



Asignatura: Problemas clínicos y controversias en hepatología

“Alcohol-related Hepatitis”

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AIMS

1. To provide a **CRITICAL** & **HOLISTIC UPDATE** on the management and future prospects in AH.
2. To try to **INSPIRE** a generation of young physicians and scientists to be interested in this disease and to love these patients.

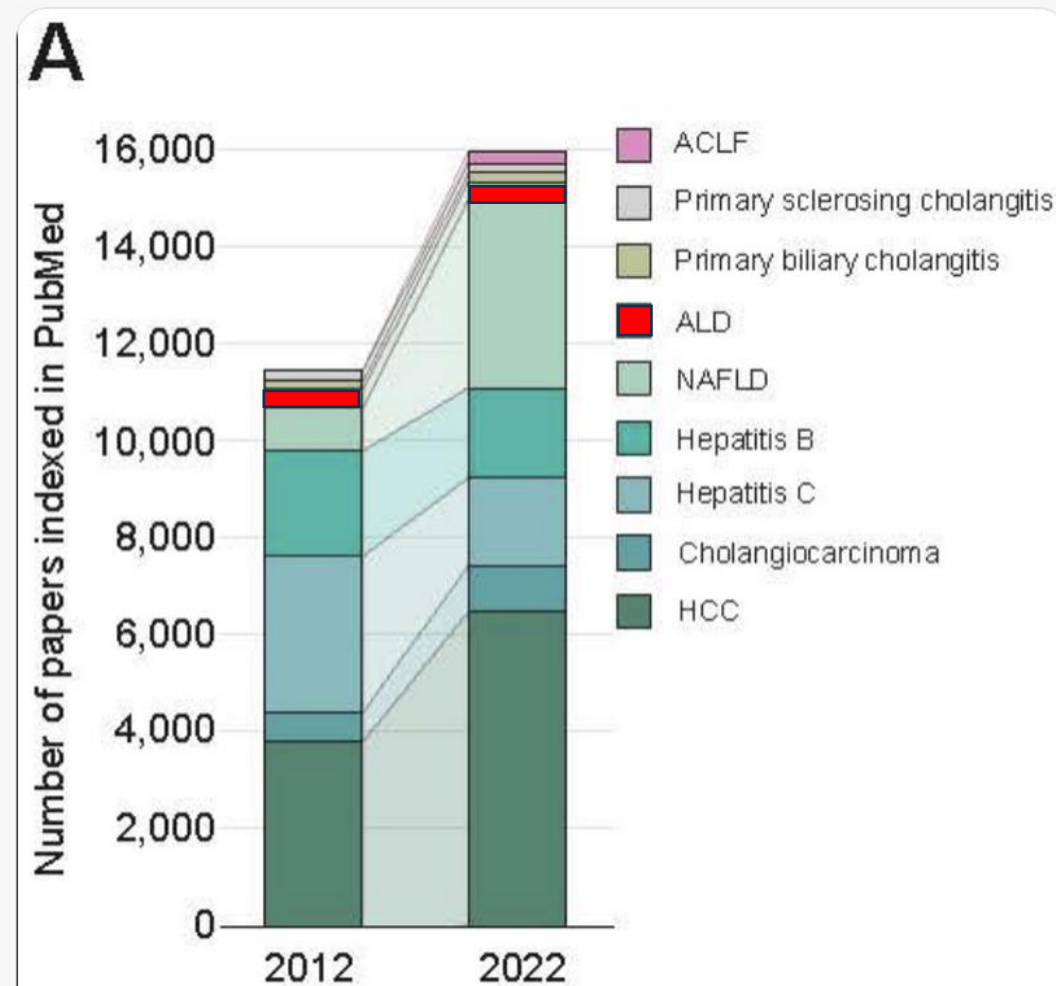


Ramon Bataller @rabataller · Jun 13

Thanks to @ThomasBerg24 & @AleksanderKrag for showing that ALD is largely overlooked.

In the State-of-the-Art lecture at #ILC2023, I will try to inspire young hepatologists to love this disease and these patients.

[@JHepatology](#) [@EASLnews](#) [#livertwitter](#)
shorturl.at/vwKU4



@rabataller

APPROACH

- 1. A presentation based on a true history.**
- 2. Limited number of slides and data.**



