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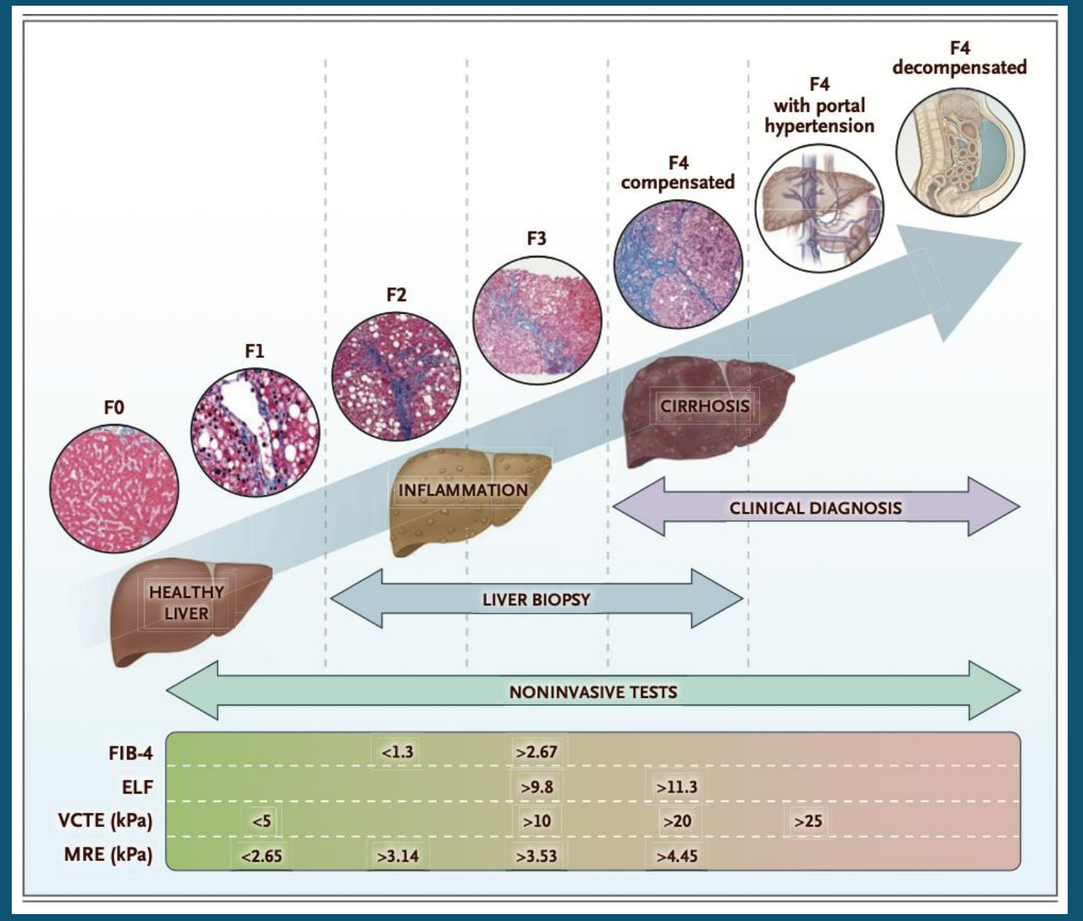
The critical role of elastography in liver disease assessment – from staging fibrosis to staging liver disease

Presented by: Annalisa Berzigotti
Department for Visceral Surgery and Medicine, Inselspital, Bern University Hospital, University of Bern
Switzerland



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EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis – 2021 update☆

J Hepatol 2021

EFSUMB Guidelines and Recommendations on the Clinical Use of Liver Ultrasound Elastography, Update 2017 (Short Version)

Ultraschall Med 2017

LIVER ULTRASOUND ELASTOGRAPHY: AN UPDATE TO THE WORLD FEDERATION FOR ULTRASOUND IN MEDICINE AND BIOLOGY GUIDELINES AND RECOMMENDATIONS

Ultrasound Med Biol 2018

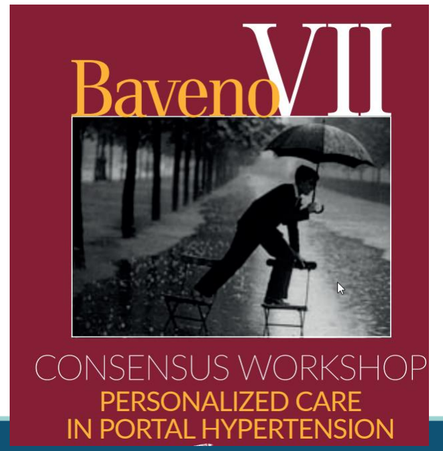
Radiology

REVIEWS AND COMMENTARY · STATEMENTS AND GUIDELINES

Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement

Richard G. Barr, MD, PhD • Stephanie R. Wilson, MD • Deborah Rubens, MD • Guadalupe Garcia-Tsao, MD • Giovanna Ferraioli, MD

Radiology 2020



J Hepatol 2022

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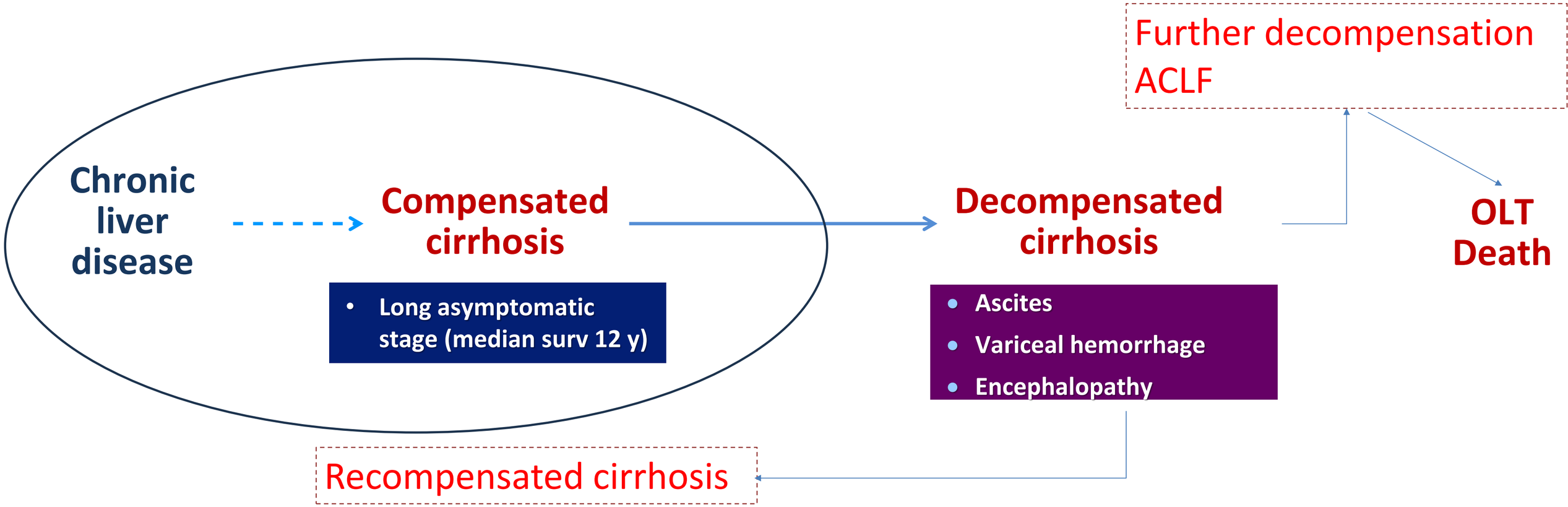
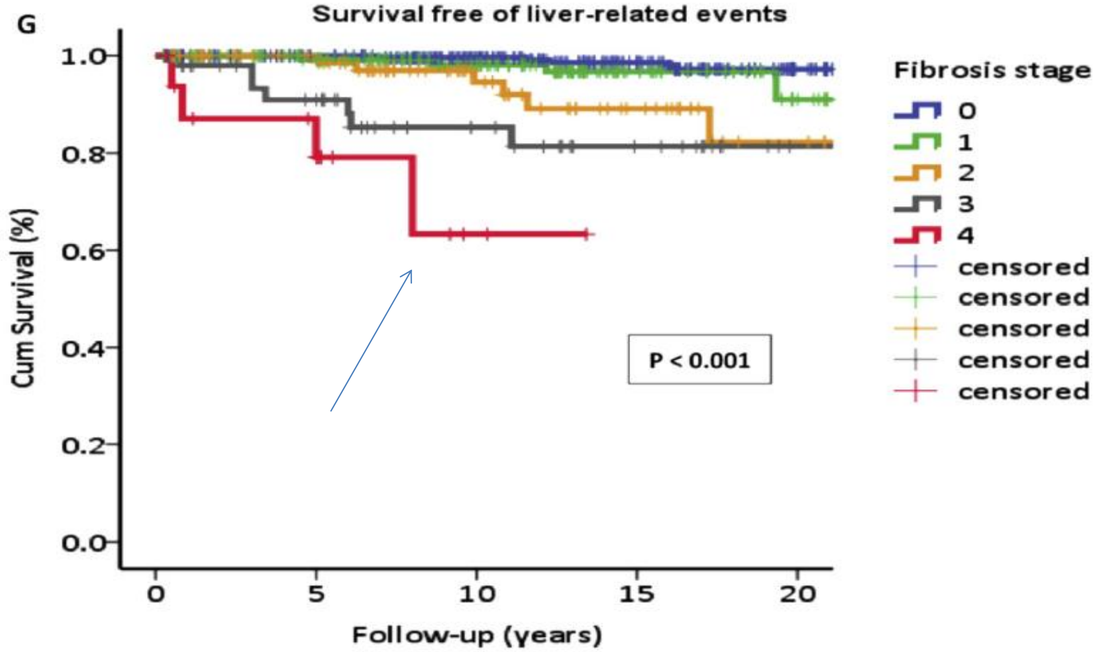
Natural history of chronic liver disease and stages of cirrhosis



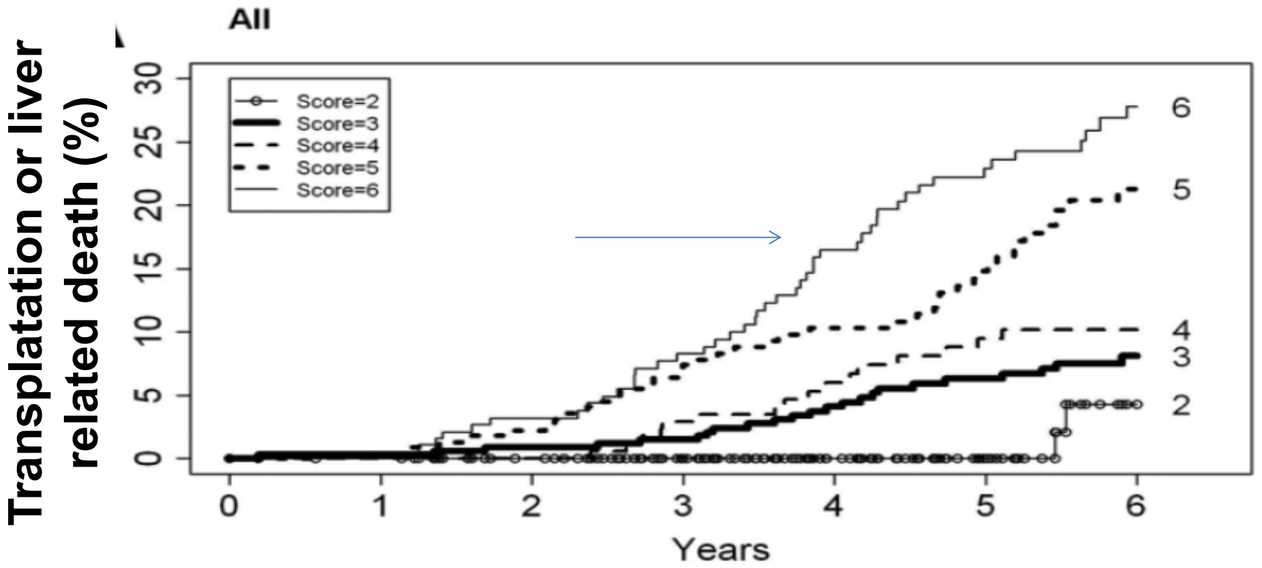
Modified from Garcia-Tsao, Abraldes, Berzigotti and Bosch, Hepatology 2017

The risk of clinical events in CLD is linked to the stage of fibrosis



MASLD/NASH

Angulo P et al. Gastroenterology 2015



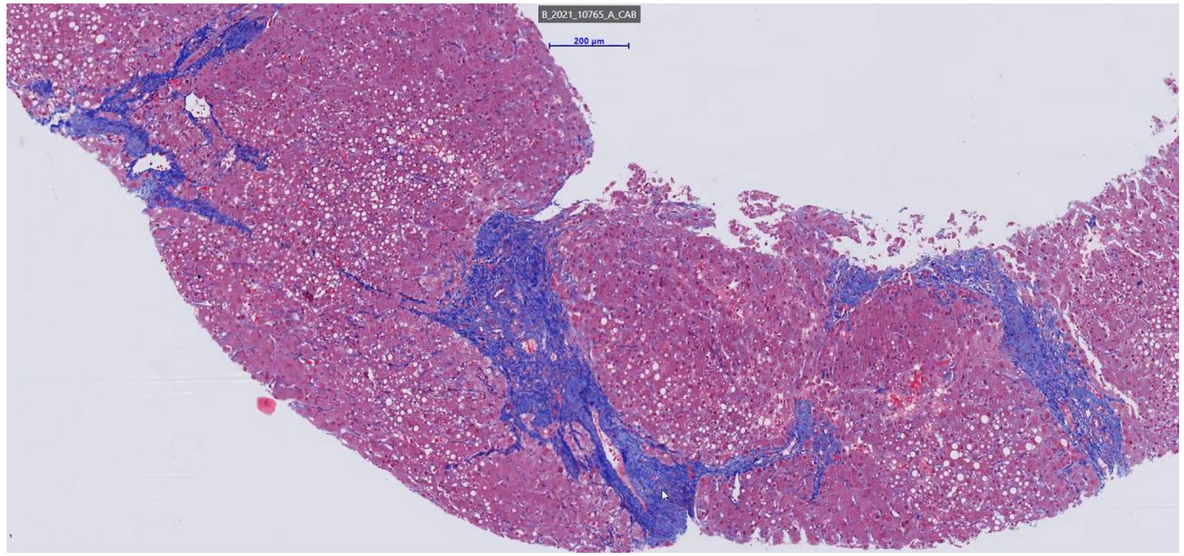
HCV

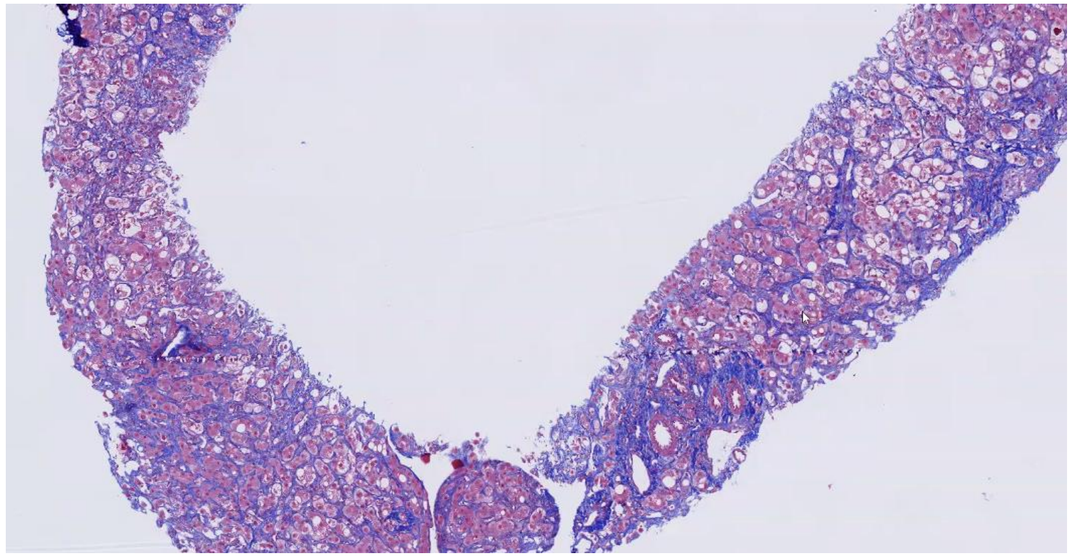
Everhart, Hepatology 2010

Bridging fibrosis and cirrhosis on histology identify patients at risk of developing clinical events (decompensation, HCC, liver-related death)

