Hepatocellular cancer surveillance in patients with Advanced Chronic Liver Disease

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Disclosures

SF holds a senior clinical investigator fellowship from the Research Foundation Flanders (FWO) (1802154N).

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He has acted as consultant for Abbvie, Actelion, Aelin Therapeutics, AgomAb, Aligos Therapeutics, Allergan, Alnylam, Astellas, Astra Zeneca, Bayer, Boehringer Ingelheim, Bristoll-Meyers Squibb, CSL Behring, Coherus, Echosens, Eisai, Enyo, Galapagos, Galmed, Genetech, Genfit, Gilead Sciences, Intercept, Inventiva, Janssens Pharmaceutica, Julius Clinical, Madrigal, Medimmune, Merck Sharp & Dome, NGM Bio, Novartis, Novo Nordisk, Promethera, Roche.

SF has been lecturer for Abbvie, Allergan, Bayer, Eisai, Genfit, Gilead Sciences, Janssens Cilag, Intercept, Inventiva, Merck Sharp & Dome, Novo Nordisk, Promethera, Siemens.

Recommendation

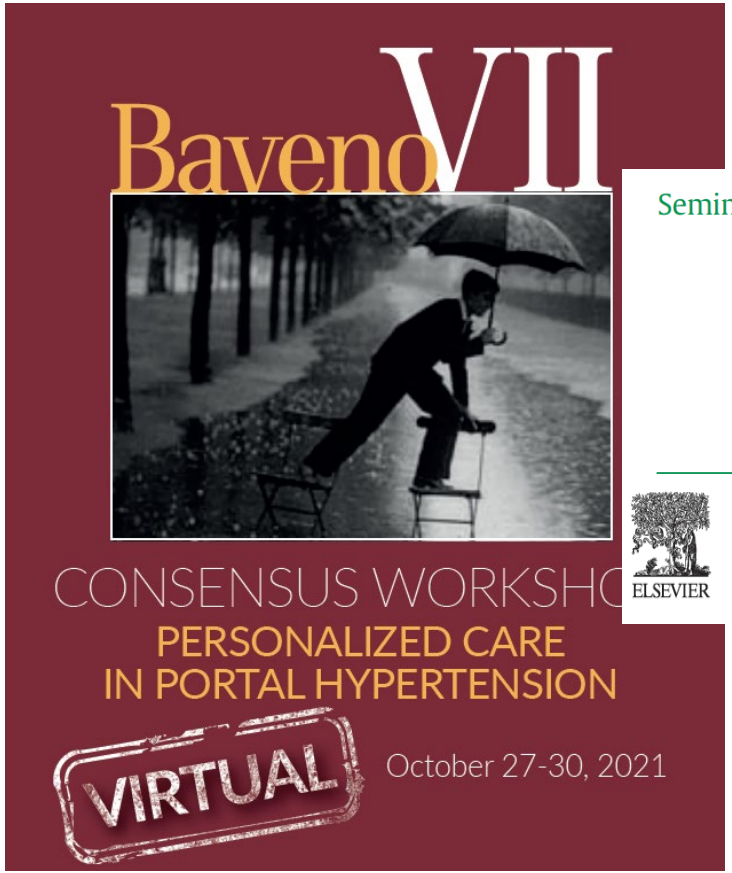
- Patients with cirrhosis should be offered surveillance for HCC unless they have a relatively high risk of death from non-HCC causes, or they could not be offered a curative-intent treatment for HCC (*e.g.*, patients with Child-Pugh class C cirrhosis ineligible for liver transplantation) **(LoE 2, strong recommendation, strong consensus).**

Definition of cirrhosis?
F4, imaging

Recommendation

- Patients with chronic liver disease and advanced fibrosis without cirrhosis have a higher risk of HCC than the general population, but HCC surveillance cannot currently be recommended in this group owing to insufficient evidence **(LoE 3, weak recommendation, strong consensus).**

EASL CPG HCC. J Hep 2024



Seminar

JOURNAL OF HEPATOLOGY

Baveno VII – Renewing consensus in portal hypertension

Roberto de Franchis[1,*], Jaime Bosch[2,3], Guadalupe Garcia-Tsao[4,5], Thomas Reiberger[6,7], Cristina Ripoll[8], on behalf of the Baveno VII Faculty[§]

ELSEVIER

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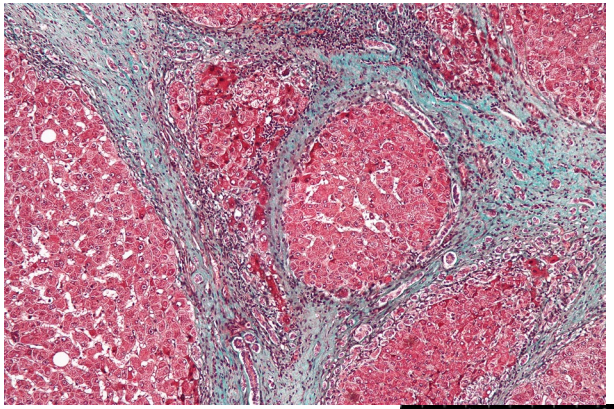
EASL The Home of Hepatology

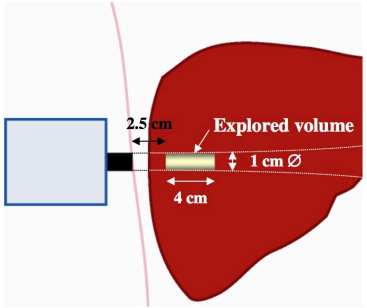
cACLD

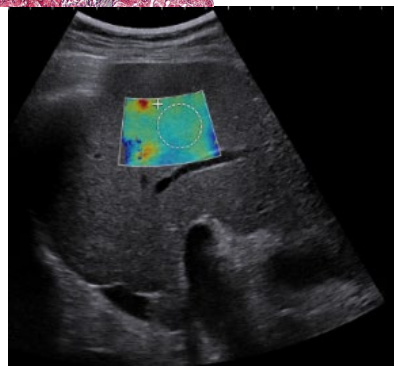
- The term “compensated advanced chronic liver disease (cACLD)” had been proposed to reflect the continuum of severe fibrosis and cirrhosis in patients with ongoing chronic liver disease.
- Pragmatic definition of cACLD based on liver stiffness measurement (LSM) is aimed at stratifying the risk of CSPH and decompensation at point of care.

