19e Congrès International d'Addictologie de l'ALBATROS

ALBATROS International Congress of Addictology

"Alcohol-related liver disease: a holistic and personalized approach"

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Liver Unit

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MAIN TOPICS

1. Never decompensated ALD
2. Alcohol-associated hepatitis
3. Treatment of underlying alcohol use disorder

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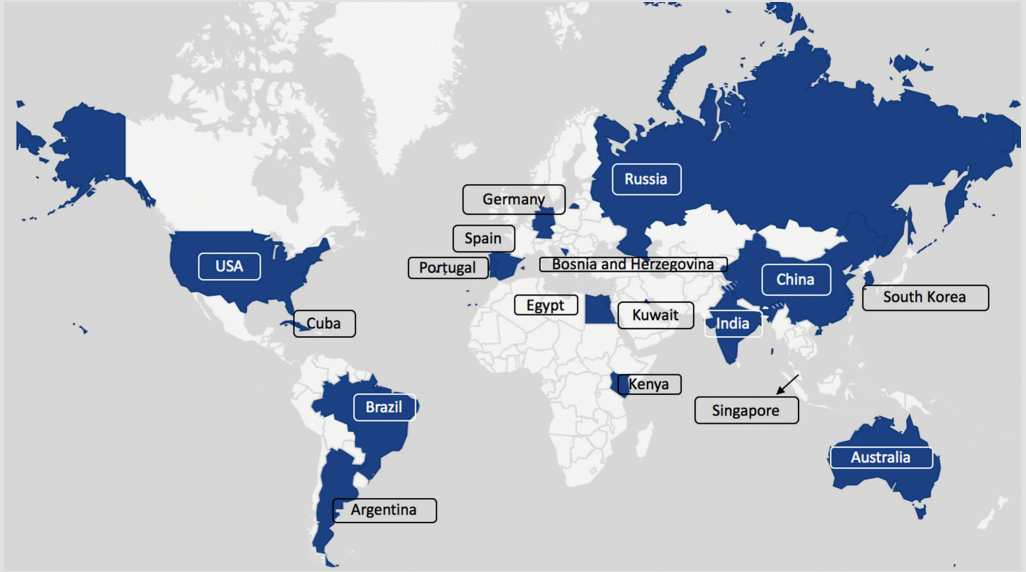
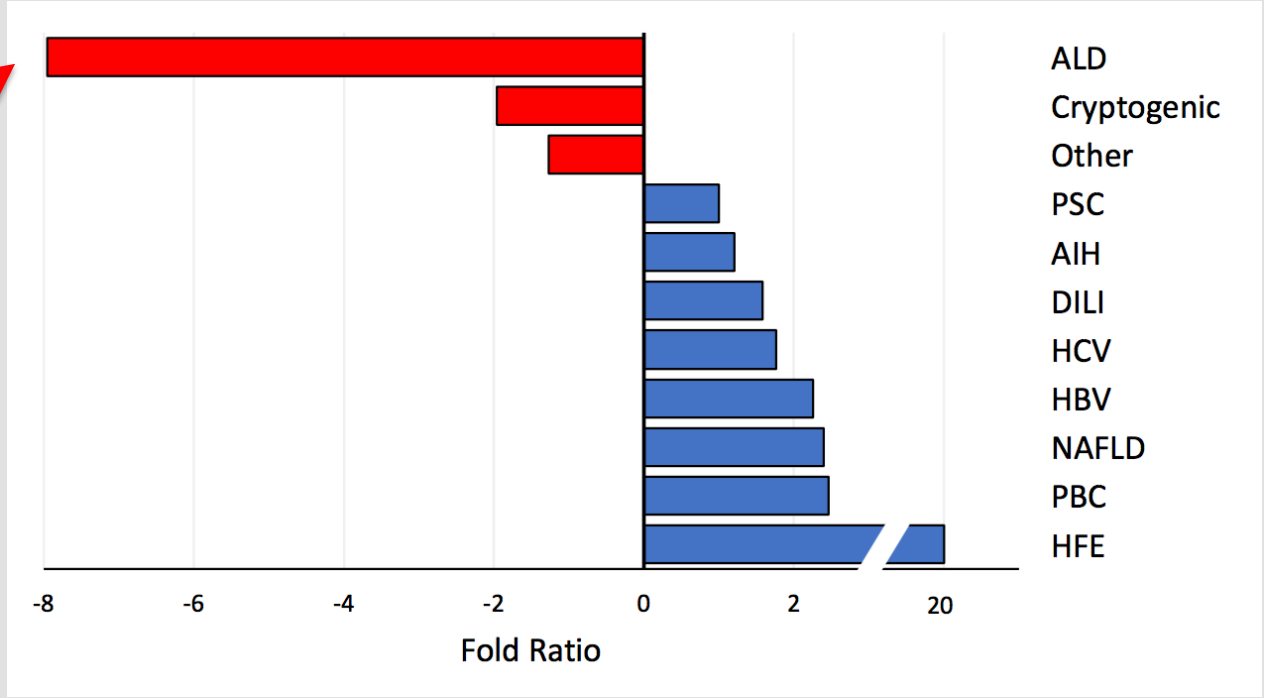
DETECTION OF EARLY vs ADVANCED ALD WORLDWIDE

Alcohol-Related Liver Disease Is Rarely Detected at Early Stages Compared With Liver Diseases of Other Etiologies Worldwide

Neil D. Shah,[*,a] Meritxell Ventura-Cots,[‡,§,a] Juan G. Abraldes,[‖] Mohamed Alboraie,[¶,#] Ahmad Alfadhli,[¶] Josepmaria Argemi,[‡,**] Ester Badia-Aranda,[‡‡] Enrique Arús-Soler,[§§] A. Sidney Barritt IV,[*] Fernando Bessone,[‖‖] Marina Biryukova,[¶¶] Flair J. Carrilho,[##] Marlen Castellanos Fernández,[§§] Zaily Dorta Guiridi,[¶¶] Mohamed El Kassas,[***] Teo Eng-Kiong,[‡‡‡] Alberto Queiroz Farias,[##] Jacob George,[§§§] Wenfang Gui,[‖‖‖] Prem H. Thurairajah,[‡‡‡] John Chen Hsiang,[‡‡‡] Azra Husić-Selimovic,[¶¶¶] Vasily Isakov,[¶¶] Mercy Karoney,[###] Won Kim,[****] Johannes Kluwe,[‡‡‡‡] Rakesh Kochhar,[§§§§] Narendra Dhaka,[§§§§] Pedro Marques Costa,[‖‖‖‖] Mariana A. Nabeshima Pharm,[##] Suzane K. Ono,[##] Daniela Reis,[‖‖‖‖] Agustina Rodil,[##] Caridad Ruenes Domech,[§§] Federico Sáez-Royuela,[‡‡] Christoph Scheurich,[‡‡‡‡] Way Siow,[§§§] Nadja Sivac-Burina,[¶¶¶] Edna Solange Dos Santos Traquino,[§§] Fatma Some,[###] Sanjin Spreckic,[¶¶¶] Shiyun Tan,[¶¶¶¶] Julio Vorobioff,[‖‖] Andrew Wandera,[###] Pengbo Wu,[¶¶¶¶] Mohamed Yacoub,[####] Ling Yang,[‖‖‖] Yuanjie Yu,[¶¶¶¶] Nerma Zahiragic,[¶¶¶] Chaoqun Zhang,[¶¶¶¶] Helena Cortez-Pinto,[‖‖‖‖] and Ramon Bataller[*,‡]



DETECTION OF EARLY vs ADVANCED ALD WORLDWIDE: THE GLADIS STUDY

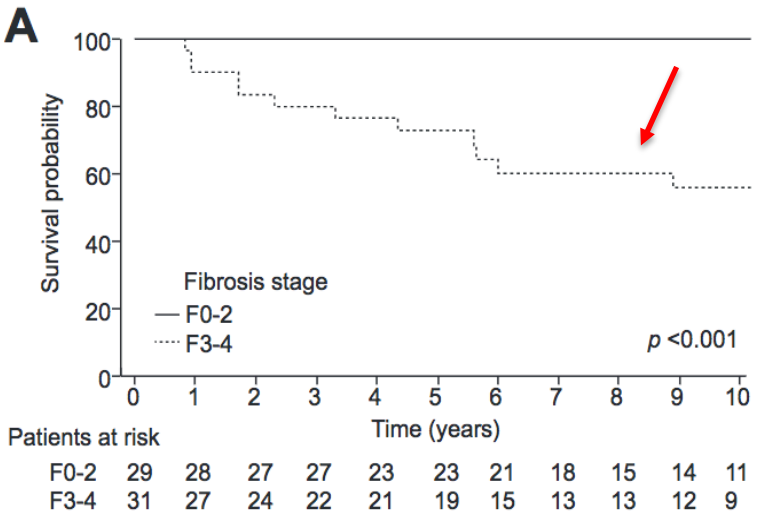


Advanced - decompensated **Early - compensated**

IMPACT OF ADVANCED FIBROSIS IN LONG TERM MORTALITY

Histological parameters and alcohol abstinence determine long-term prognosis in patients with alcoholic liver disease