EASL-ALEH CPGs J Hepatol 2015

Liver biopsy – reference standard in the past

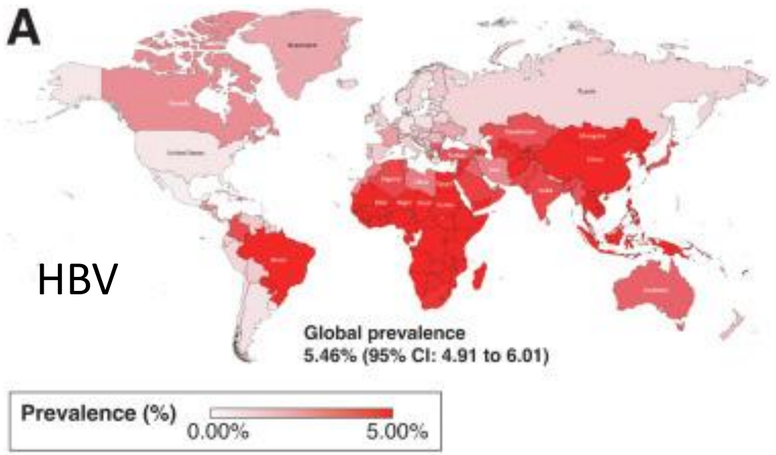


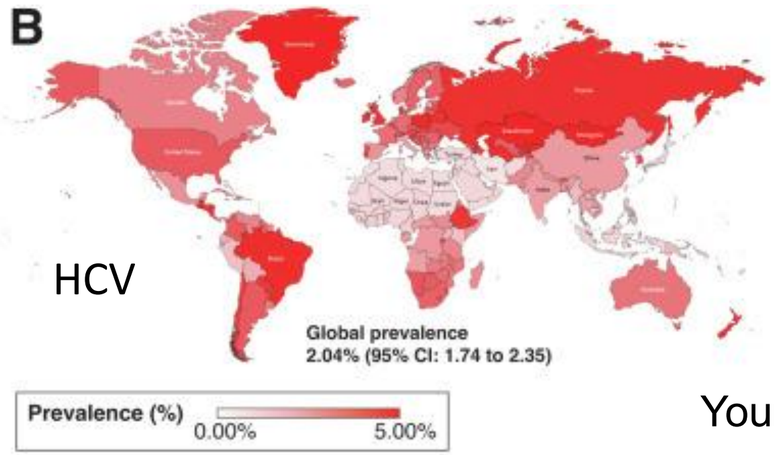


Fibrosis stage = surrogate marker for prognosis

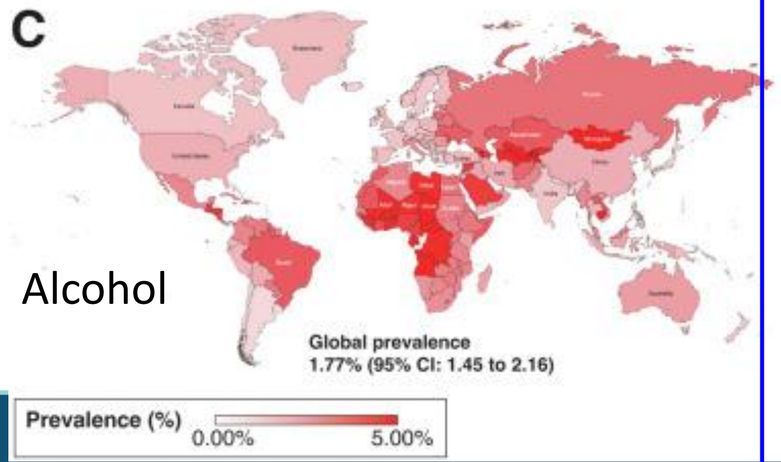
The epidemiology of CLD has changed – very high number of incident cases of CLD

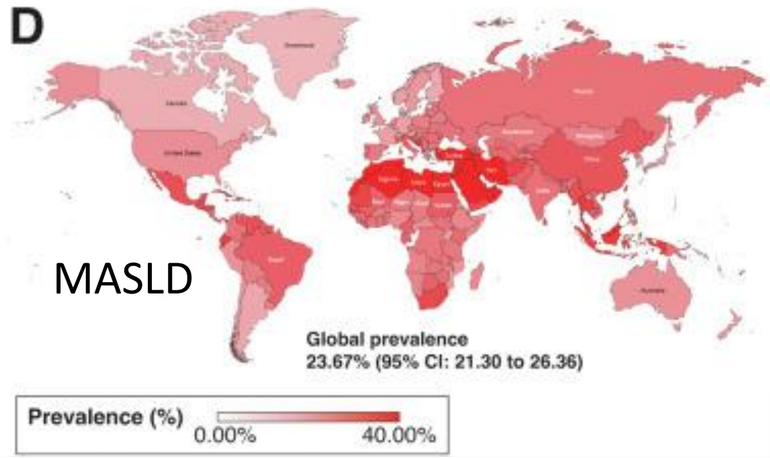
> 1500 million people has currently some degree of chronic liver disease (>> MASLD)





Younossi Z et al. CGH 2023





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In the last 20 years several non-invasive tests for liver fibrosis assessment have become available

Serum markers/Scores

- APRI
- **FIB-4**
- NFS score
- BARD
- FAST
- Agile 3 and 4

Non Patented

- **Fibrotest ®**
- **ELF ™**
- FibroMeter®
- Hepascore
- LiverPRO

Patented

Elastography

Transient Elastography

Point SWE

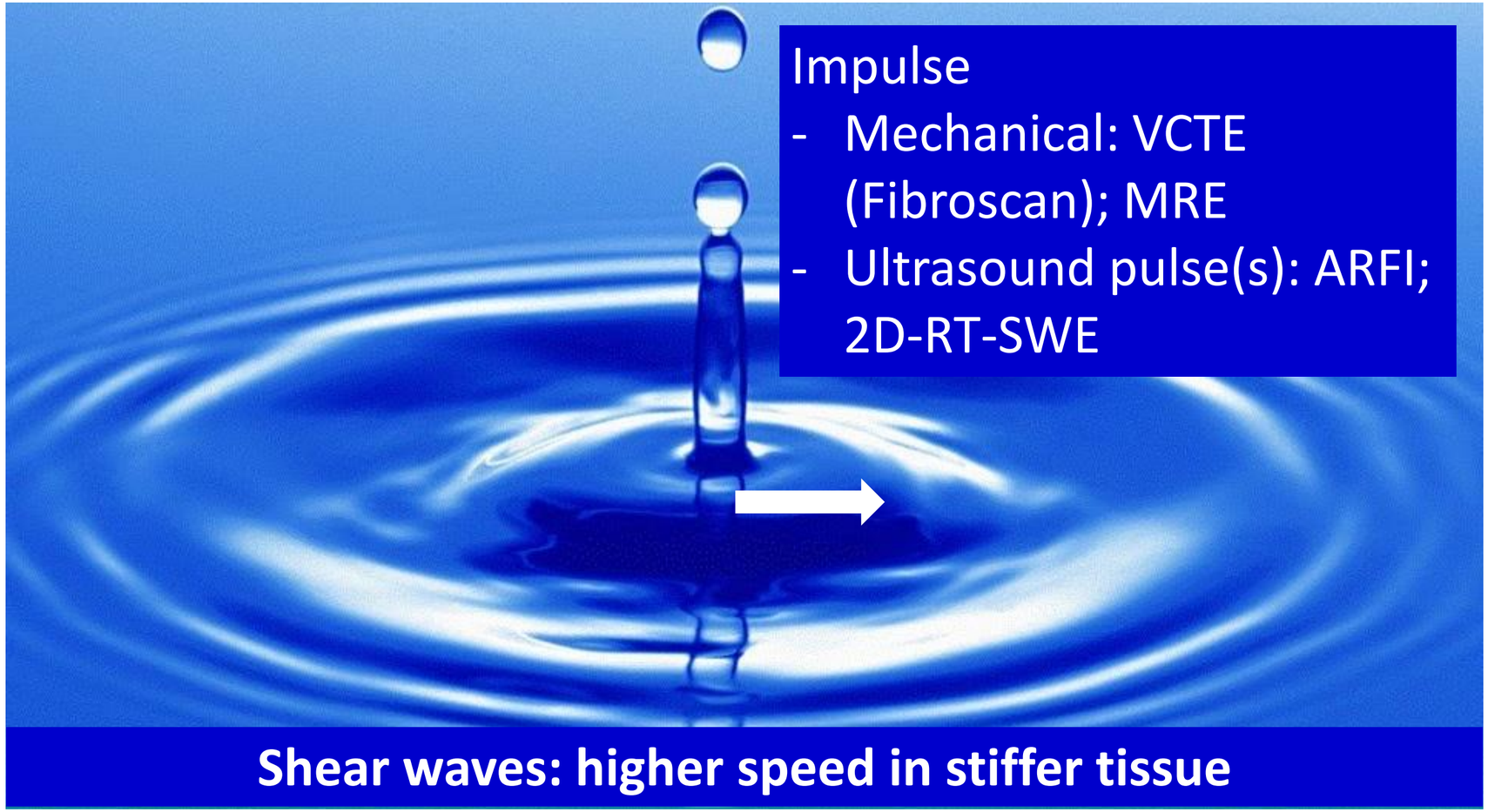
2D- SWE

MRE

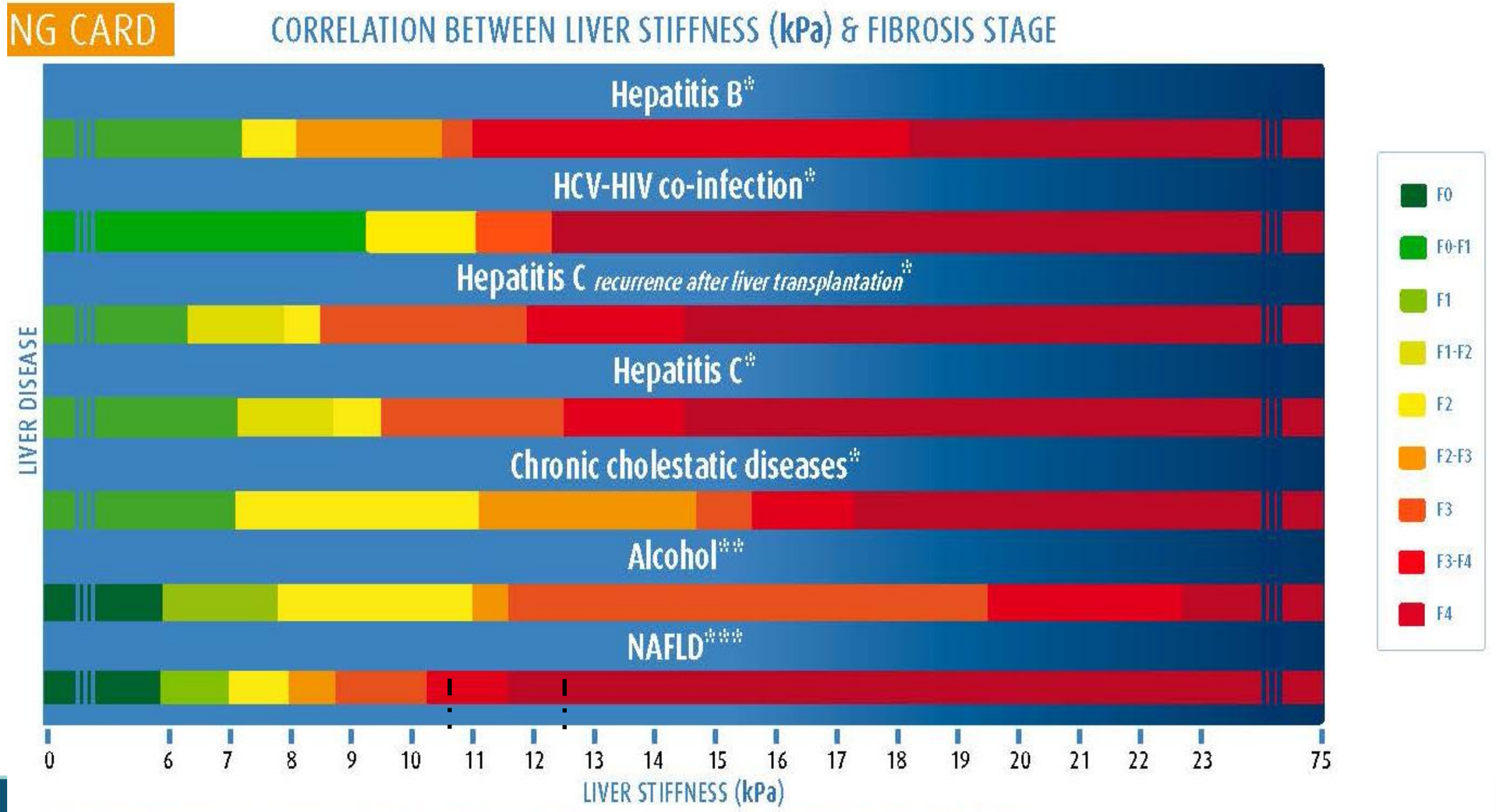
EASL Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis. J Hepatol 2021

+ Imaging / (US, CT, MR)

Elastography

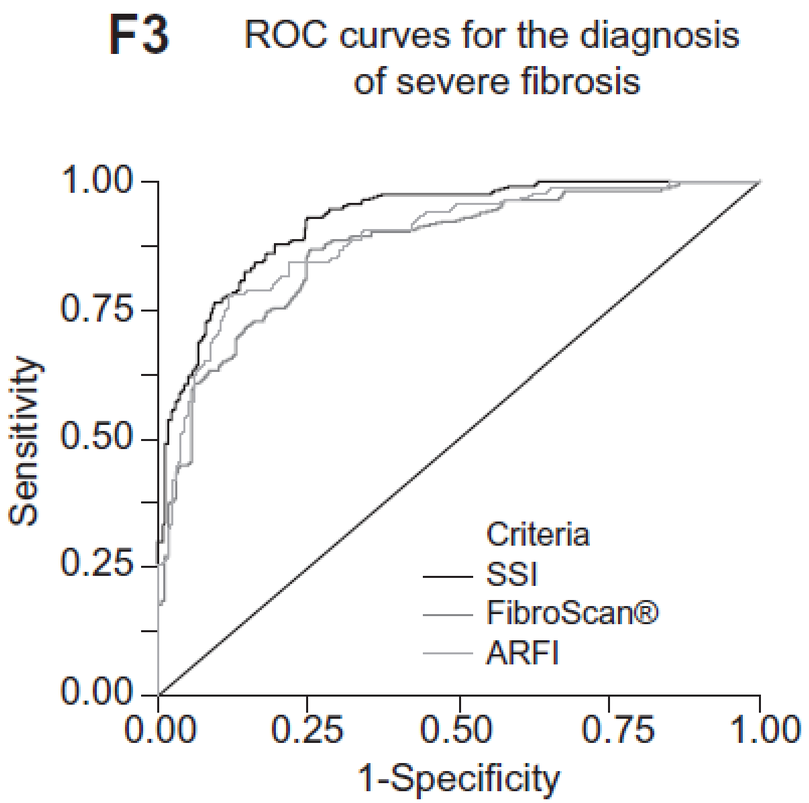


Good correlation with fibrosis in all etiologies

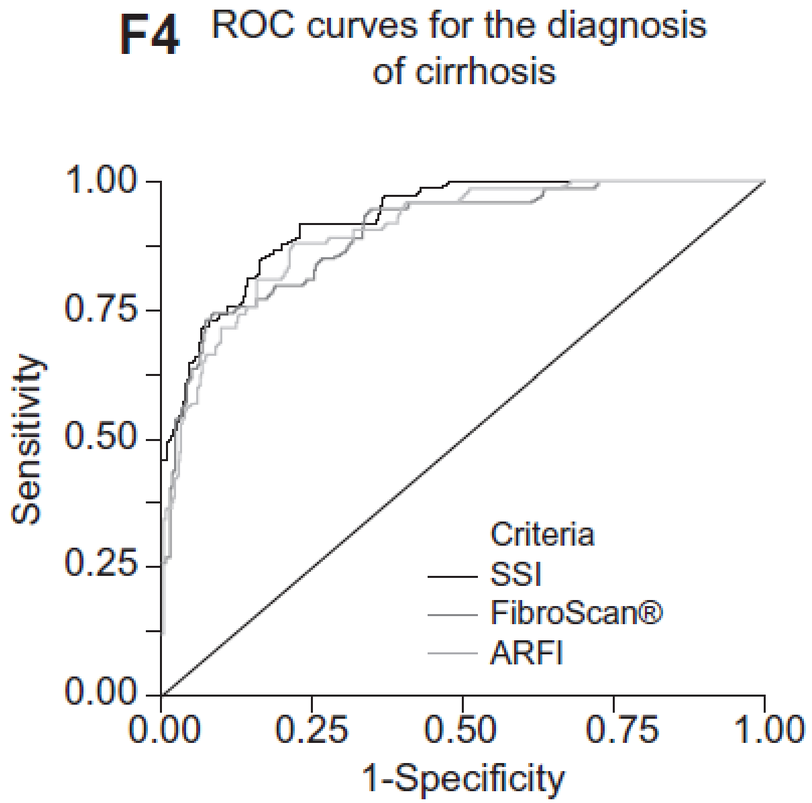


*According to Metavir score: Transient elastography (FibroScan): V. de Lédinghen, J. Vergniol, Gastroentérologie Clin Bio (2008) 32, 58-67
**According to Brunt score: Nahon et al. J Hepatol (2009) 49, 1062-68, Nguyen-Khac et al. , Aliment Pharmacol Ther (2008), 28, 1188-98
***According to Brunt score: Wong et al. Hepatology (2010) 51, 454-62Transient elastography (FibroScan®): V. de Lédinghen, J. Vergniol, Gastroentérologie Clin Bio (2008) 32, 58-67