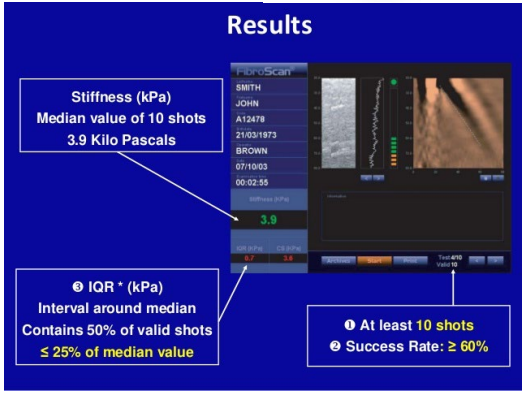
Baveno VII. J Hep 2022

Liver stiffness measurement (LSM)

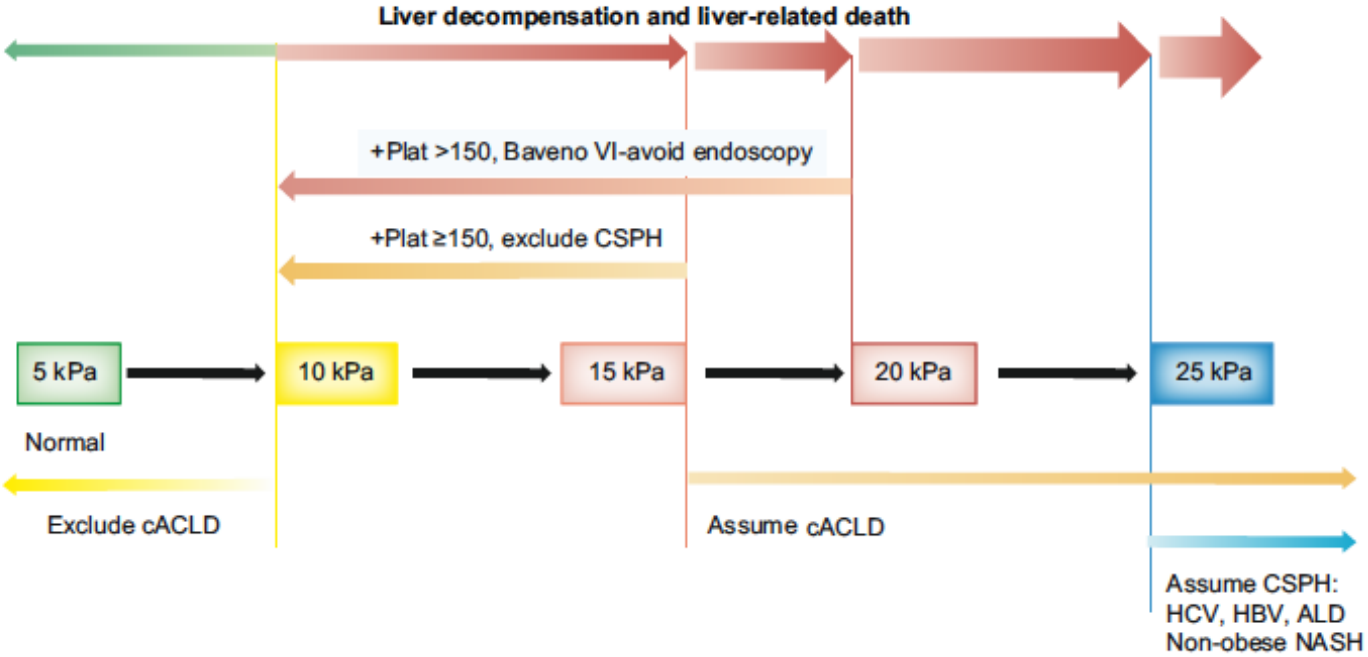








Rule of 5



Baveno VII. J Hep 2022

Elastometry
Surrogate for histology

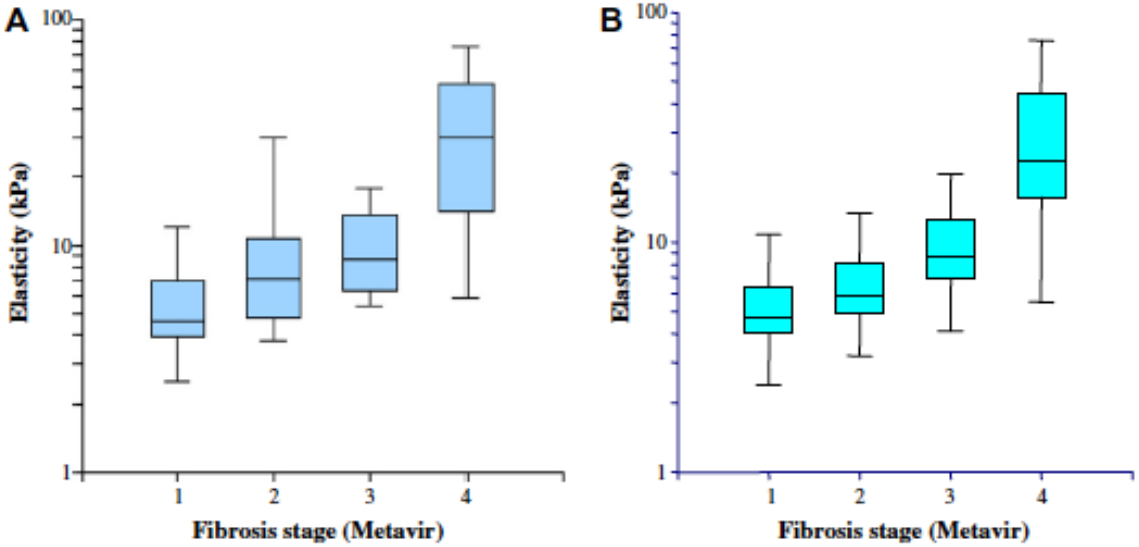
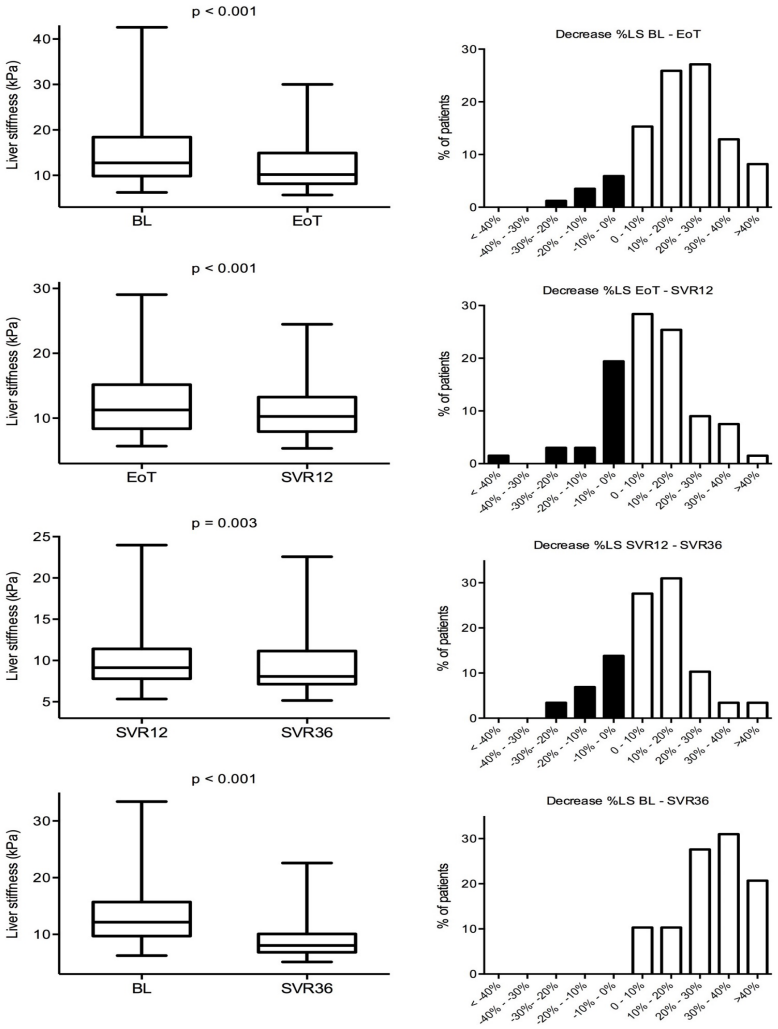


