Paris Hepatology Conference
Paris 2024

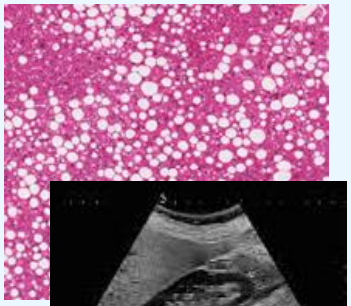
Non-invasive tests use in clinical practice

Pr Jérôme Boursier

Angers University & Angers University Hospital, France

Natural history of MASLD

LIVER STEATOSIS



Isolated steatosis
(75%)

Liver Inflammation

NASH / MASH
(25%)

Liver fibrosis

F0 – F1 – F2 – F3

Cirrhosis
(asymptomatic)

–

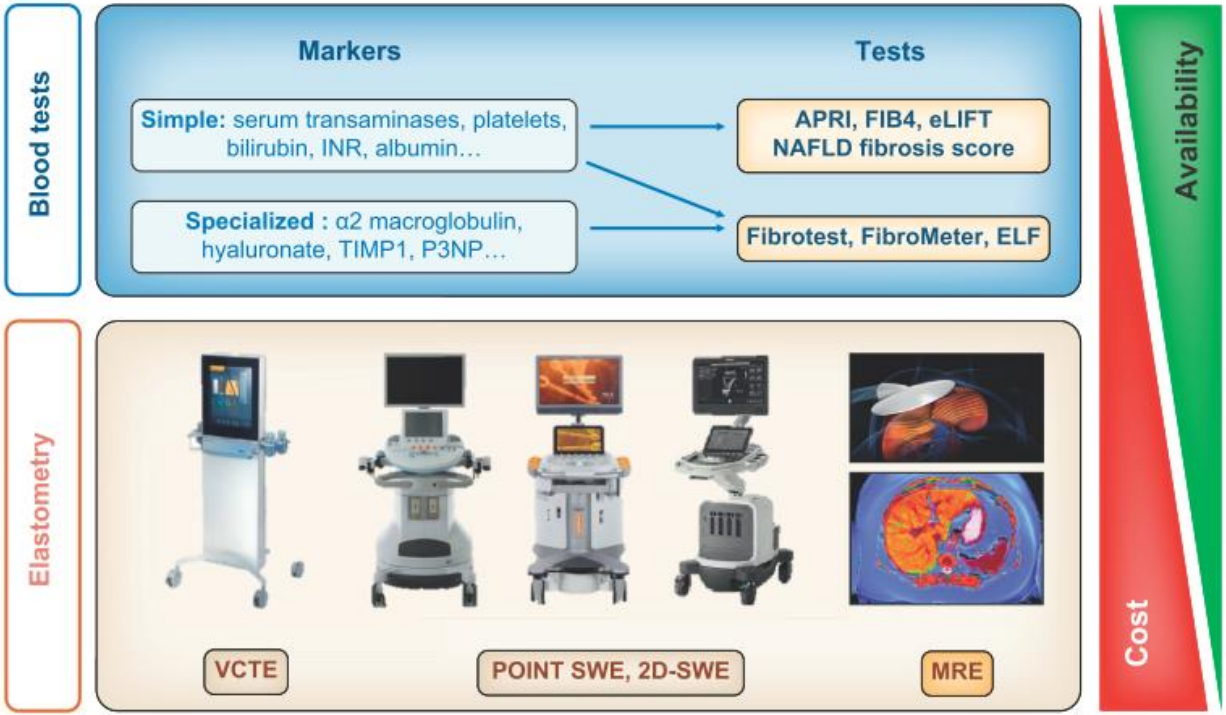
F4

Liver-related Complications

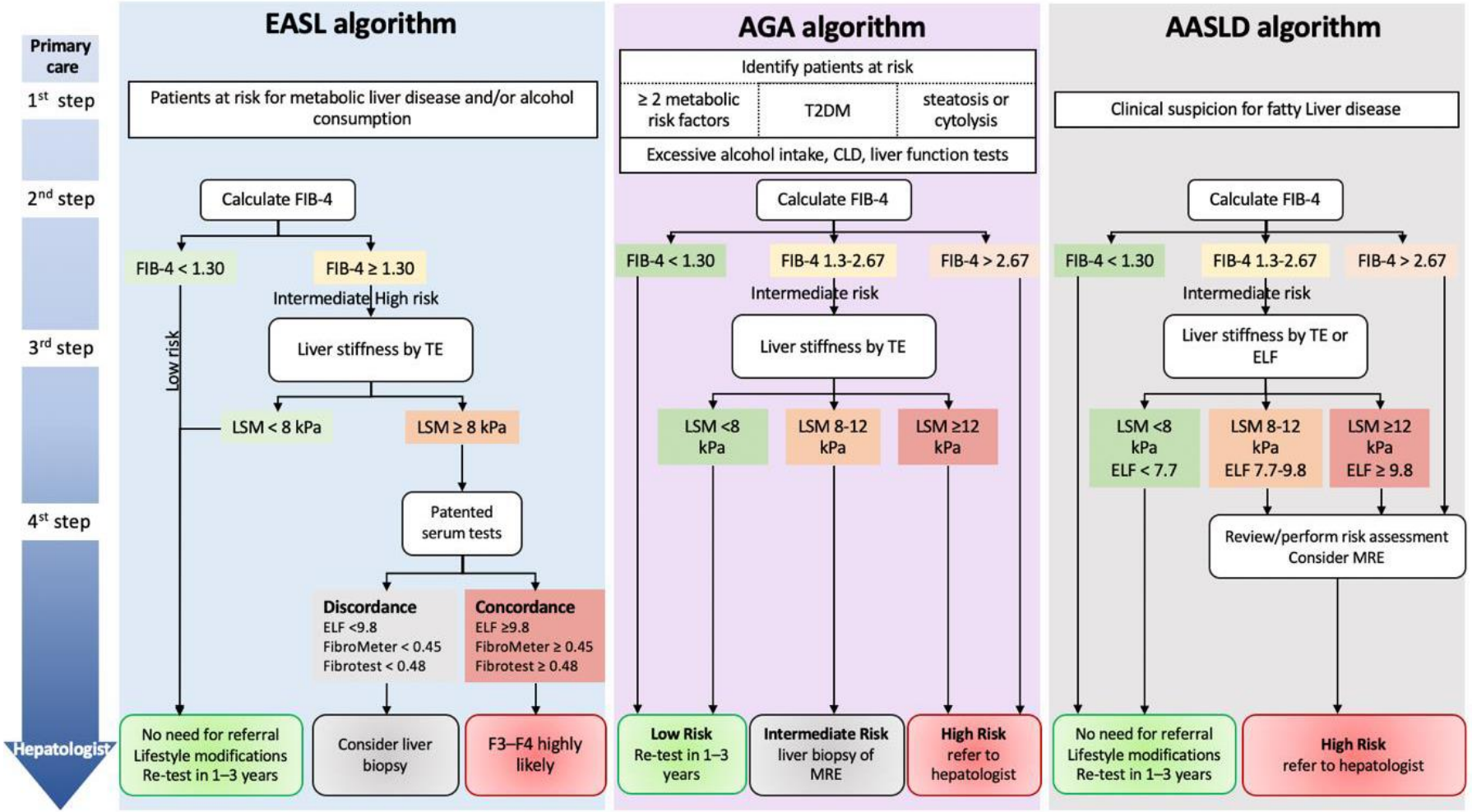
- **Decompensated cirrhosis**
  - Ascitis
  - Liver failure
  - Variceal bleeding
  - Hepatorenal syndrome
- **Hepatocellular carcinoma**