Carolin Lackner[1,*,†], Walter Spindelboeck[2,†], Johannes Haybaeck[1], Philipp Douschan[2], Florian Rainer[2], Luigi Terracciano[3], Josef Haas[4], Andrea Berghold[5], Ramon Bataller[6], Rudolf E. Stauber[2]



1. *Why some patients develop F3-F4 ?*
2. *Why not all F4 decompensate and die ?*

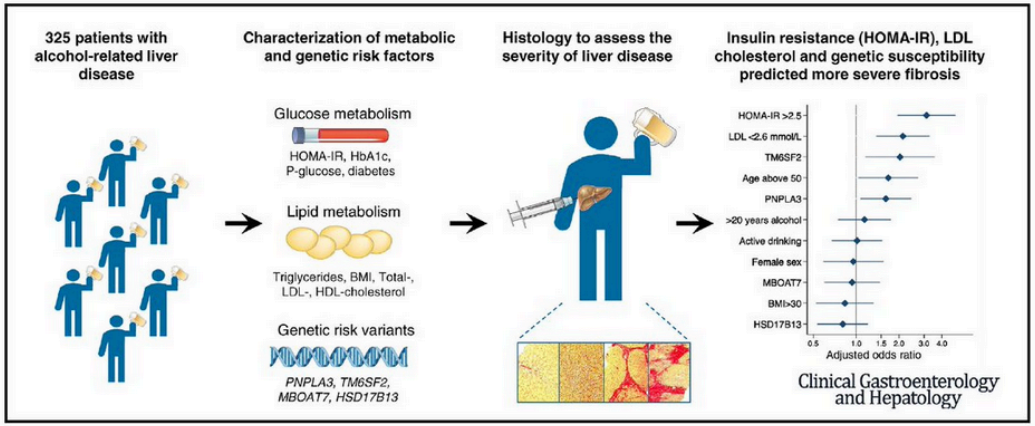
CAN WE PREDICT PATIENTS PROGRESSING TO CIRRHOSIS ?

Metabolic and Genetic Risk Factors Are the Strongest Predictors of Severity of Alcohol-Related Liver Fibrosis

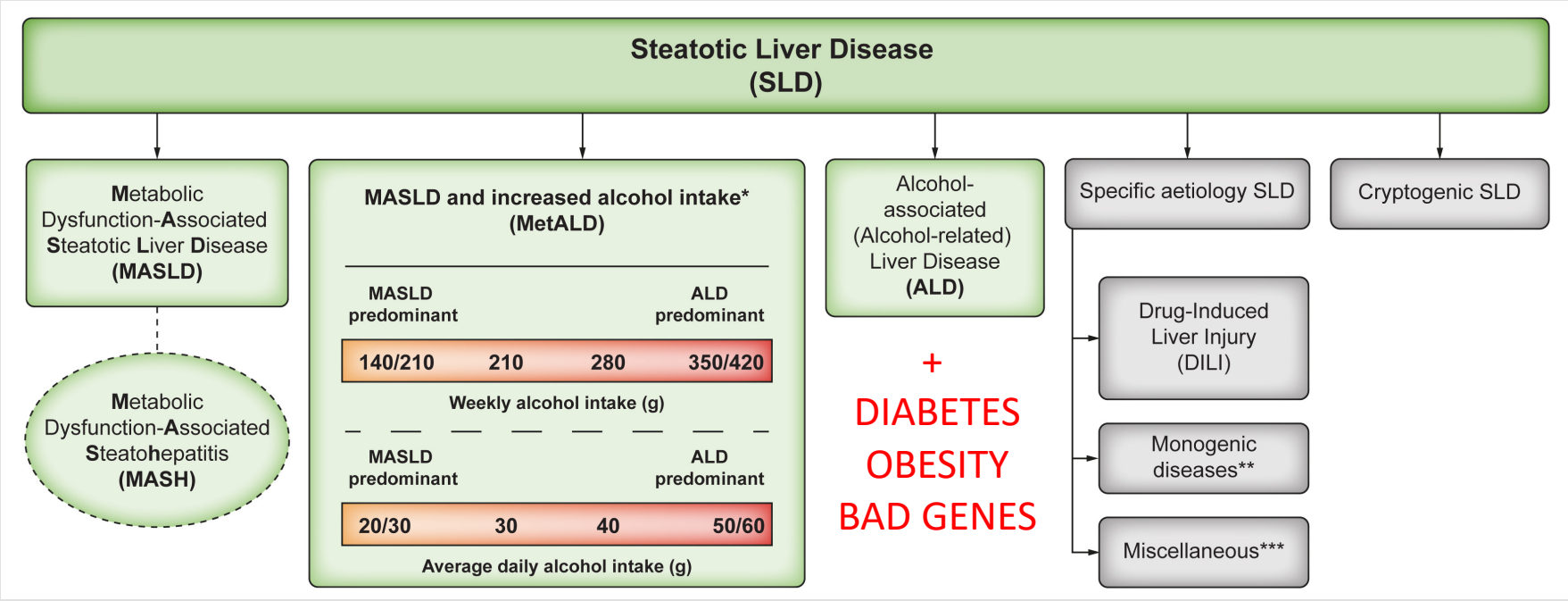
Mads Israelsen,[*,‡] Helene Bæk Juel,[§] Sönke Detlefsen,[‡,‖] Bjørn Stæhr Madsen,[*,‡] Ditlev Nytoft Rasmussen,[*,‡] Trine R. Larsen,[¶] Maria Kjærgaard,[*,‡] Mary Jo Fernandes Jensen,[§] Stefan Stender,[#,**] Torben Hansen,[§] Aleksander Krag,[*,‡] and Maja Thiele,[*,‡] on behalf of the GALAXY and MicrobLiver consortiak

*Department of Gastroenterology and Hepatology, Odense University Hospital, Odense; ‡Institute of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense; §Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, Copenhagen; ‖Department of Pathology, Odense University Hospital, Odense; ¶Department of Clinical Biochemistry, Svendborg Hospital, Svendborg; #Department of Clinical Biochemistry, Rigshospitalet, Copenhagen; and **Department of Gastroenterology and Hepatology, Hvidovre Hospital, Hvidovre, Denmark

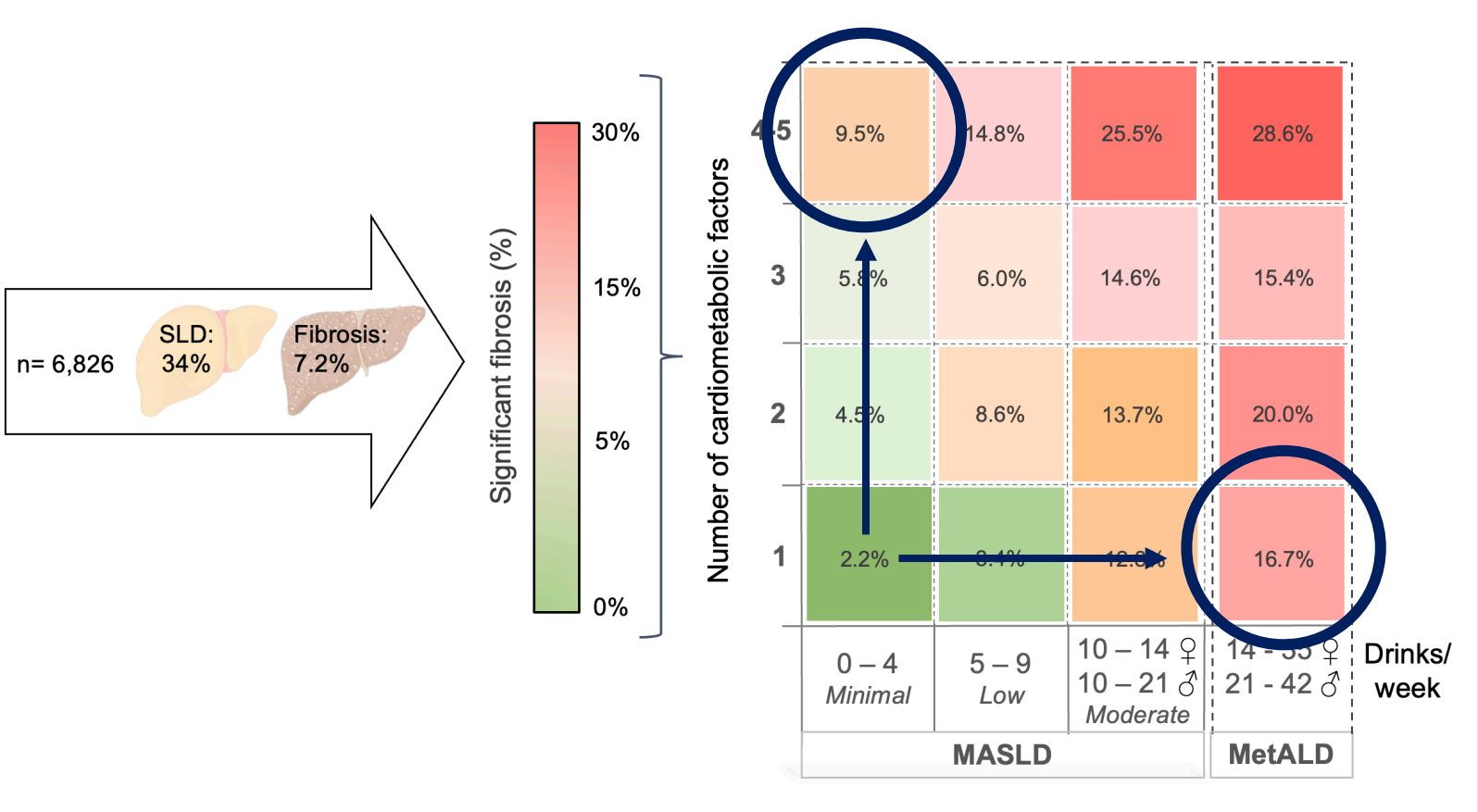
This article has an accompanying continuing medical education activity, also eligible for MOC credit on page e1529. Upon completion of this activity, successful learners will be able to identify high risk patients with a history of excessive alcohol use but without any symptoms of liver disease.