Fig. 3. Box-plots of liver stiffness values for each fibrosis stage (Metavir). Because of the wide range of FS values for *F4*, the vertical axis is in logarithmic scale. Adapted from (A) Ziol et al. [18] and (B) Castera et al. [17].

Castera et al. J Hep 2008

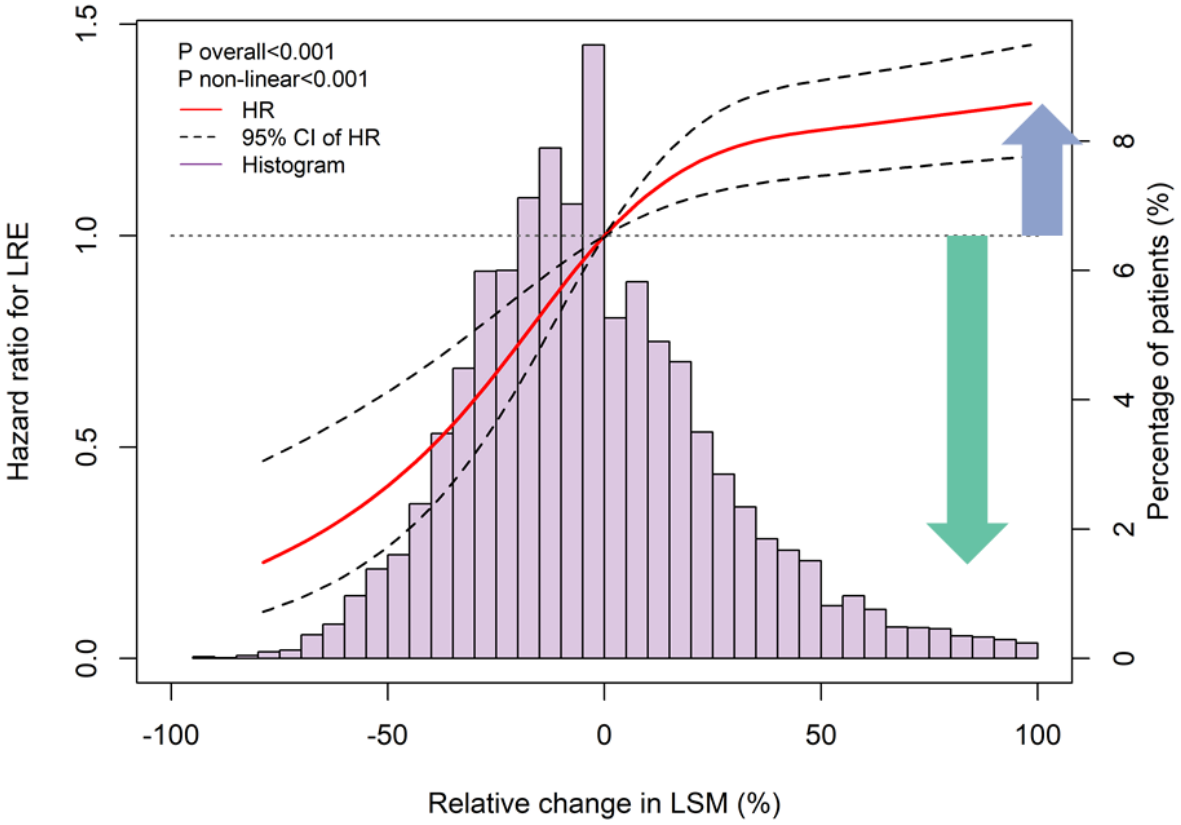


But...

Liver stiffness and antiviral treatment

Verlinden, Francque, …Vanwolleghem. Hepatology 2016

LSM & Prognosis



Yip T *et al*. ILC 2024 (GS-004)

Lin *et al*. JAMA 2024

	Number of Observations	RDC_{DDDO}	Upper 95% Confidence Bound	RC_{SDSO}	Upper 95% Confidence Bound
Vendor 1	24	31.9%	42.0%	19.0%	25.0%
Vendor 2	24	24.2%	32.1%	13.9%	18.3%
Vendor 3	24	29.9%	39.4%	14.2%	18.7%
Vendor 4	24	32.3%	42.5%	14.9%	19.6%
Vendor 5	24	34.3%	45.2%	35.0%	46.1%
Pooled SWE	**40**	**30.7%**	**34.4%**	**21.0%**	**23.5%**
VCTE	39	35.6%	43.9%	19.6%	24.1%

Pierce T. *et al*. Radiology 2024

Elastography-
Liver Stiffness Measurement (LSM)

- Quality metrics
- Need for repeat measurements
- Surrogate for histology
  - Not just fibrosis
  - Inflammation, cholestasis, congestion…
- Prognostic marker
  - Baseline and follow-up

NEJM Evidence

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ORIGINAL ARTICLE

Hepatocellular Cancer Surveillance in Patients with Advanced Chronic Liver Disease

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- Inclusion
  - Valid baseline LSM by two-dimensional shear-wave elastography (2D-SWE)
  - Comprehensive baseline lab
  - Minimum of 6 months of follow-up
    - Data censored at Y2
  - ACLD defined according to the Baveno VII

