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Country: France

Affiliation: APHP and University Paris Nord

Function: Professor of Hepatology

Main expertise (1-2 lines): HCC risk stratification and early detection, randomized control trials for HCC surveillance strategies

EASL position paper on clinical follow-up after HCV cure – Is it time to refine HCC surveillance?

Antwerp 2025

Pierre Nahon

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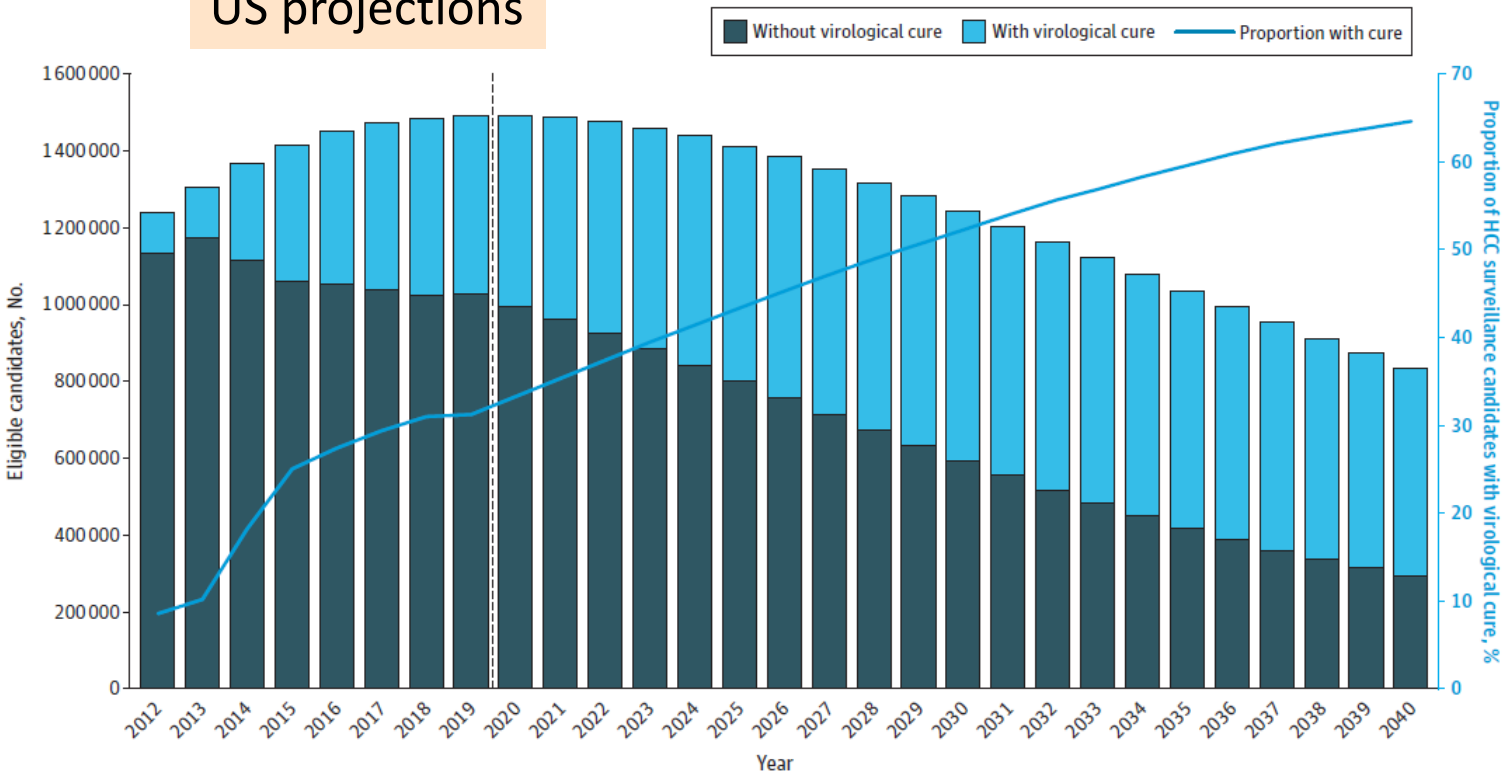
Génomique fonctionnelle des tumeurs solides

Financial Disclosures

- Honoraria or consultation fees: Abbvie, AstraZeneca, Bayer, Bristol-Myers Squibb, Eisai, Gilead Sciences, IPSEN, Roche