Death

Non-invasive tests of liver fibrosis

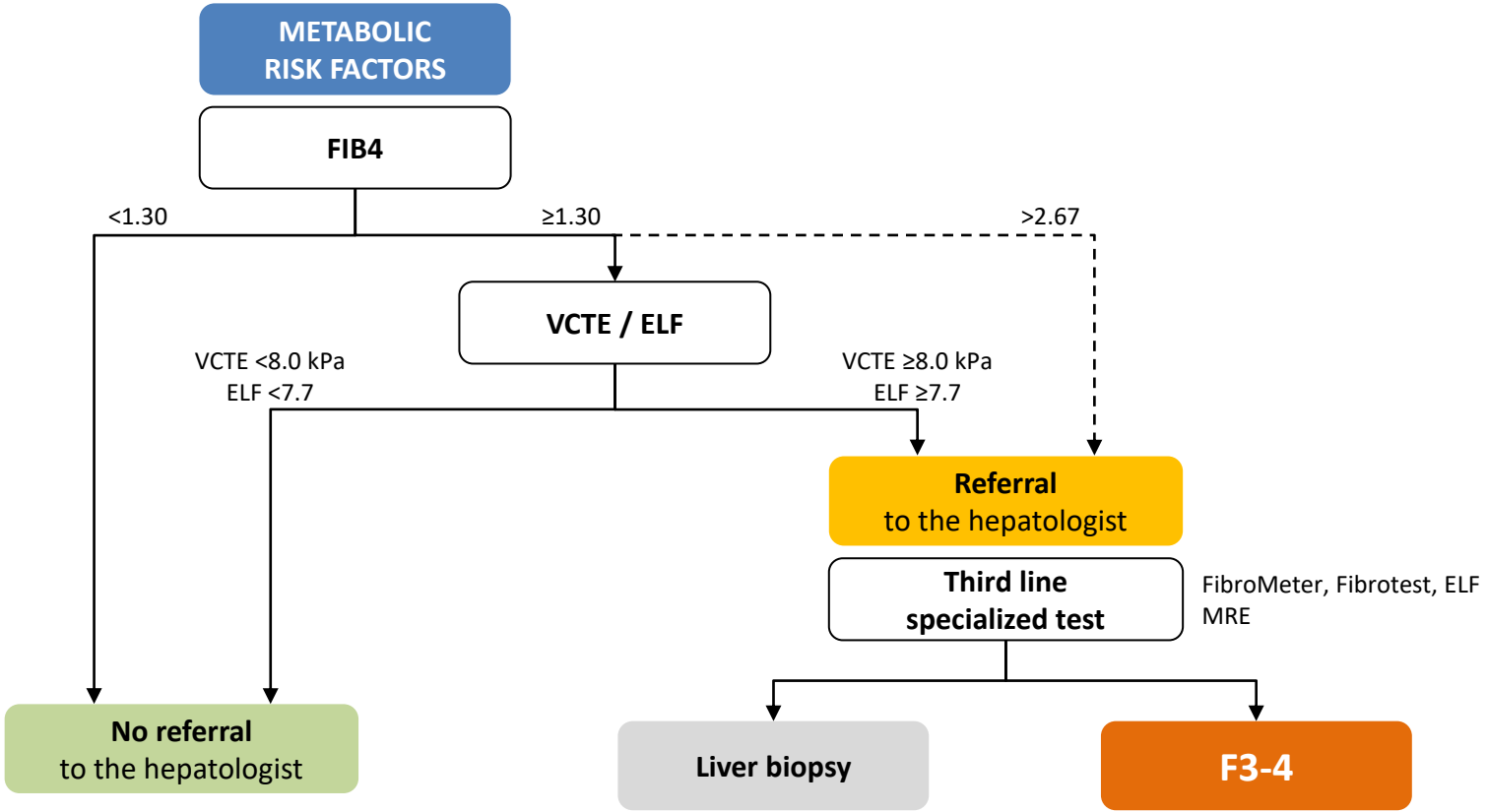


Boursier, J Hep Report 2021



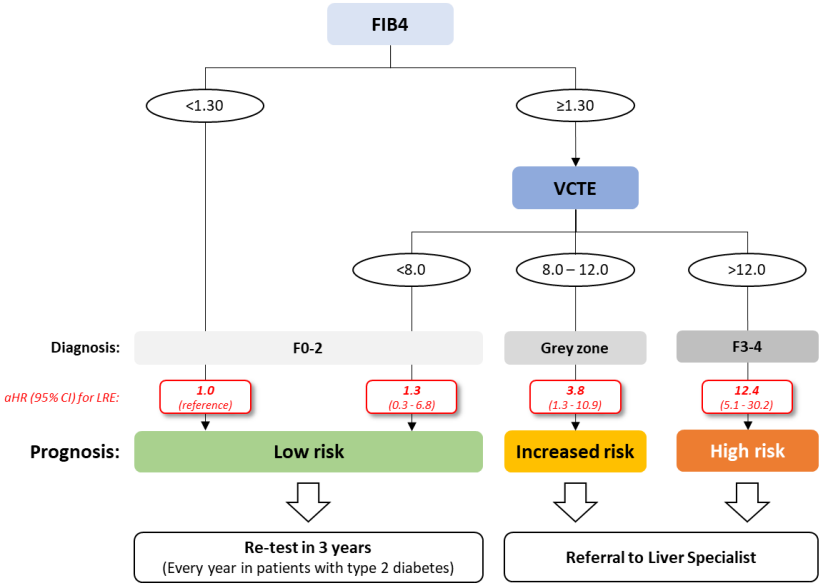
Canivet, Diagnostics 2022

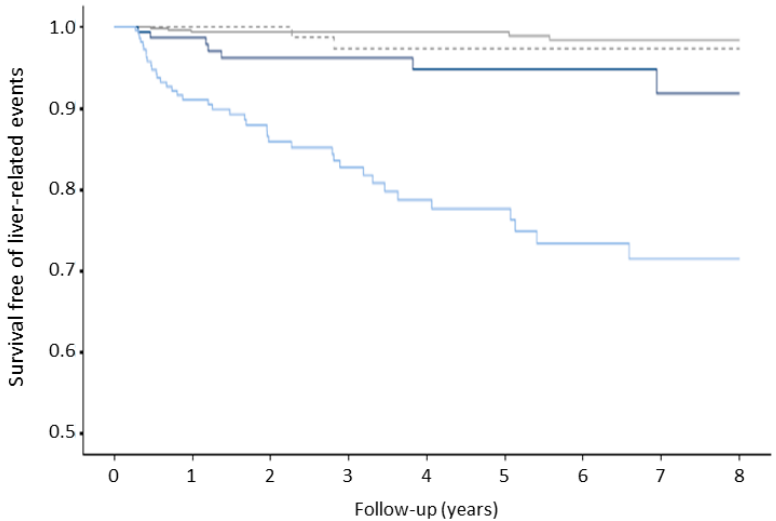
Summary of guidelines



Prognostic accuracy of non-invasive tests in MASLD

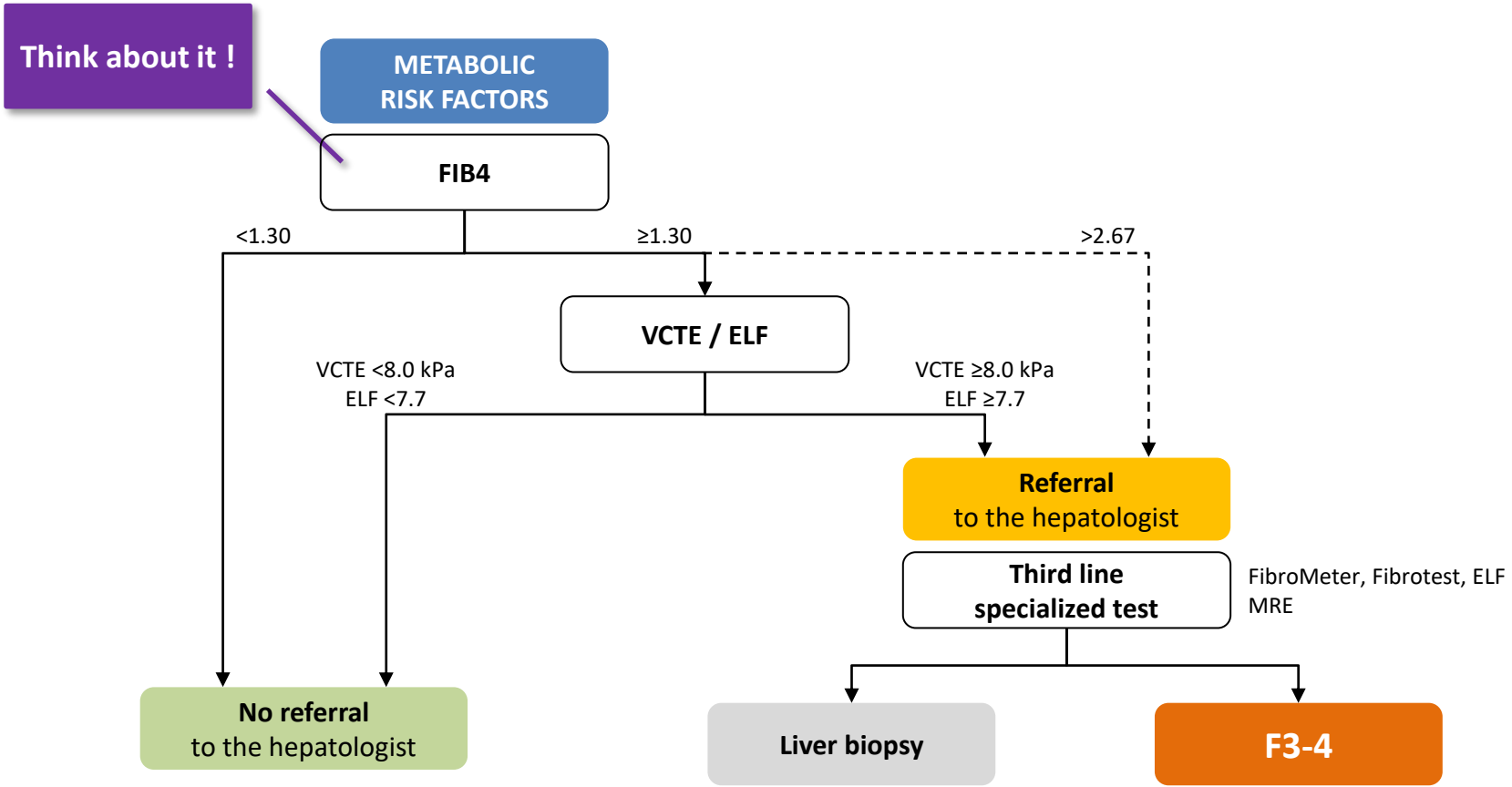
1,057 patients with MASLD in four centers (France, Spain, Sweden)
FIB4 and VCTE (liver biopsy in a subgroup, n=594)
Median follow-up: 3.1 years; 62 liver-related events (cirrhosis complication or HCC)