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Recruitment of patients

17 centres
3,016 patients
Period: 2007-2018

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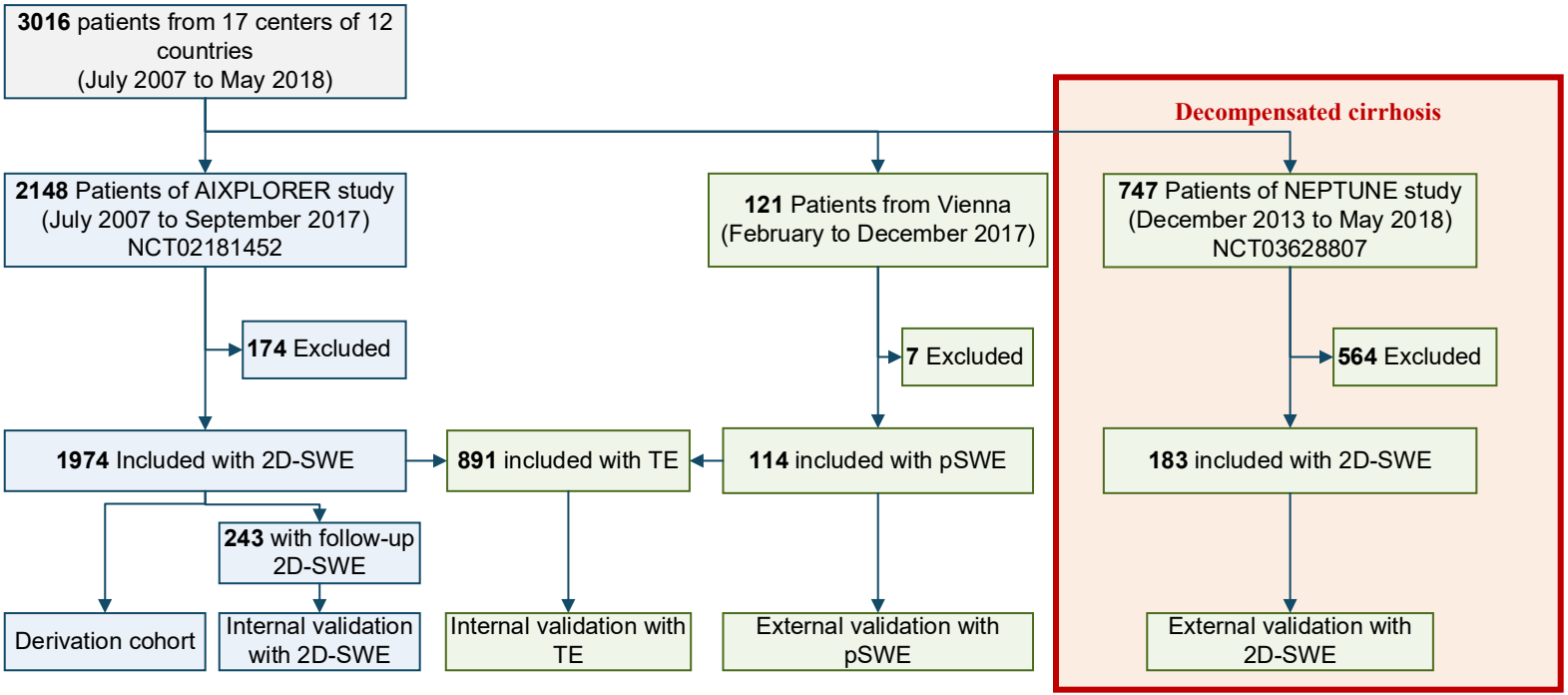

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Table 1. General Characteristics of the Derivation Cohort of the Aixplorer Study and Comparison between Patients with and without Hepatocellular Carcinoma Development during Follow-up.*

Variables†	Aixplorer Study (n=1974)	HCC (n=106)	No HCC (n=1868)
Follow-up time, months	29.4 (12.8–47.2)	13.7 (6.3–21.3)	31.1 (13.4–48.0)
Age	55.0 (45.0–62.6)	59.0 (54.0–64.0)	54.5 (44.5–62.4)
Male	1233 (62.5%)	83 (78.3%)	1150 (61.6%)
BMI, kg/m²‡	26.4 (23.0–30.5)	25.9 (23.4–29.0)	26.4 (22.9–30.7)
Etiology			
ALD	434 (22.0%)	30 (28.3%)	404 (21.6%)
MASLD	412 (20.9%)	9 (8.5%)	403 (21.6%)
HCV	296 (15.0%)	39 (36.8%)	257 (13.8%)
HCV SVR baseline	80 (27.0%)	2 (5.1%)	78 (30.4%)
HCV SVR follow-up	88 (29.7%)	1 (2.6%)	87 (33.9%)
HBV	211 (10.7%)	15 (14.2%)	196 (10.5%)
HBV control baseline	87 (41.2%)	2 (13.3%)	85 (43.4%)
HBV control follow-up	83 (39.3%)	0 (0.0%)	83 (42.3%)

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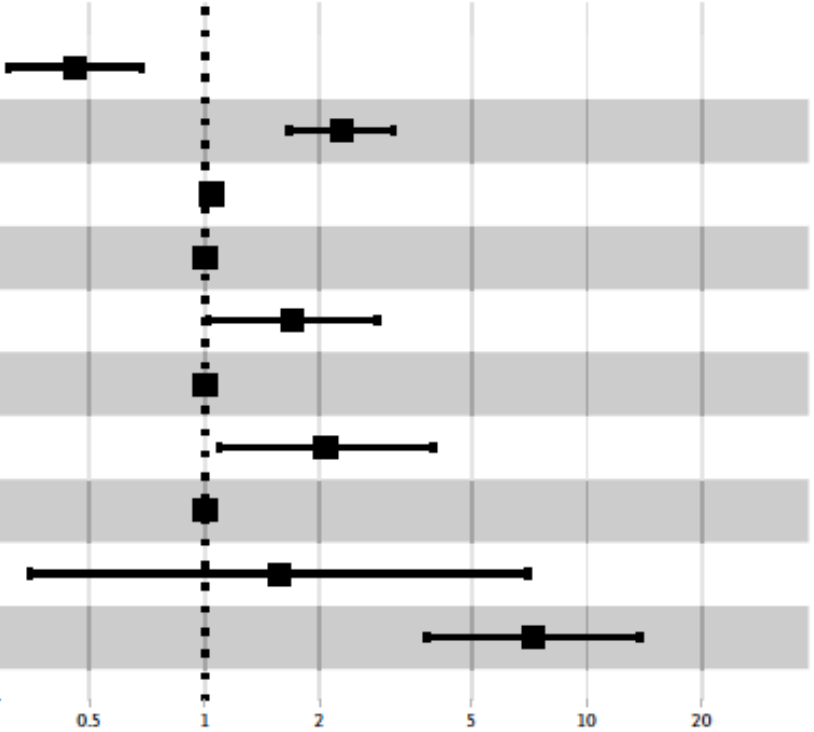
Variable		Hazard Ratio
Platelet: ln (platelet [g/l])		0.46 (0.31 to 0.68)
Elastography: ln (LSM [kPa])		2.28 (1.67 to 3.12)
Age		1.04 (1.02 to 1.06)
Sex	Female	Reference
	Male	1.70 (1.02 to 2.82)
ESLDtiology: SLD	No	Reference
	Yes	2.07 (1.09 to 3.95)
Viral	No	Reference
	Controlled	1.57 (0.35 to 7.03)
	Uncontrolled	7.24 (3.82 to 13.71)

