at 12 months	<7%	1.00	Reference	—
	7–10%	1.52	0.65–3.56	0.631
	>10%	1.45	0.76–2.76	0.944
PEth Level	<20 ng/ml	ref		
PEth Level	≥20 ng/mL	5.3	2.85–9.74	<0.001
Baseline MELDNa		1.13	1.06–1.2	<0.001

*The sHR for lack of recompensation was extremely large due to near-complete separation, reflecting no mortality among recompensated patients till their follow-up.

†Etiology analysis includes the full cohort, whereas weight loss and PEth analyses were performed using a 12-month landmark approach restricted to patients alive and transplant-free at 12 months.

A higher baseline MELD-Na was associated with increased mortality risk (sHR 1.13 per point, 95% CI 1.06–1.20; $p < 0.001$).

List of Supplementary Figures

Supplementary Figure S1: Sankey Plots showing the alcohol use patterns, results of PEth testing and weight loss trends of patients enrolled in the cardiometabolic risk cohort. (N=344)

S2A shows the change in CTP class from baseline based on the % weight loss attained by 12 months

S2B shows the attainment of Recompensation based on the baseline PEth test

S1C shows the change in CTP class from baseline based on the AUDIT-C at baseline

Supplementary Figure S2: Sankey Plots showing the alcohol use patterns, results of PEth testing and weight loss trends of patients enrolled in the cardiometabolic risk cohort. (N=344)

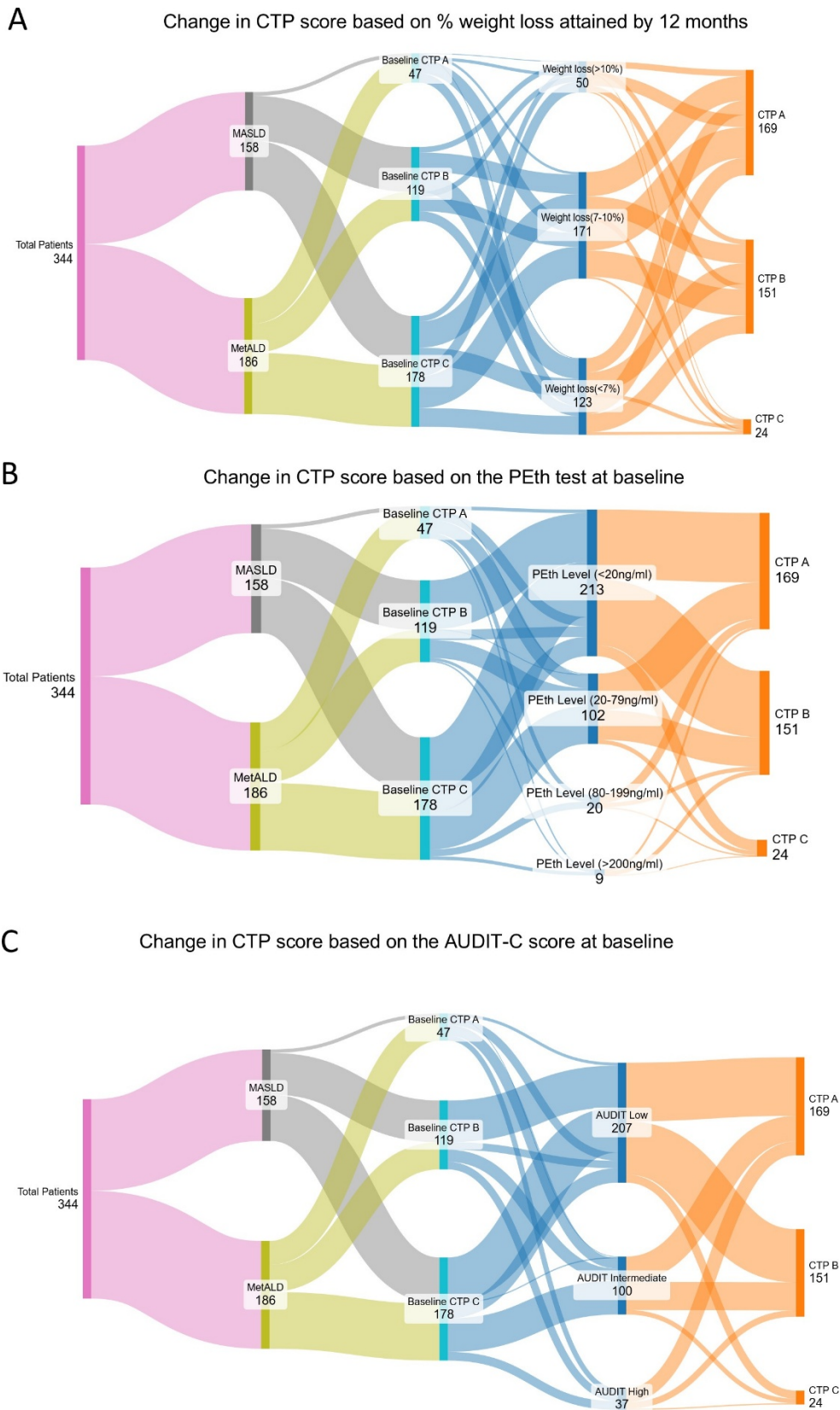
S2A shows the attainment of Recompensation based on baseline CTP class and the weight loss at 12 months