MetALD: A COMMON CONDITION THAT WAS OVERLOOKED

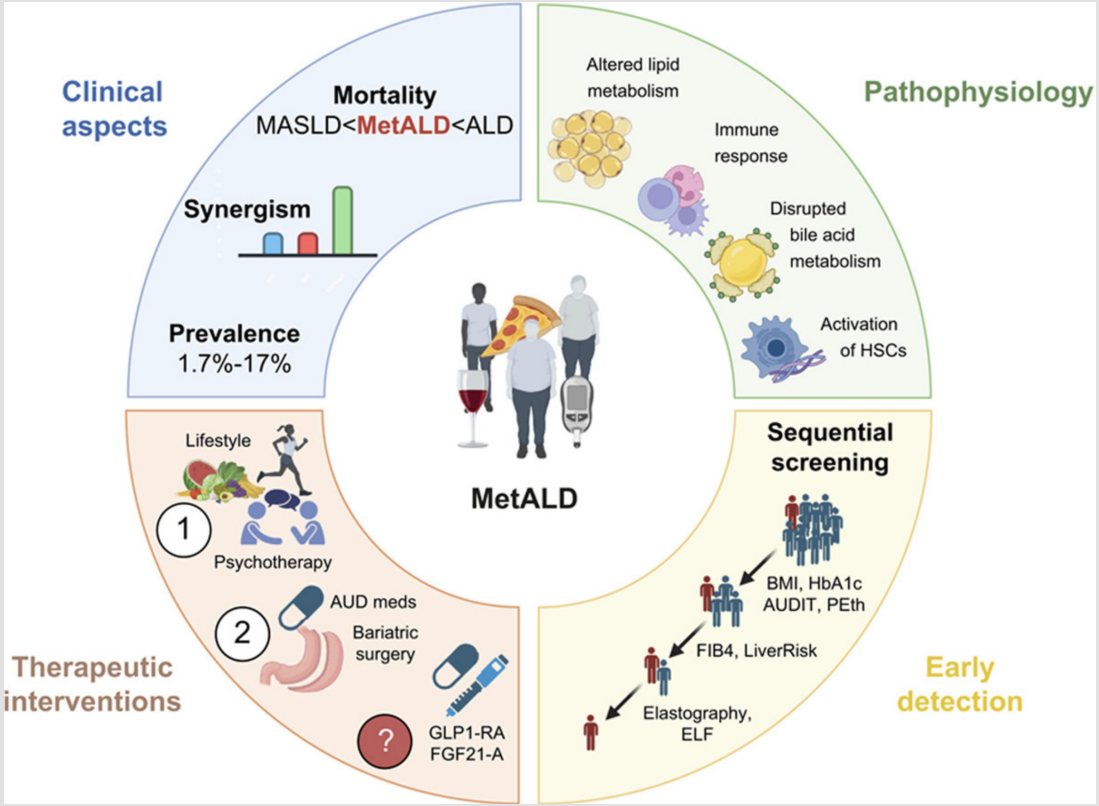


MetALD: EVEN LOW ALCOHOL INTAKE PROMOTES FIBROSIS



Marti-Aguado et al, J Hepatol 2024

MetALD: PATHOPHYSIOLOGI AND CLINICAL ASPECTS



Gratacos-Gines J et al. JHepReports 2025

PRECISION-PERSONALIZED MEDICINE IN 3 SCENARIOS

1. Never decompensated ALD
2. Alcohol-associated hepatitis
3. Treatment of underlying alcohol use disorder

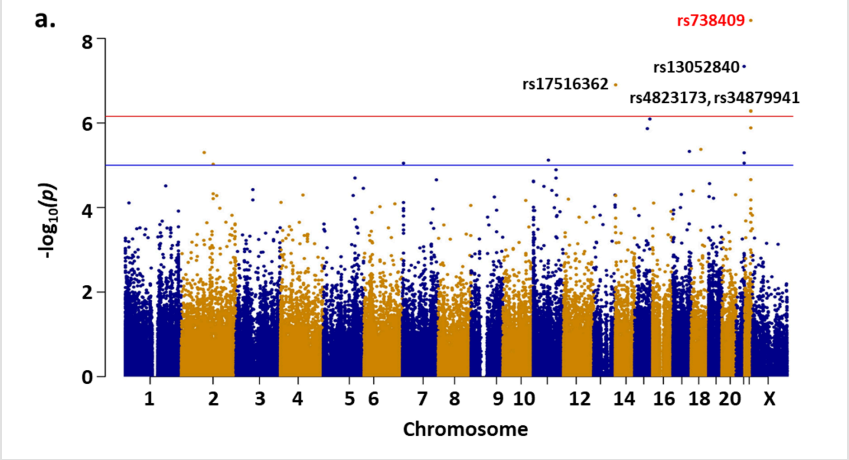
MAIN QUESTIONS IN ALCOHOL-ASSOCIATED HEPATITIS

1. *Why only a subset of patients **develop** AH ?*
2. *Can we predict **mortality** ?*
3. *Can we predict response to **corticosteroids** ?*
4. *Can we accurately select the best **candidates for early transplant** ?*

GENETIC FACTORS AND RISK OF AH DEVELOPMENT

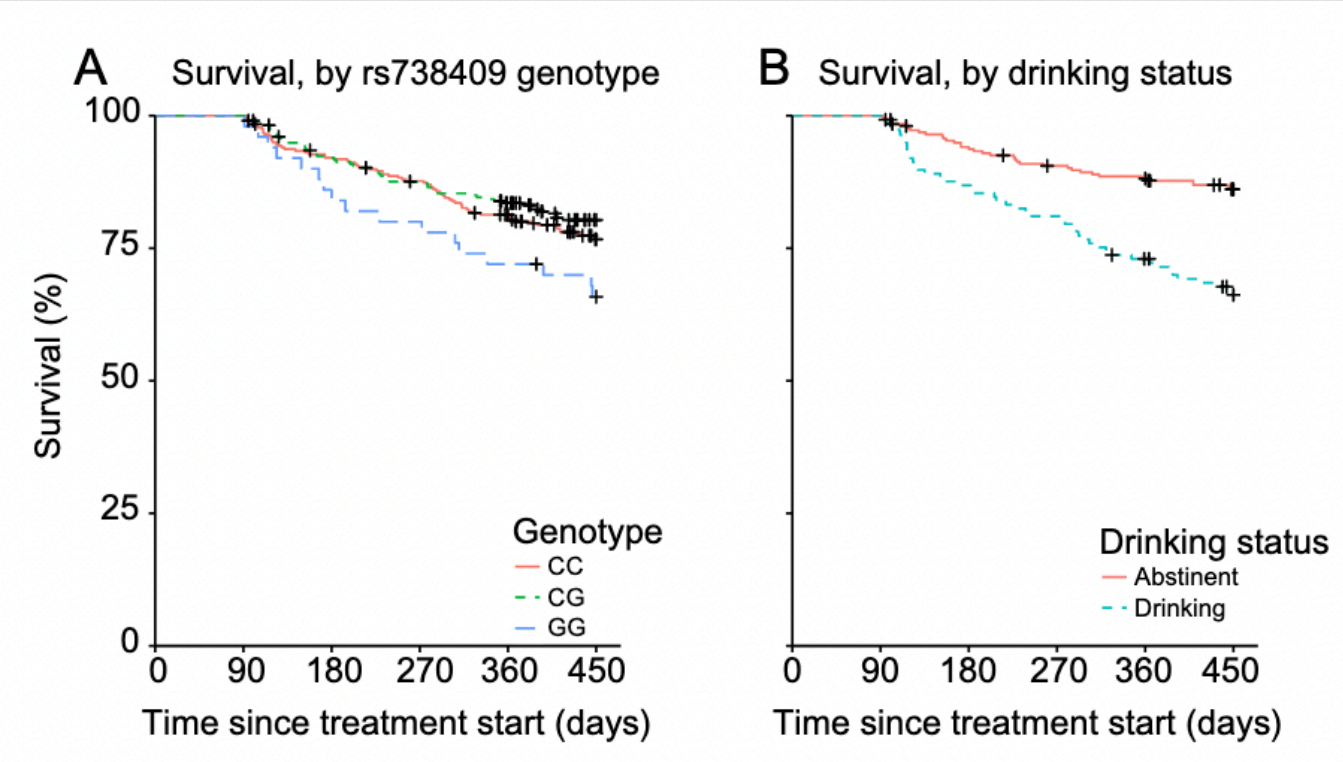
Exome-wide association analysis identifies novel risk loci for alcohol-associated hepatitis