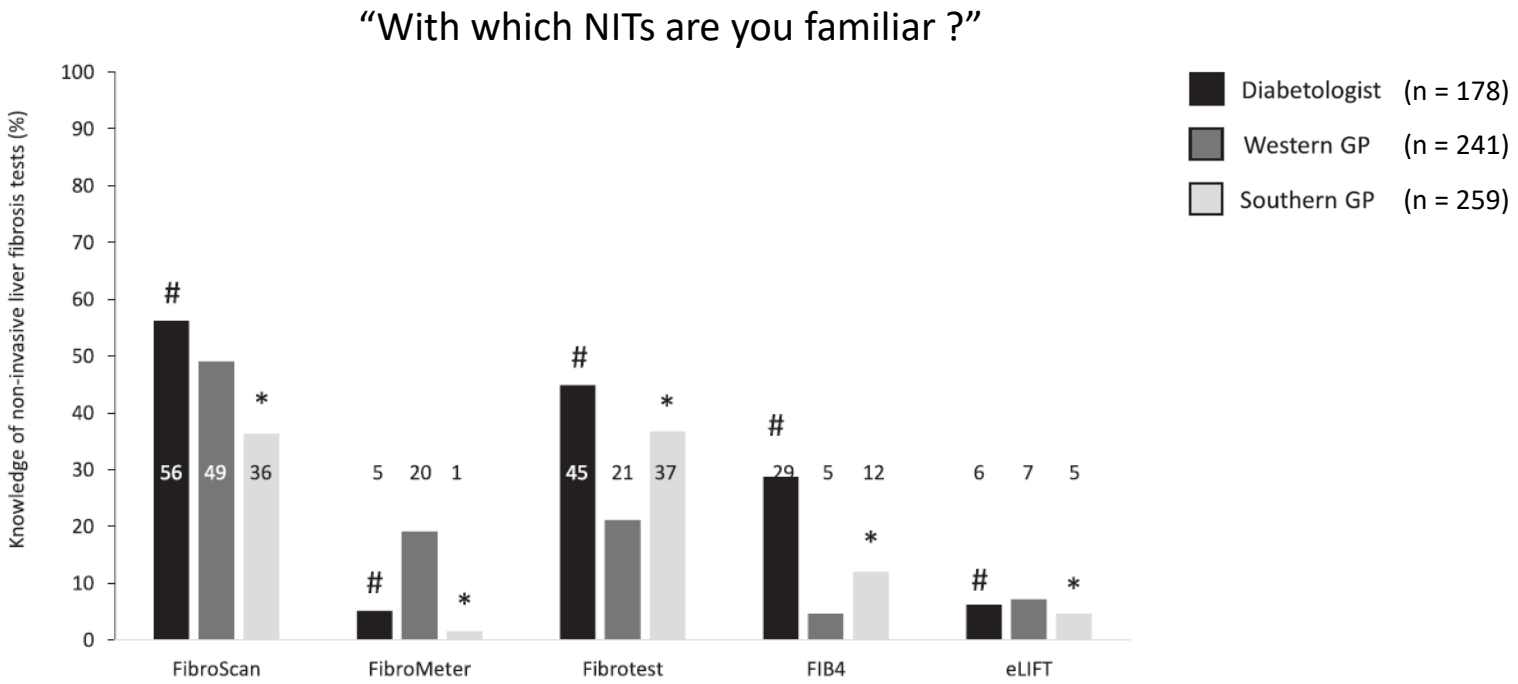


Boursier, J Hepatol 2021

Summary of guidelines

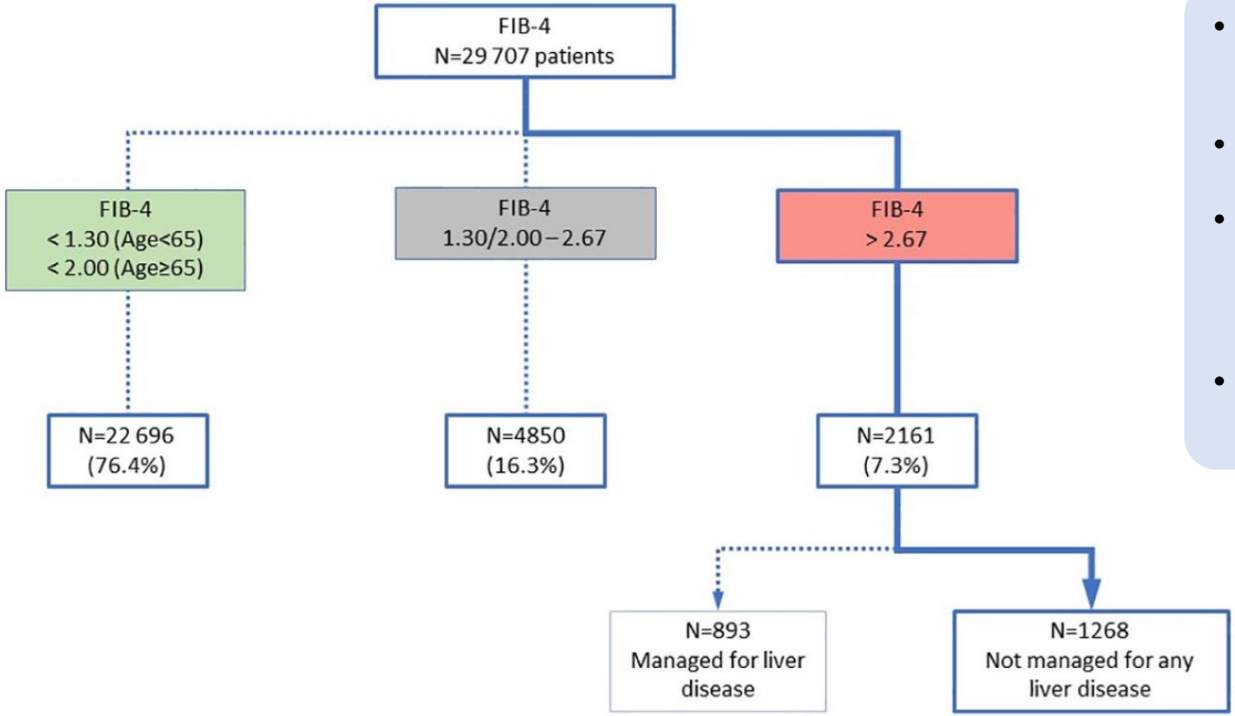


Awarness



Canivet, Clin Res Hepatol Gastroenterol 2022

Automatic calculation of FIB4 in private labs



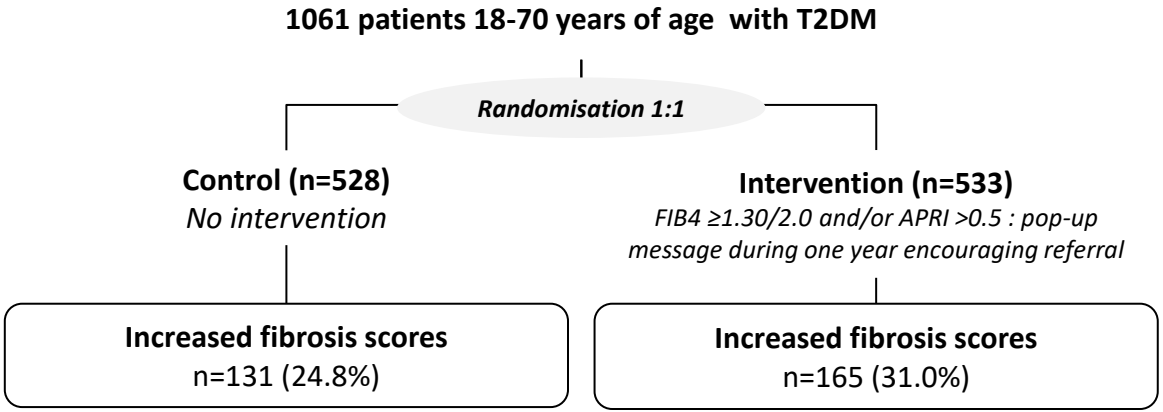
- 21 French clinical laboratories (Marseille, France)
- December 2018 - May 2019