No. events: 91; *AIC:* 1191.85; *Concordance Index:* 0.84



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PLEASE Score		Subscore = 0	Subscore = 1
Platelet (g/l)		≥150	<150
Elastography: LSM (kPa)		<15	≥15
Age (years)		<50	≥50
Sex		Female	Male
Etiology	SLD	No	Yes
	Viral hepatitis	No	Yes
		Controlled	Uncontrolled
Total Score		≥4: high-riskgroup <4:low-riskgroup	

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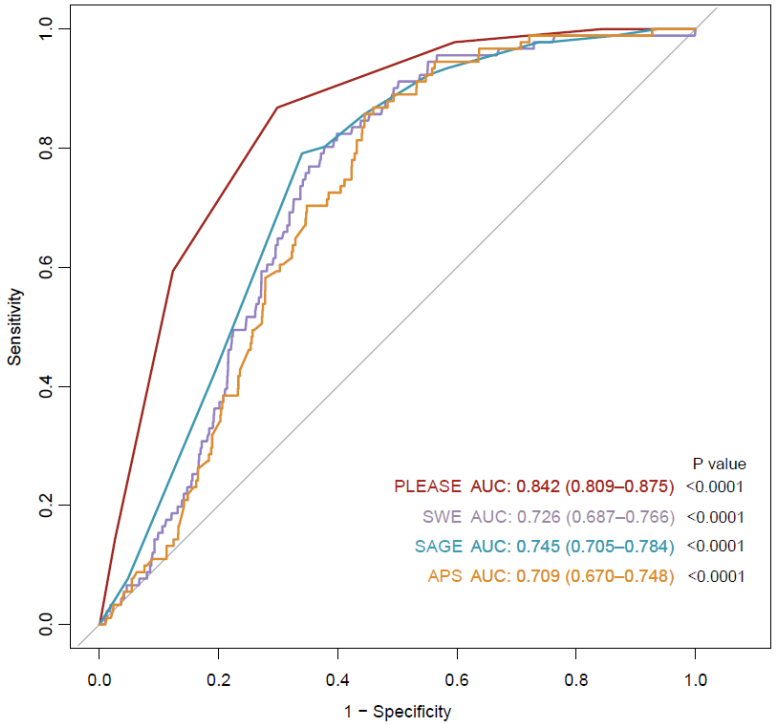
PLEASE Algorithm



https://www .medizin.uni-muenster.de/med-b/please-calculator.html

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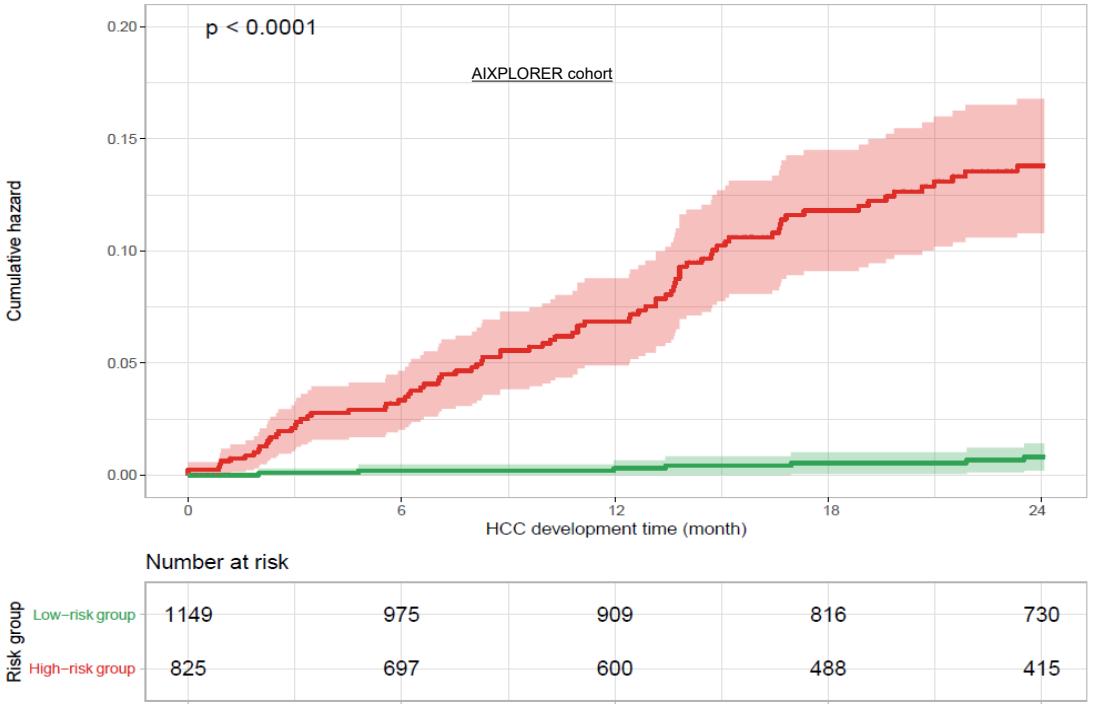
HCC risk stratification in 2 years