OUR PATIENT

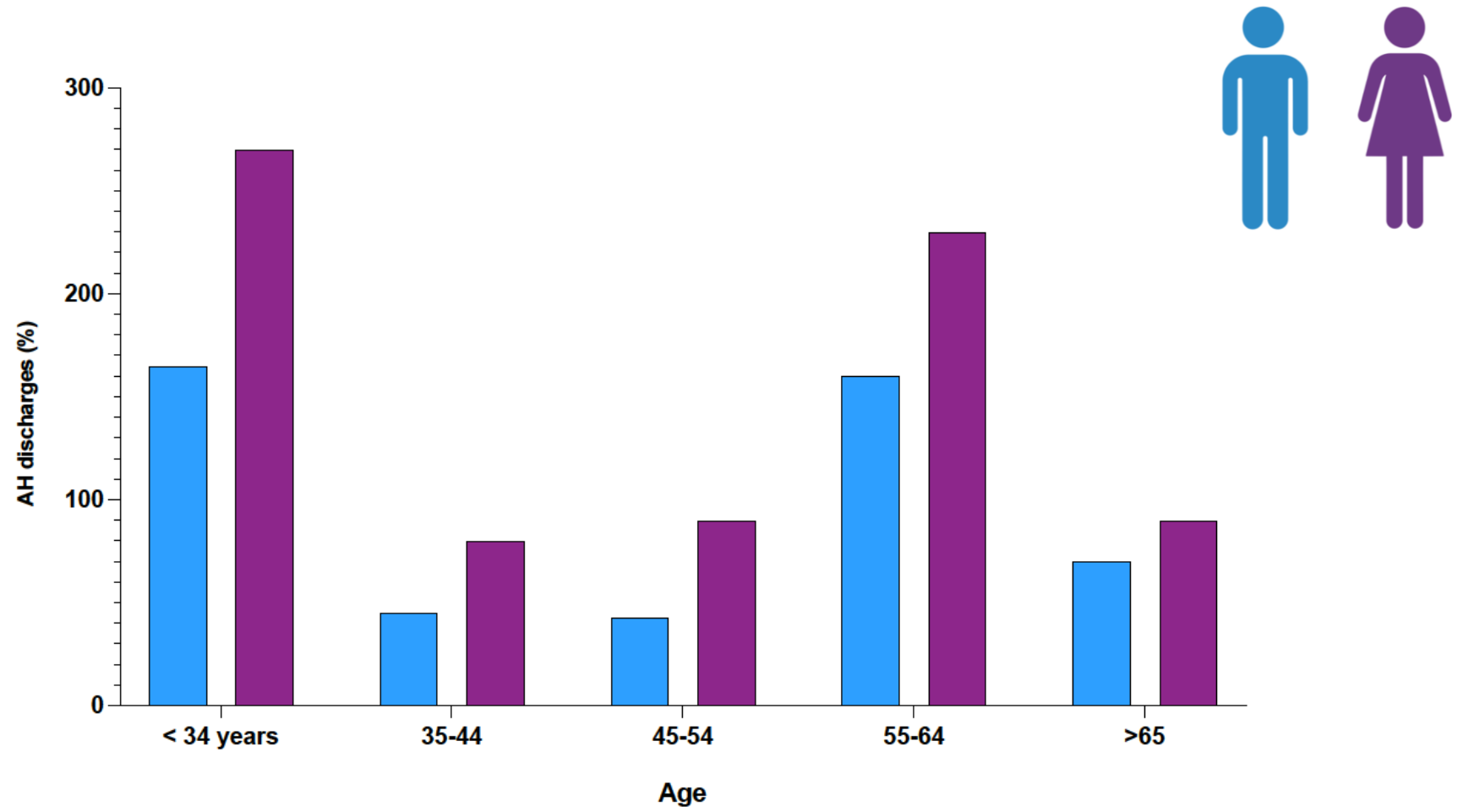


Ms. Nice

Why Ms. ?

Why Nice ?

Why Ms ?



Bertha M et al. Liver Inter 2022

Why Nice ?

The stigma of alcohol-related liver disease and its impact on healthcare

Georg Schomerus^{1,*}, Anya Leonhard¹, Jakob Manthey^{1,2,3}, James Morris⁴, Maria Neufeld⁵,
Carolin Kilian³, Sven Speerforck¹, Petr Winkler^{6,7}, Patrick W. Corrigan⁸

Women > men

Minorities > whites

Socioeconomic status

Cultural & religion



Should hepatologists get trained on addiction medicine ?



Ramon Bataller

@rabataller

In current hepatology, with the majority of hospitalized patients with alcohol-related liver disease, I think it would be very useful if liver FELLOWS have a brief rotation in ADDICTION MEDICINE.

[#MedTwitter](#) [#livertwitter](#) [@EASLedu](#) [@AASLDTweets](#)

8:47 PM · May 4, 2023 from Barcelona, Spain · **18K** Views

24 Retweets

6 Quotes

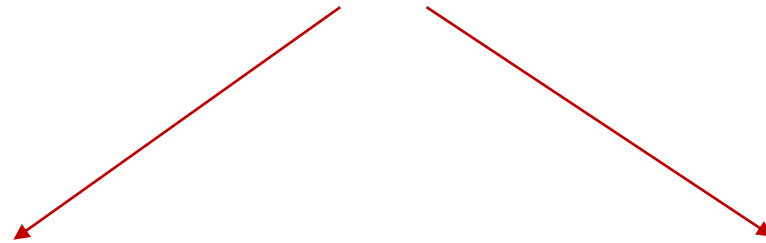
150 Likes

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Before Ms Nice was born

Father: employed, moderate drinker. No family history alcohol.

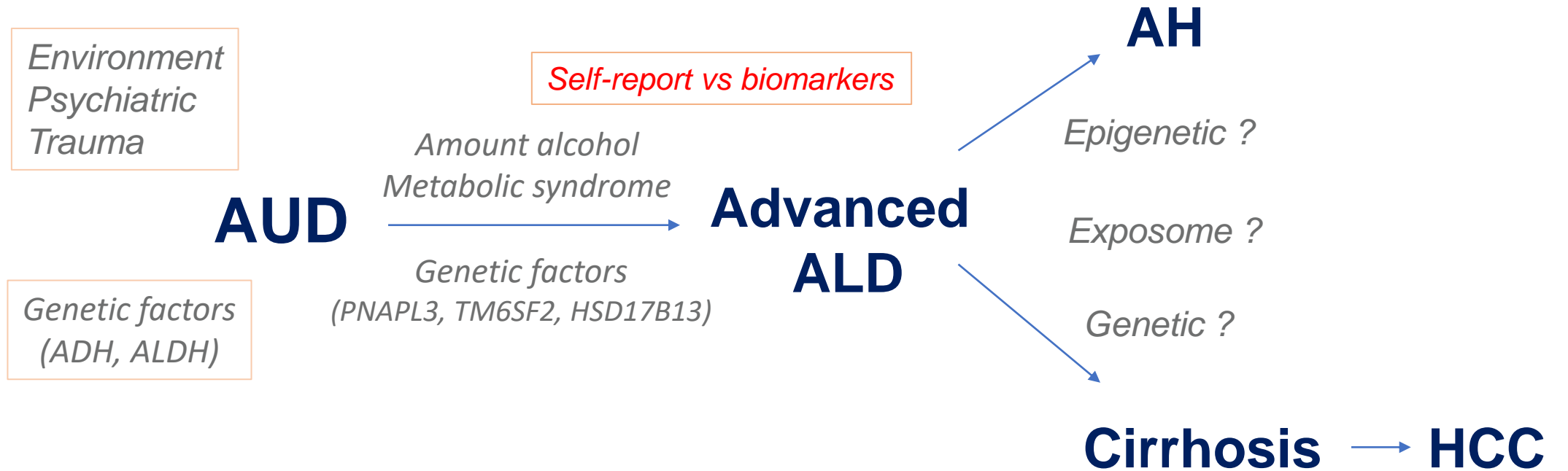
Mother: bipolar, heavy drinker. Sister & father with alcohol problems.