HCC surveillance in HCV patients: *a remaining burden despite virological cure*

US projections



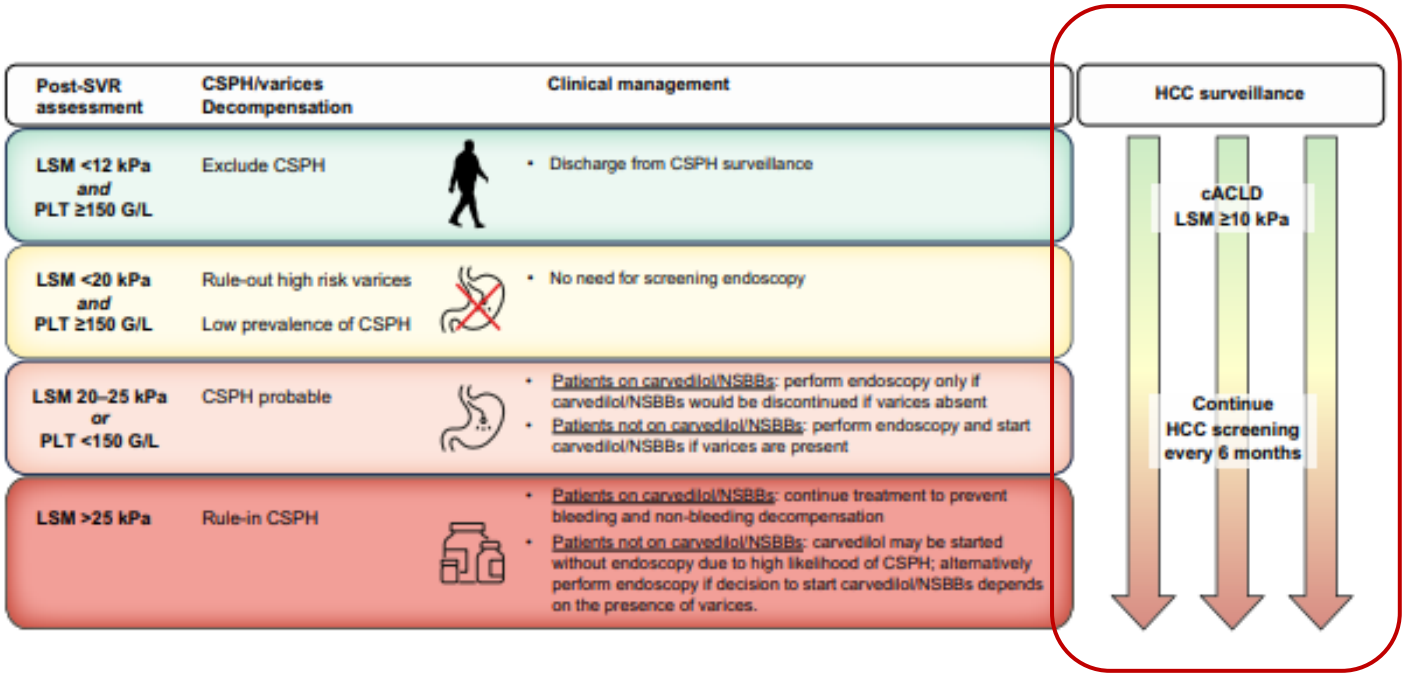
Chen et al, JAMA Nework Open 2020

Position Paper

JOURNAL
OF HEPATOLOGY

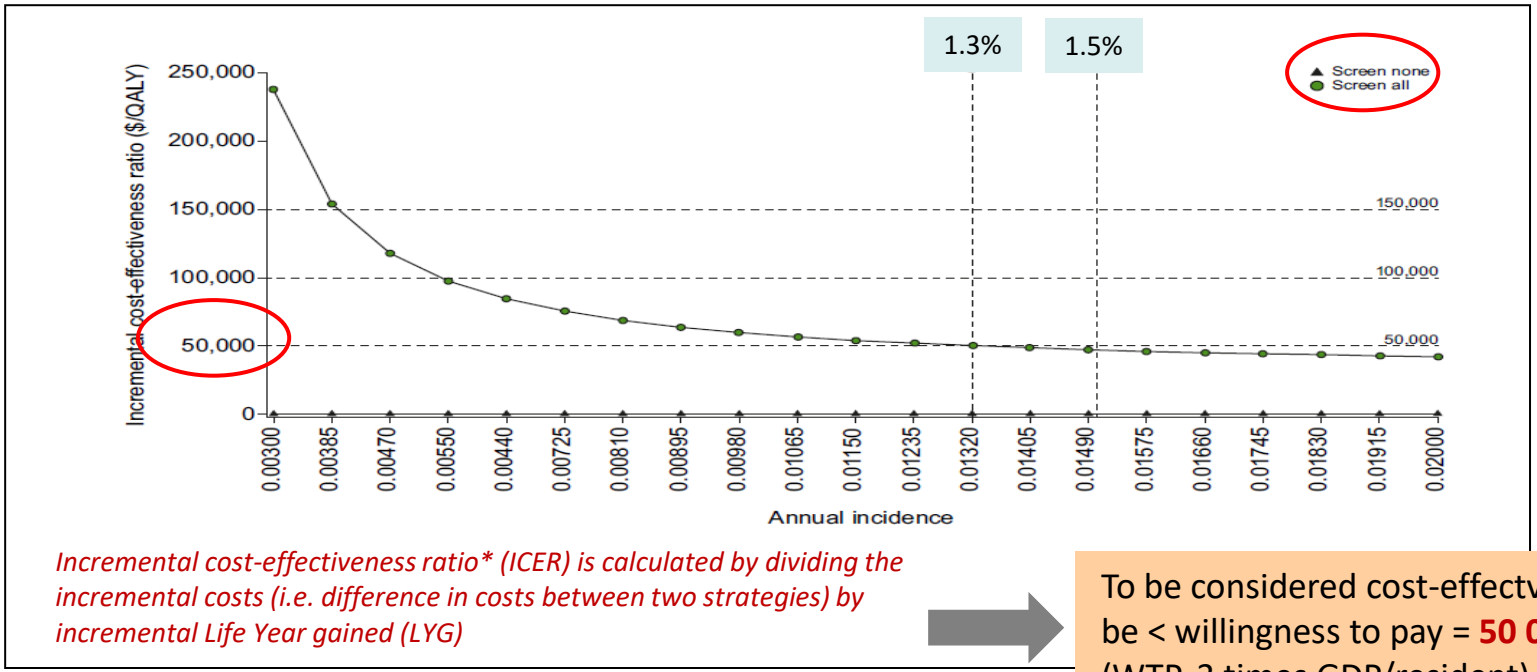
EASL position paper on clinical follow-up after HCV cure

Thomas Reiberger[1,†], **Sabela Lens**[2,†], Giuseppe Cabibbo[3], Pierre Nahon[4], Anna Linda Zignego[5], Katja Deterding[6], Ahmed M. Elsharkawy[7], Xavier Forns[2,*]



J Hep 2024

Surveillance cost-effectiveness is a major driver of decision making process and directly depends on HCC incidence

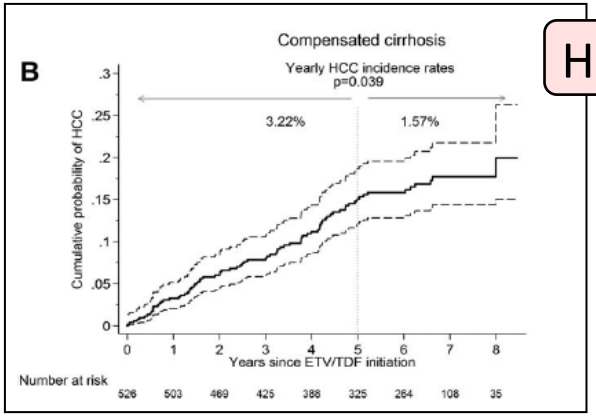


Incremental cost-effectiveness ratio (ICER) is calculated by dividing the incremental costs (i.e. difference in costs between two strategies) by incremental Life Year gained (LYG)*

To be considered cost-effectve, ICER must be < willingness to pay = **50 000€/LYG** (WTP, 3 times GDP/resident)

Farhang et al, CGH 2019

A « global » annual incidence ranging from 1.5% to 3% in cirrhosis in 2020*

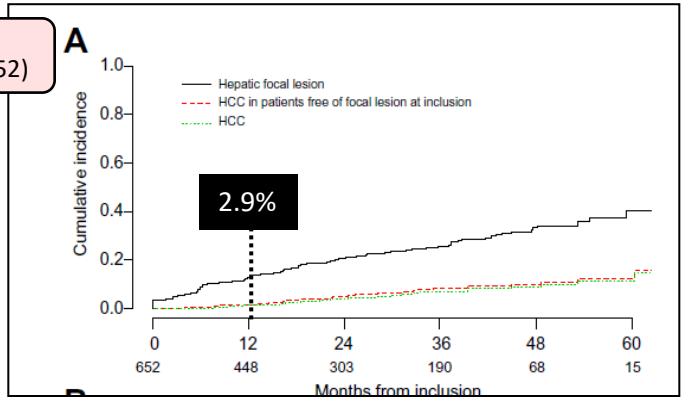


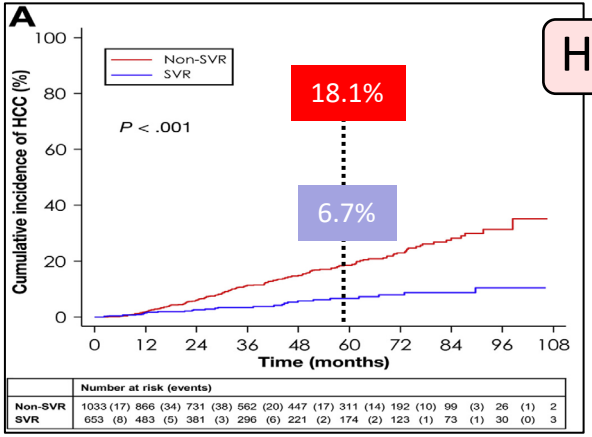
HBV (n=528)

Papatheodiris,
Hepatology 2017

Alcohol (n=652)

Ganne-Carrié,
J Hepatology 2018



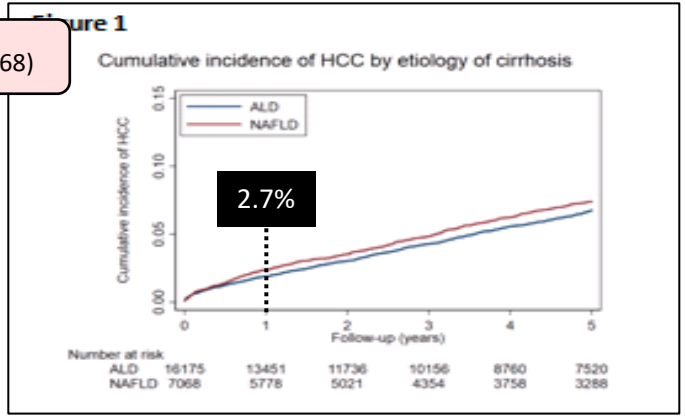


HCV (n=1372)

Nahon,
Gastroenterology 2017

NASH (n=7068)

Ioannou,
J Hepatology 2019



**Based on European multicentre prospective cohorts of patients included in surveillance programs*

Refining HCC screening in SVR patients

- **Question 1:** Can we define patients with ACLD who could be discarded from surveillance?

- **Question 2:** is there a population in whom HCC surveillance should be intensified? If yes, how?

Clinical case

- SVR obtained in a 48 yrs-old male with compensated ACLD and **LSM 19 kPa**
- Patient included in HCC surveillance program (US/AFP every 6 months)
- 5 years later:
  - AST/ALT normal
  - Liver function perfect
  - **LSM=7.8 kPa**

The patient is asking you if HCC surveillance can be stopped

Submit a Manuscript: https://www.f6publishing.com
DOI: 10.3748/wjg.v27.i40.6737
World J Gastroenterol 2021 October 28; 27(40): 6737-6749
ISSN 1007-9327 (print) ISSN 2219-2840 (online)
FRONTIER

Hepatocellular carcinoma risk after viral response in hepatitis C virus-advanced fibrosis: Who to screen and for how long?