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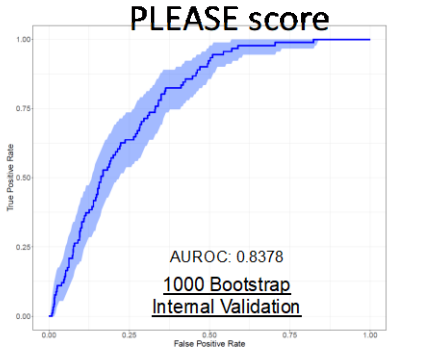
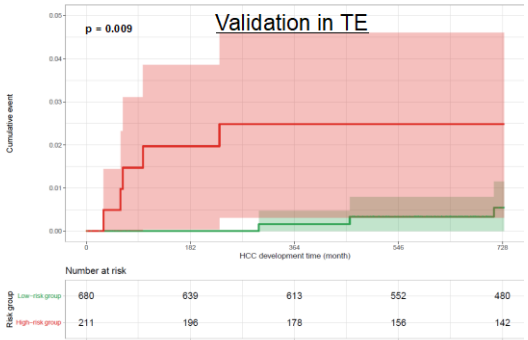
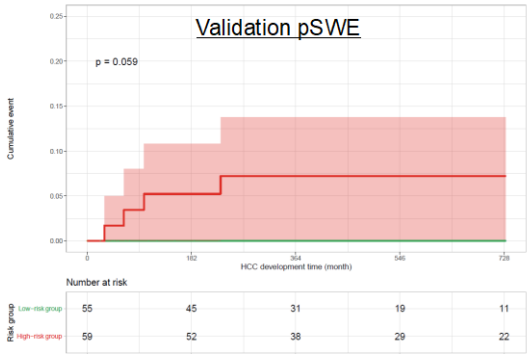
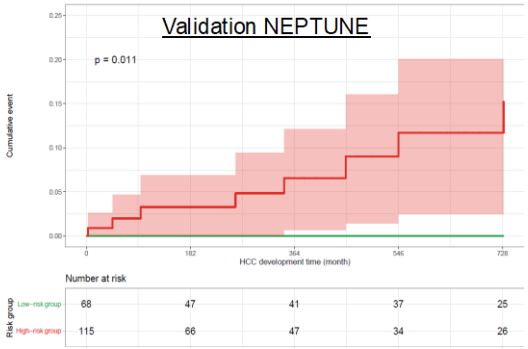
Internal and external validation









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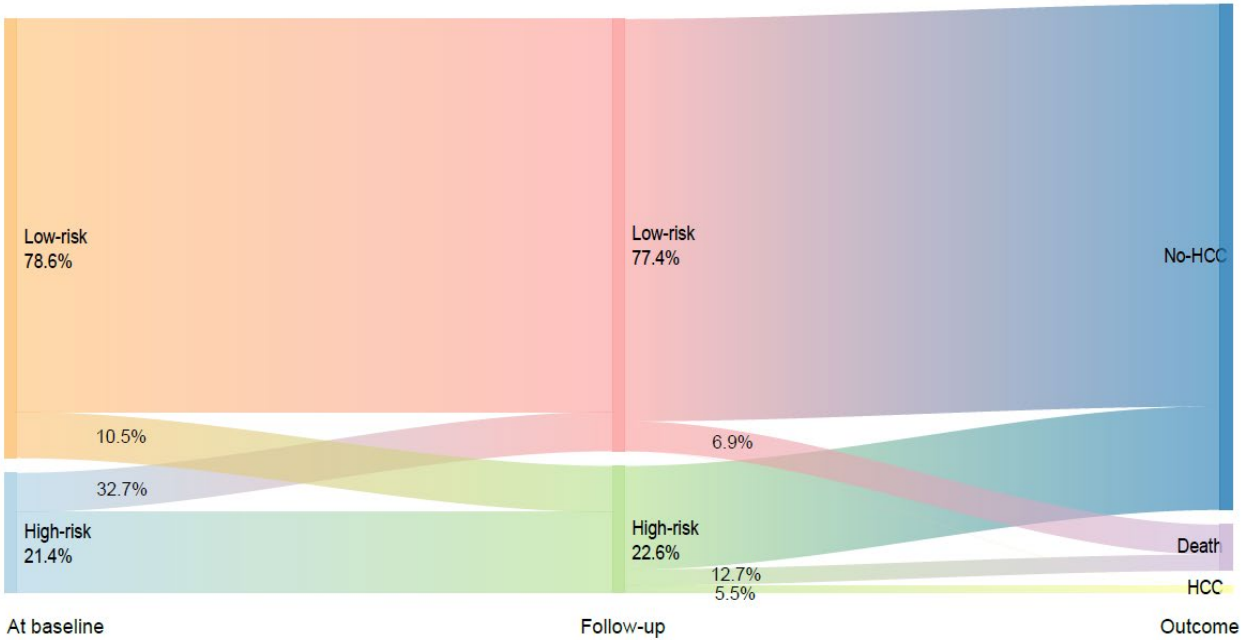
Dynamic changes of PLEASE score



Dynamic (n = 243)

- 10% deteriorated
- 33% improved
- Follow-up visit:
  - 100% true negative rate

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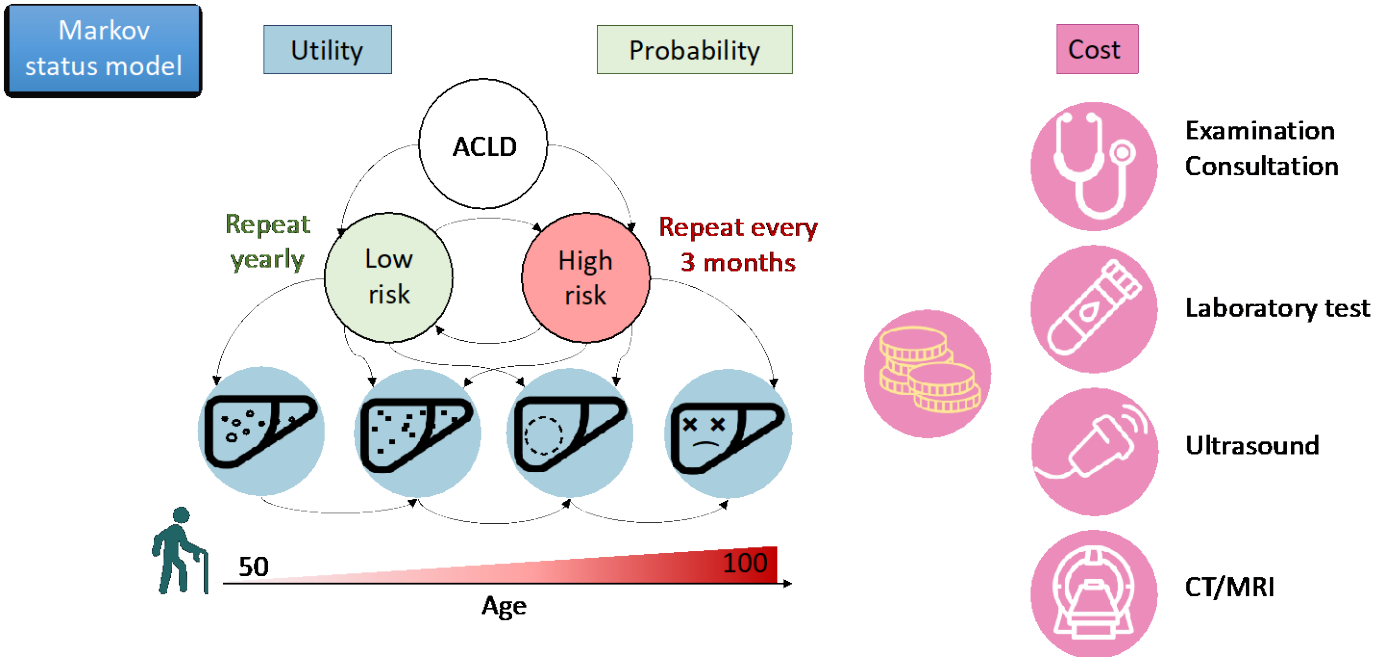
Cost claims analysis