NURTURE: ENVIROMENTAL

NATURE: GENETIC

Factors predisposing to AUD and advanced ALD



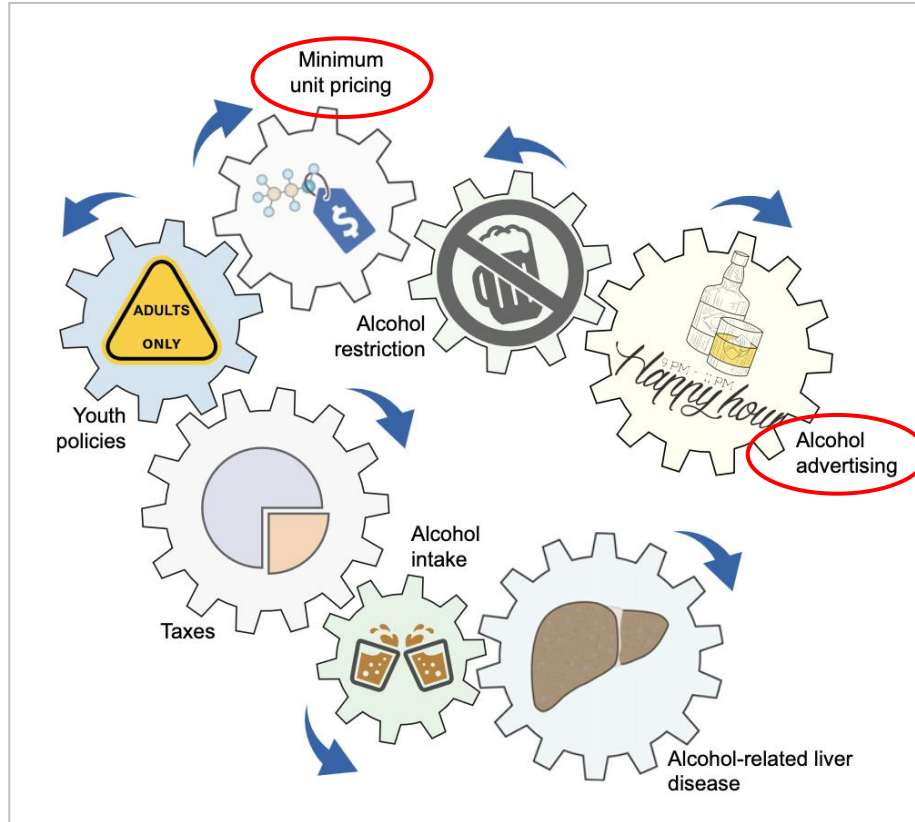
Ms Nice's adolescence

Early alcohol use: binge drinking since 16 yo and then in college

Sexual abuse: PTSD & anxiety

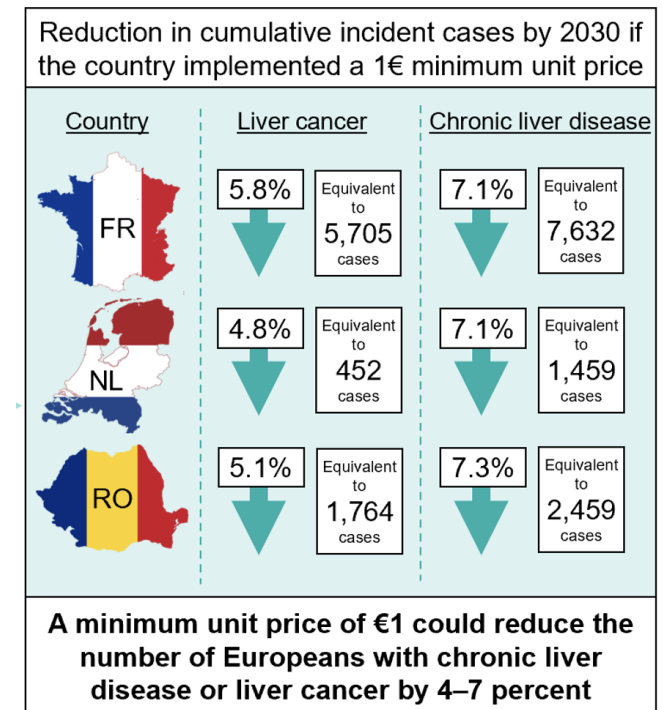


Can we prevent alcohol use disorder and AH ?



Ventura-Cots M et al, JHEP Rep 2019

Preventing liver disease with policy measures to tackle alcohol consumption and obesity: a microsimulation study



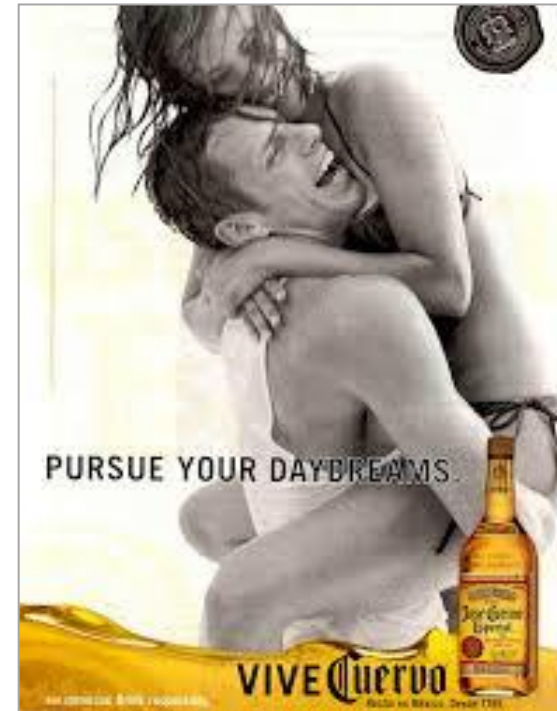
L Retat, L Webber, P Jepsen, H Cortez Pinto, M Mitchyn, JV Lazarus, A Martin, F Negro, P Nahon, J Guzek, N Sheron, J Card-Gowers, S Zelber Sagi, H Graff, M Buti.