S2B shows the change in CTP class from baseline based on the PEth level at baseline

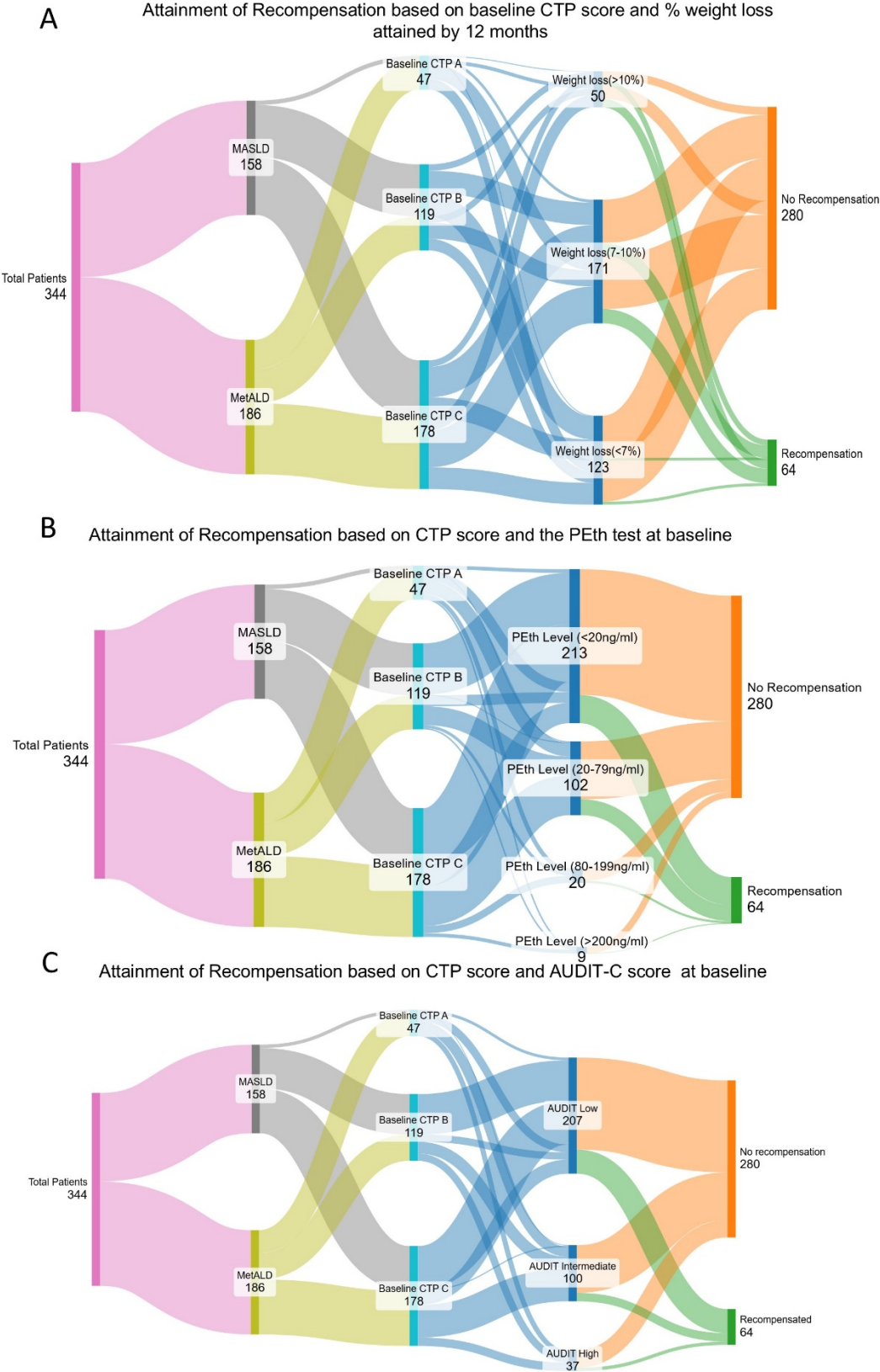
S2C shows the attainment of Recompensation based on baseline CTP class and the baseline AUDIT-C score

Supplementary Figure S3 Adjusted cumulative incidence functions for recompensation derived from Fine–Gray competing-risk regression based on (A) Number of Cardiometabolic risk factors at enrolment and (B) Number of decompensation events at enrolment, with death treated as a competing event and adjustment for baseline MELD-Na.