Fibrosis estimation by elastography: similar results with different techniques

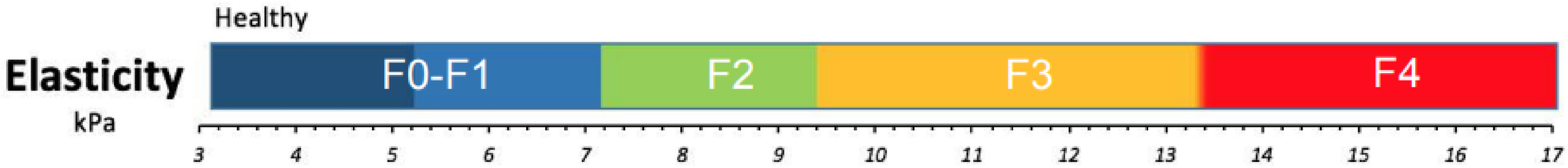


N=349



Cassinotto et al. J Hepatol 2014

Suggested cut-offs to rule-in and rule-out fibrosis using ShearWave™

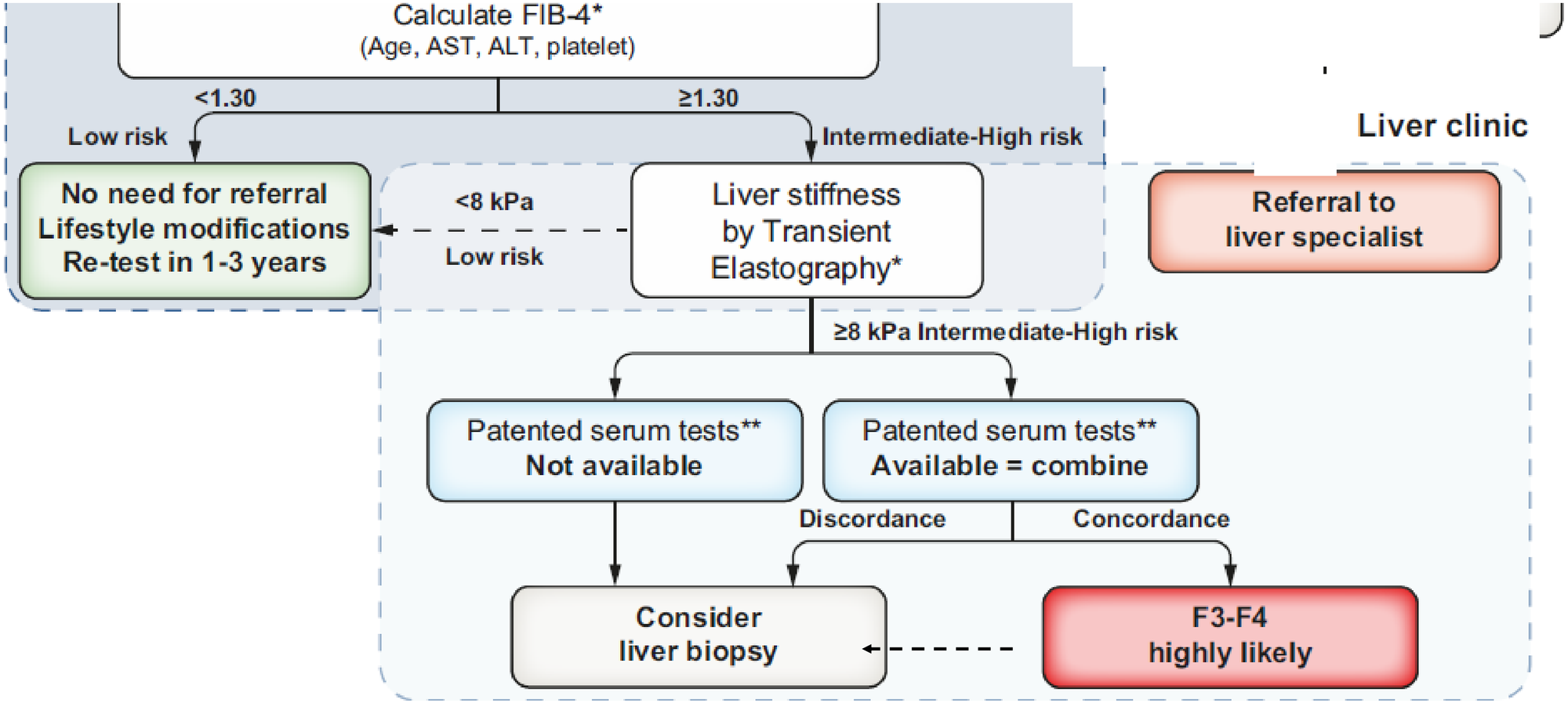


RECOMMENDATION 17

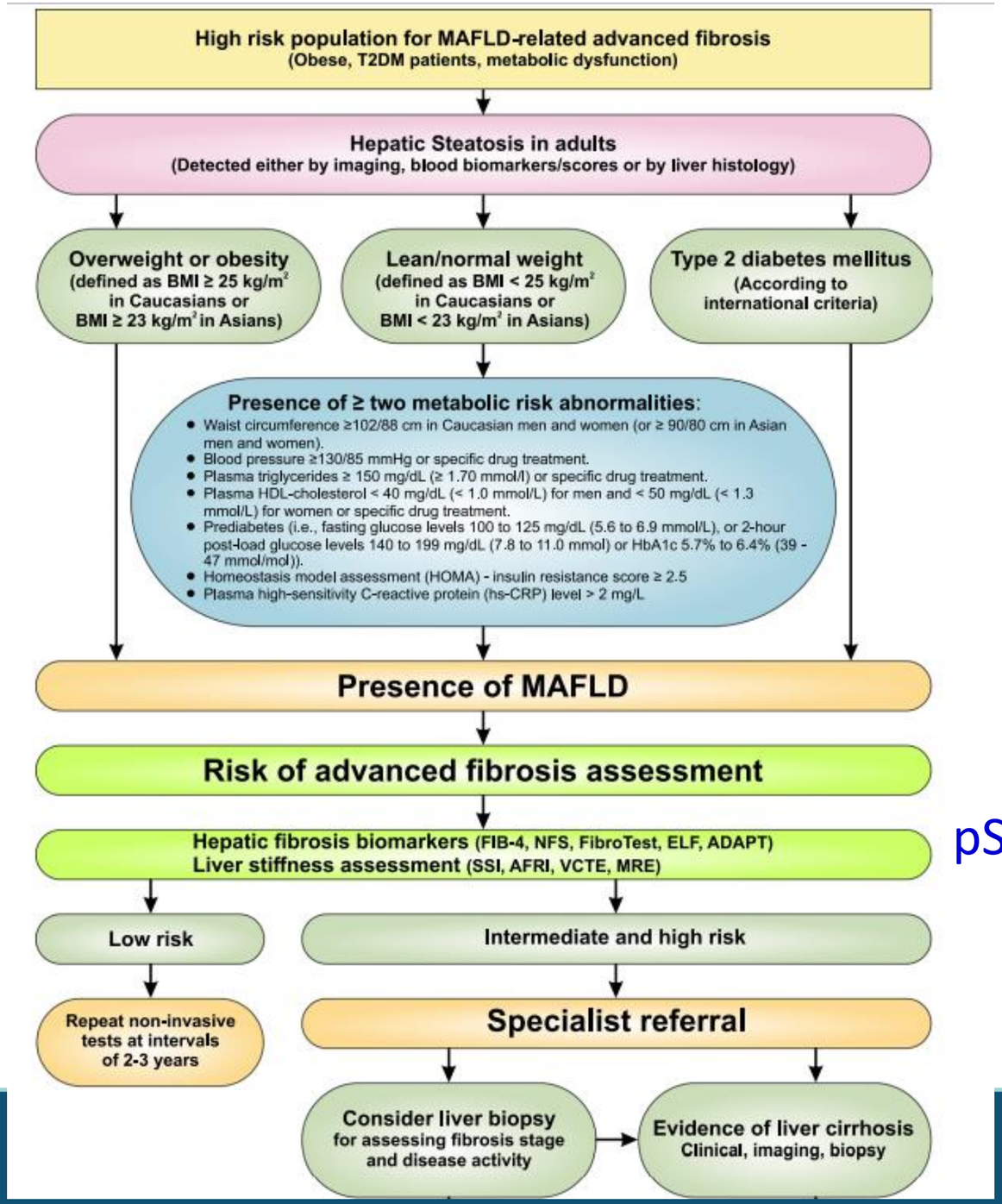
2D-SWE as demonstrated with SSI can be used as a first-line assessment for the severity of liver fibrosis in patients with chronic hepatitis C. It performs best with regard to the ruling out of cirrhosis (LoE 1b, GoR A) [106 – 108]. Broad consensus (17/0/1, 94 %)

The higher liver stiffness, the higher the risk of fibrosis

When is LSM indicated? EASL guidelines on NITs in liver disease



EASL CPG NITs J Hepatol 2021

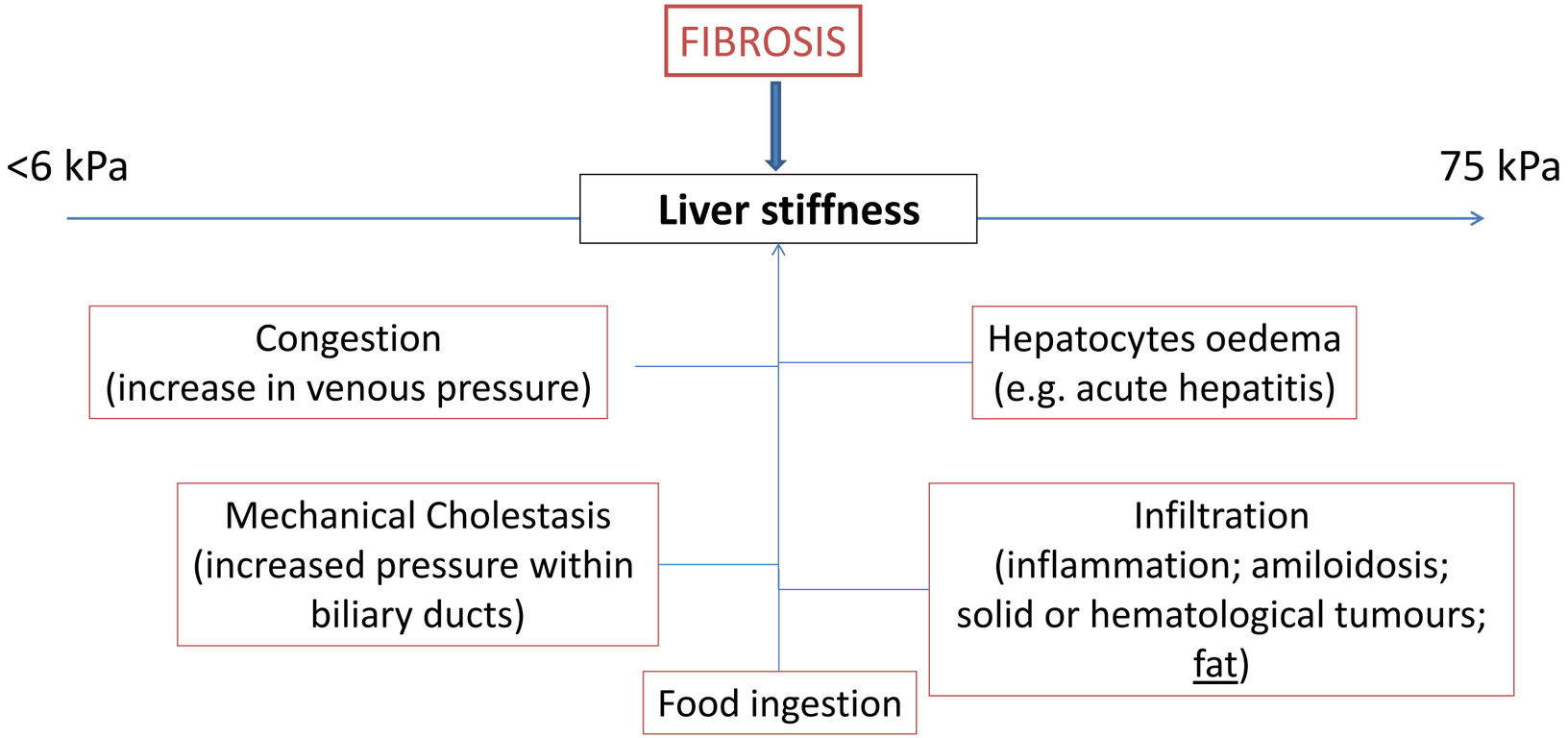


APASL guidelines on MASLD

pSWE, 2DSWE, VCTE and MRE accepted for LSM

Eslam M et al. Hepatol Int 2020

Caution on interpretation: liver stiffness is not only fibrosis

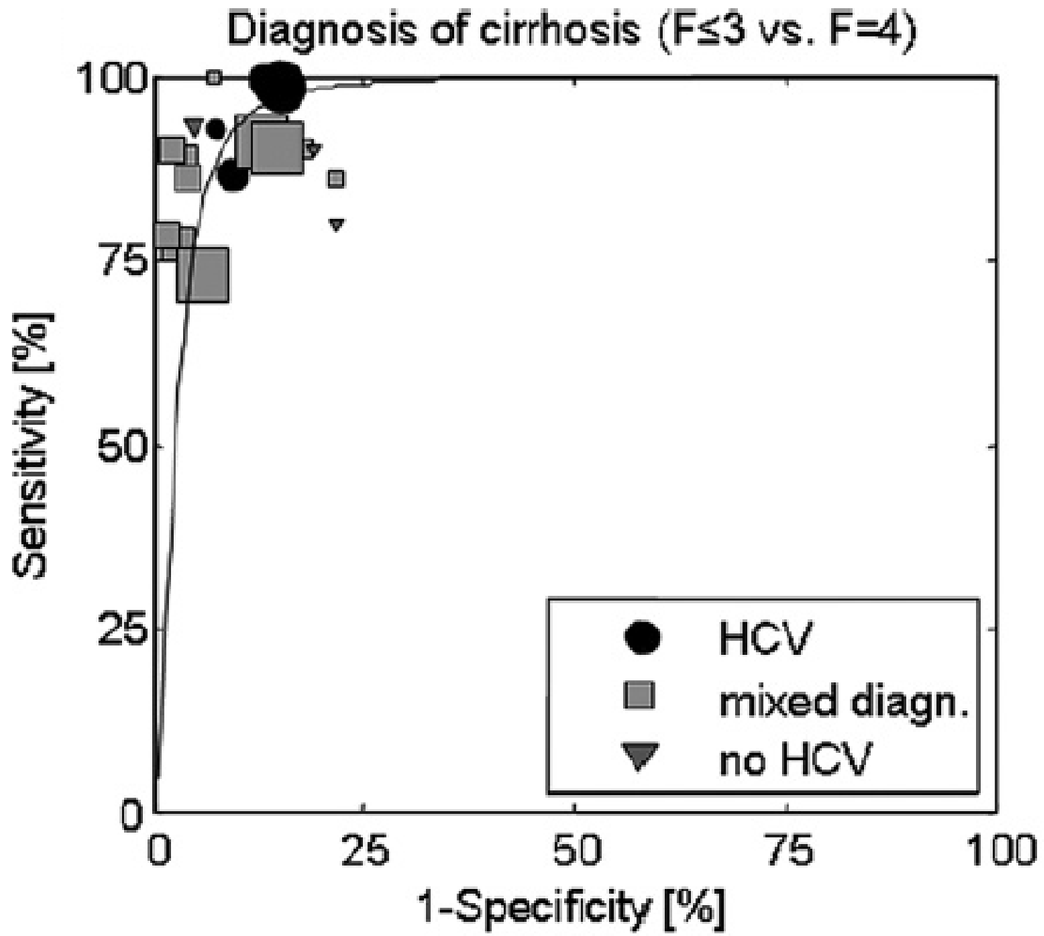


RECOMMENDATION 8

SWE within the normal range can rule out significant liver fibrosis when in agreement with the clinical and laboratory background (LoE 2A, GoR B) [34, 35]. Broad consensus (17/0/1, 94 %)