Alcohol advertisements

PERFORMANCE



SOCIAL SUCCESS



A KEY ROLE FOR EASL & ELPA

 **EASL**™ The Home of Hepatology

POLICY STATEMENT

EASL Policy Statement Reducing Alcohol Harms 2023



EXECUTIVE SUMMARY AND KEY MESSAGES

Aim: The aim of this European Association for the Study of the Liver (EASL) policy statement is to:

1. Urge policy-makers to reduce health-related, social and economic harms caused by alcohol by implementing evidence-based policies to reduce alcohol consumption in the general population, and
2. Empower health professionals, especially those working with liver disease, to use their collective voice to advocate and inform the public, policymakers, and people at risk regarding alcohol-related liver disease (ARLD) and other alcohol harms.

Main message: Europe is the highest alcohol-consuming region in the world and, as a result, has the highest level of alcohol harms. These harms include liver disease, seven types of cancer, alcohol dependence syndromes, psychiatric illnesses and suicides, heart diseases, injuries, and violence.


Evidence-based interventions that reduce population-level alcohol consumption are both effective and cost-effective at reducing deaths from ARLD and reducing other negative health, social and economic impacts of alcohol consumption.

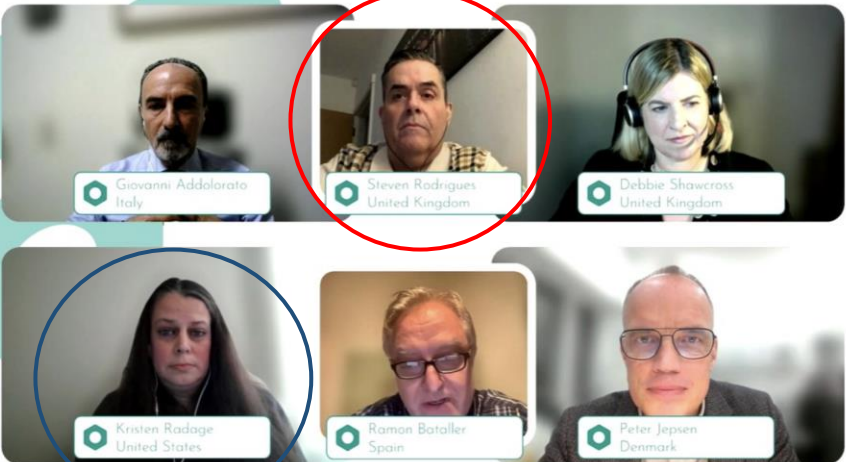
Nonetheless, many states have failed to implement these proven and effective measures, usually due to lobbying and interference by the alcohol industry.

The irreconcilable conflict of interest between the alcohol industry and health must be acknowledged and confronted. The alcohol industry should have no role in formulating public health and alcohol policy.

f t y in easloffice@easloffice.eu | www.easl.eu 1

EASL STUDIO: a 360 Approach to Treat Alcohol-related Liver Disease





Giovanni Addolorato
Italy

Steven Rodrigues
United Kingdom


Debbie Shawcross
United Kingdom

Kristen Radage
United States

Ramon Botaller
Spain

Peter Jepsen
Denmark

SALVE



Study of Alcohol-Related LiVer Disease in Europe

Ms. Nice developed jaundice at her early 30s

- Rapid development of jaundice
- Ascites, edema and painful hepatomegaly
- Sarcopenia
- AST 176, ALT 34, TBil 23, INR 1.8, Creat 1.1, Plat 148.000: **MELD 26**
- US & CT scan: heterogenous hepatomegaly, permeable veins, borderline splenomegaly, ascites

Does Ms Nice has an episode of AH ?

“Not every jaundiced patient with AUD has an episode of AH”

Rule Out Other Reasons for Jaundice

Mechanical obstruction:

HCC, biliary obstruction, or Budd–Chiari syndrome
Perform Doppler abdominal ultrasonography and,
if indicated, CT or MRI-MRCP

Drug-induced liver injury:

Review detailed history of medications, supplements,
and pharmacy records

Check <http://livertox.nih.gov>

Viral hepatitis:

Acute hepatitis A, B, C, or E, especially if first episode,
or high clinical suspicion

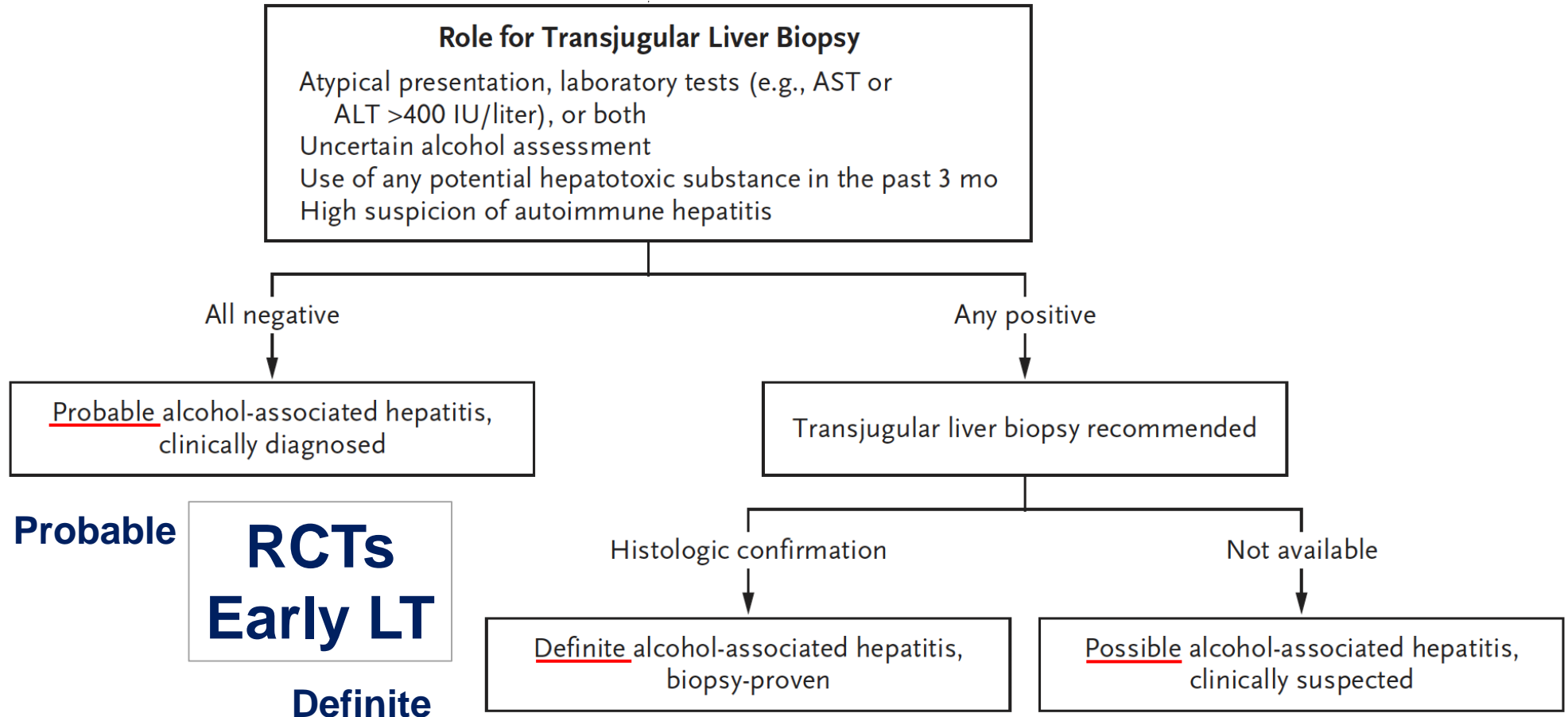
Autoimmune hepatitis:

Severe autoimmune hepatitis if first episode, clinical
suspicion (ANA, ASMA, IgG), or both

Ischemic hepatitis:

Presence of hypotension, septic shock, massive
bleeding, or recent cocaine use

Should Ms Nice undergo a liver biopsy?



NIAAA criteria

How should we treat Ms Nice ?

- Prevent and treat **withdrawal syndrome**
- Ensure adequate **caloric-protein** intake
- **Micronutrients/vitamin deficits**: folic acid, vits B and D, vit K
- Maintain MAP to **prevent AKI**
- Work-up for **infections** (procalcitonin): BSA if any suspicion

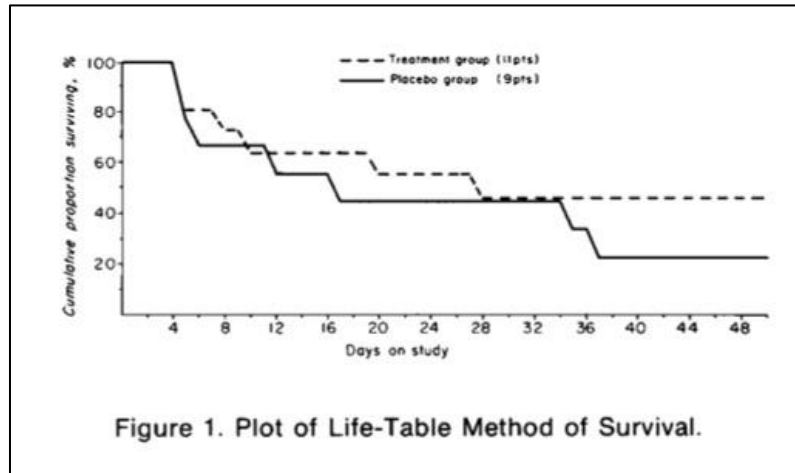
Should we start corticosteroids in Ms Nice ?

Prednisolone or Pentoxifylline for Alcoholic Hepatitis

CORTICOSTEROID THERAPY IN SEVERE ALCOHOLIC HEPATITIS*

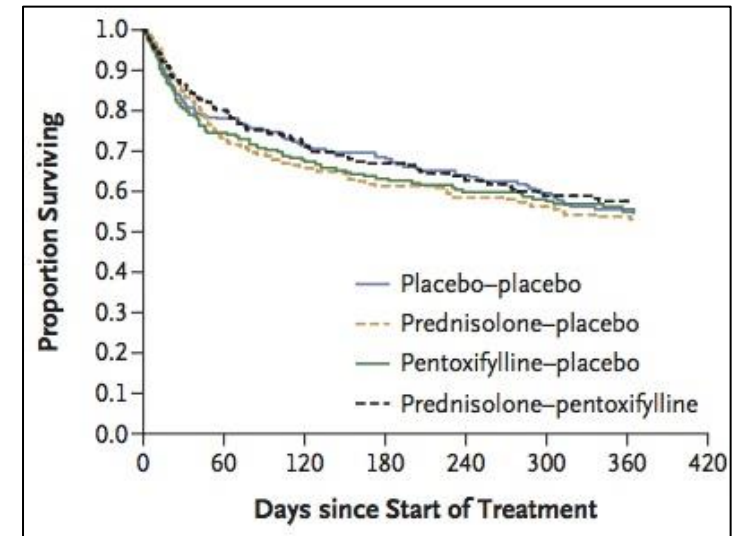
A Double-Blind Drug Trial

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.



1971

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

Should we start corticosteroids in Ms Nice ?



Ramon Bataller

@rabataller



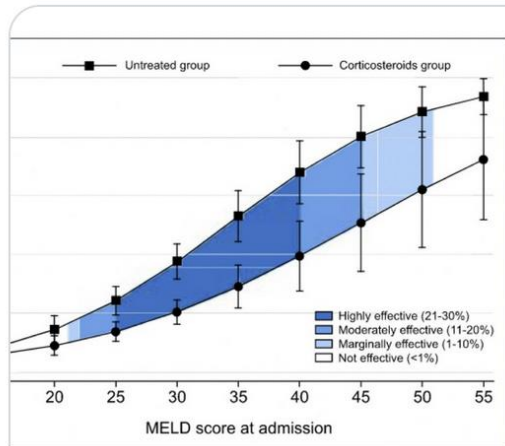
I am often asked the same question: do you still use prednisolone in Alc Hep? My answer is: YES, if the MELD is 21-39, but I apply an early Lille score at 4 days so I stop it if Bil does not quickly decrease. See below the evidence supporting this approach.