Qiaoping Yuan[1], Colin Hodgkinson[1], Trina Norden-Krichmar[4], Xiaochen Liu[4], Bruce Barton[3], Nancy Diazgranados[2], Melanie Schwandt[2], with DASH, InTEAM, SCAHC and TREAT consortia, Timothy Morgan5, Ramon Bataller[6], Suthat Liangpunsakul[3], Laura E. Nagy[7], David Goldman[1,2,] for the AH Genomics Consortia



Gene	VEP	Snp151	Chr-Pos-Ref-Alt	*p*.value	BETA	SE
PNPLA3	I148M	rs738409	chr22-44324727-C-G	**3.75E-09**	0.548	0.095
ICOSLG	Q329Q	rs13052840	chr21-45649848-T-C	**4.59E-08**	0.515	0.096
TOX4	5'-UTR	rs17516362	chr14-21944955-G-C	**1.25E-07**	-0.495	0.096
PNPLA3	intron	rs4823173	chr22-44328730-G-A	**5.14E-07**	0.499	0.102
PNPLA3	intron	rs34879941	chr22-44332878-C-T	**5.30E-07**	0.493	0.101
MESP1	intron	rs2305442	chr15-90293701-G-A	8.06E-07	0.479	0.100
PNPLA3	intron	rs2072906	chr22-44333172-A-G	1.31E-06	0.474	0.101
ADAMTS7	intron	rs3971703	chr15-79092481-G-C	1.36E-06	0.442	0.094
SIGLEC15	F273L	rs2919643	chr18-43419003-T-C	4.21E-06	-0.478	0.107
SLC25A19	intron	rs2306218	chr17-73282299-C-T	4.71E-06	0.423	0.095
CREG2	5'-UTR	rs116287156	chr2-102003962-T-C	5.00E-06	0.467	0.106
CFAP410	5'-UTR	rs73374031	chr21-45759197-G-C	5.07E-06	-0.438	0.099
ADRBK1	intron	rs10896164	chr11-67052466-G-A	7.57E-06	0.484	0.112
CFAP410	R11R	rs11870	chr21-45759045-C-T	8.89E-06	-0.426	0.099
AP5Z1	intron	rs3750012	chr7-4828593-T-C	8.94E-06	-0.551	0.128
LRP1B	intron	rs1429365	chr2-141747249-A-T	9.42E-06	-0.380	0.089

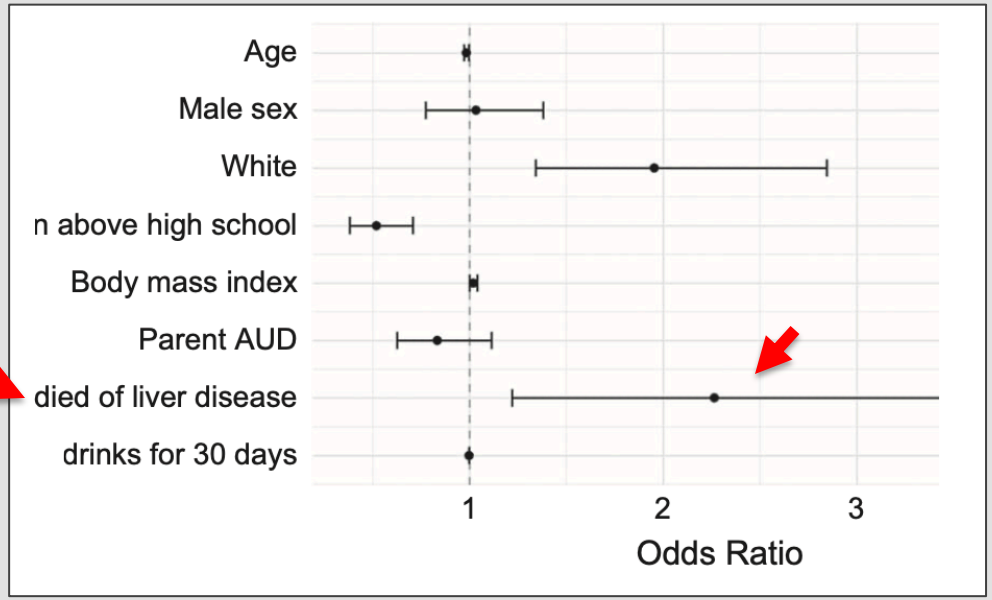
PNPAL3 VARIATIONS AND PROGNOSIS IN AH



Atkinson et al, J Hepatol 2018

Parental liver disease mortality is associated with unfavorable outcomes in patients with alcohol-associated hepatitis

Wanzhu Tu[1] | Samer Gawrieh[1] | Lauren Nephew[1] | Craig McClain[2] | Qing Tang[1] | Srinivasan Dasarathy[3] | Vatsalya Vatsalya[2] | Douglas A. Simonetto[4] | Carla Kettler[1] | Gyongyi Szabo[5] | Bruce Barton[6] | Yunpeng Yu[1] | Patrick S. Kamath[4] | Arun J. Sanyal[7] | Laura Nagy[3] | Mack C. Mitchell[8] | Suthat Liangpunsakul[1] | Vijay H. Shah[4] | Naga Chalasani[1] | Ramon Bataller[9] | on behalf of the AlcHepNet Investigators



CORTICOSTEROID THERAPY IN SEVERE ALCOHOLIC HEPATITIS*

A Double-Blind Drug Trial

HENRIK P. PORTER, M.D., FRANCIS R. SIMON, M.D., CHARLES E. POPE, II, M.D., WADE VOLWILER, M.D., AND L. FREDERICK FENSTER, M.D.

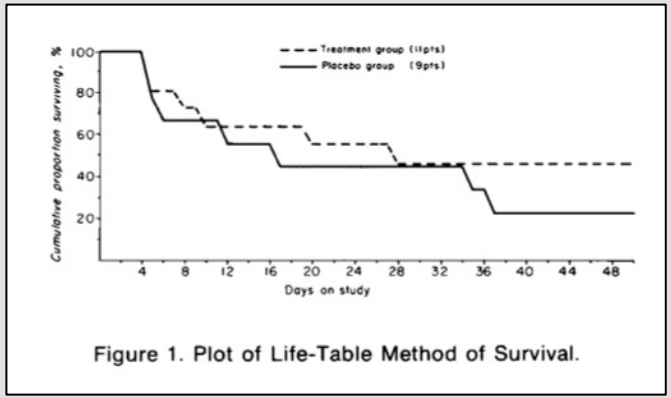
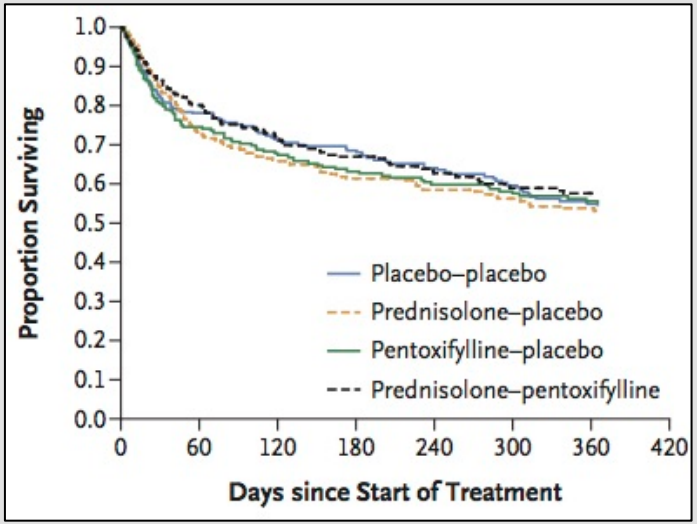


Figure 1. Plot of Life-Table Method of Survival.