Adriana Ahumada, Laura Rayón, Clara Usón, Rafael Bañares, Sonia Alonso Lopez

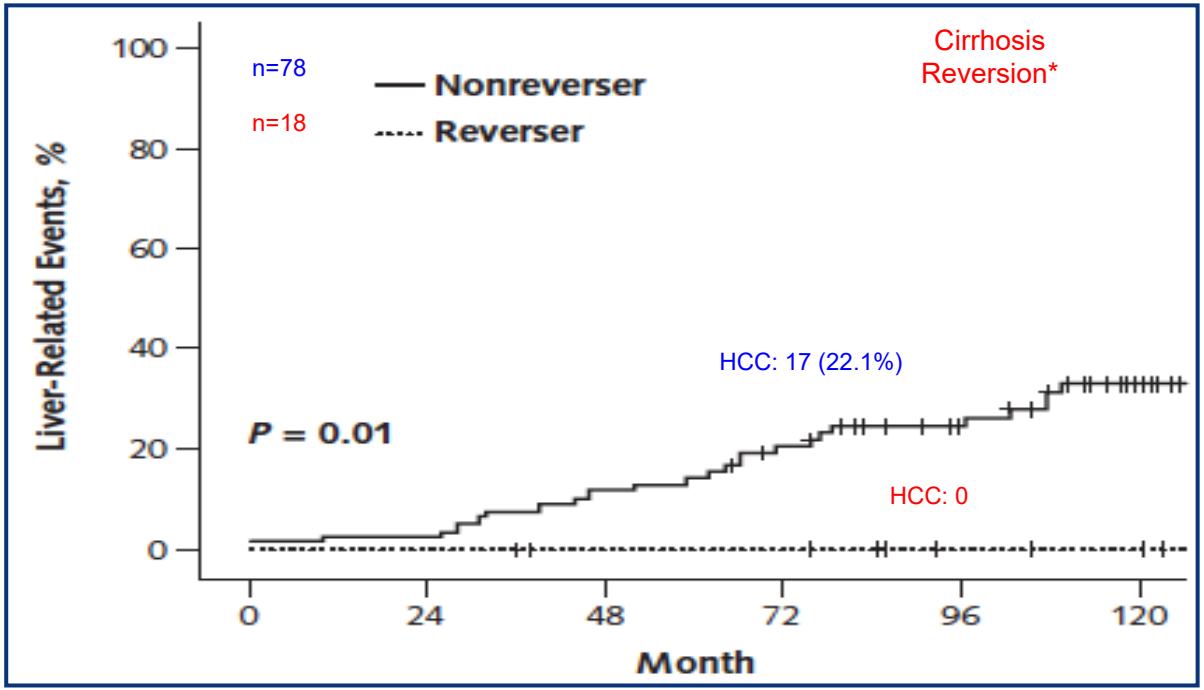
EDITORIAL | HEPATOLOGY COMMUNICATIONS, VOL. 6, NO. 3, 2022

Hepatocelluar Carcinoma Risk in Advanced Fibrosis After Sustained Virologic Response: When Can We Safely Stop Hepatocellular Carcinoma Surveillance?

Implementing HCC surveillance in « apparently » low-risk patients?

Dropping surveillance in « apparently » high-risk patients?

In case of fibrosis reversion, HCC risk may become negligible

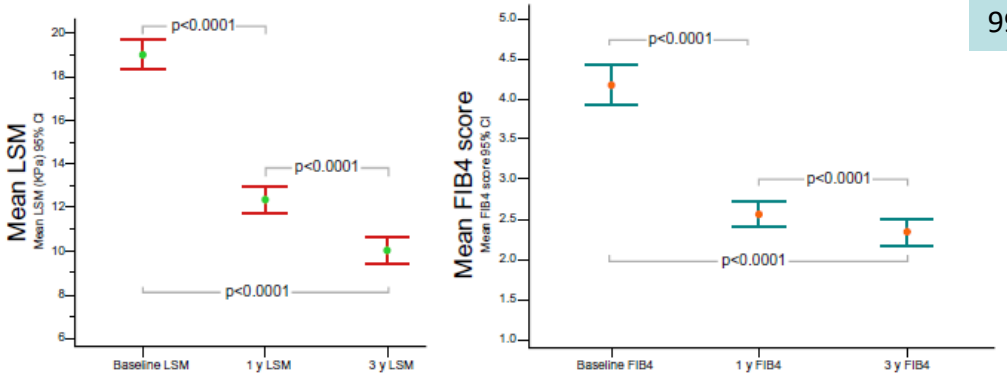


*Based on sequential histological assessment

Mallet et al. Ann Intern Med 2008;149:399–403

Dynamic variation of liver fibrosis non-invasive tests as markers of decreased HCC risk?

Evolution of non-invasive tests



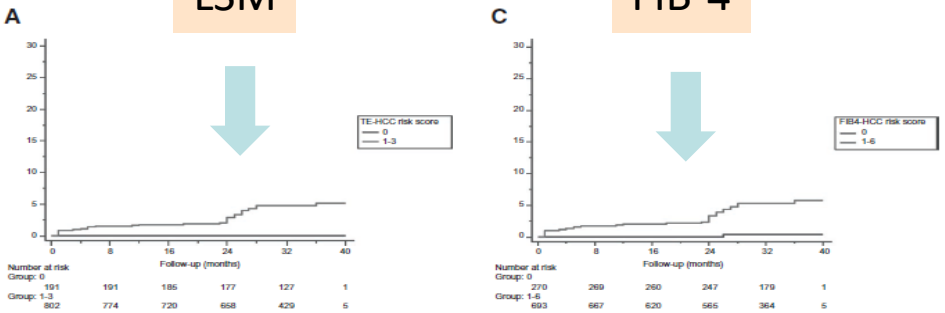
993 patients with HCV-cured ACLD

Alonso-Lopez et al, hepatology 2020

LSM

FIB-4

HCC risk



Are we able to identify patients with ACLD who should be discarded from HCC surveillance programs following SVR?

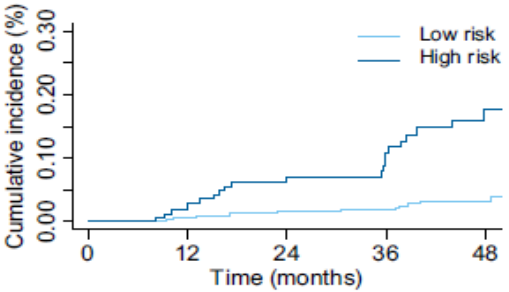
HCC risk stratification after cure of hepatitis C in patients with cACLD

AFP/LSM/albumin-based

AFP ≥4.6 ng/ml	→ 3 points
Age ≥59 years	→ 2 points
LSM ≥19 kPa	→ 1 point
Albumin <42 g/L	→ 1 point

Optionally: Alcohol consumption >30 g/d ♂/>20 g/d ♀ → 2 points

Risk group	Proportion of patients	HCC incidence at 4 years (%)	HCC per 100py
Low-risk (0-3)	70.8%	3.3	0.9
High-risk (≥4)	29.2%	17.5	4.4



Semmler J Hep 2022

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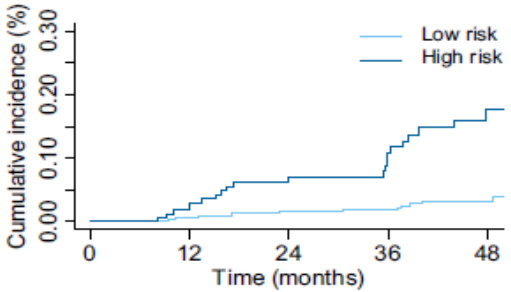
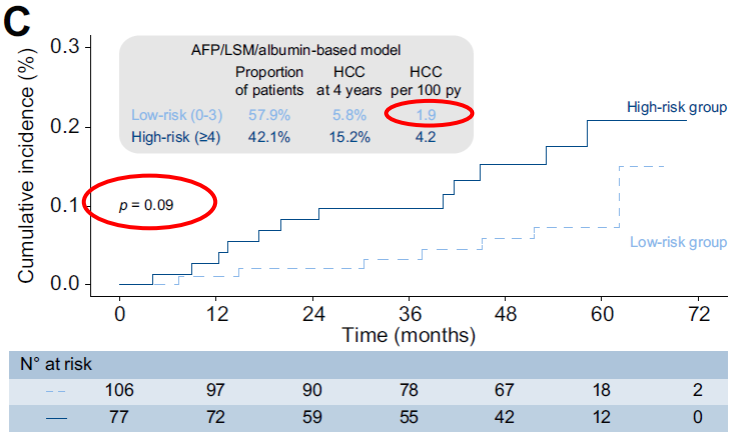


Semmler J Hep 2022

Nakatsuka et al J Hep 2022

However, further risk stratification of patients with cACLD using the proposed models was unsuccessful. This is probably because our cohort was on average 10 years older than that reported by Semmler *et al.*

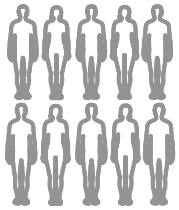


Aging as the strongest HCC risk factor in this population?