#Livertwitter

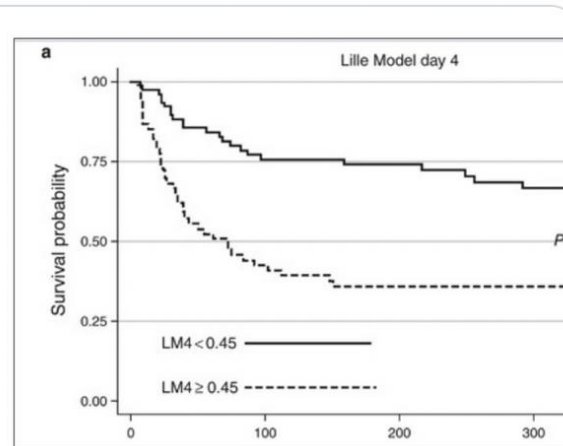


Global AlcHep

A BIG DATA NETWORK



Arab et al, J Hepatol 2021



Duarte-Rojo et al, Am J Gastroenterol 2011

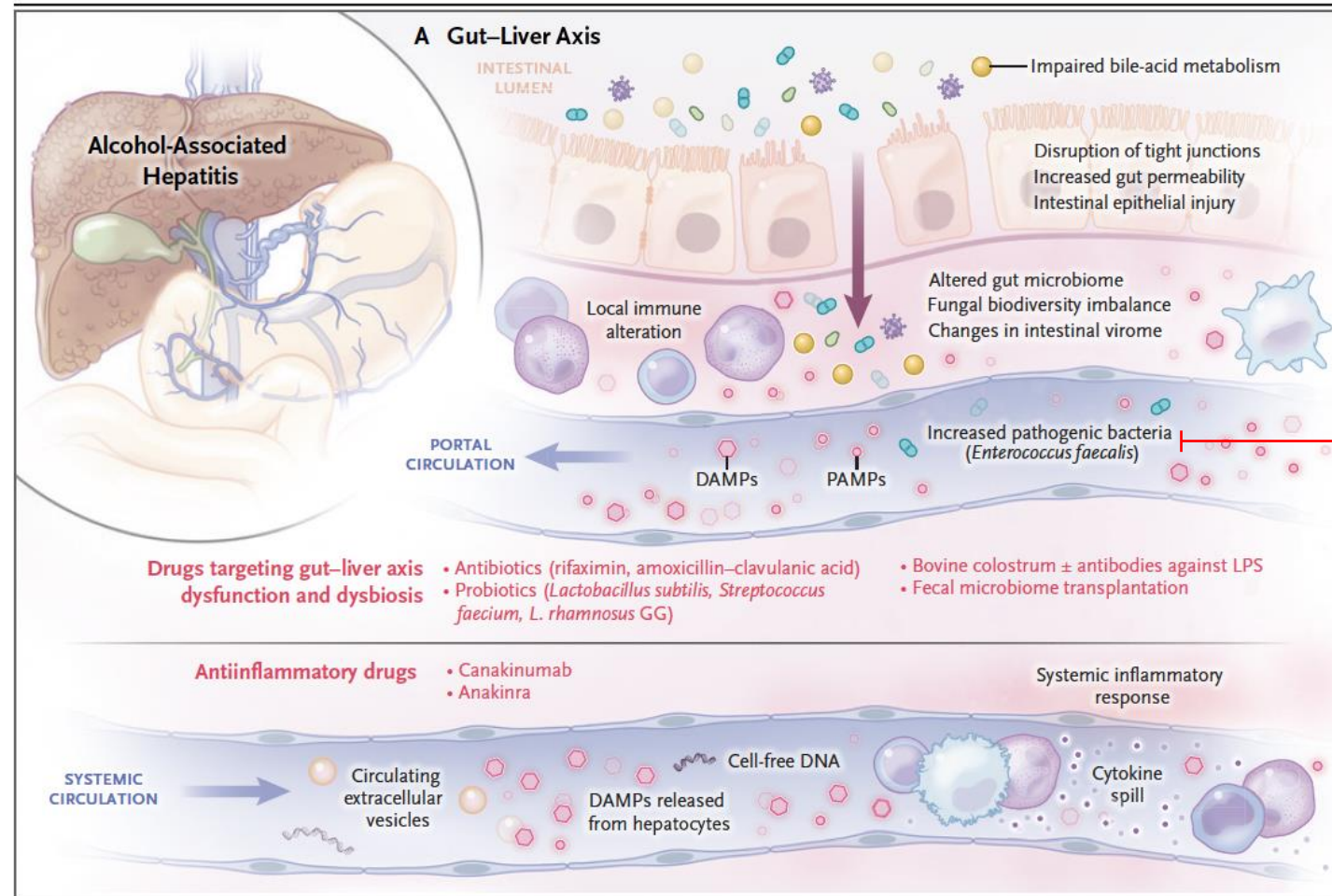
Ms Nice has not responded to corticosteroids: any promising therapy ?

- Targeting the gut-liver axis
- Improving hepatocellular function
- Preventing ACLF and multiorgan failure