1971

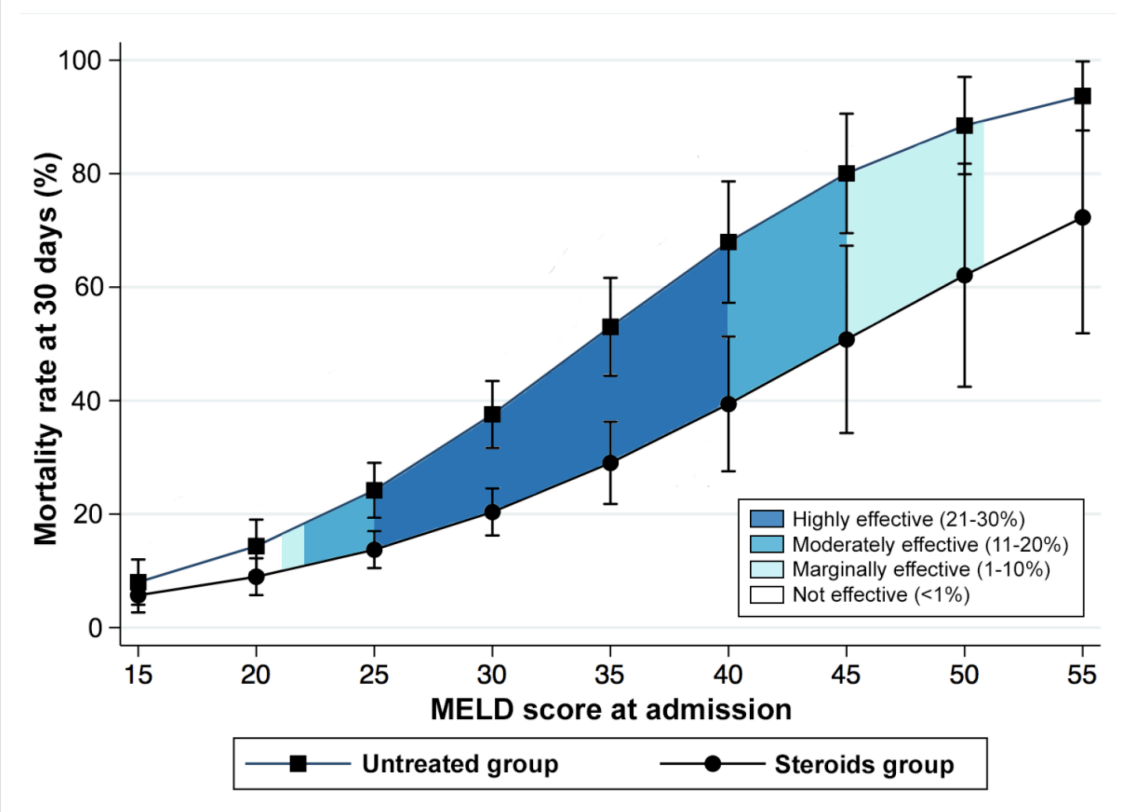
Prednisolone or Pentoxifylline for Alcoholic Hepatitis

Mark R. Thursz, M.D., Paul Richardson, M.D., Michael Allison, Ph.D., Andrew Austin, M.D., Megan Bowers, M.Sc., Christopher P. Day, M.D., Ph.D., Nichola Downs, P.G. Cert., Dermot Gleeson, M.D., Alastair MacGilchrist, M.D., Allister Grant, Ph.D., Steven Hood, M.D., Steven Masson, M.A., Anne McCune, M.D., Jane Mellor, M.Sc., John O'Grady, M.D., David Patch, M.D., Ian Ratcliffe, M.Sc., Paul Roderick, Ph.D., Louise Stanton, M.Sc., Nikhil Vergis, M.B., B.S., Mark Wright, Ph.D., Stephen Ryder, D.M., and Ewan H. Forrest, M.D., for the STOPAH Trial*



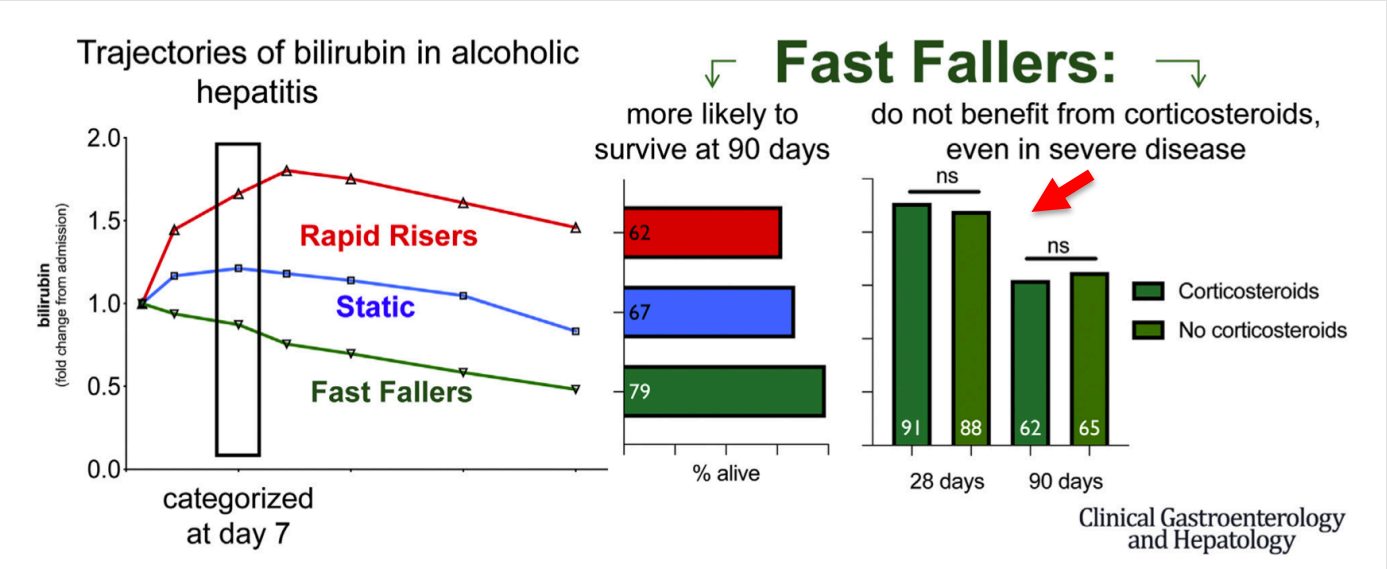
2015

THERAPEUTIC WINDOW FOR THE USE OF CORTICOSTEROIDS IN AH



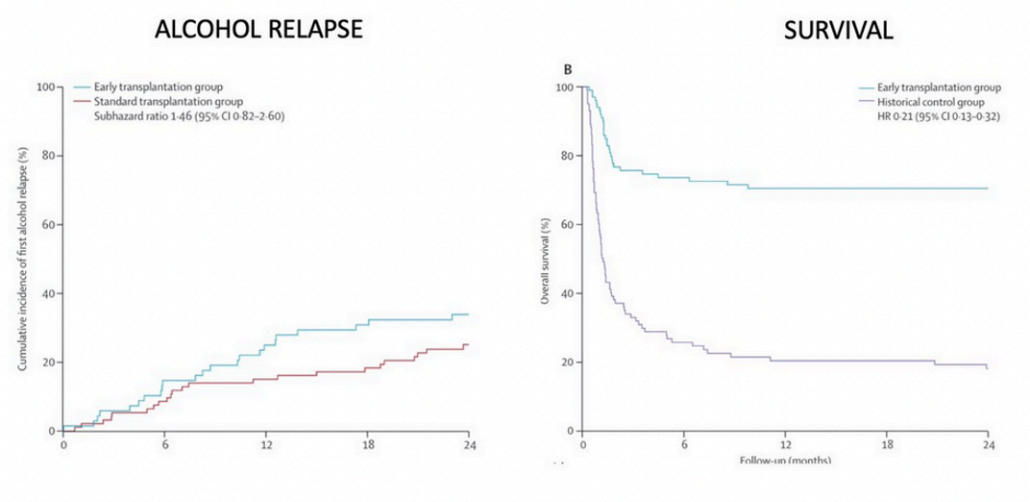
Arab JP et al, J Hepatol 2021

BILIRUBIN TRAJECTORY IN ALC HEP



Parker et al, Clin Gastroenterol Hepatol 2022

SELECTING THE BEST CANDIDATES FOR EARLY LIVER TRANSPLANT



MAIN SELECTION CRITERIA

- 1st episode AH
- No major psychiatric co-morbidities
- Reasonable alcohol insight
- Good family support
- No multiple rehab attempts
- Consensus of selection committee
- Use of scoring systems ??

Louvet et al, Lancet Gastroenterol Hepatol 2022

PRECISION-PERSONALIZED MEDICINE IN 3 SCENARIOS

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PUBLIC POLICIES TO PREVENT ALD

nature reviews gastroenterology & hepatology
https://doi.org/10.1038/s41575-025-01084-6

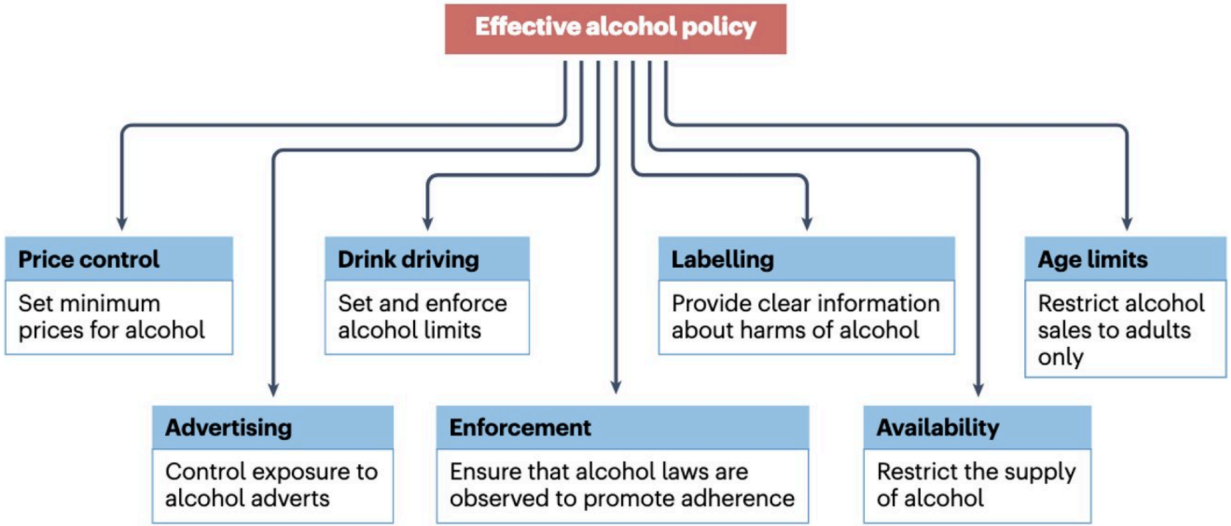
Perspective

Check for updates

Public health policies to prevent alcohol-related liver disease

Richard Parker[1], Juan P. Arab[2,3], Jeffrey V. Lazarus[4,5], Ramon Bataller[6] & Ashwani K. Singal[7,8,9]