- 134 158 patients : routine blood tests addressed by primary care physicians
- Data for Fib-4 calculation in 29 707 patients

Halfon, PLoS One 2021

Targeted automatic NITs calculation

Three general medical and two diabetes clinics in Hong Kong and Malaysia.

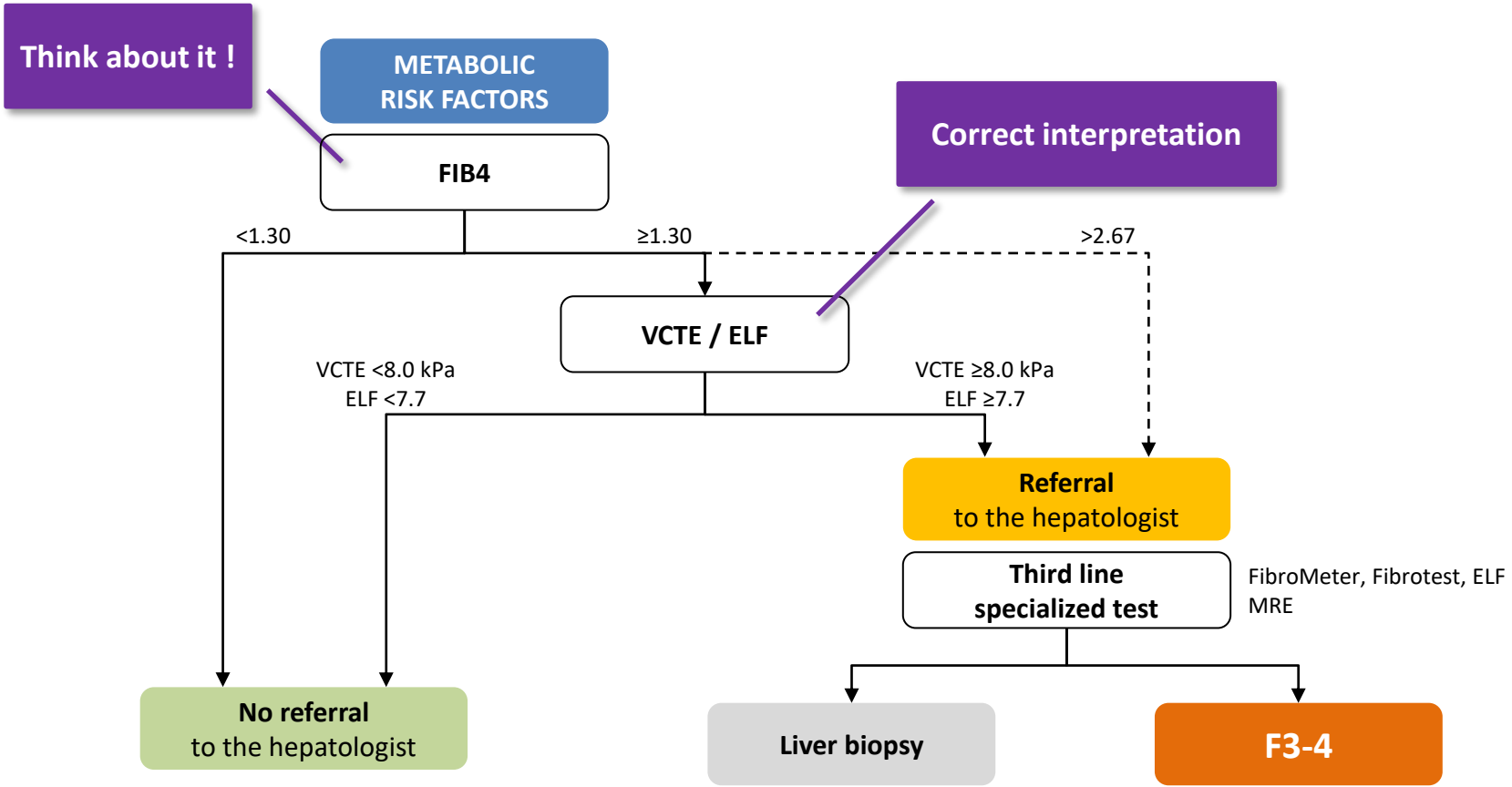
10–20 family doctors, general medical clinicians, endocrinologists or trainees at each clinic.