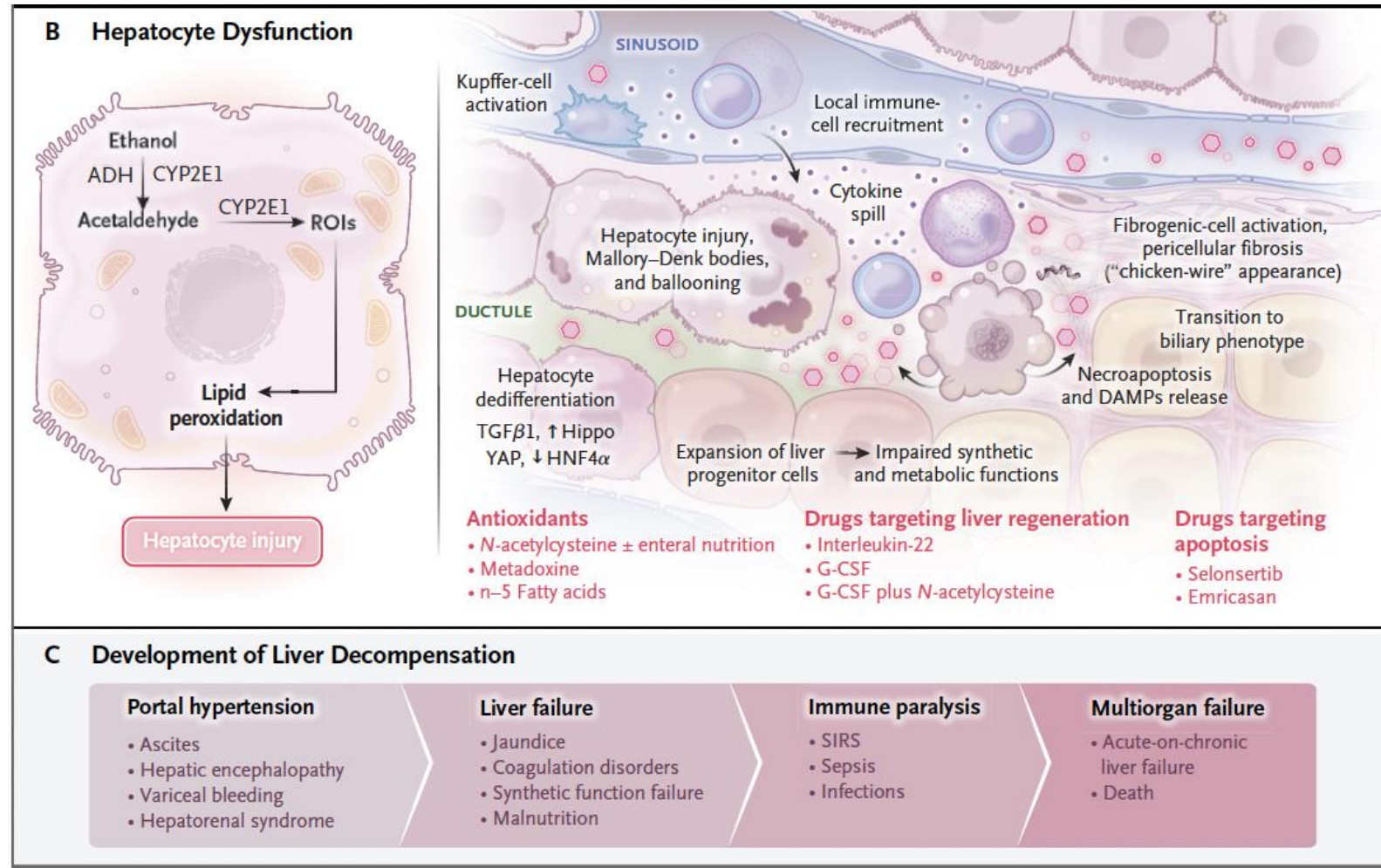
Improve short-term survival → Prevent relapse → Promote re-compensation

Targeting the gut-liver axis



Bacteriophages that target cytolytic *E. faecalis*

Improving hepatocellular function



Bataller, Arab & Shah, NEJM 2022

Preventing ACLF and multiorgan failure

- **Early referral** to a specialized center (with transplant program)
- Characterize and treat **AKI** (HRS vs ATN)
- **Early** identification and therapy **nosocomial infections** (eg. corticosteroids, fungal)
- Identify and target mediators of **systemic inflammation**
- **Plasmapheresis, artificial liver devices ??**

Is Ms Nice a good candidate for early transplantation ?

1. First AH episode
2. Good social support
3. Absence of severe psychiatric co-morbidities
4. No multiple previous rehabilitation attempts

- **Long discussions in transplant committees: difficult decision**
- **Use a scoring system tested in a similar geographic area**
- **Aggressive relapse prevention after early LT is key !**

How can we assist Ms Nice to be sober before and after LT ?

TREAT THE UNDERLYING CONDITION

PTSD
Depression
Anxiety
Sleep
Pain

MULTIDISCIPLINARY / INTEGRATED CLINIC



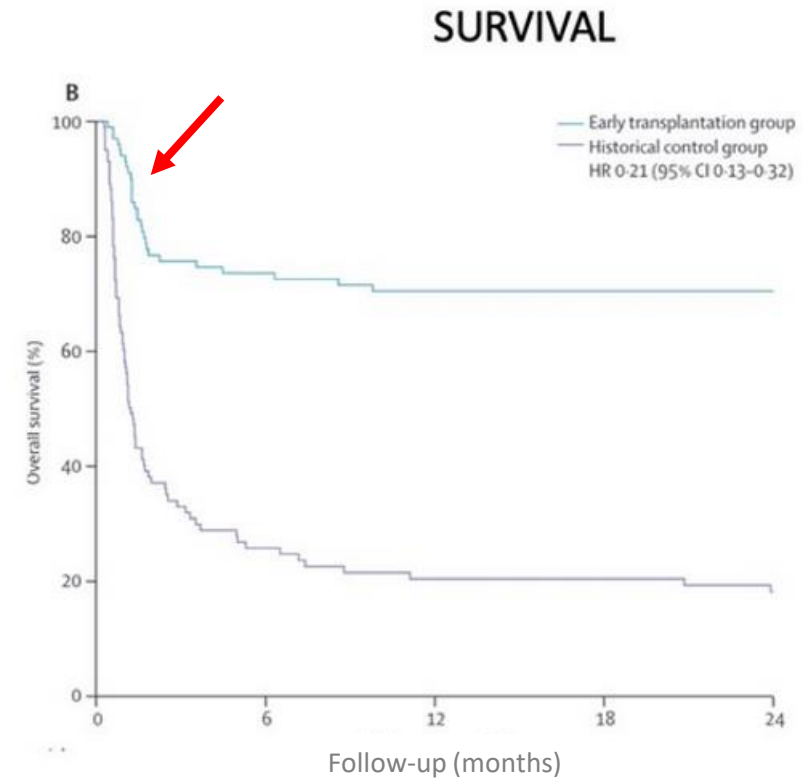
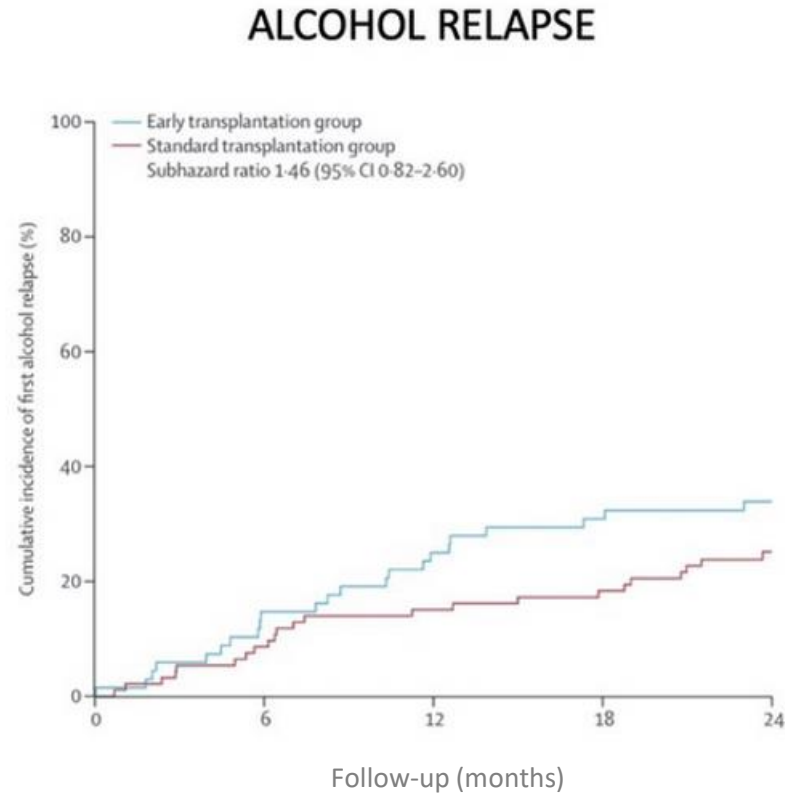
- *Specialized nurse*
- *Addiction therapist*
- *Social worker*
- *Hepatologist*