EFSUMB Guidelines
EASL CPGs

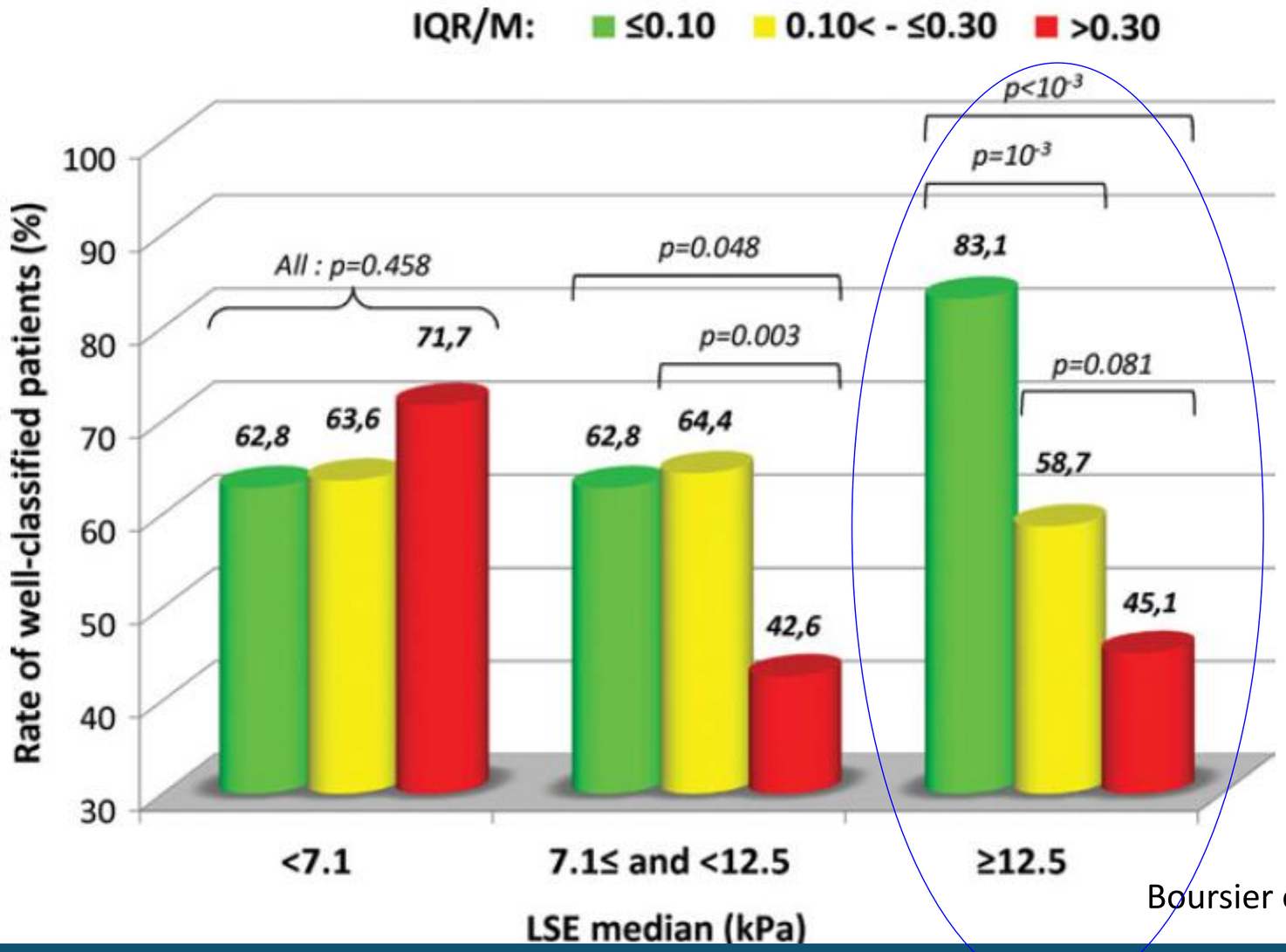
Performance of LSM by TE to diagnose cirrhosis: meta-analysis



AUROC:
0.94 (0.93-0.95)

Friedrich-Rust et al. Gastroenterology 2008

FibroScan® reliability: strict criteria are needed to accurately diagnose cirrhosis



Very strict IQR/M criteria should be used to correctly diagnose cirrhosis

Boursier et al. Hepatology 2013

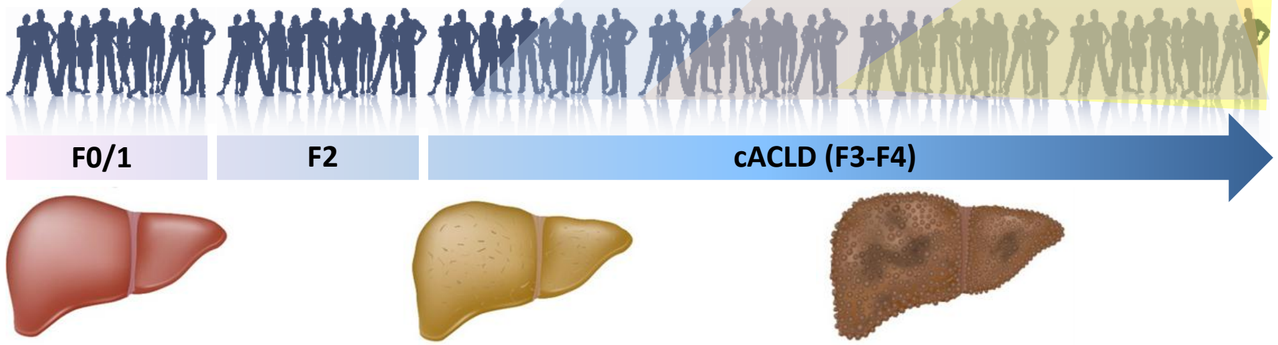
Baveno VI

But is the diagnosis of cirrhosis the thing that most matters?

TRANSIENT ELASTOGRAPHY

LIVER BIOPSY

CLINICAL DIAGNOSIS



The introduction of elastography (most data with VCTE) in clinical practice has allowed the early identification of patients with chronic liver disease (CLD) at risk of developing clinically significant portal hypertension (CSPH) (1b; A).

Courtesy of Joan Genescá

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In 2015 Baveno VI proposes for the first time to use NITs to classify patients as « high risk » or « low risk », of carrying HR varices

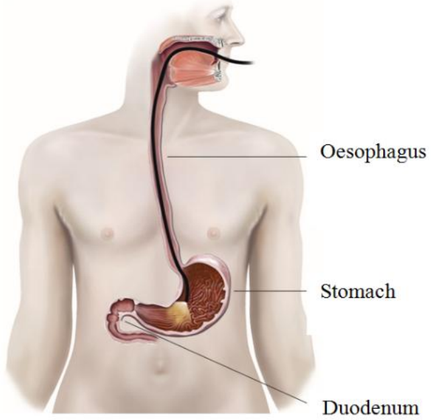
Platelet count
> 150 G/L

+

LSM < 20 kPa

De Franchis et al. J Hepatol 2015

Largely validated (> 50 studies)
Cost-effective



High risk varices in less than 3% of cases
Endoscopy can be safely skipped in this group

β blockers to prevent decompensation of cirrhosis in patients with clinically significant portal hypertension (PREDESCI): a randomised, double-blind, placebo-controlled, multicentre trial

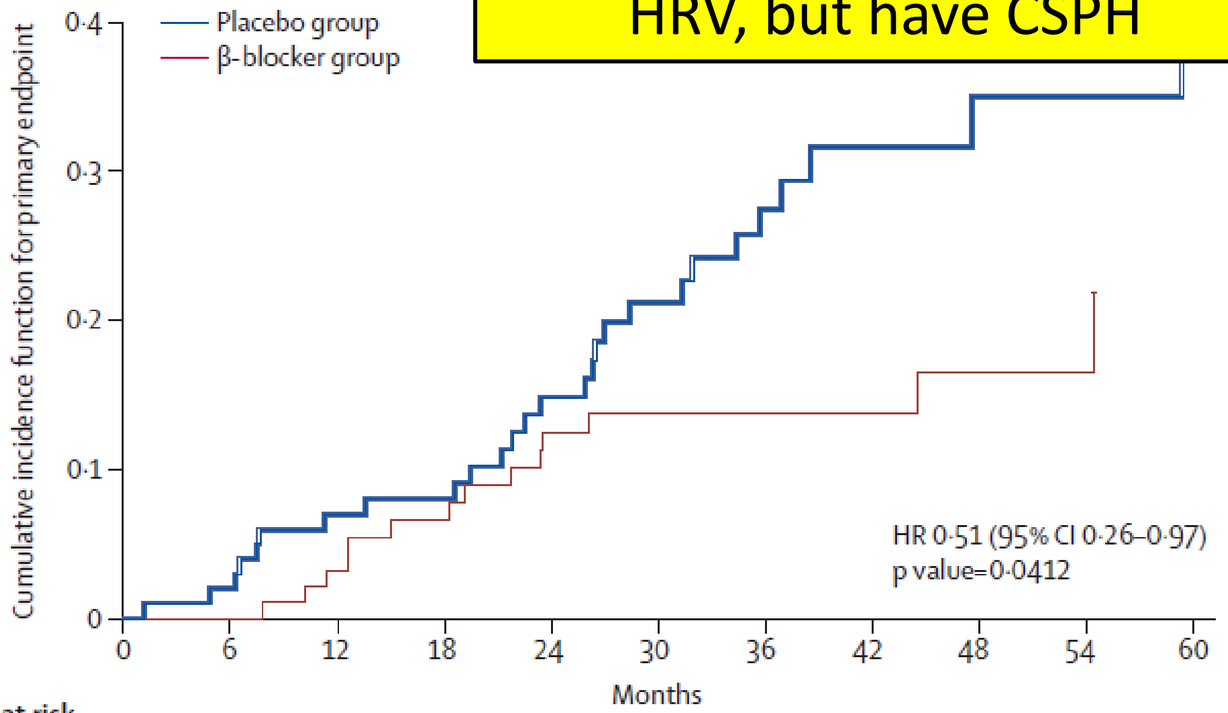
Càndid Villanueva, Agustín Albillos, Joan Genescà, Joan C Garcia-Pagan, José L Calleja, Carles A*
Beatriz Peñas, Salvador Augustin, Juan G Abraldes, Edilmar Alvarado, Ferran Torres, Jaume Bosc

Villanueva et al. Lancet 2019

After Baveno VI, new data emerged: reducing PP reduces the risk of all complications in patients who do not yet have HRV, but have CSPH

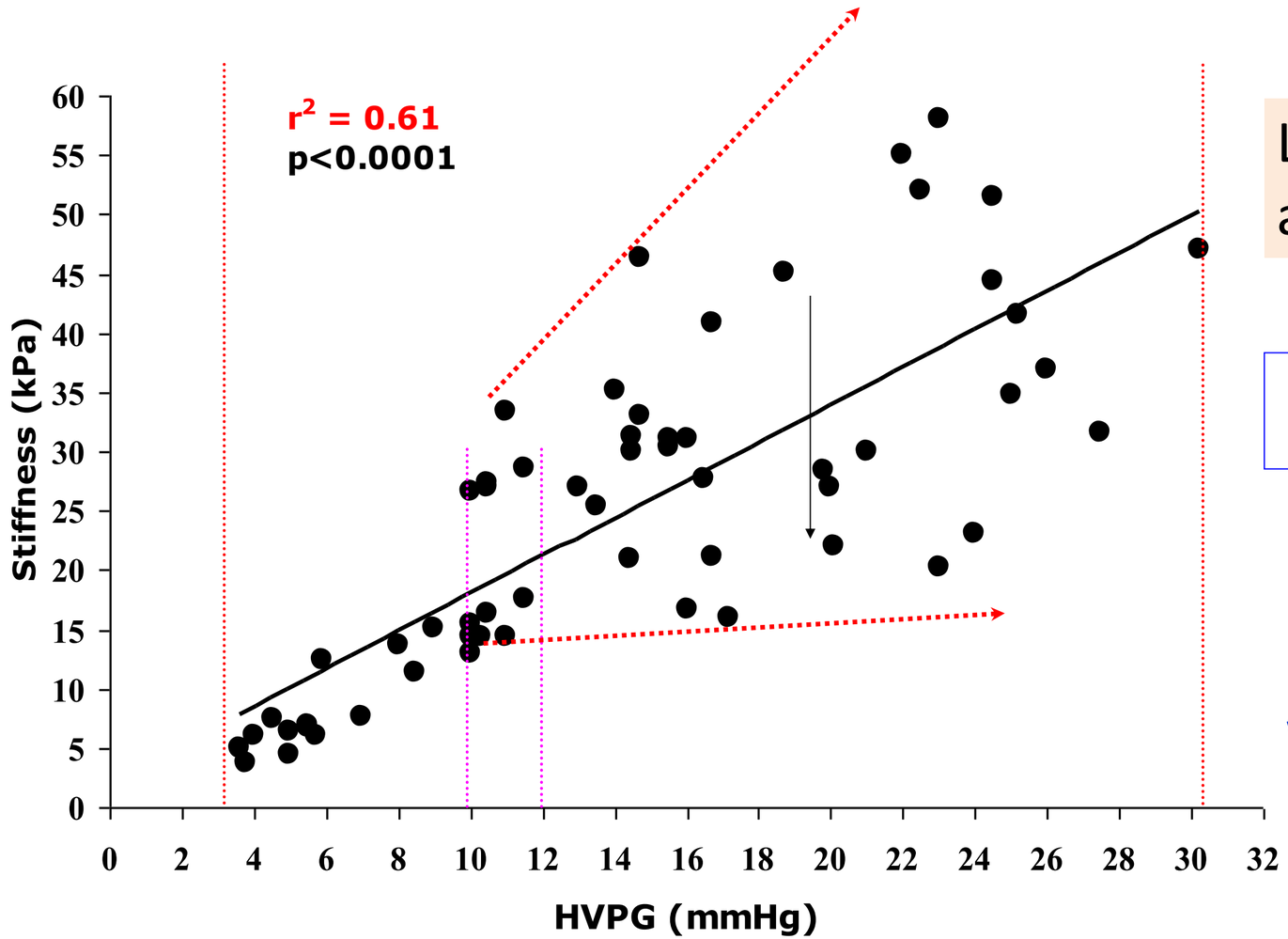
Baveno VII new paradigm: Identifying CSPH as early as possible is needed to start NSBBs as soon as CSPH is diagnosed

A



Patients at risk											
β blockers	100	96	87	80	69	60	48	31	20	15	7
Placebo	101	99	94	86	72	59	42	26	19	13	6
Primary outcome (deaths)											
β blockers		1 (1)	3 (1)	4 (2)	5 (2)	1 (1)	0	0	1 (1)	0	1
Placebo		2 (2)	5 (1)	1	6 (2)	5 (1)	4 (3)	2 (1)	1 (1)	0	1
Censoring events											
β blockers		3	6	3	6	8	12	17	10	5	7
Placebo		0	0	7	8	8	13	14	6	6	6

LSM shows a very good correlation with HVPG in compensated patients



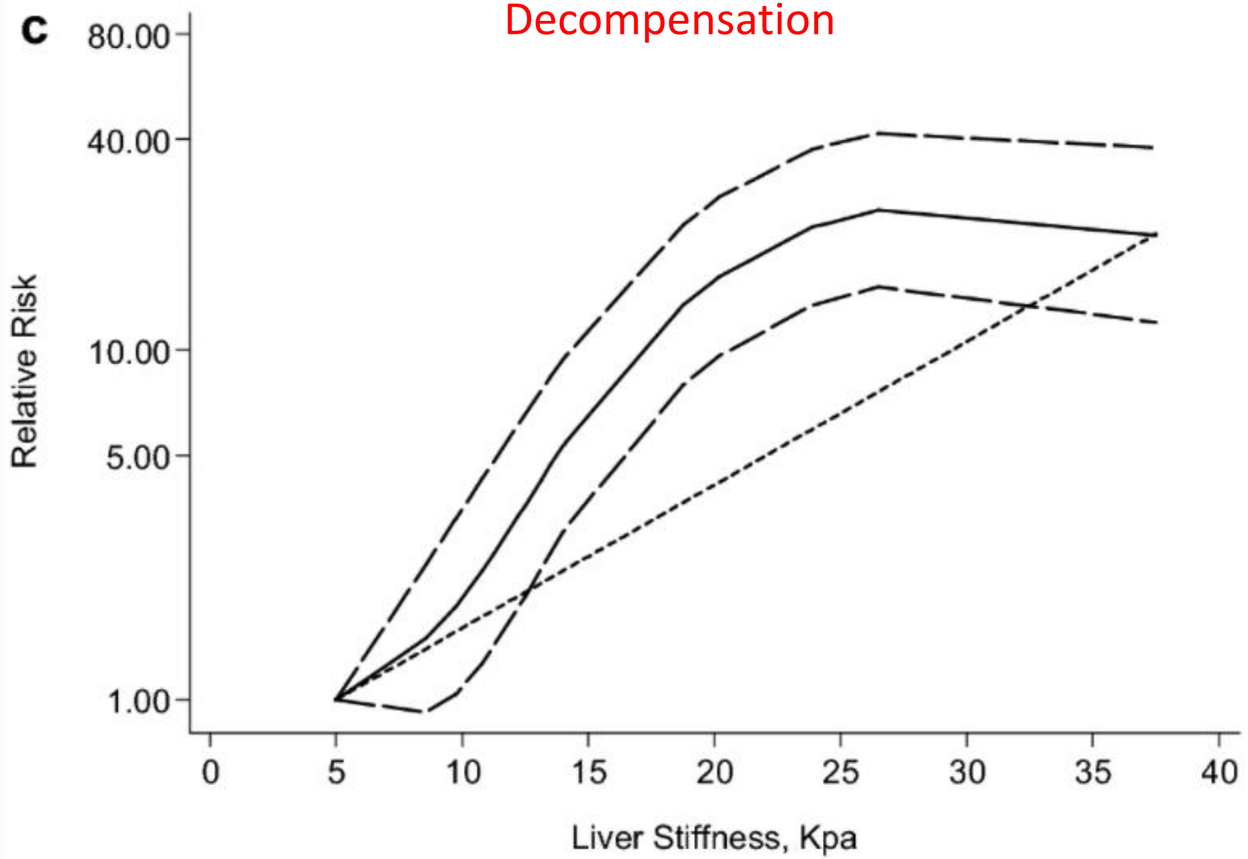
LSM allows ruling-out and ruling-in CSPH