Abstract | Sections



Ramon Bataller
@rabataller

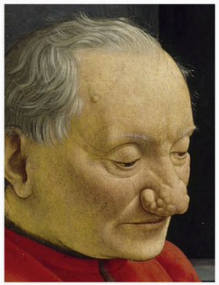
Can we detect chronic alcohol just using MEDICAL HISTORY and PHYSICAL EXAM? Of course ! This is my summary:

- Physical signs of alcohol use (Dupuytren)
- Multisystemic involvement (neuropathy)
- Associated conditions
- Periods of compensation and decompensation

#livertwitter

Medical history and physical exam to identify a chronic alcohol user

1. **SIGNS CHRONIC ALCOHOL USE**: DUPUYTREN, RHYNOPHIMA, VASCULAR ECTASIA, FACIAL MALAR ERTHEMA, PAROTID HYPERTROPHY.
2. **MULTISYSTEMIC INVOLVEMENT** : MALNOURISHMENT, SARCOPENIA, COGNITIVE IMPAIRMENT (FLAT AFFECT), PERIPHERAL NEUROPATHY.
3. **ASSOCIATED CONDITIONS**: CIGARETTE SMOKING, SOCIAL ISOLATION, FRACTURES.
4. **LIVER-RELATED DECOMPENSATION**: ALTERNATE COMPESATED AND DECOMPENSATED PERIODS.



TREATING AUD IN A PATIENT-CENTERED MANNER

GENETIC-ENVIRONMENTAL FACTORS

- Family history
- Genetic risk
- Other addictions

SOCIAOECONOMIC FACTORS

- Isolation
- Stigma
- Transportation
- Insurance

COMMON ASSOCIATED CONDITIONS

- PTSD
- Sexual abuse
- Depression
- Anxiety
- Sleep
- Pain

MULTIDISCIPLINARY ALD CLINIC

- *Specialized nurse*
- *Addiction therapist*
- *Social worker*
- *Financial counselor*
- *Hepatologist*

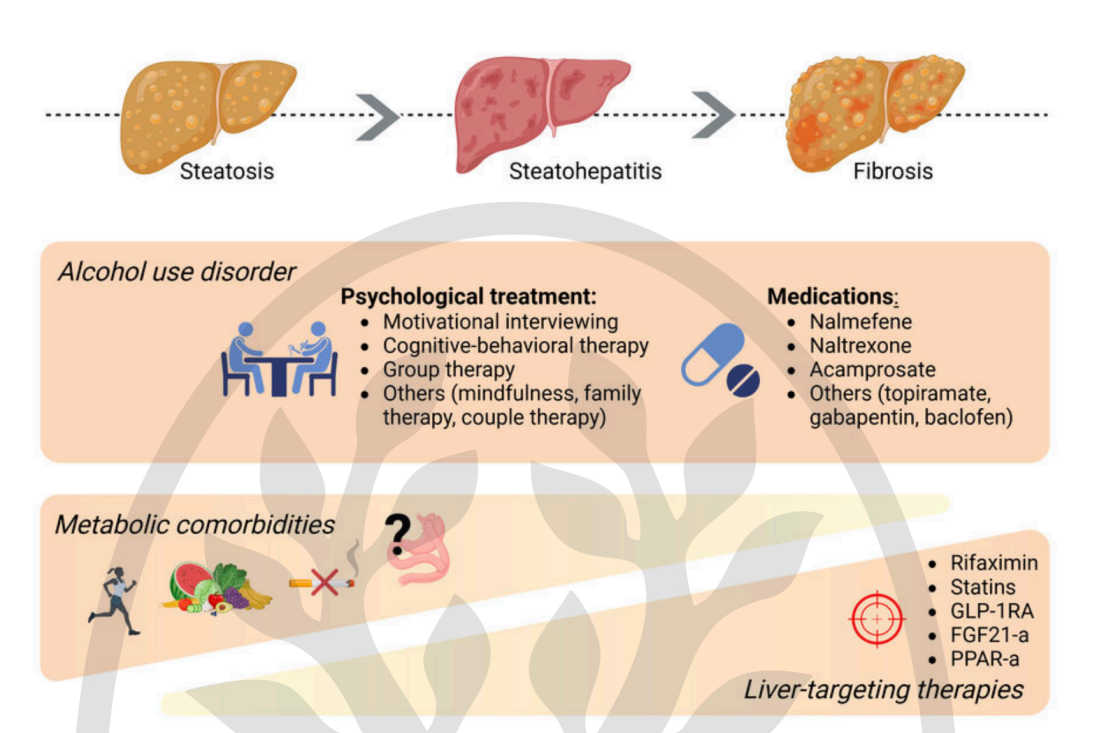
ROLE OF PHARMACOTHERAPY IN AUD IN LIVER PATIENTS

FDA approved for AUD

- **Disulfiram:** unsafe if significant fibrosis. Risk of liver failure.
- **Acamprosate:** observational studies suggest is safe and efficacious.
- **Naltrexone:** safe in compensted cirrhosis. Caution if opioid use.
- **Baclofen:** a positive placebo-control trial in cirrhosis. Anti-craving.

Arab, Izzy, Leggio, Bataller & Shah, Nat Rev Gastroenterol Hepatol 2021

TREATING AUD IN ALCOHOL-RELATED LIVER DISEASE



Seminars in Liver Disease

Diagnosis and management of early stages of ALD

Jordi Gratacós-Ginès, Edilmar Alvarado-Tapias, David Marti-Aguado, Hugo López-Pelayo, Ramon Bataller, Elisa Pose.

PROMISING APPROACHES TO TREAT AUD: SEMAGLUTIDE

Association between glucagon-like peptide-1 receptor agonists use and change in alcohol consumption: a systematic review

Mohsen Subhani, Ashwin Dhanda, James A. King, Fiona C. Warren, Siobhan Creanor, Melanie J. Davies, Sally Eldeghaidy, Stephen Bawden, Penny A. Gowland, Ramon Bataller, Justin Greenwood, Stephen Kaar, Neeraj Bhala, and Guruprasad P. Aithal

Received: 30 December 2023 | Accepted: 29 August 2024
DOI: 10.1111/add.16679
RESEARCH REPORT
ADDICTION SSA

The association between glucose-dependent insulinotropic polypeptide and/or glucagon-like peptide-1 receptor agonist prescriptions and substance-related outcomes in patients with opioid and alcohol use disorders: A real-world data analysis

Fares Qeadan | Ashlie McCann | Benjamin Tingey

JCI insight
RESEARCH ARTICLE

The glucagon-like peptide-1 (GLP-1) analogue semaglutide reduces alcohol drinking and modulates central GABA neurotransmission

Vicky Chuong, Mehdi Farokhnia, Sophia Khom, Claire L. Pince, Sophie K. Elvig, Roman Vlkolinsky, Renata C.N. Marchette, George F. Koob, Marisa Roberto, Leandro F. Vendruscolo, and Lorenzo Leggio

www.nature.com/scientificreports
scientific reports
OPEN

Semaglutide and Tirzepatide reduce alcohol consumption in individuals with obesity

Fatima Quddos[1,2], Zachary Hubshman[1,3], Allison Tegge[1], Daniel Sane[1,3], Erin Marti[1], Anita S. Kablinger[4], Kirstin M. Gatchalian[1], Amber L. Kelly[1,2], Alexandra G. DiFeliceantonio[1] & Warren K. Bickel[1]

Alcohol Use Disorder (AUD) contributes significantly to global mortality. GLP-1 (Glucagon-like peptide-1) and GLP-1/GIP (Glucose-dependent Insulinotropic Polypeptide) agonists, FDA-approved for managing type 2 diabetes and obesity, where the former has shown to effectively reduce the consumption of alcohol in animal models but no reports exist on the latter. In this report, we conducted two studies. In the first study, we conducted an analysis of abundant social media texts. Specifically, a machine-learning based attribution mapping of ~68,250 posts related to GLP-1 or GLP-1/GIP agonists on the Reddit platform. Secondly, we recruited participants (n = 153; current alcohol drinkers; BMI ≥ 30) who self-reported either taking Semaglutide (GLP-1 agonist), Tirzepatide (the GLP-1/GIP combination) for ≥ 30 days or, as a control group; no medication to manage diabetes or weight loss for a within and between subject remote study. In the social media study, we report 8 major themes including effects of medications (30%); diabetes (21%); and Weight loss and obesity (19%). Among the alcohol-related posts (n = 1580), 71% were identified as craving reduction, decreased desire to drink, and other negative effects. In the remote study, we observe a significantly lower self-reported intake of alcohol, drinks per drinking episode, binge drinking odds, Alcohol Use Disorders Identification Test (AUDIT) scores, and stimulating, and sedative effects in the Semaglutide or Tirzepatide group when compared to prior to starting medication timepoint (within-subjects) and the control group (between-subjects). In summary, we provide initial real-world evidence of reduced alcohol consumption in people with obesity taking Semaglutide or Tirzepatide medications, suggesting potential efficacy for treatment in AUD comorbid with obesity.