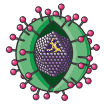
Nahon et al J Hep 2025

ANRS cohorts

3067 patients, 39 French Centres



Patients with cirrhosis included in surveillance programs

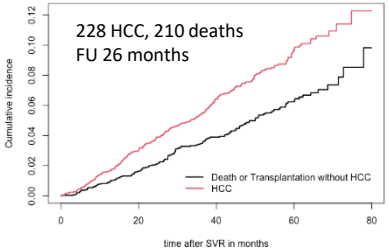


Cured HCV

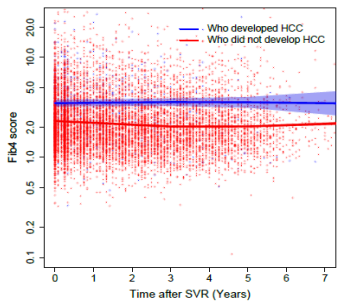
Noninvasive tests (NIT) following SVR

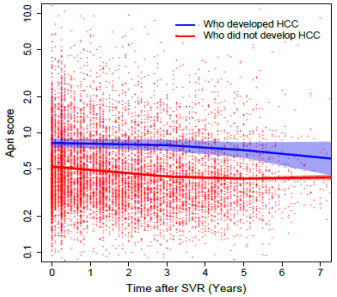
Fib4
APRI

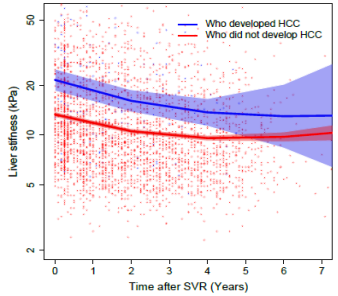
Liver stiffness Measurment (LSM)



- Joint modeling approach integrating continuous values of NITs and HCC occurrence
- Simultaneous assessment of NIT current value and slope impacts on HCC risk







HCC risk	FIB4	APRI
NIT current value	HR=2.98 [2.47;3.36]	HR=2.74 [2.38;3.21]
NIT slope	HR=1.56 [0.70;3.51]	HR=1.24 [0.67;2.31]

- NIT slope does not accurately inform HCC risk
- HCC surveillance should not be discontinued in case of NITs improvement
- NIT current value should guide HCC risk stratification

Position Paper

JOURNAL
OF HEPATOLOGY

EASL position paper on clinical follow-up after HCV cure

Thomas Reiberger[1,†], **Sabela Lens**[2,†], Giuseppe Cabibbo[3], Pierre Nahon[4], Anna Linda Zignego[5], Katja Deterding[6], Ahmed M. Elsharkawy[7], Xavier Forns[2,*]

Statement

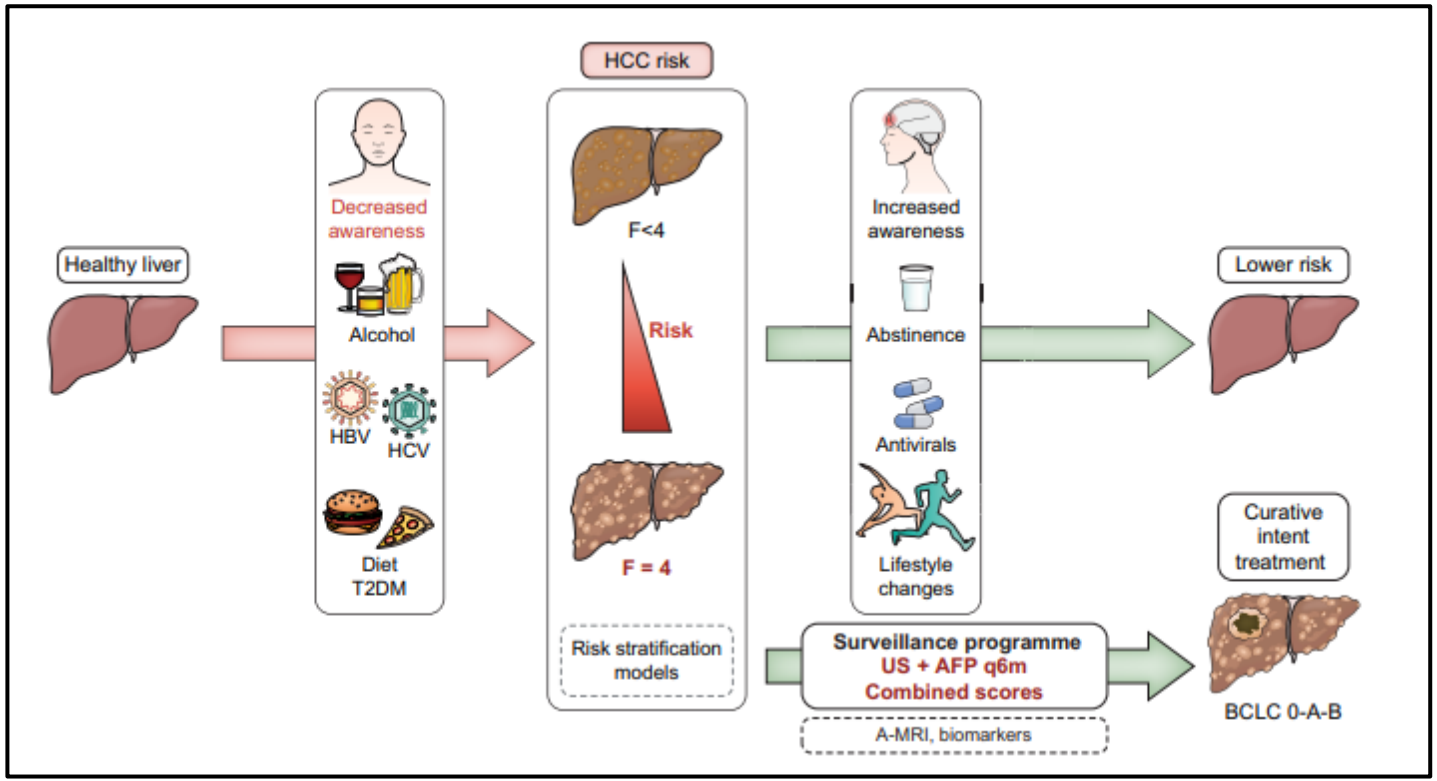
- A tailored approach to surveillance as a function of NIT trajectory following SVR requires additional research aimed at establishing a reliable correlation with changes in HCC incidence.

Refining HCC screening in SVR patients

- **Question 1:** Can we define patients with ACLD who could be discarded from sureillance?

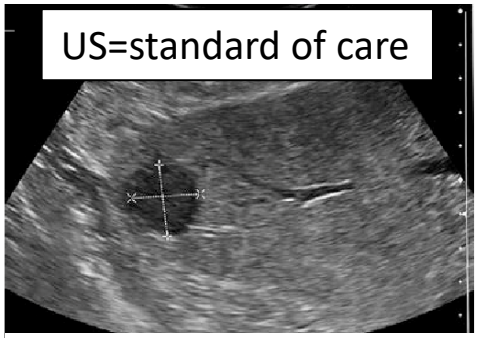
- **Question 2:** is there a population in whom HCC surveillance should be intensified? If yes, how?