P = R * Q

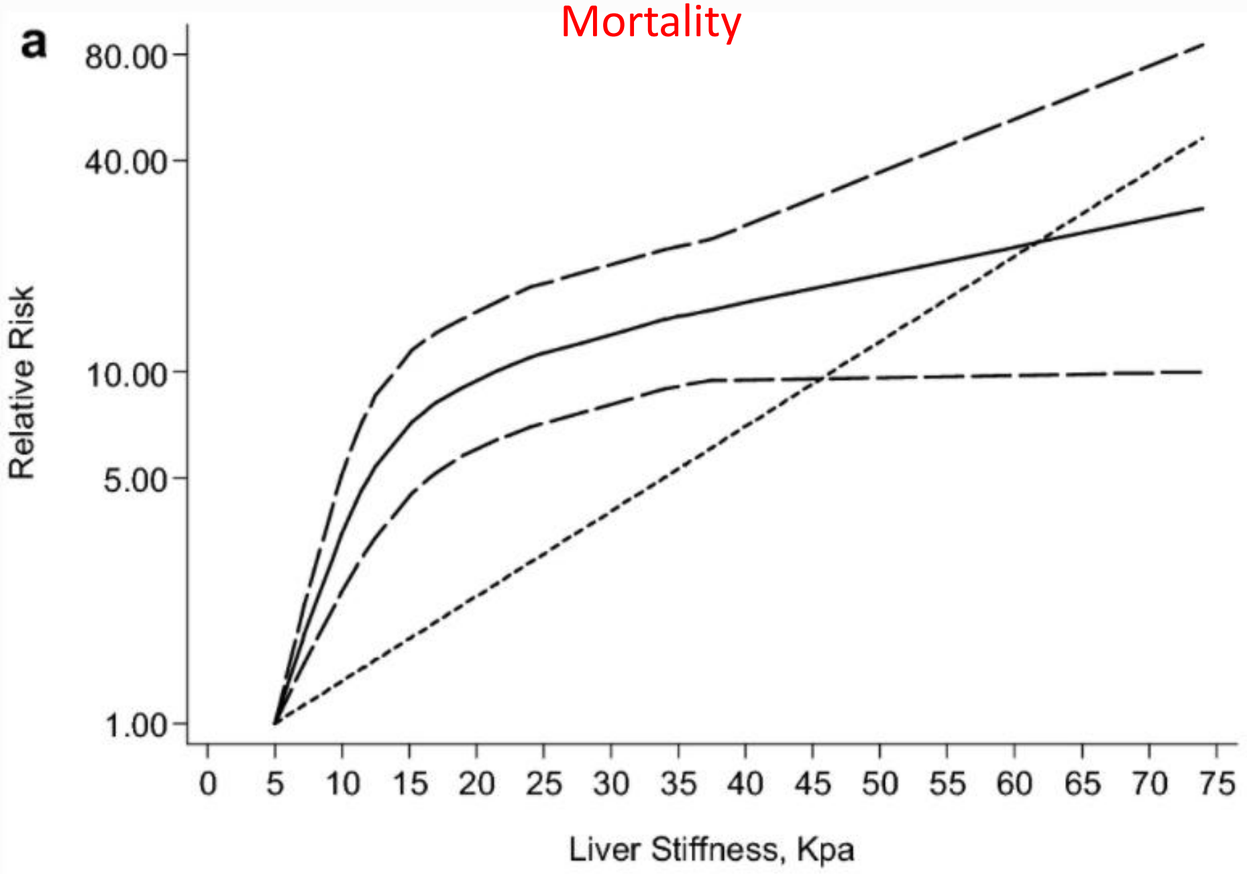
Vizzutti et al Hepatology 2007

In addition, the higher the liver stiffness, the higher the risk of decompensation and mortality

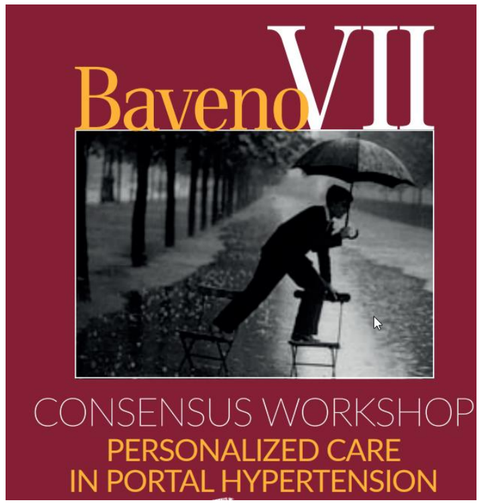
Decompensation



Mortality



Shen Y et al. Hepatol Int 2019



The ”rule of five” to pragmatically assess CSPH and risk of liver-related events

Monica Pons

Relative risk of decompensation & liver-related death

+Plat >150, Baveno VI - avoid endoscopy

+Plat ≥150, Exclude CSPH

“Grey Zone” for CSPH

5 kPa → 10 kPa → 15 kPa → 20 kPa → 25 kPa

Normal

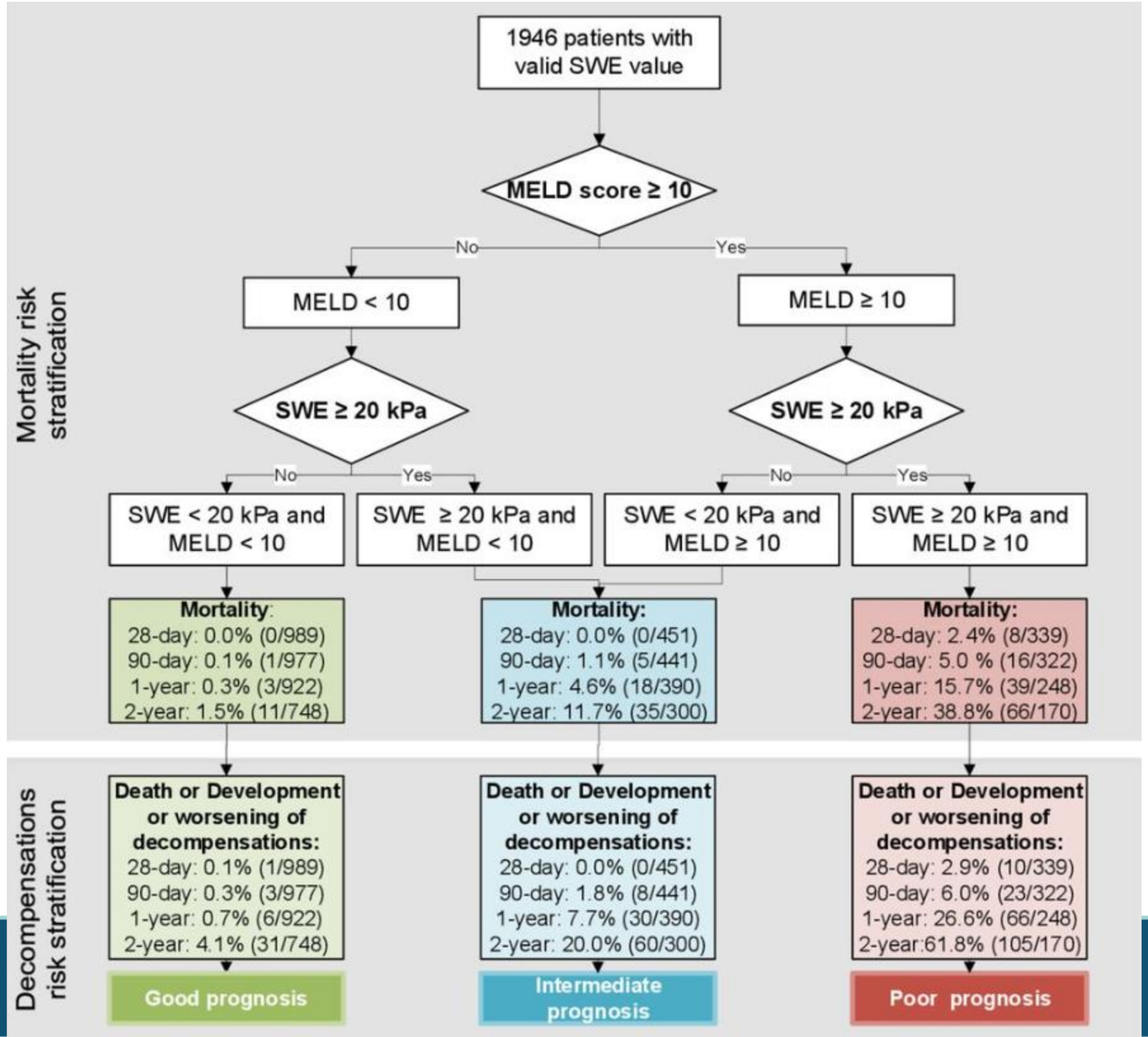
CSPH > 90%

40-60% of patients…

LSM < 15 kPa + Platelet count >150 G/L: very low risk of CSPH (<5%)

LSM > 20 kPa + Plt < 150 G/L
CSPH > 90%

LS using ShearWave™ allows an accurate risk stratification in CLD



Trebicka J et al. Gut 2022

If we use pSWE and 2D-SWE: the « rule of four »

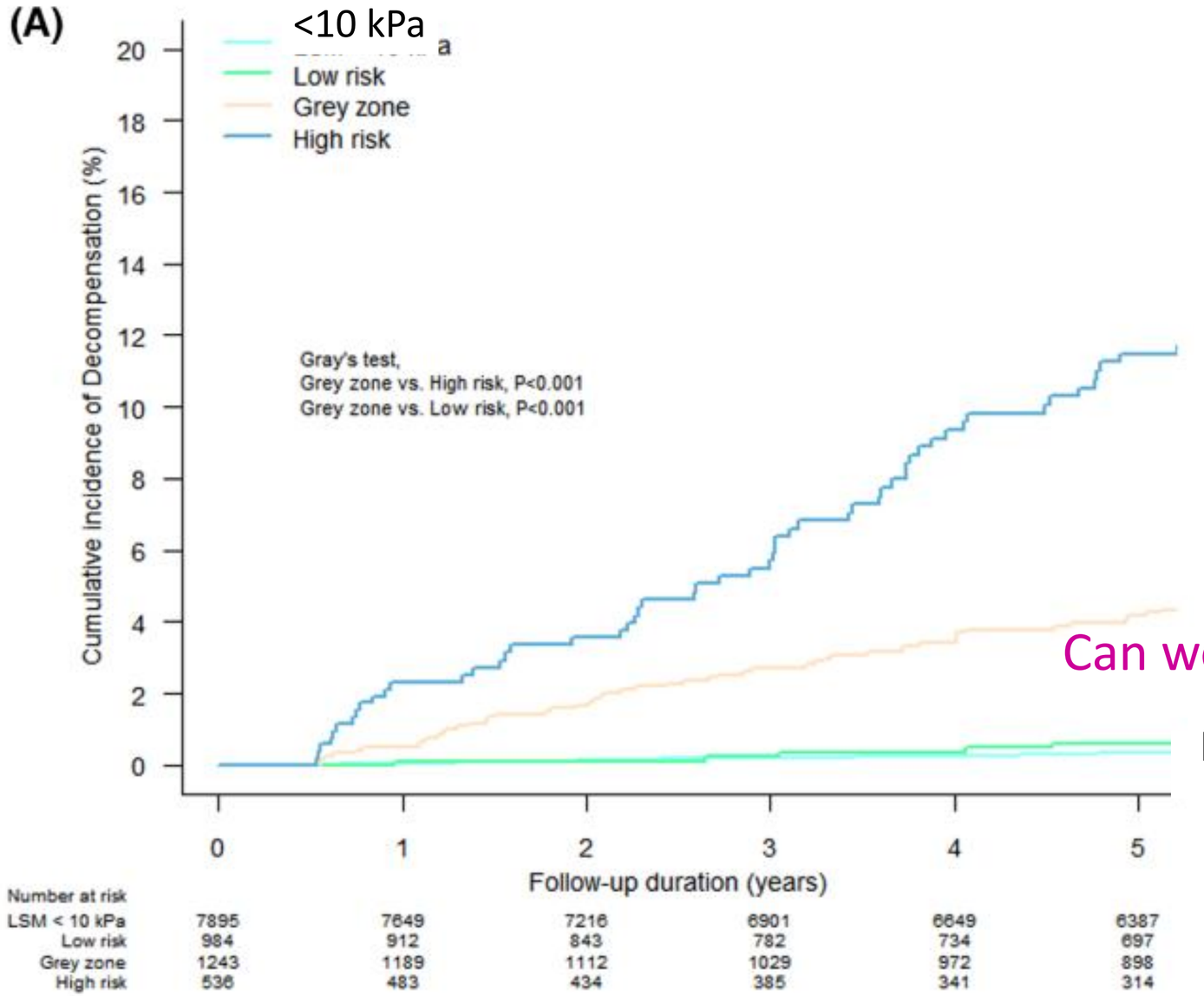
Table 2: Recommendation for Interpretation of Liver Stiffness Values Obtained with ARFI Techniques in Patients with Viral Hepatitis and NAFLD

Liver Stiffness Value	Recommendation
≤5 kPa (1.3 m/sec)	High probability of being normal
<9 kPa (1.7 m/sec)	In the absence of other known clinical signs, rules out cACLD. If there are known clinical signs, may need further test for confirmation
9–13 kPa (1.7–2.1 m/sec)	Suggestive of cACLD but need further test for confirmation
>13 kPa (2.1 m/sec)	Rules in cACLD
>17 kPa (2.4 m/sec)	Suggestive of CSPH

Note.—ARFI = acoustic radiation force impulse, cACLD = compensated advanced chronic liver disease, CSPH = clinically significant portal hypertension, NAFLD = non-alcoholic fatty liver disease.

SRU –
Barr et al. Radiology 2020

Validation of the Baveno VII rule of five: clinical events



N=2763

High risk: >25 kPa

Grey zone (indeterminate risk of CSPH)

Can we better stratify risk in this group?