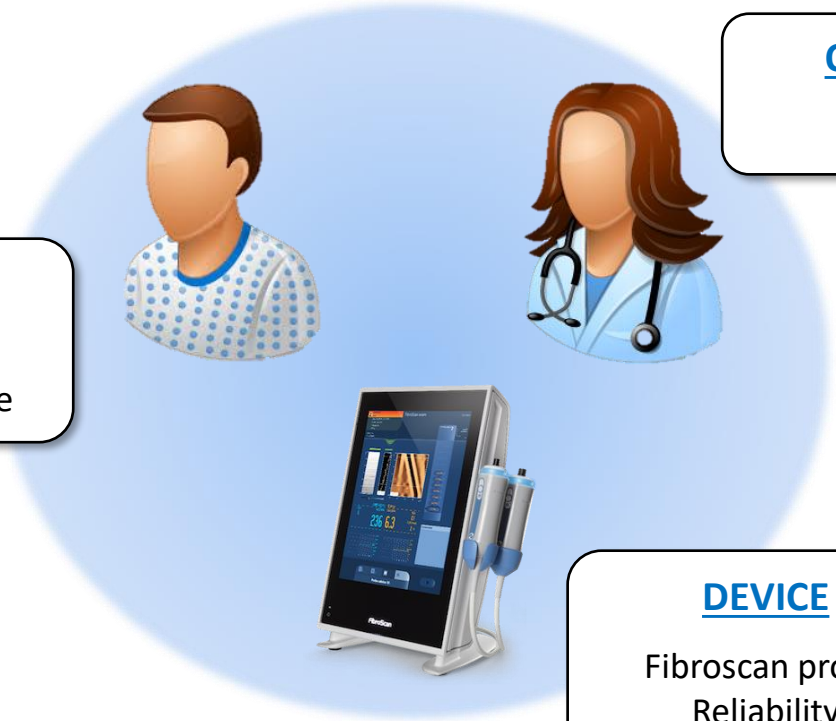
% referral to hepatologists among increased fibrosis scores	**3.1%** (4/131)	**33.3%** (55/165)	p < 0.001
- *Diabetology clinics*	*8% (3/40)*	*47% (18/38)*	*p < 0.001*
- *General mdical clinics*	*1% (1/91)*	*29% (37/127)*	*p < 0.001*
% of patients confirmed with advanced liver disease	**0.2%** (1/528)	**2.1%** (11/533)	p = 0.006

Zhang, Gut 2023

Summary of guidelines



Conditions to consider during liver stiffness measurement



OPERATOR

Experience

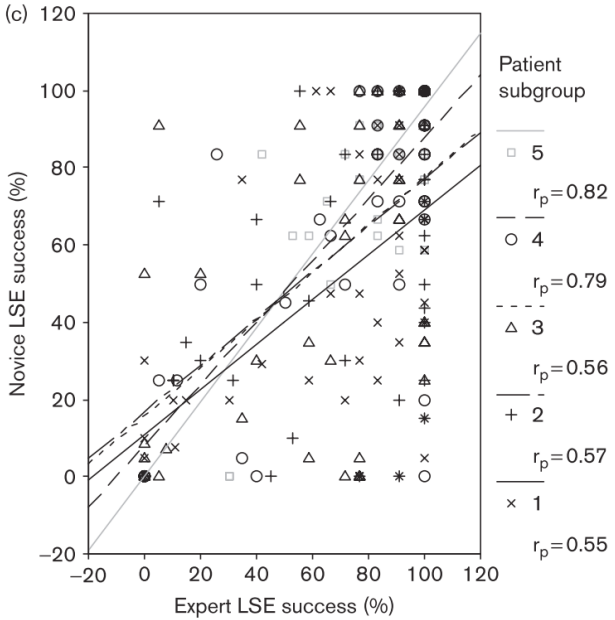
PATIENT

Fasting
Measurement site

DEVICE

Fibroscan probe
Reliability

Training with liver stiffness measurement



Factors Associated with Unreliable LSM Results

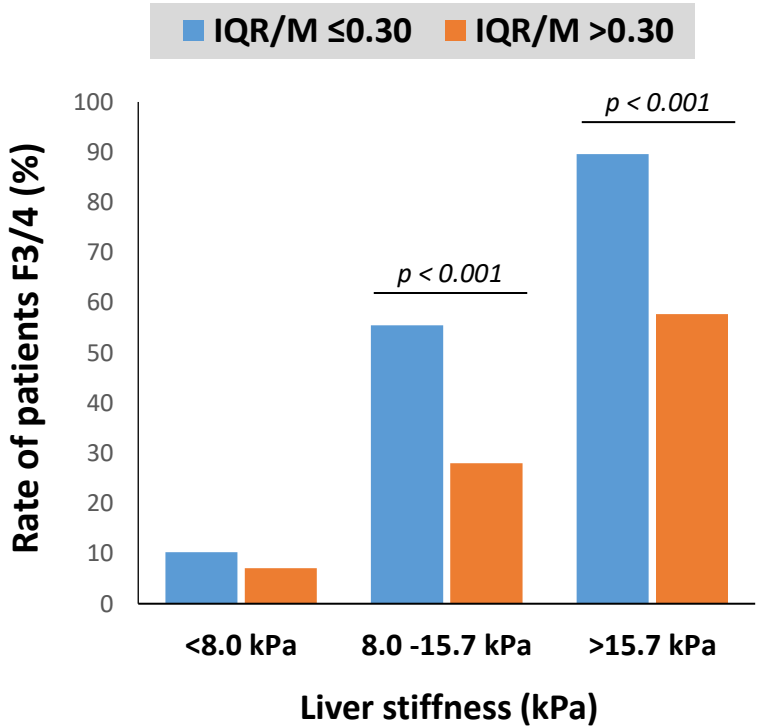
Parameter	Multivariate OR	95% CI	*P*
Operator experience (<500 versus >500 examinations)	3.3	2.7–4.0	0.0001
BMI (>30 kg/m^2)	3.1	2.7–3.6	0.0001
Age (>52 years)	1.8	1.6–2.0	0.0001
Type 2 diabetes (yes versus no)	1.2	1.0–1.4	0.02
Hypertension (yes versus no)	1.2	1.1–1.4	0.003
Female sex	1.2	1.1–1.3	0.004
Time of examination (first versus others)	1.1	1.0–1.2	0.048
ALT (>3× ULN)	0.8	0.7–0.9	0.042

Valid shots <10, SR <60%, or IQR/LSM >30%.
n = 12949 examinations.

Boursier, Eur J Gastroenterol Hepatol 2008; Castera, Hepatology 2010

Fibroscan reliability

	Liver stiffness	
IQR/M	< 8.0 kPa	≥ 8.0 kPa
≤0.10	**Very reliable**	
0.10 - 0.30	**Reliable**	
0.30<		**Poorly reliable**



Boursier, J Hepatol 2019

Consistency of blood test biomarkers

	Case 1
AST (IU/l)	37
Urea (mmol/l)	4,3
Platelets (G/l)	148
Prothrombin time (%)	81
A2macroglobulin (mg/dl)	322
Haluronate (µg/l)	94
FibroMeter	**0.86**

Personnal data

Consistency of blood test biomarkers

	Case 1	Case 2
AST (IU/l)	37	87
Urea (mmol/l)	4,3	4.4
Platelets (G/l)	148	170
Prothrombin time (%)	81	99
A2macroglobulin (mg/dl)	322	112
Haluronate (µg/l)	94	311
FibroMeter	**0.86**	**0.80**