Risk stratification: allocating ACLD patients at higher risk to more sensitive (and costly) tools and increase the proportion of HCC patients eligible for curative procedures



EASL CPG 2024

Is it justified? *Yes if we have performant tools for early HCC detection…*



BCLC 0 HCC (single<2cm)

[Sensitivity < 30%]

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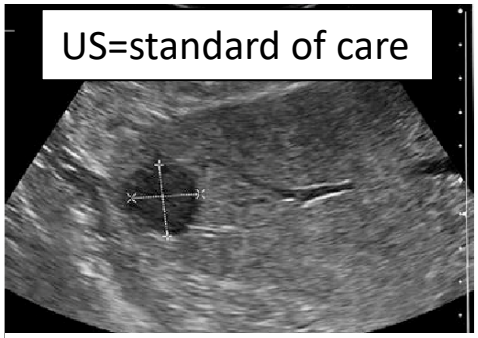

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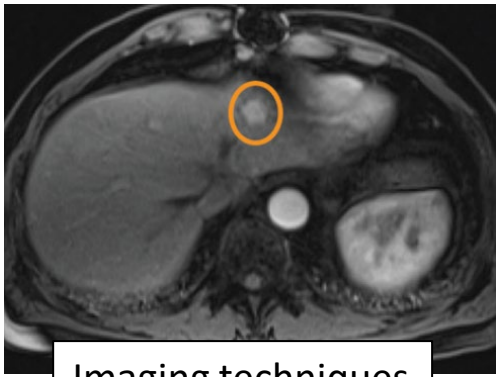
Rates of non HCC nodules detection ?
Increased recall procedures

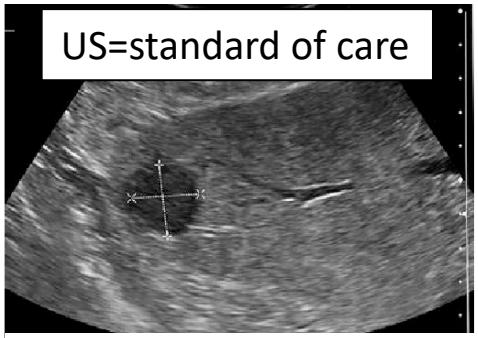


Imaging techniques

Is a 2 cm HCC detectable in the bloodstream?
Increased rates of false negatives

Circulating biomarkers

Is it justified? *Yes if we have performant tools for early HCC detection…*



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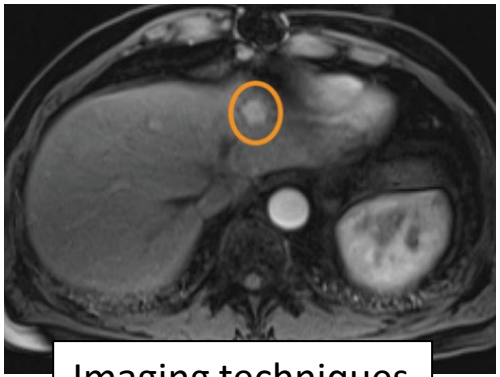

Imaging techniques

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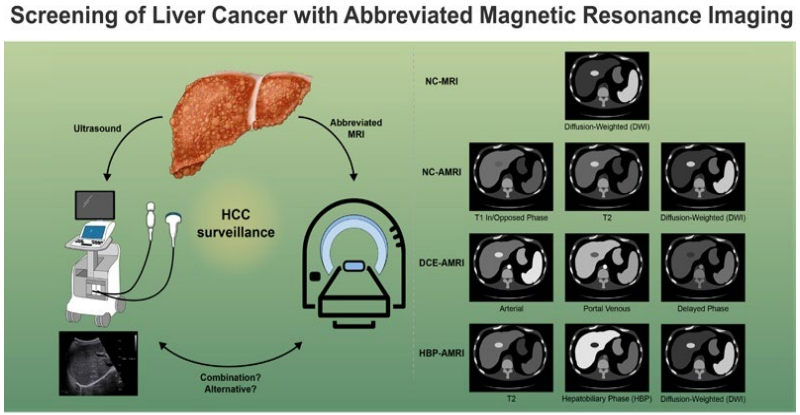
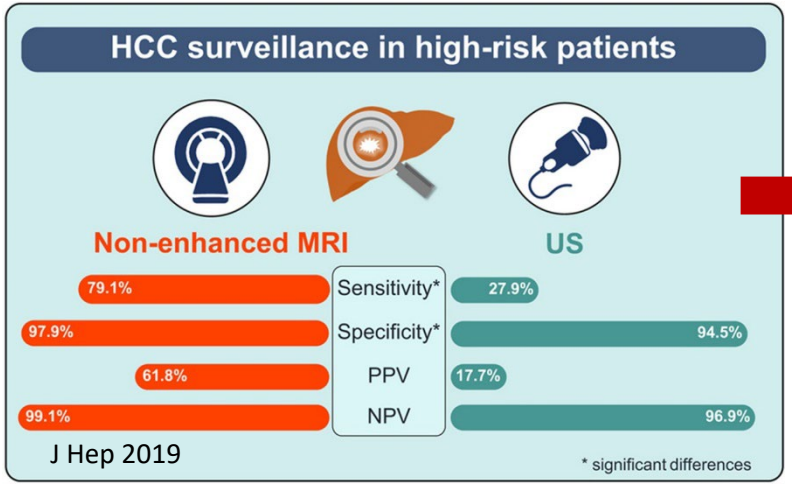


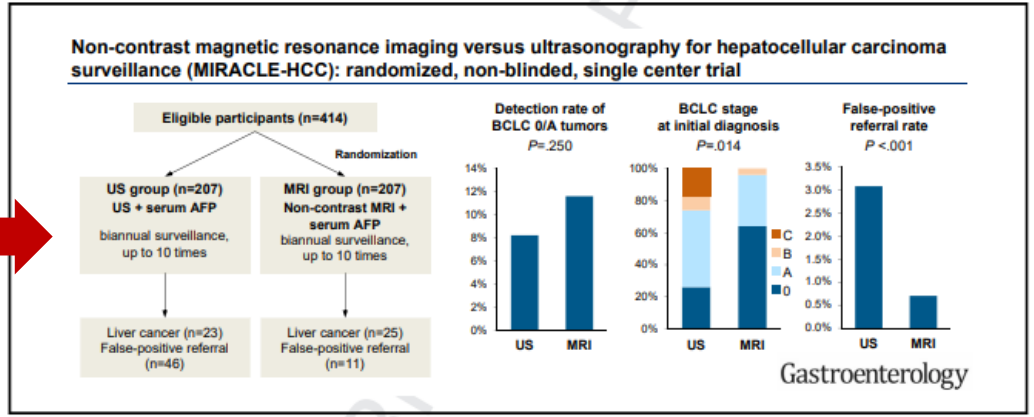
Ronot, Nahon, Rimola. *Hepatology 2023*

HEPATOLOGY

The example of abbreviated MRI (AMRI): from performance studies to clinical trials



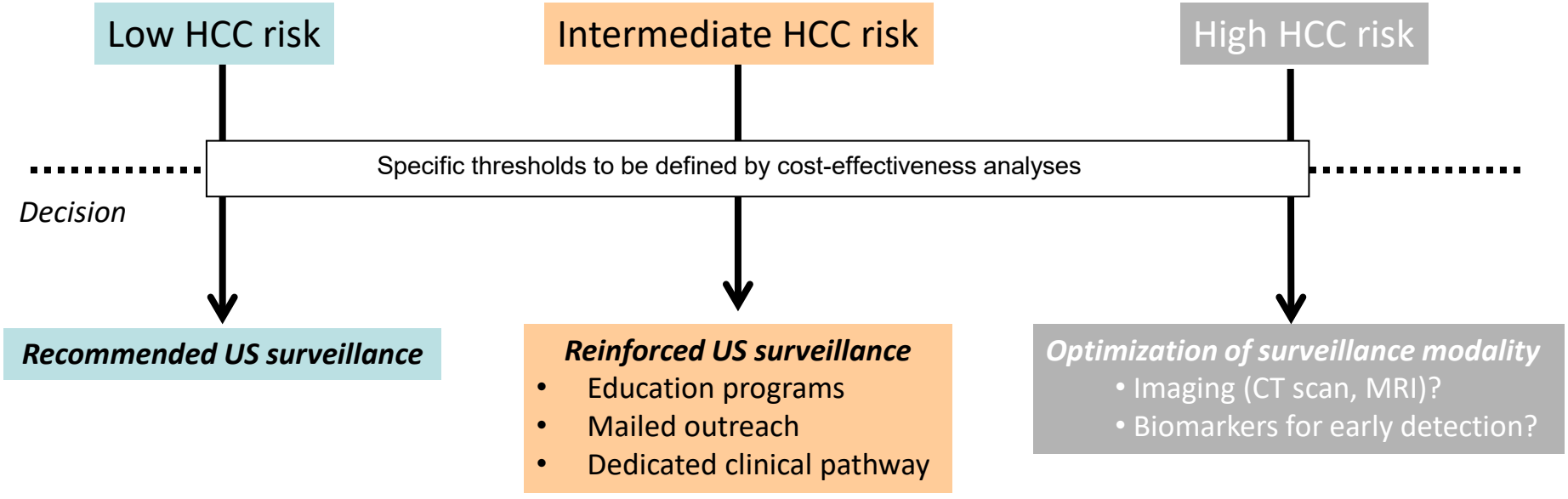
J Hep 2019



Rhee et al Gastro 2025

Personalisation of HCC screening: *can we improve early detection in patients with ACLD?*