Low risk (< 15 kPa and Plt ≥ 150 G/L)

Lin H et al. APT 2023

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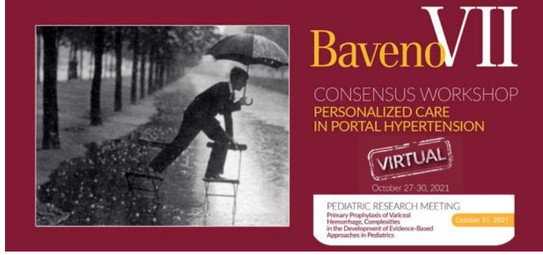


Spleen stiffness as an additional tool

LSM increases as fibrosis accumulates in the liver and **indirectly** reflects PH in patients with ACLD

Hepatic vascular R is mostly due to liver fibrosis

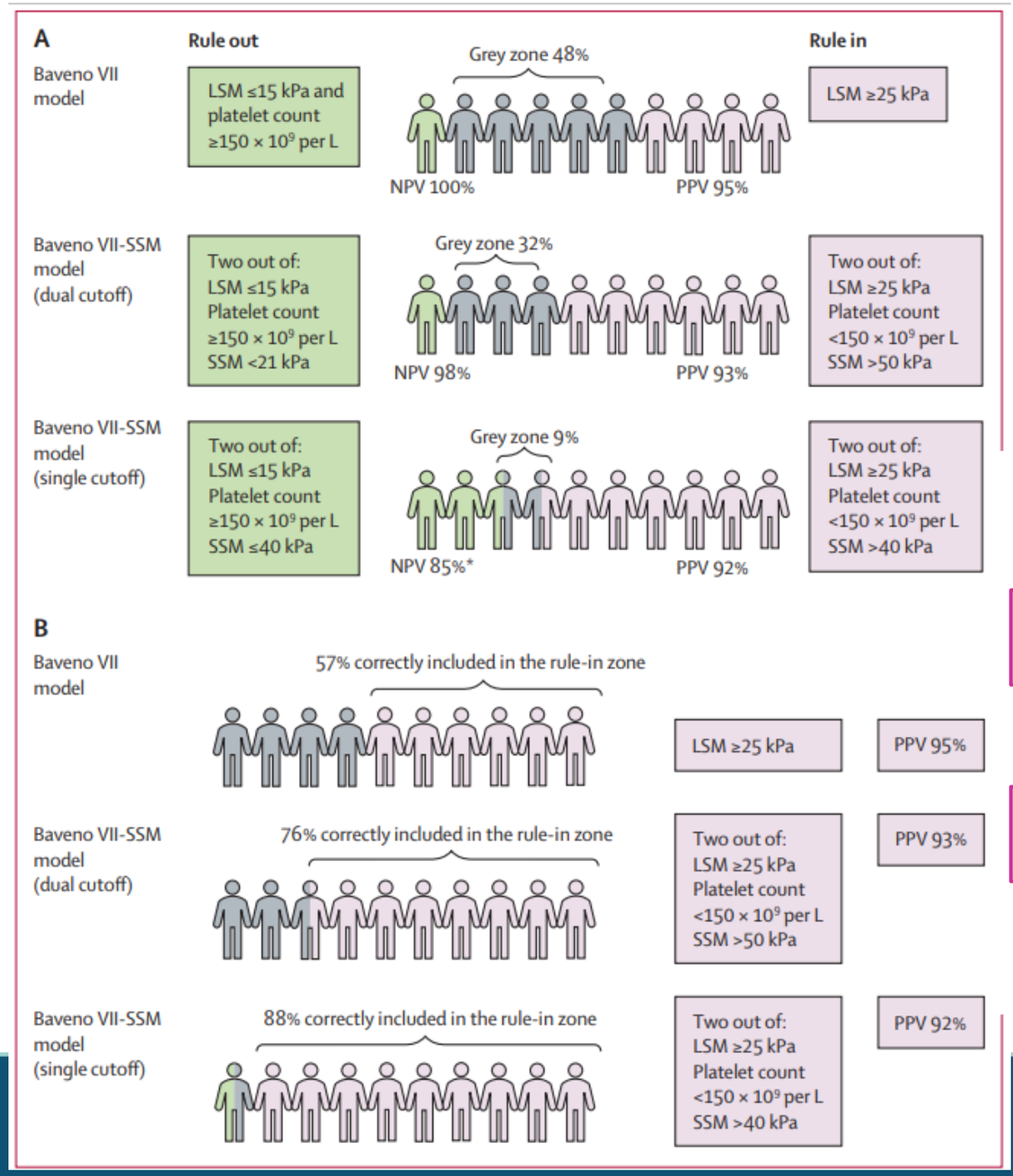
P = R * Q

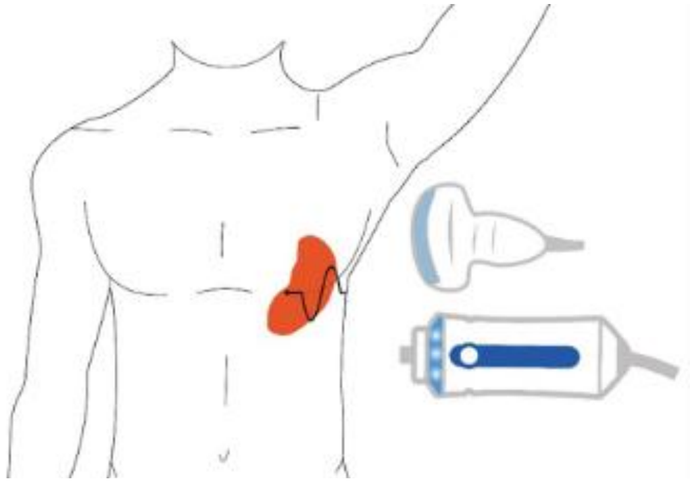
SSM **directly** reflects PH

Stiffness is due to congestion and other changes related directly to PH independent of its cause

Berzigotti, J Hepatol 2017

Individual patients data meta-analysis: SSM for CSPH





	Baveno VII–SSM single-cutoff model	Baveno VII–SSM dual-cutoff model
Rule out CSPH if	≥2 of the following criteria: LSM <15 kPa Platelet count ≥150 × 10^9/L SSM ≤40 kPa	≥2 of the following criteria: LSM <15 kPa Platelet count ≥150 ×10^9/L SSM <21 kPa
Rule in CSPH if	≥2 of the following criteria: LSM ≥25 kPa Platelet count <150 × 10^9/L SSM >40 kPa	≥2 of the following criteria: LSM ≥25 kPa Platelet count <150 × 10^9/L SSM >50 kPa

Dajti et al. Lancet Gastroenterol Hepatol 2023

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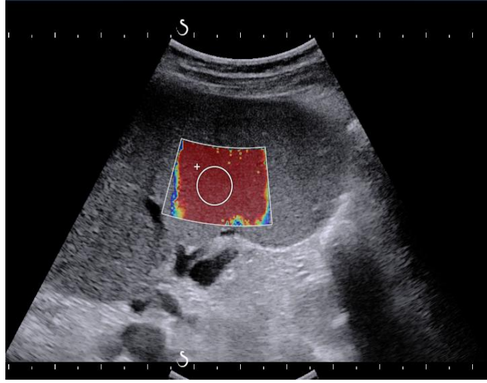
Studies reporting on SSM using 2D-SWE

SSM by 2D-SWE									
Elkrief et al.	2015	2D-SWE (SSI) TE	79, mixed, most decompensated, 89% CSPH, 69% Child-Pugh B-C	3% 58%	CSPH LEV CSPH LEV	0.640 0.580 0.630 0.650	34.7 kPa 32.3 kPa 56.3 kPa 73.5 kPa	40% 48% 73% 54%	100% 71% 67% 78%
Procopet et al.	2015	2D-SWE (SSI)	55, mixed, most compensated	34%	CSPH	0.725	22.7 kPa (rule-out) 40 kPa (rule-in)	90% N/A	N/A 90%
Cassinotto et al.	2015	2D-SWE (SSI)	401, mixed, some decompensated	29.2%	EV HRV	0.80 0.78 (all) 0.75 (compensated)	N/A N/A 25.6 kPa (with NPV >90%)	N/A N/A 94%	N/A N/A 36%
Grgurevic et al.	2015	2D-SWE (SSI)	126, mixed	29.4%	EV	0.790	30.3 kPa	79.6%	75.8%
Jansen et al.	2017	2D-SWE (SSI)	158, mixed, some decompensated	18.8%	CSPH	0.840	26.3 kPa 21.7 kPa (rule-out) 35.6 kPa (rule-in)	79.7% 91.9% 51.4%	84.2% 50% 92%
Zhu et al.	2019	2D-SWE (SSI)	104, HBV, most compensated	24.6%	CSPH	0.810	23.2 kPa (rule-out) 34.2 kPa (rule-in)	>90% N/A	N/A >90%
Karagiannakis et al.	2019	2D-SWE (SSI)	64, mixed, compensated	9.8%	HRV	0.792 (all) 0.854 (excluding cholestatic LD)	33.7 kPa (rule-out) 35.8 kPa (rule-out)	91.7% 88.9%	60.0% 72.4%
Cho et al.	2020	2D-SWE	274, mixed, compensated	N/R	HRV	0.844	≤27.3 kPa (rule-out)	98.1%	35.9%



SSM by 2D-SWE

< 21-25 kPa: rules out CSPH

< 35 kPa: rules out HRV

Limited evidence; some studies include decompensated pts

Not yet recommended by EASL and Baveno guidelines

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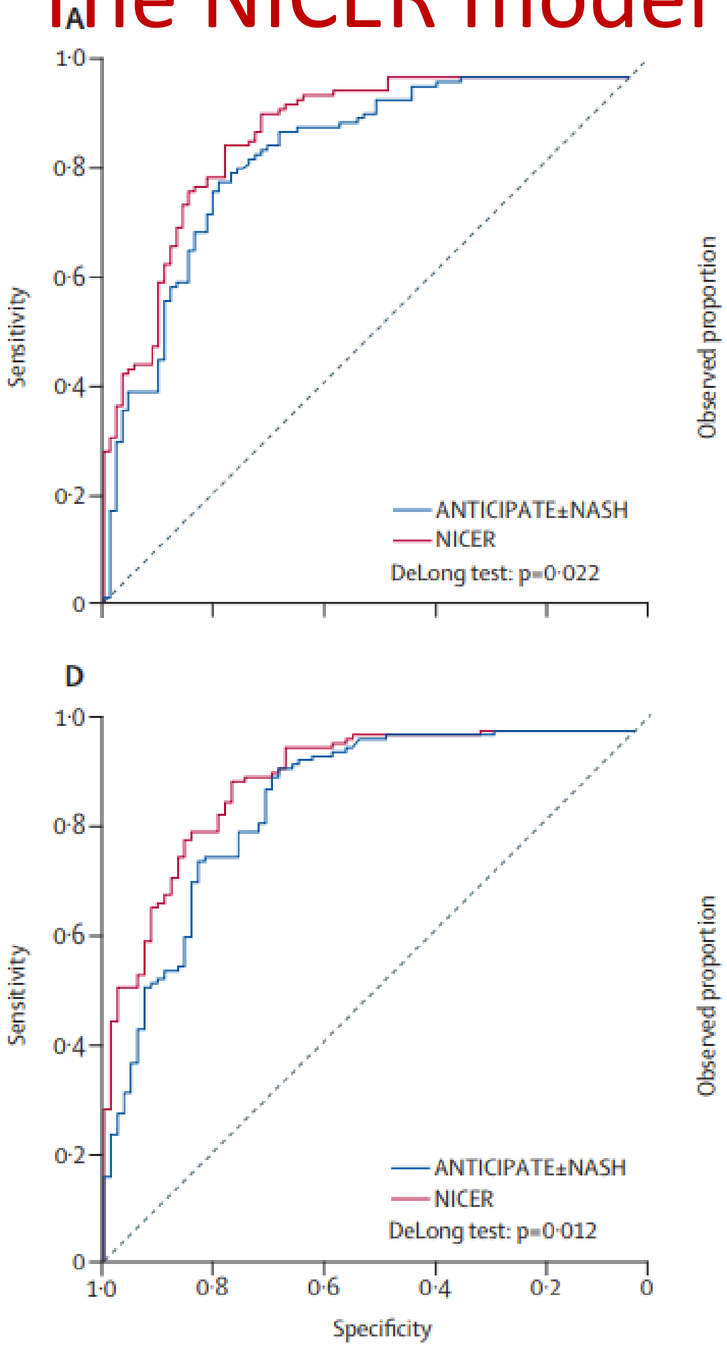
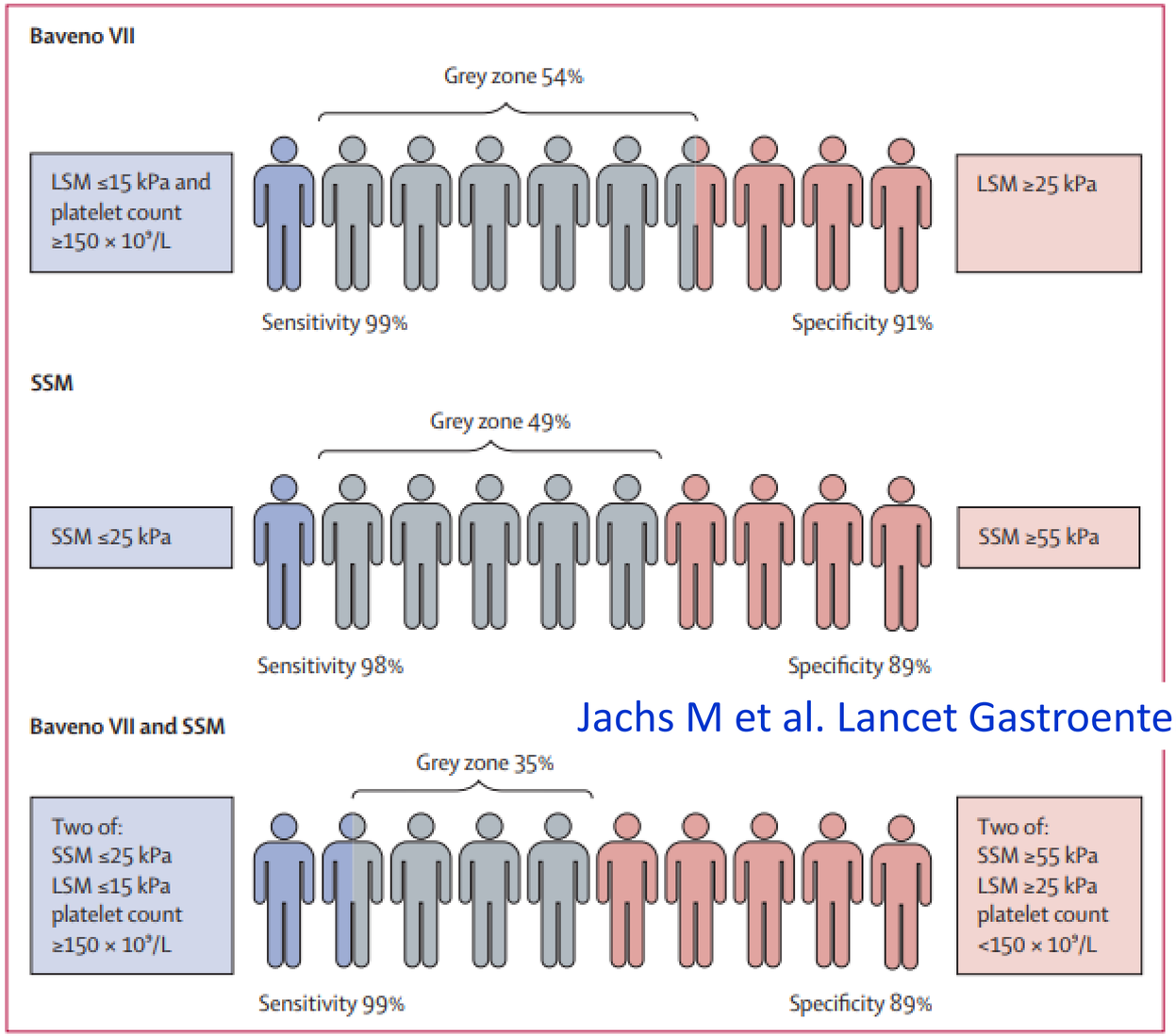
The NICER model integrates LSM, SSM, BMI and platelet count