Personnal data

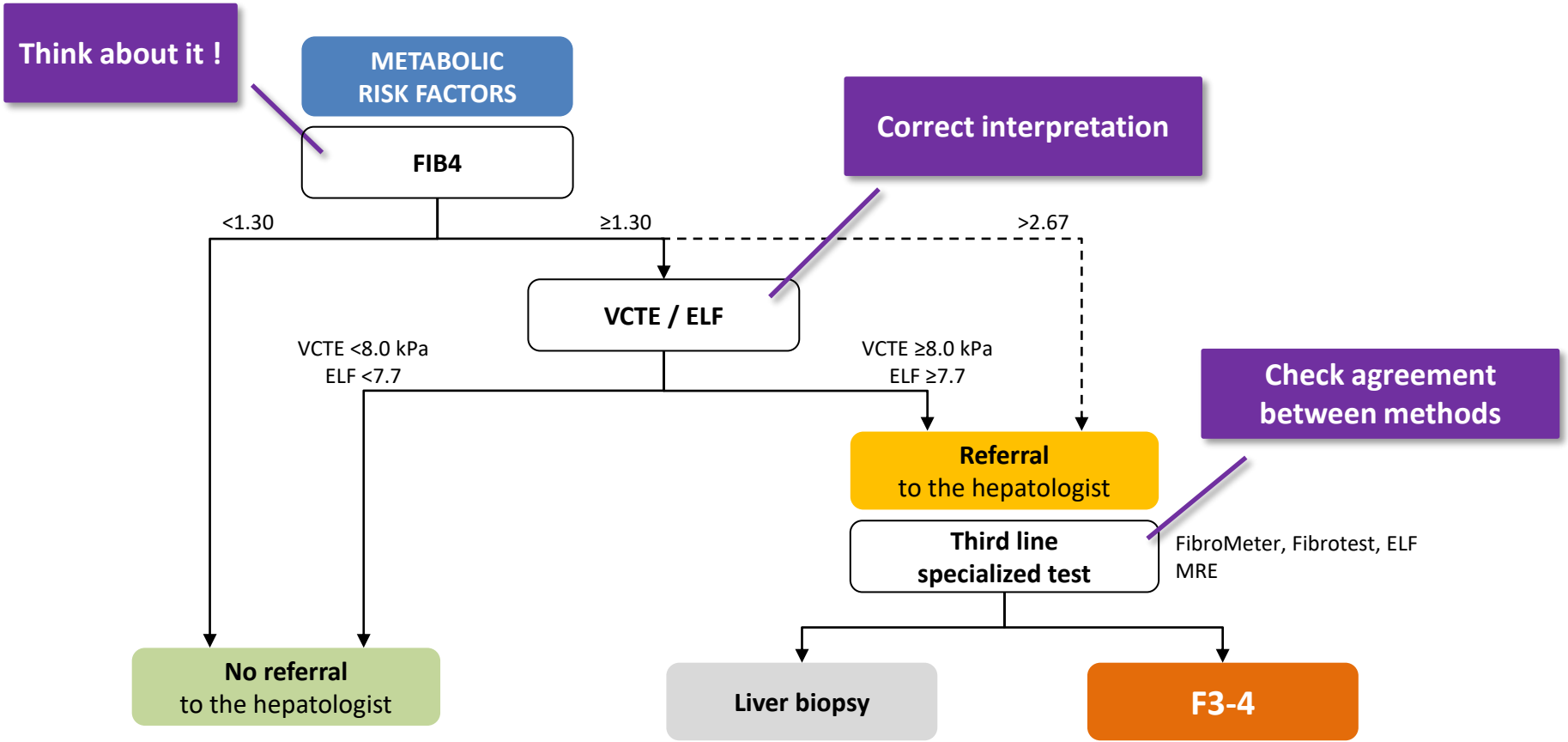
Consistency of blood test biomarkers

	Case 1	Case 2
AST (IU/l)	37	87
Urea (mmol/l)	4.3	4.4
Platelets (G/l)	148	170
Prothrombin time (%)	81	99
A2macroglobulin (mg/dl)	322	112
Haluronate (µg/l)	94	311
FibroMeter	**0.86**	**0.80**

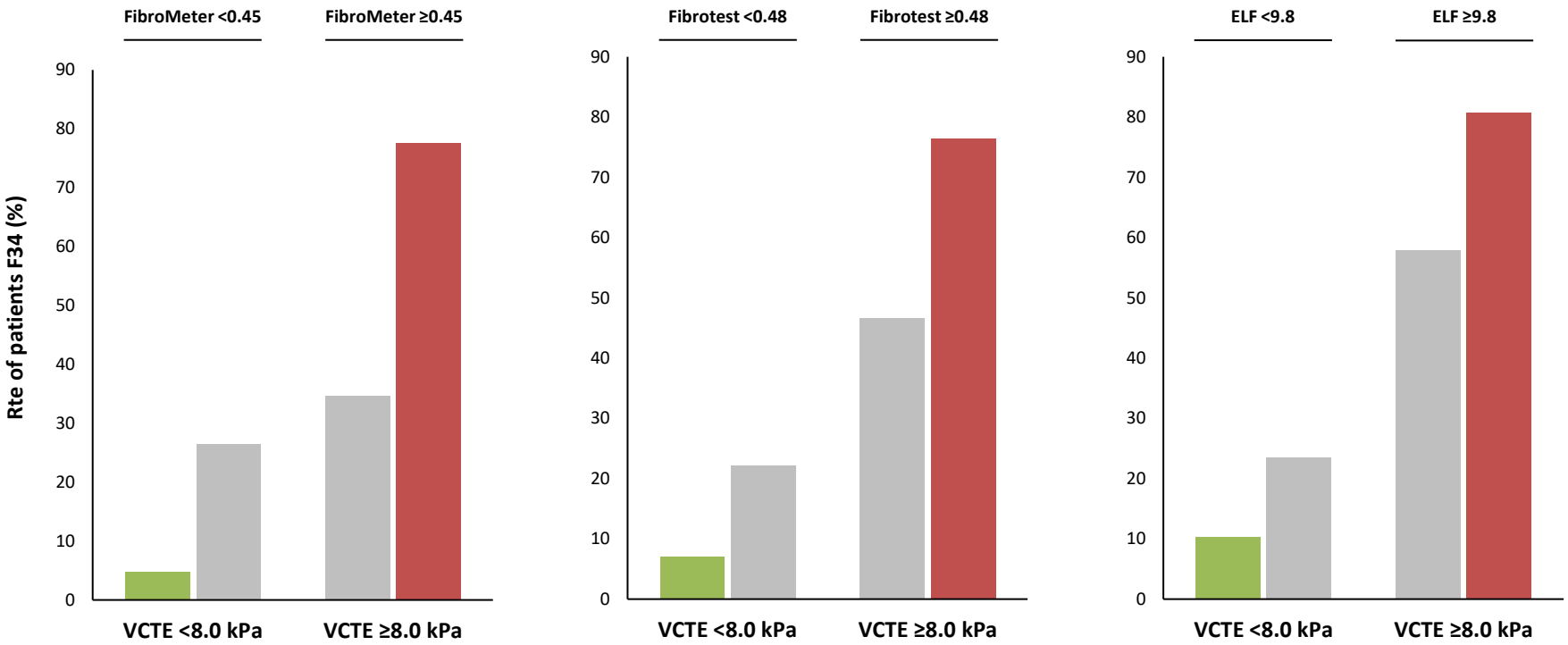
	Case 3
GammaGT (IU/l)	65
Bilirubin (µmol/l)	46
Haptoglobin (g/l)	1.52
ApolipoproteinA1 (g/l)	1.18
A2macroglobulin (mg/dl)	281
Fibrotest	**0.76**