How can we assist Ms Nice to be sober before and after LT ?

FDA approved for AUD

- **Disulfiram**: unsafe if underlying advanced ALD. Risk of liver failure.
- **Acamprosate**: retrospective studies suggest is safe and efficacious. Caution if renal failure.
- **Naltrexone**: safe in cirrhosis. Caution if opioid use.
- **Baclofen**: a positive placebo-control trial in cirrhosis.

What is the expected outcome after Ms Nice transplant ?



Louvet A et al, Lancet Gastroenterol Hepatol 2022

What are the 5 main unmet needs in AH ?

- 1. Prevention policies and early referral**
- 2. Determinants of AH:** exposome, genetics and epigenetics
- 3. Molecular subtypes** for precision medicine
- 4. Preclinical models** (human-based)
- 5. Integrated RCTs** including liver recovery and relapse prevention

Acknowledgements

Mentors: Pere Gines, Massimo Pinzani and David Brenner

Lab group: Pau Sancho-Bru, Silvia Affo, Jose Altamirano, Cristina Millan, Montserrat Moreno, Jordi Colmenero, Marlene Dominguez, Neus Gorbig, Oriol Morales, Teresa Gonzalo, Javier Michelena, Edilmar Alvarado-Tapias, Dalia Morales-Arreaez, Samitha Savi, Elena Lopez, Joel Pat Gue, Meritxell Ventura, Eva Stein, Nambi Ndugga, Josepmaria Argemi, A Oliveira-Mello Joaquin Cabezas, Ariel Watts, J Cheong, Ana Clemente-Sanchez, Carlos Fernandez-Carrillo, Maria Fernandez-Tejero, Veronica Massey, Amir Gougil, Leandra Ramalho, A Loeza-del-Castillo, Juanjo Lozano, Steve Atkinson, Gemma Odena, Jiegen Chen, Maria P Ballester-Ferrrer, Carole Rimer, Nikole Jones, David Marti-Aguado

Collaborators: Vicente Arroyo, Joan Caballeria, Juan G Abraldes, Josep M Nicolas, Juan C Garcia-Pagan, Xavier Gasull, Hugo Lopez-Pelayo, Anna Lligona, Klaus Poesltra, Robert Schwabe, Bin Gao, Juan Pablo Arab, Luis Antonio Diaz, Javier F Chaves, Matias Avila, Uxue Latasa, Jelena Mann, Phillippe Mathurin, Laurent Dubuquoy, Alexandre Louvet, Diego Rincon, Peter Starkel, Pranoti Mandrekar, Laura Nagy, Mark Thursz, Carolin Lackner, PE Ratou, Vijay Shah, Fabio Marra, Scott Cao, Ivan Rusyn, Shinji Furuya, Dinia Tiniakos, Eikiro Seki, Sebastian Mueller, Scott Magness, Fulton Crews, Claes Wahlestedt, Fatima Higuera-de laTijera, Ilya Blokhin, Pal Monga, Lans Taylor, Larry Vernetti, Michael Jurzak, Elisa Pose, Ashwani Singal, Waj Mehal, Jeff Lazarus, Hide Tsukamoto, Bernd Schnabl, Patrick Kamath, Guadalupe Garcia-Tsao, Neil Shah, Michael Lucey, Debbie Shawcross, Tim Morgan, Malu Martinez-Chantar, Victor Vargas, Rotonya Carr, Vik Rachakonda, Eric Orman, Shari Rogal, Gavin Arteel, Dirah Yadav, Jaideep Behari, Andres Duarte-Rojo, Sid Barrit, Andrew Moon, Andrea diMartini, Raj Vadigepalli, Devanshi Seth, Marco Arrese.....

Funding agencies:



A text message from Ms Nice



Thank you so much for your help, as always. I appreciate you so much! Thank you !!!

8:38 AM

Why should you become interested in ALD ?



Ramon Bataller

@rabortaller



A young physician asked me after a talk: why do you LOVE the alcohol field ? I said:

- I feel very rewarded helping vulnerable patients.
- Science in the field is fascinating.
- It's a land of opportunities.