N=407; prospective multicentric (16 centers) study vs. HVPG



LSM
BMI
Platelet count
SSM @100 Hz

Jachs M et al. Lancet Gastroenterol Hepatol 2024

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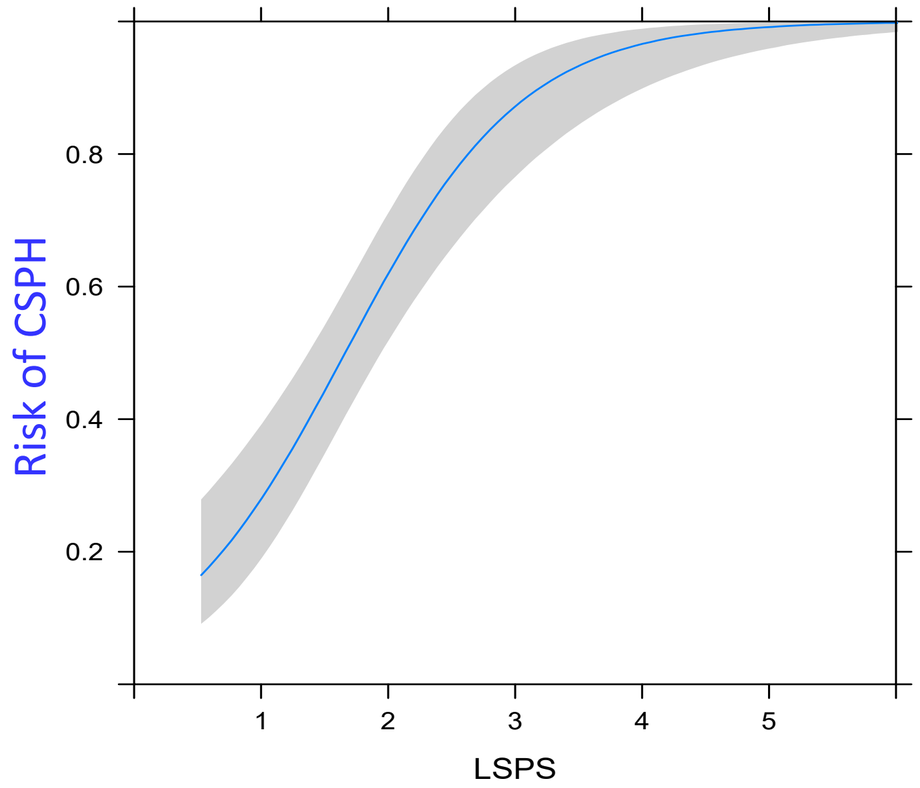
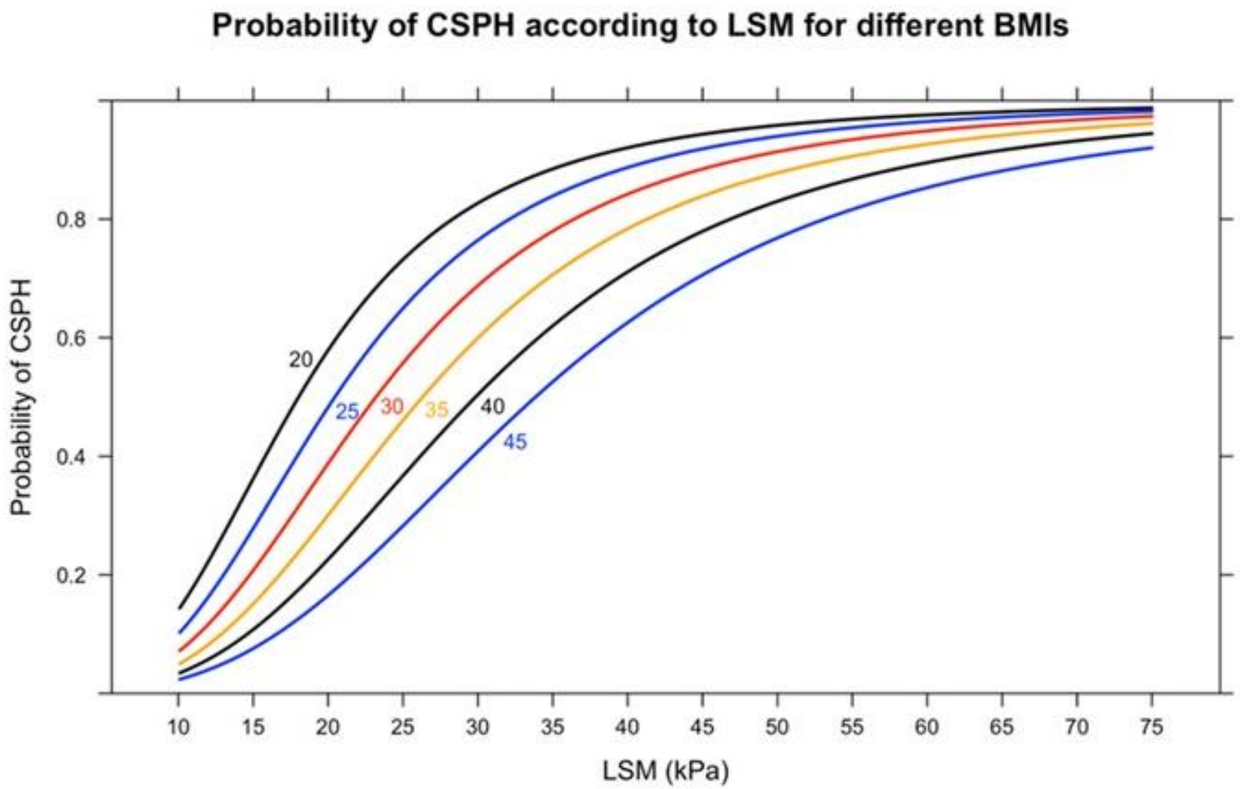
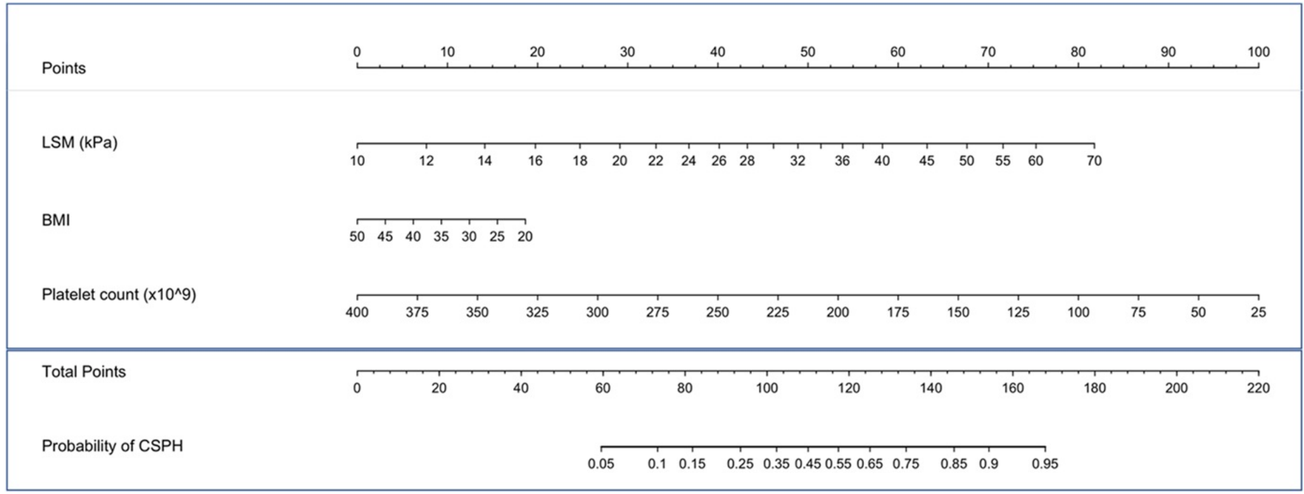
Another approach: NITs should be seen as continuous values and modeling the individual risk is possible



Abraldes JG ...Berzigotti A. Hepatology 2016

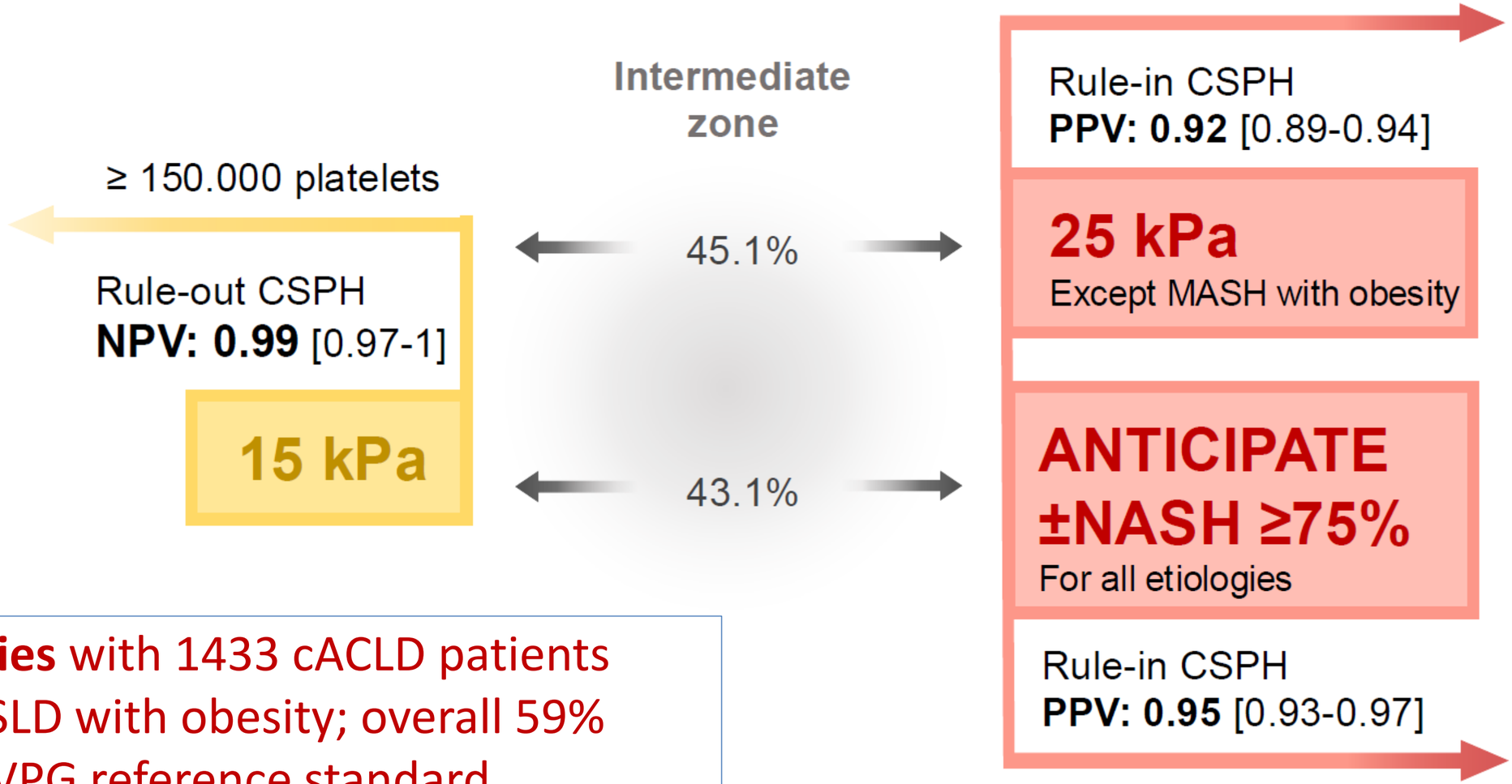
In patients with cACLD due to MASLD and obesity: ANTICIPATE-NASH model (LSM, Plt count; BMI)





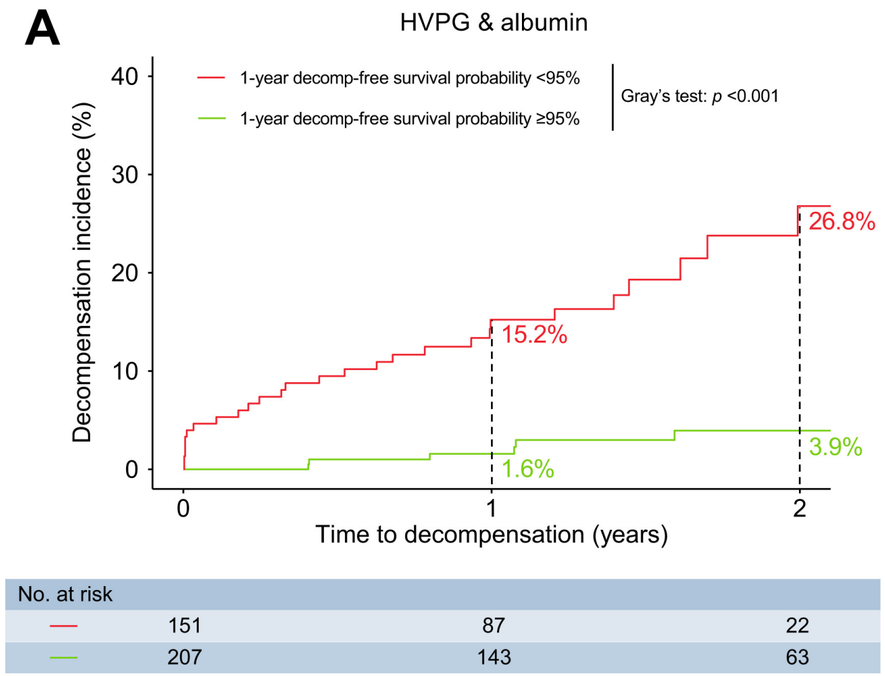
Pons M et al, AJG 2021

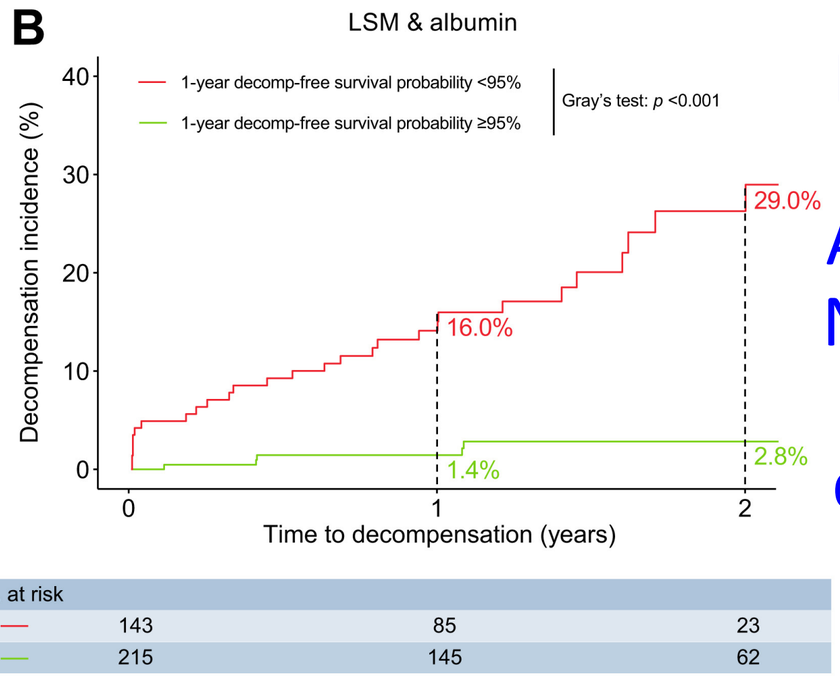
The ANTICIPATE models using a threshold of ≥ 75% allow refining the identification of CSPH: individual patients data meta-analysis

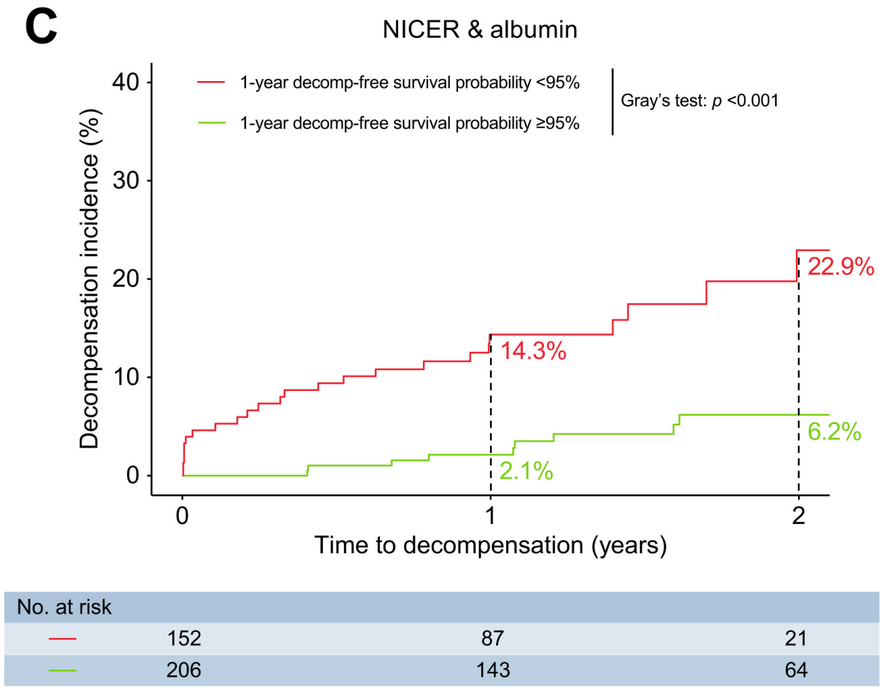


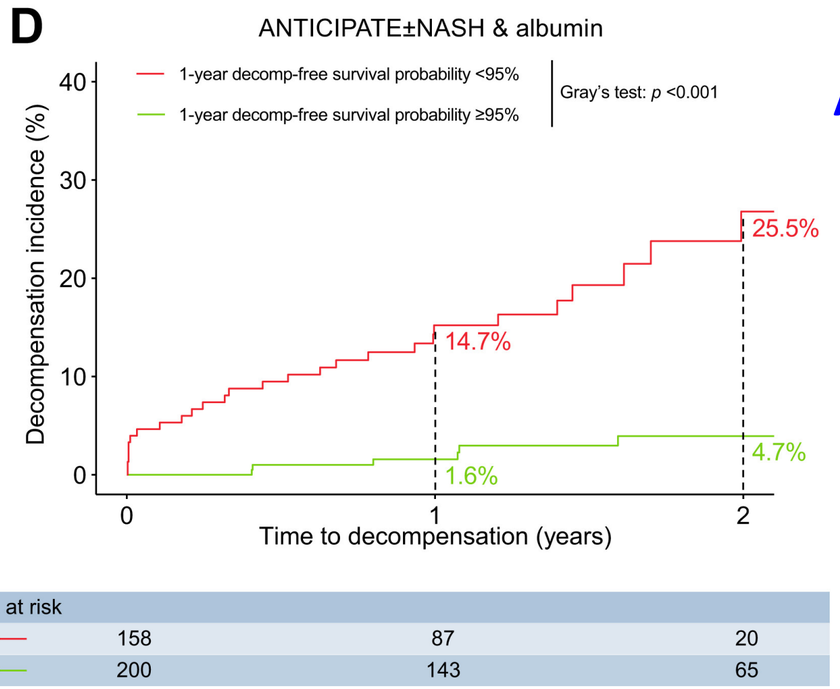
Five studies with 1433 cACLD patients (205 MASLD with obesity; overall 59% CSPH); HVPG reference standard

Bañares J et al. J Hepatol, 2025









In a large contemporary cohort the NICER and ANTICIPATE/ANTICIPATE NASH model predict the first clinical decompensation with a similar accuracy as HVPG