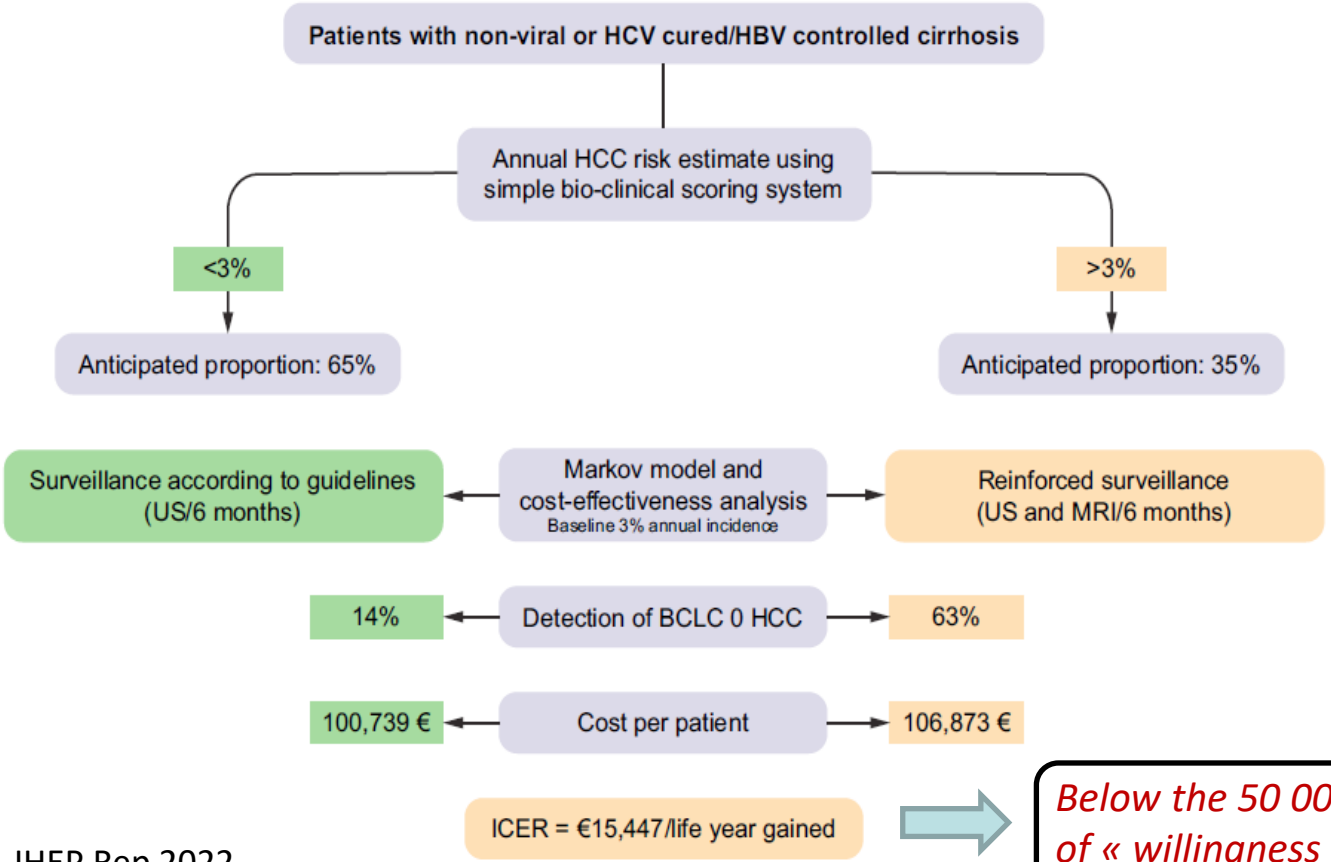
Allocation of HCC risk classes



Nahon et al, JCM 2020

INCREASED COSTS

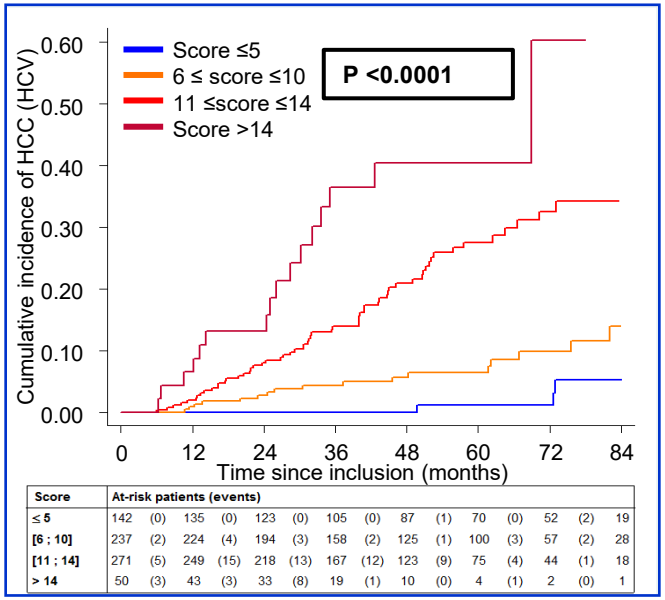
Assessing cost-effectiveness of 2 surveillance strategies based on HCC risk stratification



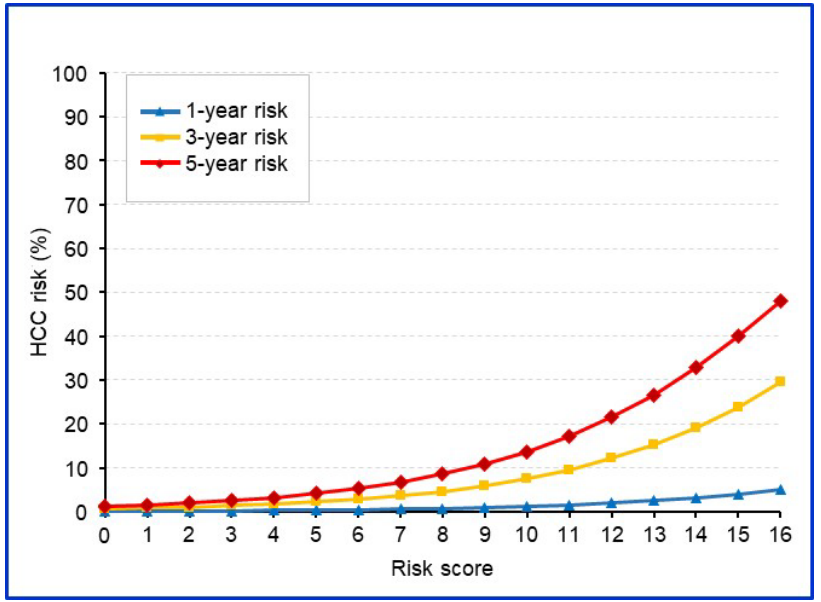
Nahon et al, JHEP Rep 2022

From risk stratification to personalized management of HCV-cured patients

Cir »Vir CO12



Score	At-risk patients (events)														
≤ 5	142	(0)	135	(0)	123	(0)	105	(0)	87	(1)	70	(0)	52	(2)	19
[6 ; 10]	237	(2)	224	(4)	194	(3)	158	(2)	125	(1)	100	(3)	57	(2)	28
[11 ; 14]	271	(5)	249	(15)	218	(13)	167	(12)	123	(9)	75	(4)	44	(1)	18
> 14	50	(3)	43	(3)	33	(8)	19	(1)	10	(0)	4	(1)	2	(0)	1