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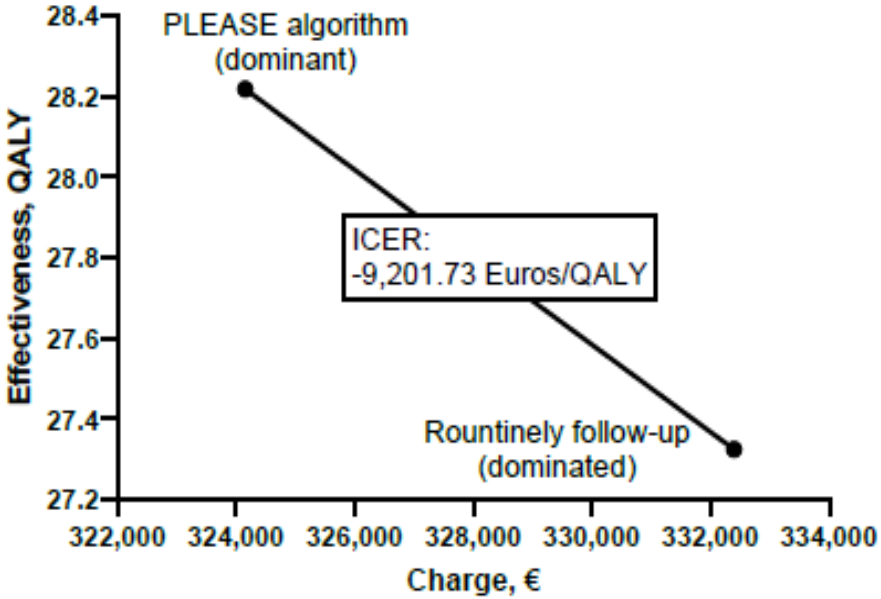

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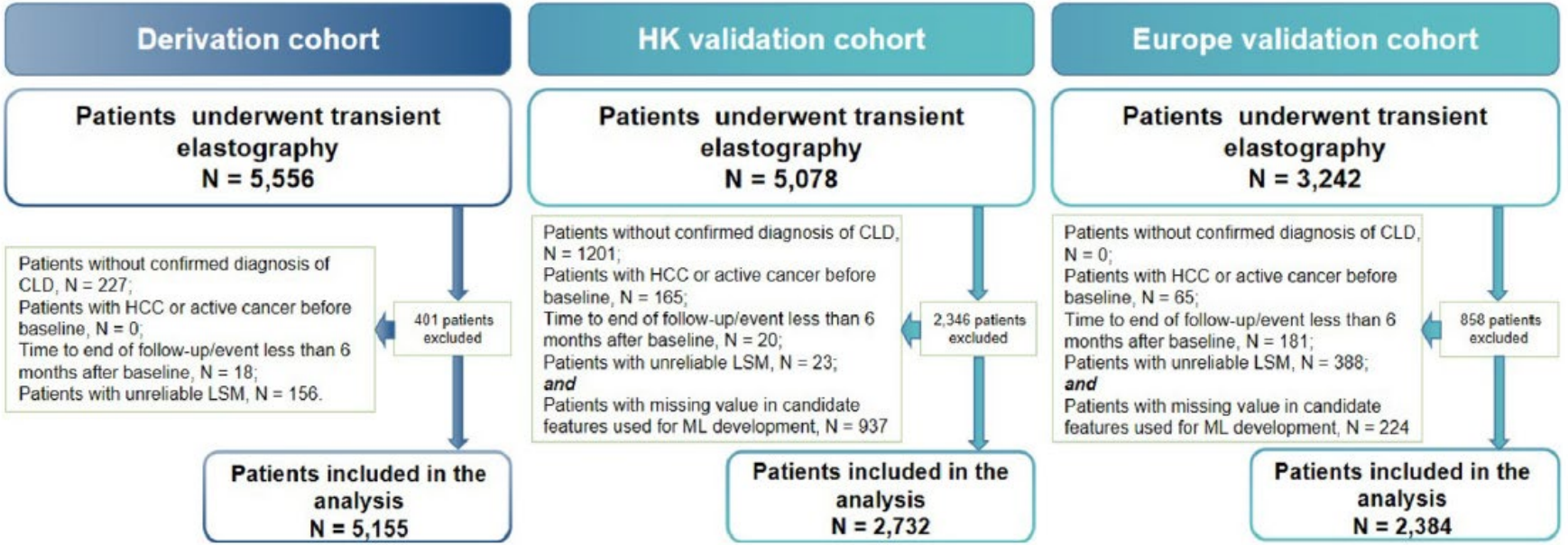
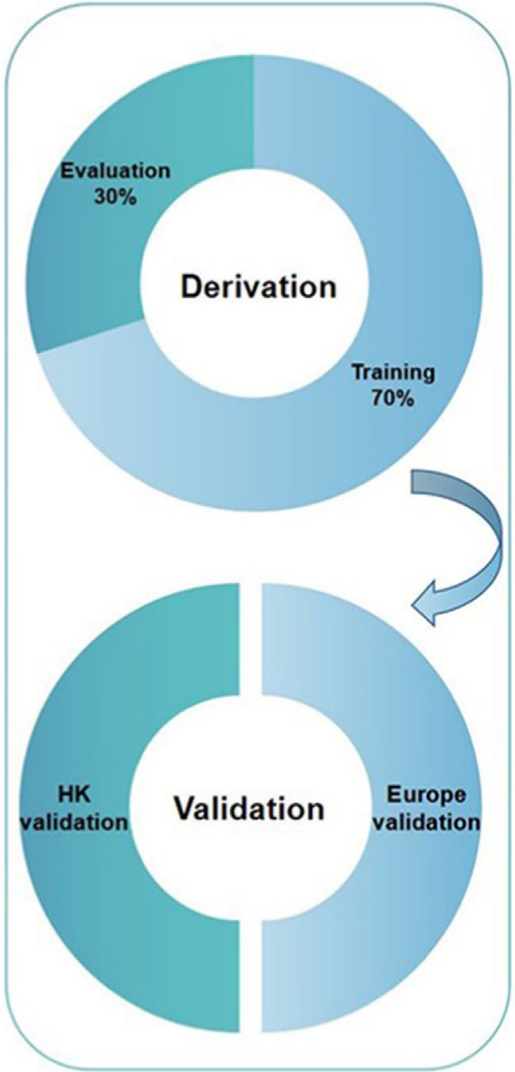
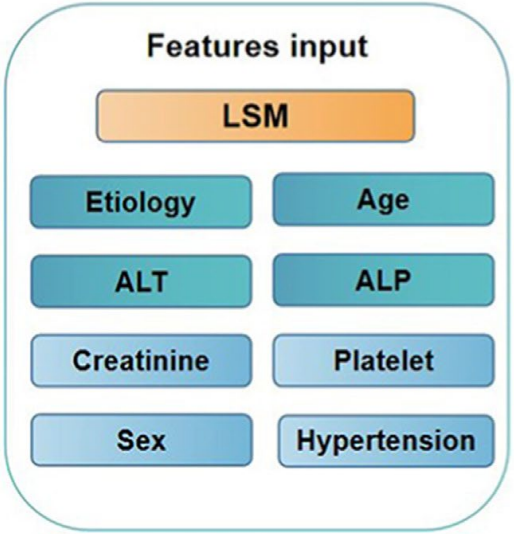
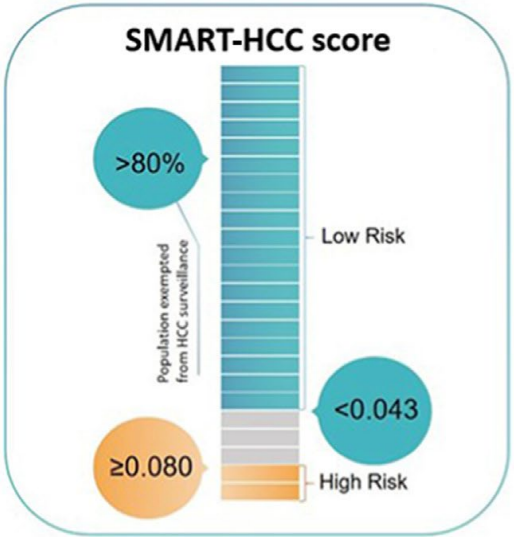
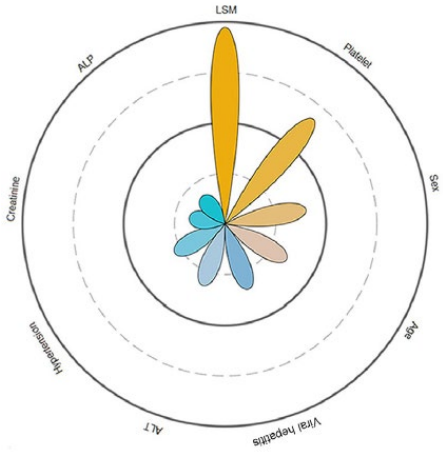