Adding albumin further improves this stratification

Jachs M et al. J Hepatol 2025

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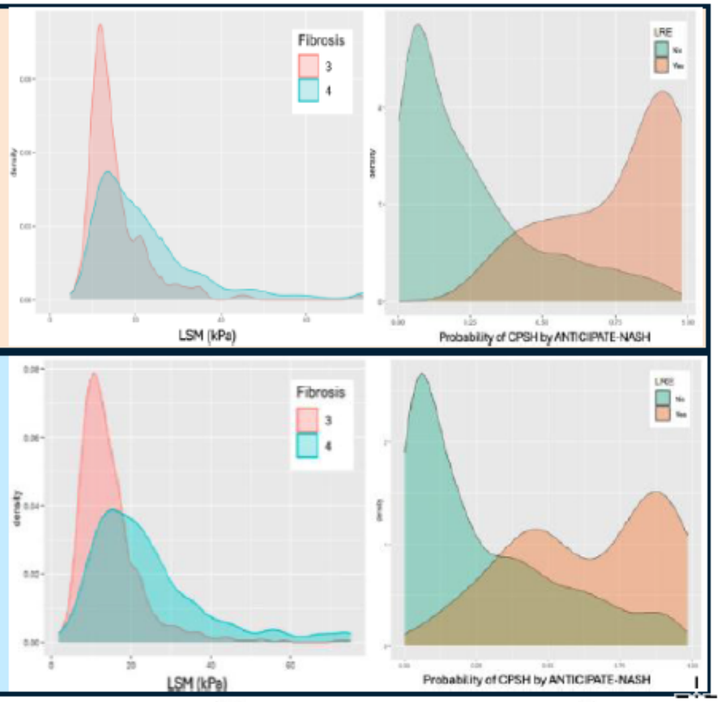
The ANTICIPATE-NASH models stratify better the risk of clinical events than histology in cACLD MASLD patients

		BASELINE ASSESSMENT	FOLLOW-UP	RESULTS
COHORT 1	**699 F3-F4 MASLD cACLD.** Multicenter cohort	Histology : • F3 • F4 + Non-invasive tool: LSM +Platelet count+BMI **ANTICIPATE-NASH** models: risk of CSPH and LRE	Until end of follow-up or development of **liver-related event** (LRE): •First decompensation HCC Liver transplantation Liver-related death	• 56 LRE (8.0%), 91.1% in F4. • The ANTICIPATE-NASH model showed excellent discrimination (c-statistic 0.93) for LRE vs histology (0.67). • Adding histology did not improve the prediction.
COHORT 2	*Validation cohort* **1396 F3-F4 MASLD cACLD.** From 4 clinical trials		Until end of follow-up or development of **clinical endpoint**: •First decompensation Worsening liver function Liver transplantation All-cause mortality	• 33 clinical endpoints (2.3%), 81.8% in F4. • The ANCITIPATE-NASH model showed a high discrimination (c-statistic, 0.84) vs. fibrosis stage (0.64).

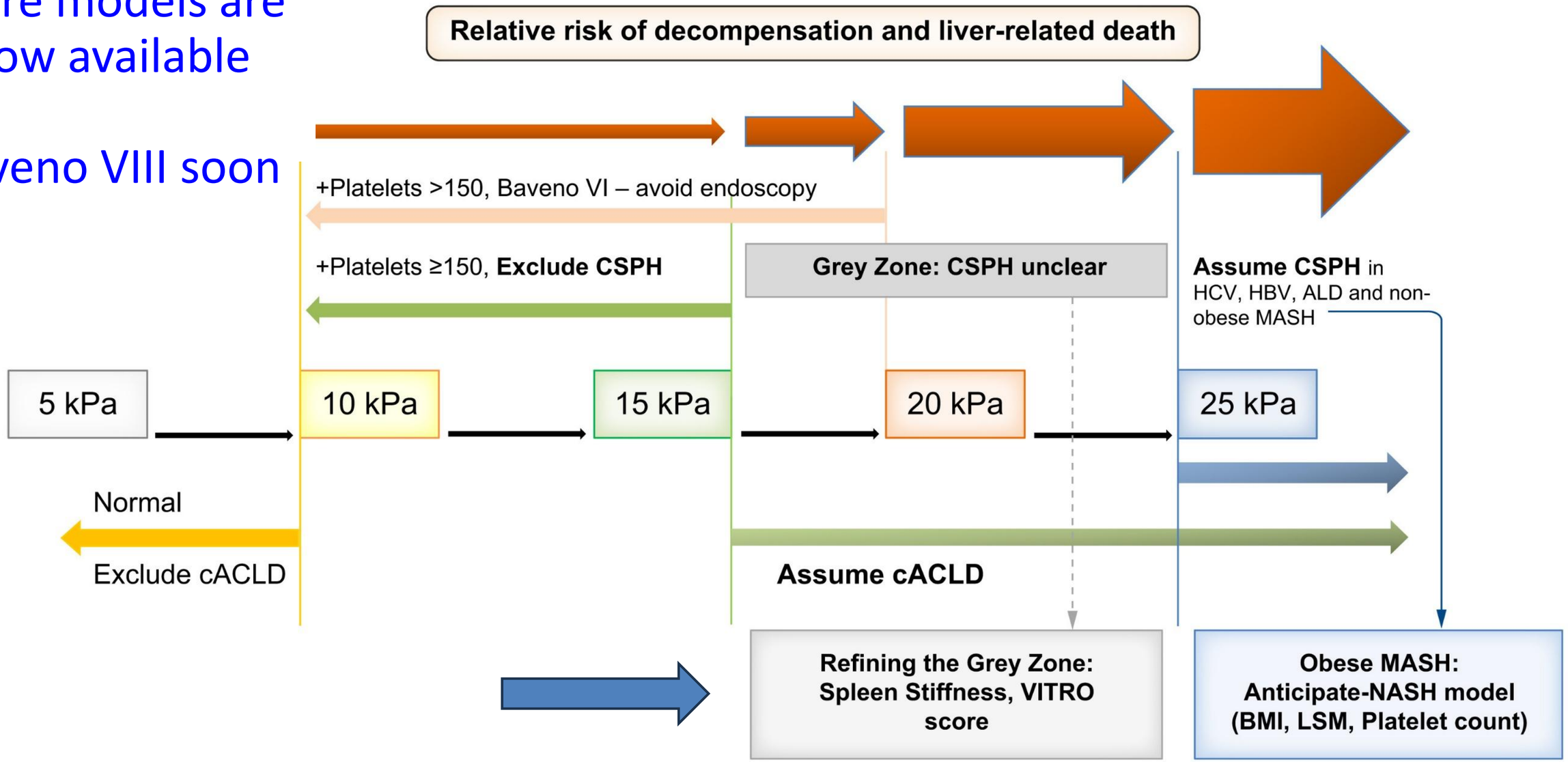


Gastroenterology

Aceituno L. et al. Gastroenterology 2025

More models are now available

Baveno VIII soon



Mandorfer M, Abraldes JG, Berzigotti A. JHep Reports 2024

Based on existing data, can we then use elastography to start NSBBS?

Are non-invasive methods accurate enough to select candidates to NSBB treatment?

Prevention of decompensation

Many studies, mostly retrospective

No data from a prospective, trial setting

Design: post-hoc analysis from a RCT (PREDESCI trial)

Dajti E… Bosch J. J Hepatol 2024

A study by the Baveno Cooperation, an EASL Consortium

PREDESCI cohort

Patients with HVPG, endoscopy and LSM available, both from screened for the trial but not randomized since no CSPH (n = 52) and from randomized in the trial (n = 118)

Prediction rules for CSPH presence

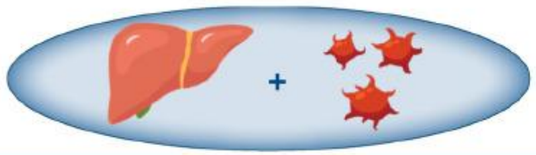
LSM ≥25 kPa — *Baveno VII (rule-in criteria)*

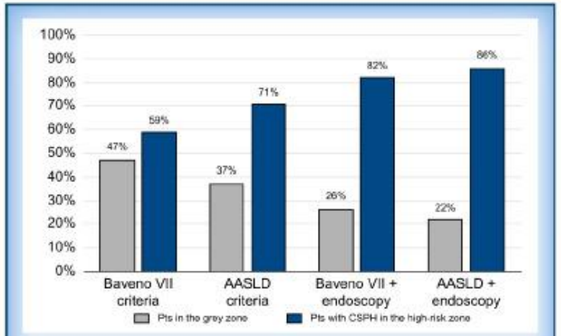
LSM ≥25 kPa *or* LSM >20 kPa + PLT <150x10⁹/L — *AASLD (rule-in criteria)*

- Wide "grey zone"
- Many CSPH pts outside rule-in criteria

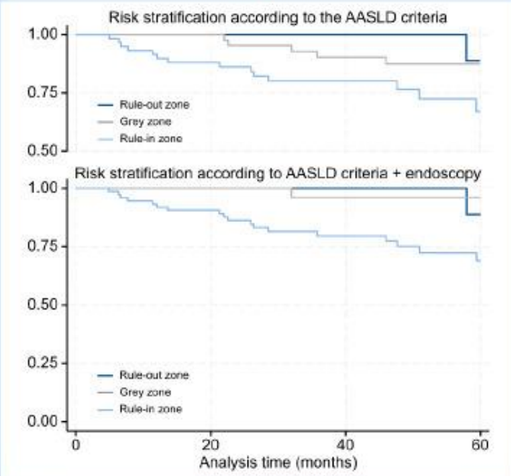
Perform endoscopy in "grey zone" pts

rule-in CSPH if varices





- Significantly reduced grey zone
- More patients with CSPH included, with similar PPV
- Improved risk stratification for decompensation

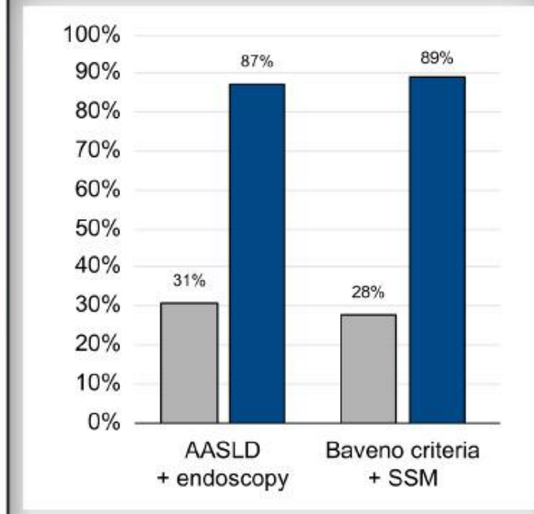


Endoscopy in the Baveno VII grey zone

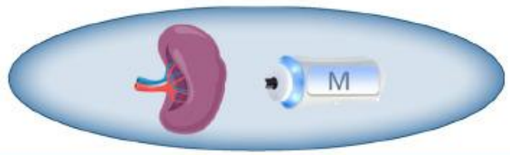
External validation

Observational cohort

n = 195 patients with available LSM, SSM, HPVG, and endoscopy



- Full validation of results
- Comparable results using SSM instead of endoscopy
- Further validation from prospective cohorts required



Might NITs guide the selection of patients who require NSBB in cACLD? Yes

	REMOTE PAST - until Baveno VI 2015	RECENT PAST - Baveno VI criteria 2015-2021	PRESENT – Baveno VII criteria 2021-2026	FUTURE – After Baveno VIII?
Candidates to NSBB therapy in compensated	High-risk varices	High-risk varices	All patients with CSPH	All patients with CSPH
Identification/ Screening strategy	Endoscopy to all at diagnosis	LSM > 20 kPa or Plt < 150 G/L: endoscopy In the others no endoscopy	LSM ≥ 25 kPa or other signs of CSPH (porto-systemic collaterals; HVPG ≥ 10 mmHg) SSM maybe useful	LSM ≥ 25 kPa (non-obese MASLD) ANTICIPATE/ANTICIPATE-NASH or NICER models (includes obese MASLD) (or imaging / HVPG criteria) SSM useful to refine the «indeterminate» group
«Rescue» strategy	-	-	In patients with contraindications/intolerance to NSBB: BVI criteria to indicate/skip endoscopy	Shift from a diagnostic prospective to a prognostic prospective, irrespective of endoscopy findings; endoscopy in patients with contraindications/intolerance to NSBBs

Personal summary – Annalisa Berzigotti

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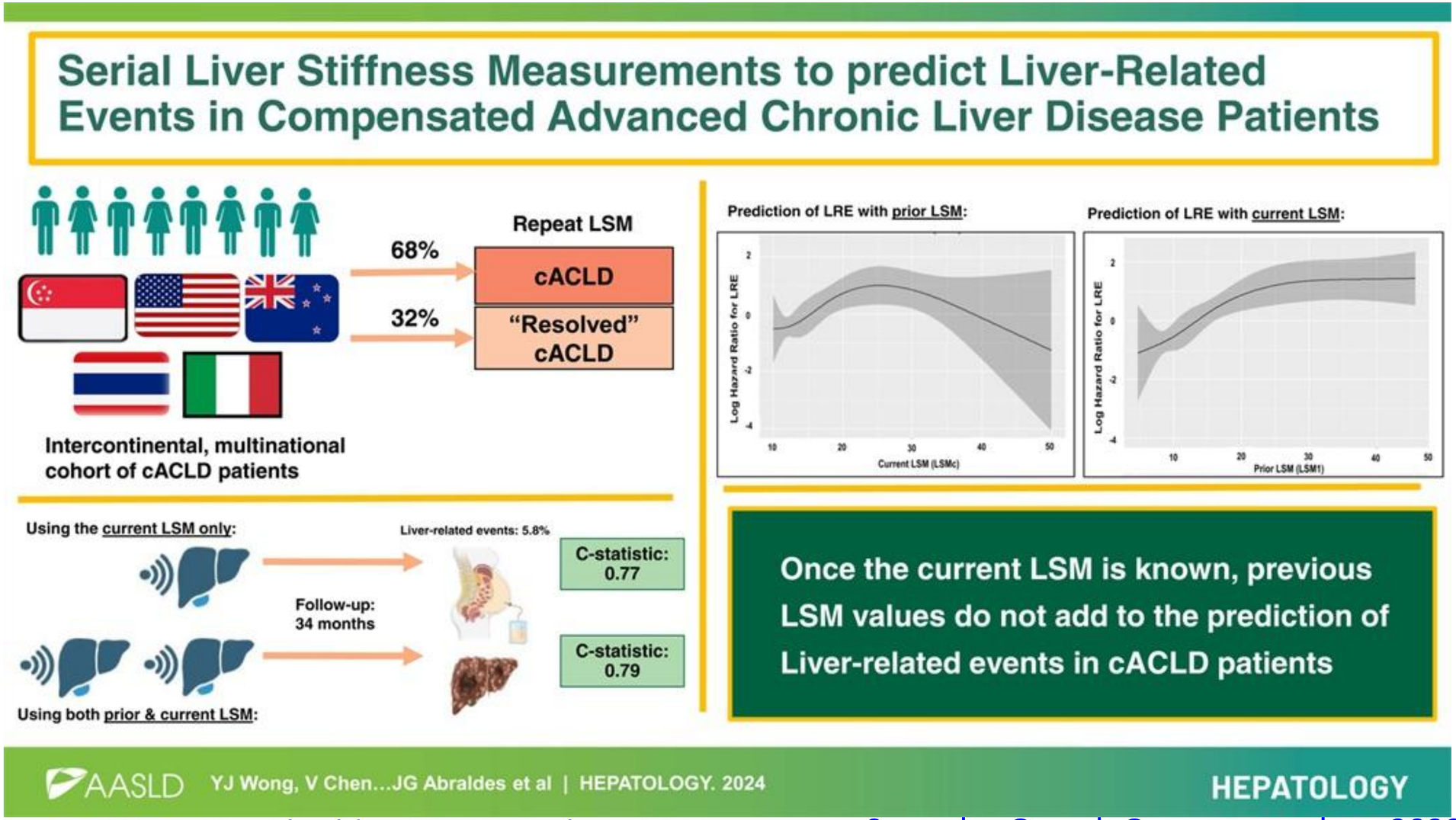
And we should use LSM (and SSM) to follow-up patients

Repeat on a yearly basis; the last value is the most important to predict the risk of events



Wong YJ… Abraldes JG. Hepatology 2024

Semmler G et al. Gastroenterology 2023

Take home messages

- ✓ Elastography is a cornerstone of non-invasive assessment of liver disease in 2026
  - ✓ Liver fibrosis
  - ✓ Cirrhosis
  - ✓ Portal hypertension
  - ✓ Prognosis
- ✓ Everything worth doing should be done right: technical aspects!
- ✓ Use two cut-offs (rule-in/rule-out); in the indeterminate zone: further tests
- ✓ Pragmatic risk assessment VCTE: rule of five; 2D-SWE and pSWE rule of four
- ✓ Avoid comparison among different techniques/machines
- ✓ Combine unrelated methods to achieve more accurate results:
  - ✓ LSM + platelet count (and spleen size); spleen stiffness
- ✓ Remember ultrasound: collaterals; confounders of LSM; point of care!

https://baveno8.org/registration/

Thank you for your attention