- Age >50 years
- Alcohol
- GGT >N
- Plat <100 10^3
- SVR

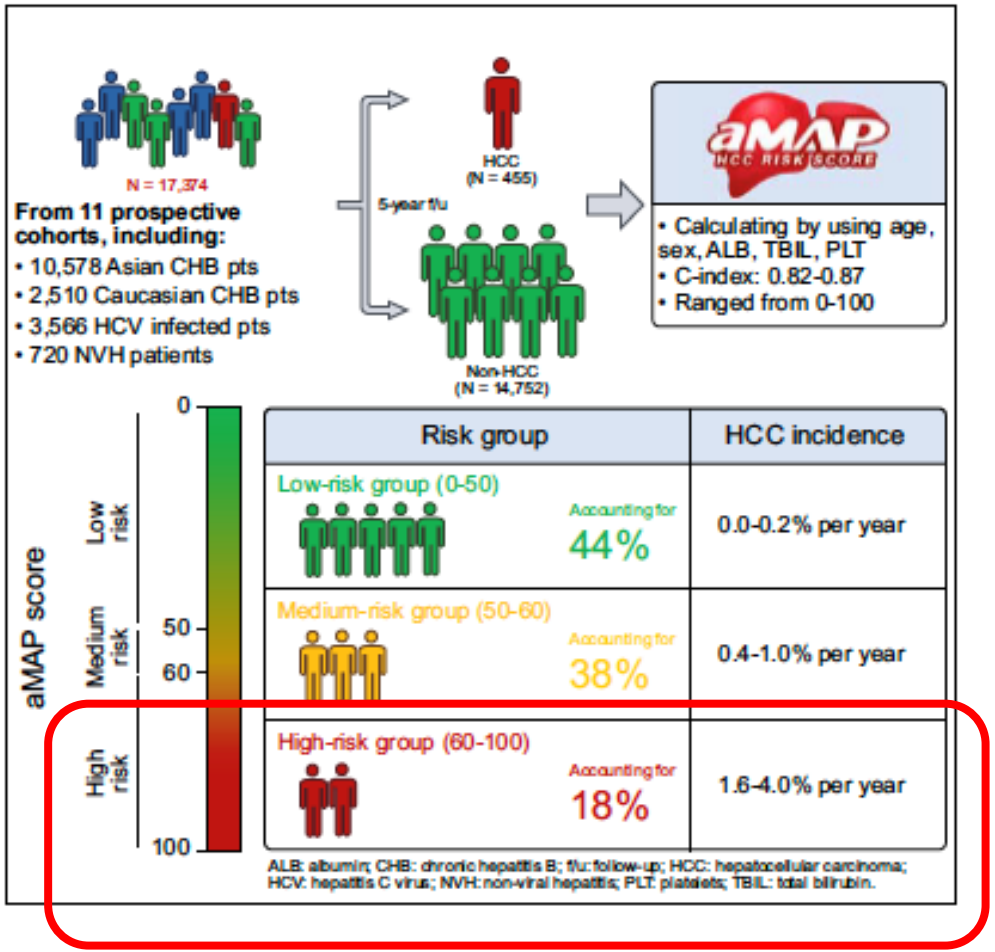
Risk modelling

Score ≤5: low
Score 6–10: intermediate
Score 11–14: high
Score >14: maximal

Ganne-Carrié et al, Hepatology 2016

Towards “universal” HCC risk stratification scoring systems

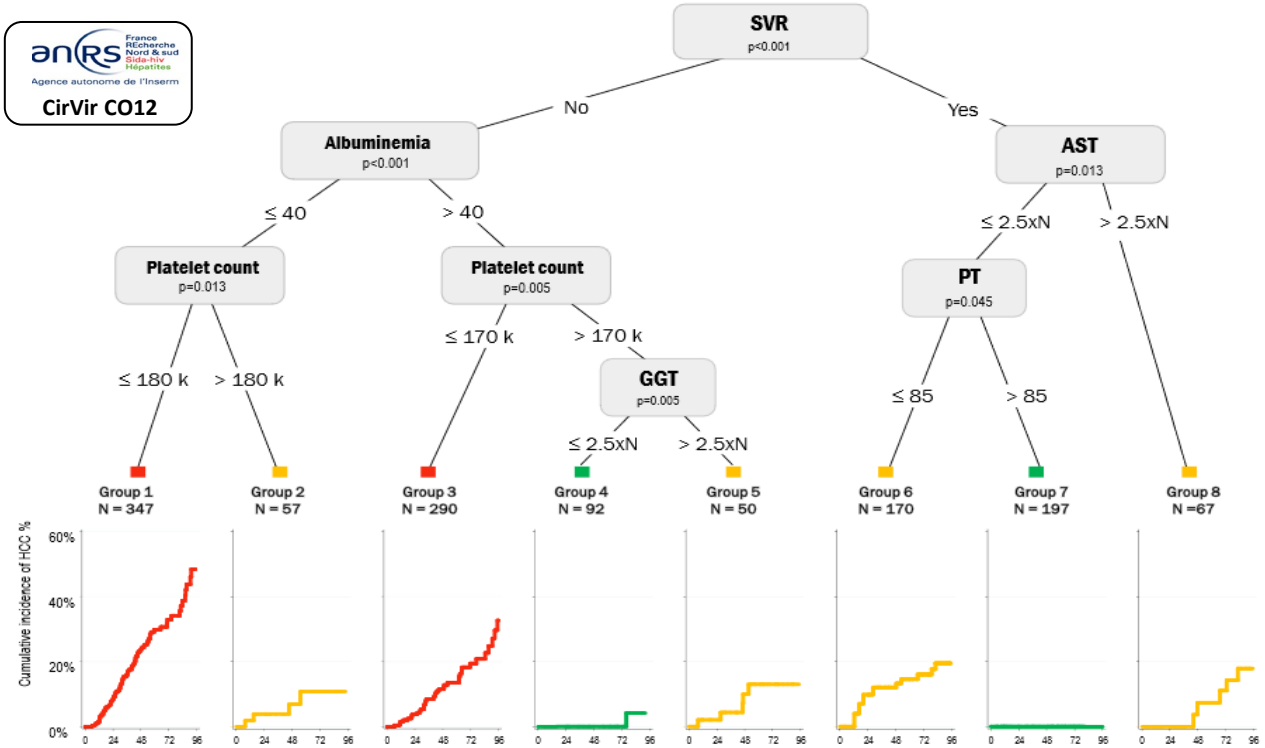
- Patients without active viral replication
- Regardless of the cause of chronic liver disease
- Multiple ethnicity
- Not all with cirrhosis

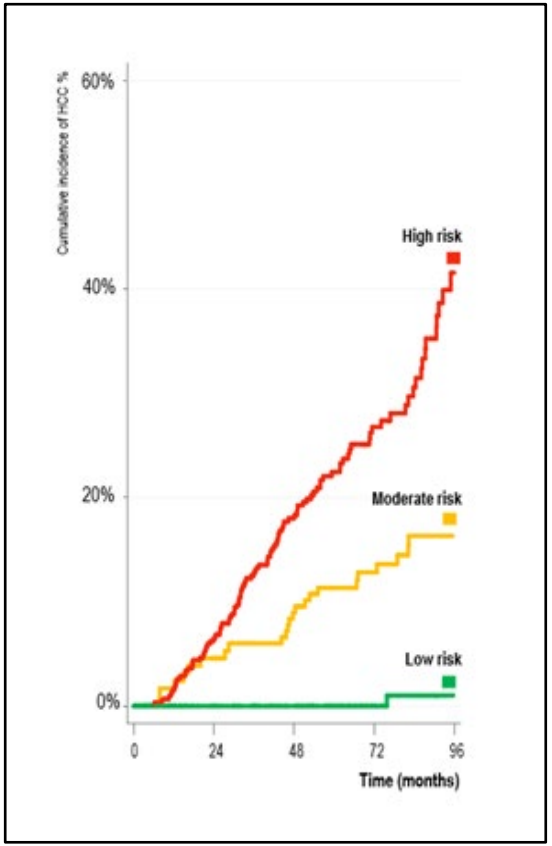


Fan et al, J Hep 2020

Precision medicine to improve risk stratification: *Machine learning approaches and AI*