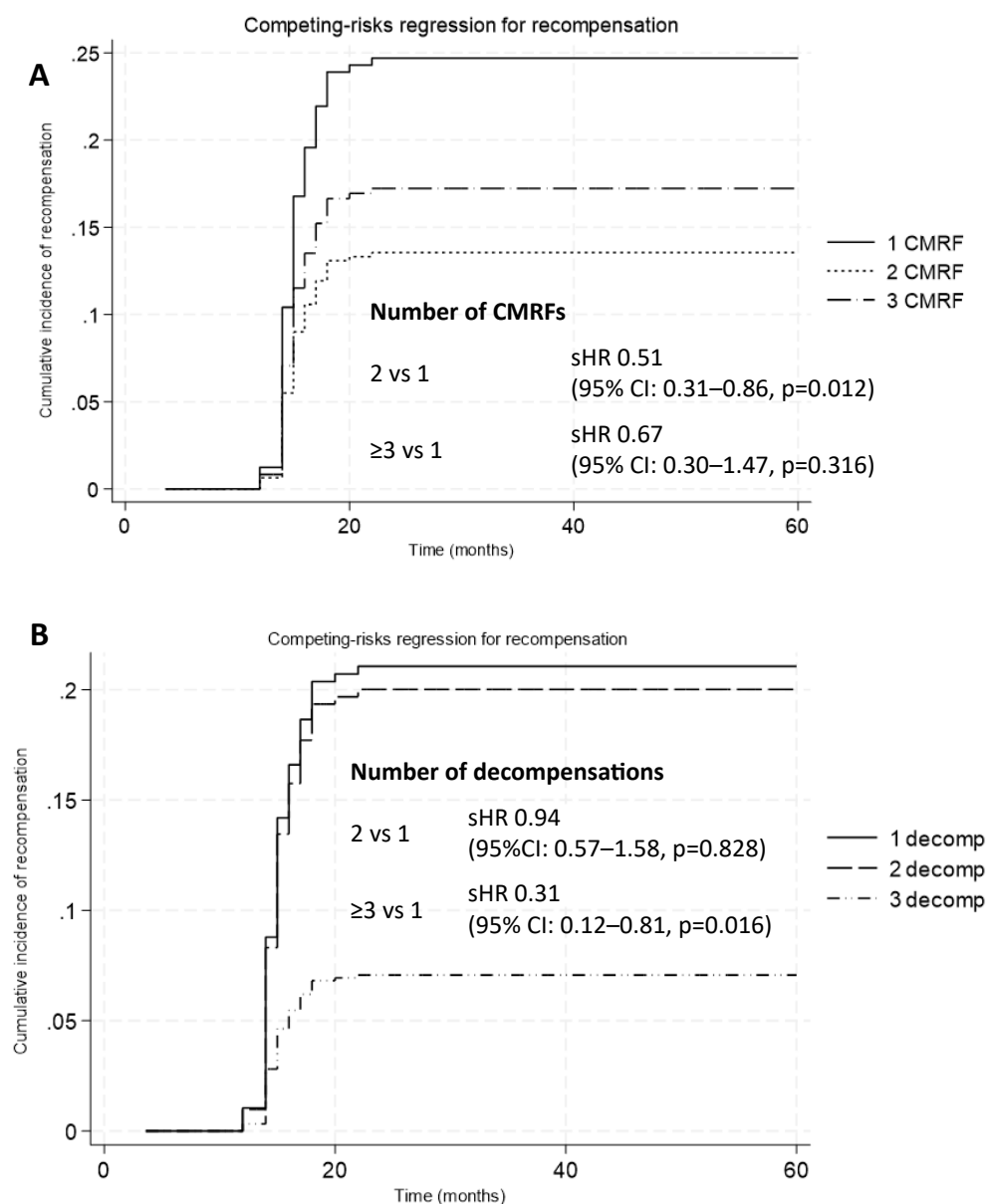
Supplementary Figure S1: Sankey Plots showing the alcohol use patterns, results of PEth testing and weight loss trends of patients enrolled in the cardiometabolic risk cohort. (N=344).S2A shows the change in CTP class from baseline based on the % weight loss attained by 12 months. S2B shows the change in the CTP class based on the baseline PEth test. S1C shows the change in CTP class from baseline based on the AUDIT-C at baseline



Supplementary Figure S2: Sankey Plots showing the attainment of recompensation based on weight loss trends, results of PEth testing and AUDIT C scores of patients enrolled in the cardiometabolic risk cohort. (N=344)



Supplementary Figure S3: Adjusted cumulative incidence functions for recompensation derived from Fine–Gray competing-risk regression with death treated as a competing event and adjustment for baseline MELD-Na. Panels show results by number of CMRF (A), and number of decompensation events (B).



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