Personnal data

Summary of guidelines



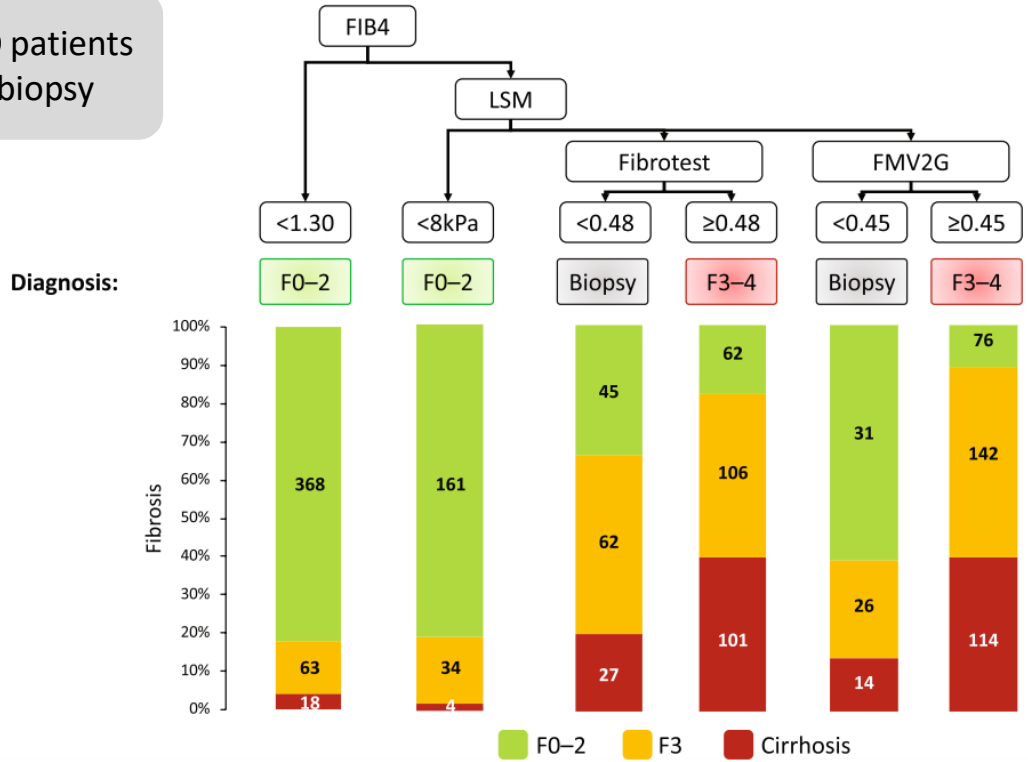
Agreement between specialized blood tests and elastography



Canivet, Hepatology 2022

EASL diagnostic pathway (2021)

1051 NAFLD patients wth liver biopsy

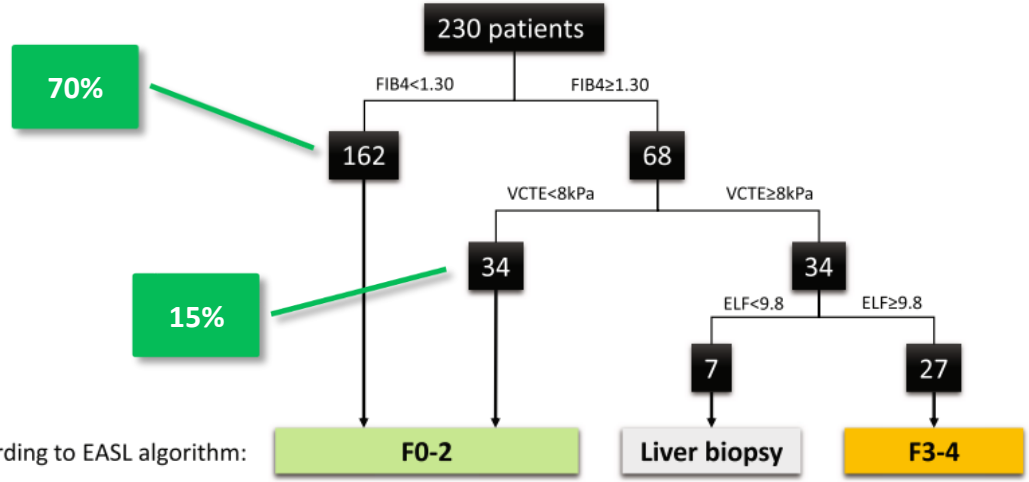


Same results in the subroup of 396 patients with ELF available

Canivet, Hepatology 2022

Rate of patients referred following the EASL algorithm

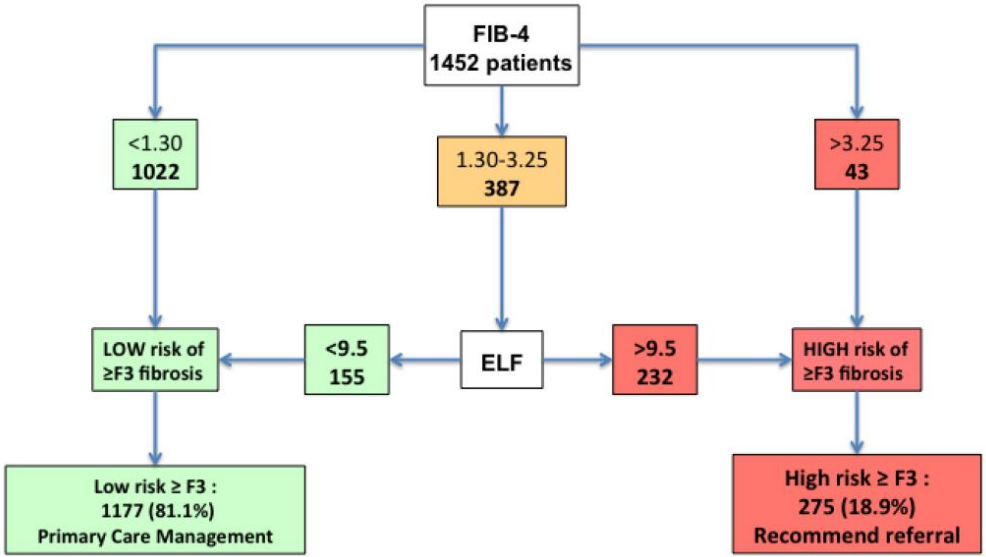
230 patients MASLD
Primary care/
diabetology

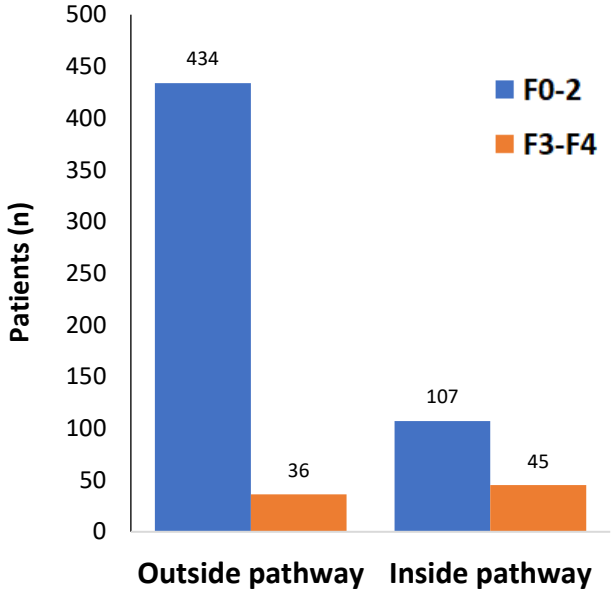


Patients who underwent liver biopsy (n)	F0-2	18	4	0	0
	F3	6	2	2	5
	F4	3	0	1	6
Imaging diagnosis of cirrhosis (n)	F4	3	0	0	9