CirVir CO12





Audureau et al, J Hepatology 2020

Position Paper

JOURNAL
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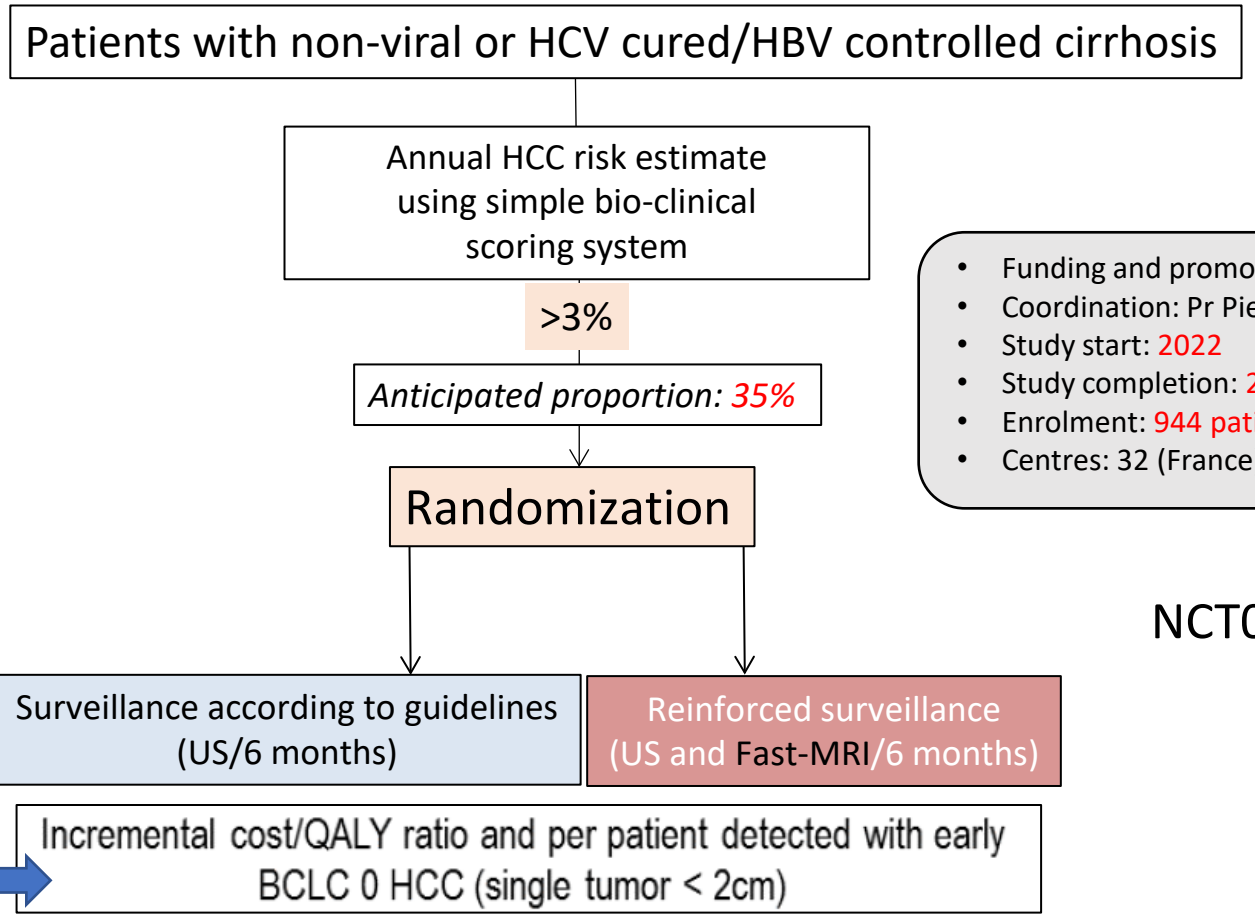
EASL position paper on clinical follow-up after HCV cure

Thomas Reiberger[1,†], **Sabela Lens**[2,†], Giuseppe Cabibbo[3], Pierre Nahon[4], Anna Linda Zignego[5], Katja Deterding[6], Ahmed M. Elsharkawy[7], Xavier Forns[2,*]

Statement

- HCC risk stratification models enable the identification of patients with a particularly high HCC incidence following SVR. Individualised HCC surveillance strategies could be proposed in these individuals using more sensitive and potentially also more expensive HCC screening procedures. The latter must first be proven to be superior to liver ultrasound in randomised trials that also consider cost-effectiveness.

FASTRAK trial (FAST-MRI for HCC suRveillance in pAtients with high risK of liver cancer)



- Funding and promotion: APHP
- Coordination: Pr Pierre Nahon
- Study start: 2022
- Study completion: 2028
- Enrolment: 944 patients
- Centres: 32 (France)

NCT05095714

Conclusions: the long road to incorporate precision medicine in HCC surveillance

- Prospective cohorts of HCV-cured patients included in HCC surveillance programs enabled to estimate the proportion of high risk individuals using stratification models

- Medico-economic projections and analyses are key to ultimately set up pragmatic surveillance strategies

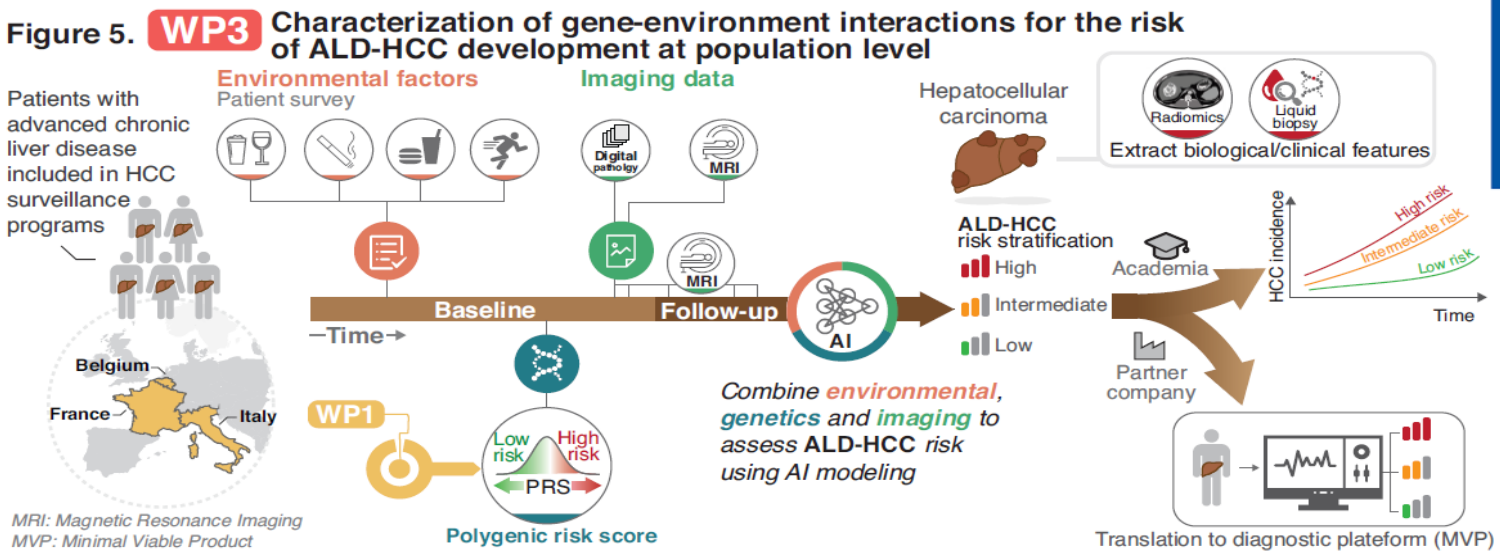
- Randomized trials taking into acccount risk stratification and mixing clinical and economic endpoints will ultimately pave the way for refinement of HCC surveillance using more sensitive and costly early detection tools.

- Until then, HCC surveillance based on semi-annual US must remain a lifelong commitment in post-SVR ACLD patients, even in case of NIT decrease.

Joint international efforts: the example of the GENIAL consortium

Call: HORIZON-MISS-2021-CANCER-02

(Research and Innovation actions supporting the implementation of the Mission on Cancer)



Five prospective cohorts of patients with chronic liver disease included in HCC surveillance programs (n =3,990), recruited in France, Belgium, and Italy will be used in WP3 (**Table 1**). GENIAL is designed to use available biobanks of these four already constituted European cohorts of compensated patients prospectively followed-up and included in HCC surveillance programs in whom all clinical data at baseline and during follow-up are already monitored. These cohorts are **already funded.**