The Journal of Clinical Investigation
CLINICAL RESEARCH AND PUBLIC HEALTH

Glucagon-like peptide-1 receptor agonists, but not dipeptidyl peptidase-4 inhibitors, reduce alcohol intake

Mehdi Farokhnia, John Tazare, Claire L. Pince, Nicolaus Bruns VI, Joshua C. Gray, Vincent Lo Re III, David A. Fiellin, Henry R. Kranzler, George F. Koob, Amy C. Justice, Leandro F. Vendruscolo, Christopher T. Rentsch, and Lorenzo Leggio

JAMA Psychiatry | Original Investigation

Once-Weekly Semaglutide in Adults With Alcohol Use Disorder
A Randomized Clinical Trial

Christian S. Hendershot, PhD; Michael P. Bremmer, MA; Michael B. Paladino, BS; Georgios Kostantinis, BA; Thomas A. Gilmore, BA; Neil R. Sullivan, BA; Amanda C. Tow, MD, PhD; Sarah S. Dermody, PhD, CPsych; Mark A. Prince, PhD; Robyn Jordan, MD, PhD; Sherry A. McKee, PhD; Paul J. Fletcher, PhD; Eric D. Claus, PhD; Klara R. Klein, MD, PhD

IMPORTANCE Preclinical, observational, and pharmacoepidemiology evidence indicates that glucagon-like peptide 1 receptor agonists (GLP-1RAs) may reduce alcohol intake. Randomized trials are needed to determine the clinical significance of these findings.

OBJECTIVE To evaluate the effects of once-weekly subcutaneous semaglutide on alcohol consumption and craving in adults with alcohol use disorder (AUD).

DESIGN, SETTING, AND PARTICIPANTS This was a phase 2, double-blind, randomized, parallel-arm trial involving 9 weeks of outpatient treatment. Enrollment occurred at an academic medical center in the US from September 2022 to February 2024. Of 504 potential participants assessed, 48 non-treatment-seeking participants with AUD were randomized.

INTERVENTION Participants received semaglutide (0.25 mg/week for 4 weeks, 0.5 mg/week for 4 weeks, and 1.0 mg for 1 week) or placebo at weekly clinic visits.

MAIN OUTCOMES AND MEASURES The primary outcome was laboratory alcohol self-administration, measured at pretreatment and posttreatment (0.5 mg/week). Secondary and exploratory outcomes, including prospective changes in alcohol consumption and craving, were assessed at outpatient visits.

RESULTS Forty-eight participants (34 [71%] female; mean [SD] age, 39.9 [10.6] years) were randomized. Low-dose semaglutide reduced the amount of alcohol consumed during a posttreatment laboratory self-administration task, with evidence of medium to large effect sizes for grams of alcohol consumed (β, −0.48; 95% CI, −0.85 to −0.11; $P = .01$) and peak breath alcohol concentration (β, −0.46; 95% CI, −0.87 to −0.06; $P = .03$). Semaglutide treatment did not affect average drinks per calendar day or number of drinking days, but significantly reduced drinks per drinking day (β, −0.41; 95% CI, −0.73 to −0.09; $P = .04$) and weekly alcohol craving (β, −0.39; 95% CI, −0.73 to −0.06; $P = .01$), also predicting greater reductions in heavy drinking over time relative to placebo (β, 0.84; 95% CI, 0.71 to 0.99; $P = .04$). A significant treatment-by-time interaction indicated that semaglutide treatment predicted greater relative reductions in cigarettes per day in a subsample of individuals with current cigarette use (β, −0.10; 95% CI, −0.16 to −0.03; $P = .005$).

CONCLUSIONS AND RELEVANCE These findings provide initial prospective evidence that low-dose semaglutide can reduce craving and some drinking outcomes, justifying larger clinical trials to evaluate GLP-1RAs for alcohol use disorder.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT05520775

Article
https://doi.org/10.1038/s41467-024-48780-6

Associations of semaglutide with incidence and recurrence of alcohol use disorder in real-world population

Received: 8 November 2023
Accepted: 8 May 2024
Published online: 28 May 2024

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Alcohol use disorders are among the top causes of the global burden of disease, yet therapeutic interventions are limited. Reduced desire to drink in patients treated with semaglutide has raised interest regarding its potential therapeutic benefits for alcohol use disorders. In this retrospective cohort study of electronic health records of 83,825 patients with obesity, we show that semaglutide compared with other anti-obesity medications is associated with a 50%-56% lower risk for both the incidence and recurrence of alcohol use disorder for a 12-month follow-up period. Consistent reductions were seen for patients stratified by gender, age group, race and in patients with and without type 2 diabetes. Similar findings are replicated in the study population with 598,803 patients with type 2 diabetes. These findings provide evidence of the potential benefit of semaglutide in AUD in real-world populations and call for further randomized clinical trials.

PROMISING APPROACHES TO TREAT AUD: FMT

HEPATOLOGY
AASLD
HEPATOLOGY, VOL. 73, NO. 5, 2021
STEATOHEPATITIS/METABOLIC LIVER DISEASE

A Randomized Clinical Trial of Fecal Microbiota Transplant for Alcohol Use Disorder

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BACKGROUND AND AIMS: Alcohol use disorder (AUD) is associated with microbial alterations that worsen with cirrhosis. Fecal microbiota transplant (FMT) could be a promising approach.

APPROACH AND RESULTS: In this phase 1, double-blind, randomized clinical trial, patients with AUD-related cirrhosis with problem drinking (AUDIT-10 > 8) were randomized 1:1 into receiving one placebo or FMT enema from a donor enriched in *Lachnospiraceae* and *Ruminococcaceae*. Six-month safety was the primary outcome. Alcohol craving questionnaire, alcohol consumption (urinary ethylglucuronide/creatinine), quality of life, cognition, serum IL-6 and lipopolysaccharide-binding protein, plasma/stool short-chain fatty acids (SCFAs), and stool microbiota were tested at baseline and day 15. A 6-month follow-up with serious adverse event (SAE) analysis was performed. Twenty patients with AUD-related cirrhosis (65 ± 6.4 years, all men, MoDel for End-Stage Liver Disease 8.9 ± 2.7) with similar demographics, cirrhosis, and AUD severity were included. Craving reduced significantly in 90% of FMT versus 30% in placebo at day 15 ($P = 0.02$) with lower urinary ethylglucuronide/creatinine ($P = 0.03$) and improved cognition and psychosocial quality of life. There was reduction in serum IL-6 and lipopolysaccharide-binding protein and increased butyrate/isobutyrate compared with baseline in FMT but not placebo. Microbial diversity increased with higher *Ruminococcaceae* and other SCFAs, producing taxa following FMT but not placebo, which were linked with SCFA levels. At 6 months, patients with any SAEs (8 vs. 2, $P = 0.02$), AUD-related SAEs (7 vs. 1, $P = 0.02$), and SAEs/patient (median [interquartile range], 1.5 [1.25] vs. 0 [0.25] in FMT, $P = 0.02$) were higher in placebo versus FMT.

CONCLUSIONS: This phase 1 trial shows that FMT is safe and associated with short-term reduction in alcohol craving and consumption with favorable microbial changes versus placebo in patients with alcohol-associated cirrhosis with alcohol misuse. There was also a reduction in AUD-related events over 6 months in patients assigned to FMT. (HEPATOLOGY 2021;73:1688-1700).

Alcohol use disorder (AUD) and alcohol-associated cirrhosis are major causes of morbidity and mortality.[1] Continued alcohol misuse in the setting of end-organ damage, such as cirrhosis, can hasten disease progression. Therefore, therapies that encourage alcohol abstinence or reduce alcohol misuse are relevant. Pharmaco-therapies for craving in alcohol-associated cirrhosis have yielded partial success and focus largely on neuromodulation.[2] AUD is associated with major changes in the gut-brain axis, which is worsened with the occurrence of cirrhosis.[3] In addition, other studies

Original Article
JOURNAL OF CLINICAL AND EXPERIMENTAL HEPATOLOGY

Long-term Outcomes of Stool Transplant in Alcohol-associated Hepatitis—Analysis of Clinical Outcomes, Relapse, Gut Microbiota and Comparisons with Standard Care☆