Lin *et al*. CGH 2024









Lin *et al*. CGH 2024

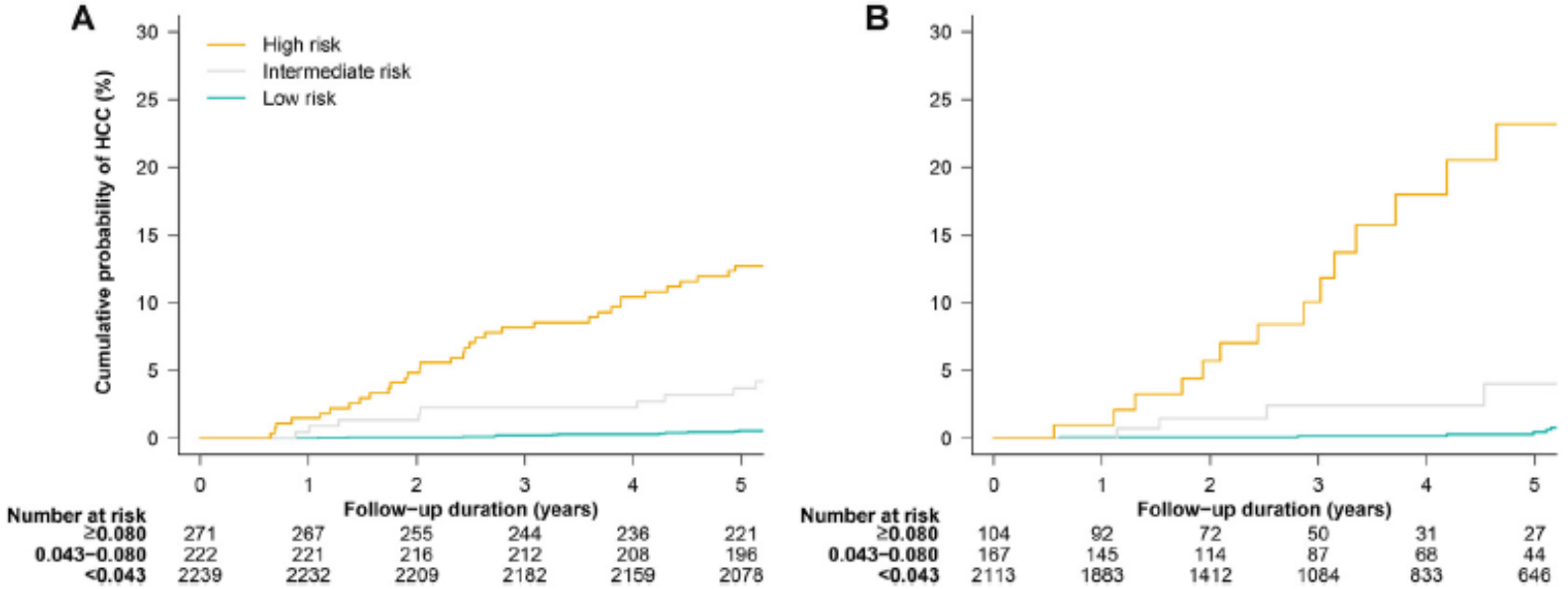


Figure 3. HCC risk stratification by SMART-HCC score in the (*A*) HK and (*B*) Europe validation cohorts.

Lin *et al*. CGH 2024

- Performance not significantly different
  - Aetiology
  - Diabetes
  - Viral hepatitis–related features
    - viral load and anti-viral treatment: no impact on performance

Lin *et al*. CGH 2024

Conclusions

- Risk-based strategy refines surveillance policy in ACLD
  - Elastography
  - Platelets, age, sex, aetiology (SLD/Viral)
- 3 m *vs*. 1 y
  - Incrementally cost-effective
- Validated in different cohorts and with different techniques
- Further validation needed
- Broader application outside ACLD?
  - Lin *et al.* small numbers HCV and more variables

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