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Background: **Healthy donor fecal microbiota transplantation (FMT) was preliminarily shown to have clinical benefits in hepatic encephalopathy (HE), severe alcohol-associated hepatitis (SAH), and alcohol use disorder. However, the long-term outcomes of FMT and the gut microbiota (GM) changes in patients with SAH are unknown.** ***Methods:*** **Patients with SAH who underwent FMT (N = 35) or standard of care (SoC, N = 26) from May 2017 to June 2018 were included, and their stored stool samples were analyzed prospectively. Clinical outcomes, including infections, hospitalizations, critical illness, alcohol relapse, and survival, were evaluated. Metagenomic analysis was undertaken to identify the relative abundances (Ras) and significant taxa at baseline and post-therapy (up to three years) among survivors between the two groups.** ***Results:*** **At follow-up, the incidences of ascites, HE, infections, and major hospitalizations were significantly higher in the SoC than in the FMT group ($P < 0.05$). Alcohol relapse was lower (28.6% versus 53.8%), and the time to relapse was higher in the FMT than in the SoC group ($P = 0.04$). Three-year survival was higher in the FMT than in the SoC group (65.7% versus 38.5%, $P = 0.052$). Death due to sepsis was significantly higher in the SoC group (N = 13/16, 81.2%; $P = 0.008$). GM analysis showed a significant increase in the RA of Bifidobacterium and a reduction in the RA of Acinetobacter in the FMT group. Beyond one to two years, the RA of Porphyromonas was significantly higher and that of Bifidobacterium was lower in the SoC than in the FMT group.** ***Conclusions:*** **In terms of treatment for patients with SAH, healthy donor FMT is associated with significantly lesser ascites, infections, encephalopathy, and alcohol relapse (with a trend toward higher survival rates) than SoC, associated with beneficial GM modulation. Larger controlled studies on FMT are an unmet need.** (J Clin Exp Hepatol 2022;12:1124-1132)

Alcohol-associated Hepatitis

frontiers | Frontiers in Nutrition
TYPE Original Research
PUBLISHED 18 April 2024
DOI 10.3389/fnut.2024.1393014

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RECEIVED 28 February 2024
ACCEPTED 02 April 2024
PUBLISHED 18 April 2024

CITATION
Lamas-Paz A, Mesquita M, García-Lacarte M, Estévez-Vázquez O, Benedé-Ubieto R, Gutierrez AH, Wu H, Leal Lasalle H, Vaquero J, Bañares R, Martínez-Naves E, Roa S, Nevzorova YA, Jorquera G and Cubero FJ (2024) Fecal microbiota transplantation from female donors restores gut permeability and reduces liver injury and inflammation in middle-aged male mice exposed to alcohol. *Front. Nutr.* 11:1393014.
doi: 10.3389/fnut.2024.1393014

Fecal microbiota transplantation from female donors restores gut permeability and reduces liver injury and inflammation in middle-aged male mice exposed to alcohol

Arantza Lamas-Paz[1,2†], Mariana Mesquita[1,3†], Marcos García-Lacarte[4,5,6], Olga Estévez-Vázquez[1], Raquel Benedé-Ubieto[1], Alejandro H. Gutierrez[2], Hanghang Wu[1], Hector Leal Lasalle[1], Javier Vaquero[7,8,9], Rafael Bañares[7,8,9], Eduardo Martínez-Naves[1,2], Sergio Roa[4,5,6,10], Yulia A. Nevzorova[1,8,9], Gonzalo Jorquera[11,12*†] and Francisco Javier Cubero[1,8,9*†]

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Fecal microbiota transplantation in alcohol-associated acute-on-chronic liver failure: an open-label clinical trial

Original Article | Published: 28 March 2022
Volume 16, pages 433–446, (2022) Cite this article

Anima Sharma, Akash Roy, Madhumita Premkumar, Nipun Verma, Ajay Duseja, Sunil Taneja, Sandeep Grover, Madhu Chopra & Radha K. Dhiman

Abstract

Background

Severe alcoholic hepatitis (SAH) presenting as acute-on-chronic liver failure (ACLF) carries a high short-term mortality. Alteration of gut microbiota is a crucial component implicated in its pathogenesis, whose modulation has been suggested as a potential therapeutic tool. We evaluated the safety of fecal microbiota transplantation (FMT) and its efficacy in improving short-term survival and clinical severity scores in patients with SAH–ACLF.

Methods

Thirty-three patients [13 in the FMT arm; 20 in the standard of care arm (SOC)] with SAH–ACLF were included in this open-label study. A single FMT session was administered as a freshly prepared stool suspension from pre-identified healthy family member stool donors through a nasojejunal tube. Patients were followed up on days 7, 28, and 90.

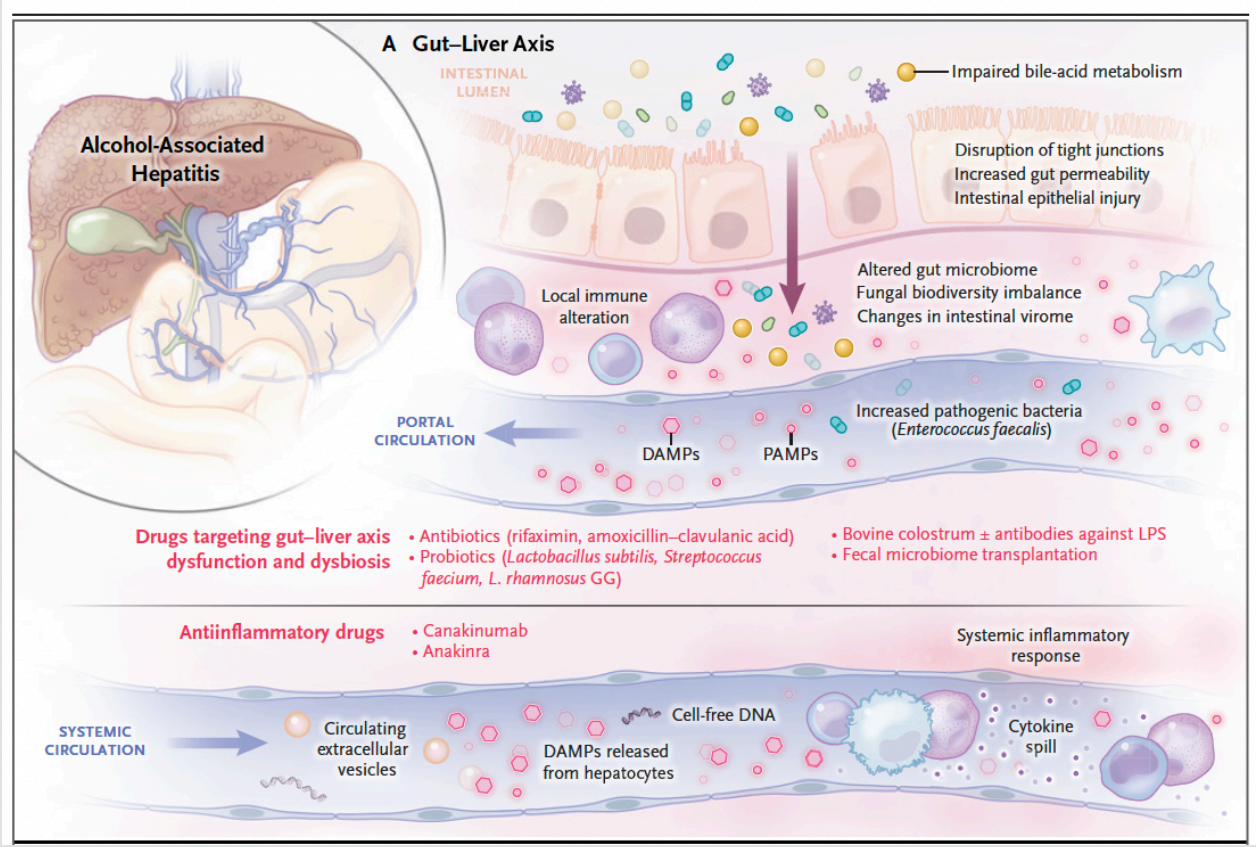
Results

Survival at 28 and 90 days was significantly better in the FMT arm (100% versus 60%, $p = 0.01$; 53.84% versus 25%, $p = 0.02$). Hepatic encephalopathy resolved in 100% versus 57.14% (FMT versus SOC, $p = 0.11$) patients, while ascites resolved in 100% versus 40% survivors ($p = 0.04$). Major adverse event rates, including spontaneous bacterial peritonitis and gastrointestinal bleeding, were similar in both groups ($p = 0.77$; $p = 0.070$). Median IL1beta decreased by 21.39% (IQR − 73.67 to 7.63) in the FMT group, whereas it increased in the SOC by 27.44% (IQR − 0.88 to 128.11) ($p = 0.01$). Percentage changes in bilirubin and ALT between baseline and day 7 emerged as predictors of 90-day mortality.

Conclusion

FMT is safe, improves short-term and medium-term survival, and leads to improvement in clinical severity scores in patients with SAH–ACLF.

PROMISING APPROACHES TO TREAT AUD: FMT



Bataller, Arab & Shah, NEJM 2022

TAKE HOME MESSAGES

- **Most patients with ALD are detected at late stages: early detection campaigns are needed.**
- **Corticosteroids improve 30-day survival in AH patients with MELD 21-39. Early Lille Score at 4 day could be applied.**
- **Early LT in highly selected patients with severe AH has good outcomes.**
- **There is a clear need to carry out clinical trials to treat alcohol use disorder in patients with ALD.**

Ramon Bataller
@rabataller

Promote

I'm devastated by the news of the sudden passing of **Kristen Radage**.

She was our social worker that helped many patients with **alcohol use disorder** at UPMC. I'll never forget Kristen's kindness and compassion. She left a beautiful mark on every patient and colleague she met.

She participated in a recent @EASLedu studio on ALD and gave us useful advice. RIP.