Canivet, Hepatology 2022

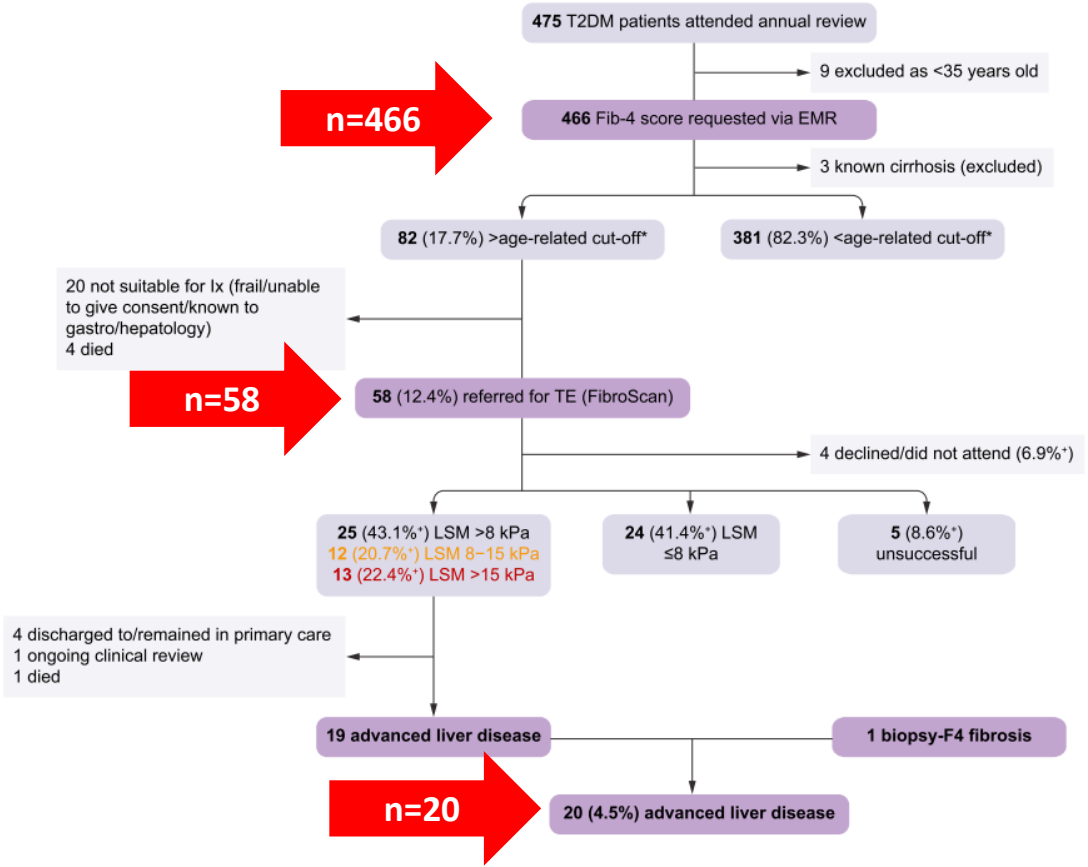
Camden and Islington NAFLD pathway





Srivasta, J Hepatol 2019

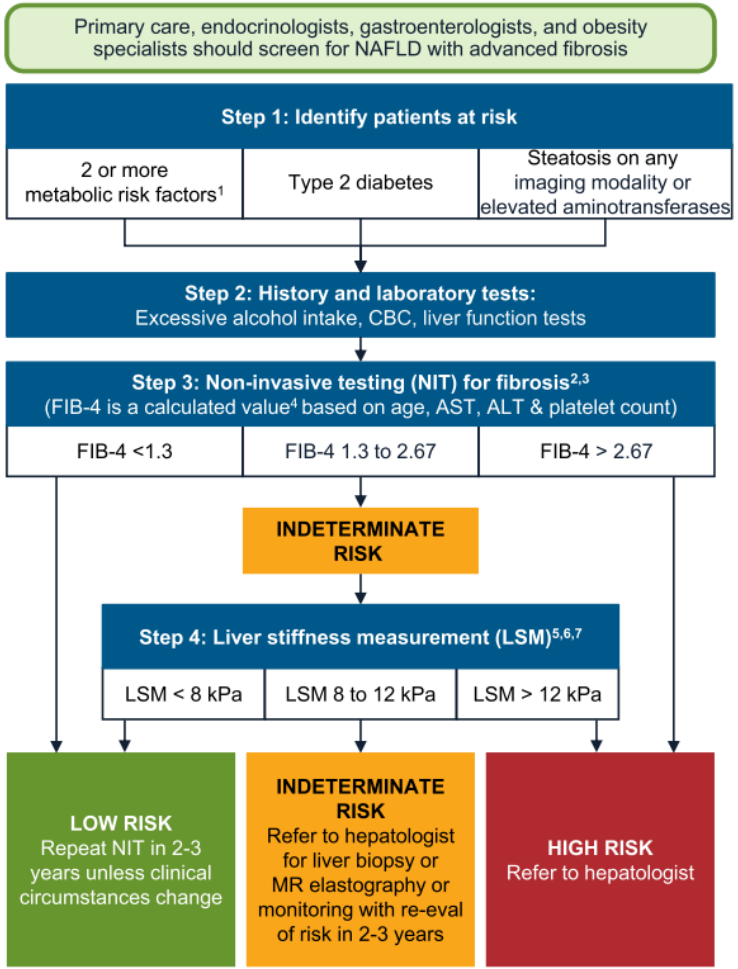
Liver fibrosis screening in patients with type 2 diabetes



There was an almost **7-fold increase in the detection of advanced liver disease** compared with standard care in place before the pilot (4.55% vs. 0.67%)

Overall, 45.5% of patients with advanced disease in this study had a normal ALT

Mansour, J Hep Reports 2021



Flux of patients in the US

Estimation from NHANES 2017-2018

AGA pathway	EASL pathway	
4.6 millions	2.8 millions	Referrals
14.5 millions		VCTE
1.2 millions		VCTE >12 kPa
2.4 millions		Missed VCTE >12 kPa

Kanwal, Gastroenterology 2021; Udompap, Hepatology 2023

FDA NEWS RELEASE

FDA Approves First Treatment for Patients with Liver Scarring Due to Fatty Liver Disease

"Today, the U.S. Food and Drug Administration approved Rezdiffra (resmetirom) for the treatment of adults with noncirrhotic non-alcoholic steatohepatitis (NASH) with **moderate to advanced** liver scarring (fibrosis), to be used along with diet and exercise."

Non-invasive diagnosis of fibrotic NASH

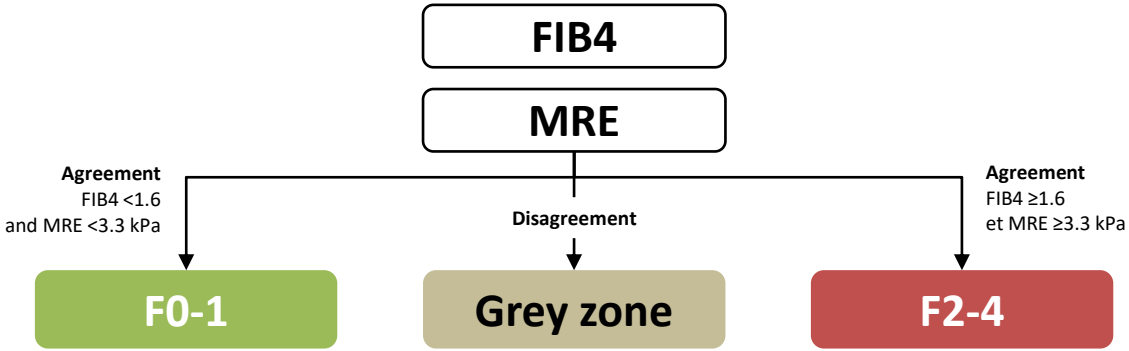
Fibrotic NASH: NASH + NAS ≥4 + F ≥2

Blood tests			Elastography-based scores	
AST Hba1c HDL cholesterol	AST HOMA CK18	HbA1c, A2macroglobulin YKL-40, mir-34a	AST VCTE (kPa) CAP (dB/m)	AST MRE (kPa) MRI-PDFF (%)
⇩	⇩	⇩	⇩	⇩
FNI	**MACK-3**	**NIS4 / NIS2+**	**FAST**	**MAST**
AUROC 0.83	AUROC 0.80 – 0.92	AUROC 0.76 – 0.83	AUROC 0.74 – 0.95	AUROC 0.86 – 0.93

Tavaglione, Clincal Gastroenterol Hepatol 2022; Boursier, Aliment Pharmacol Ther 2018; Harrison, Lancet Gastroenterol 2020; Newsome, Lancet Gastroenterol 2020; Noureddin, J Hepatol 2021

MEFIB algorithm

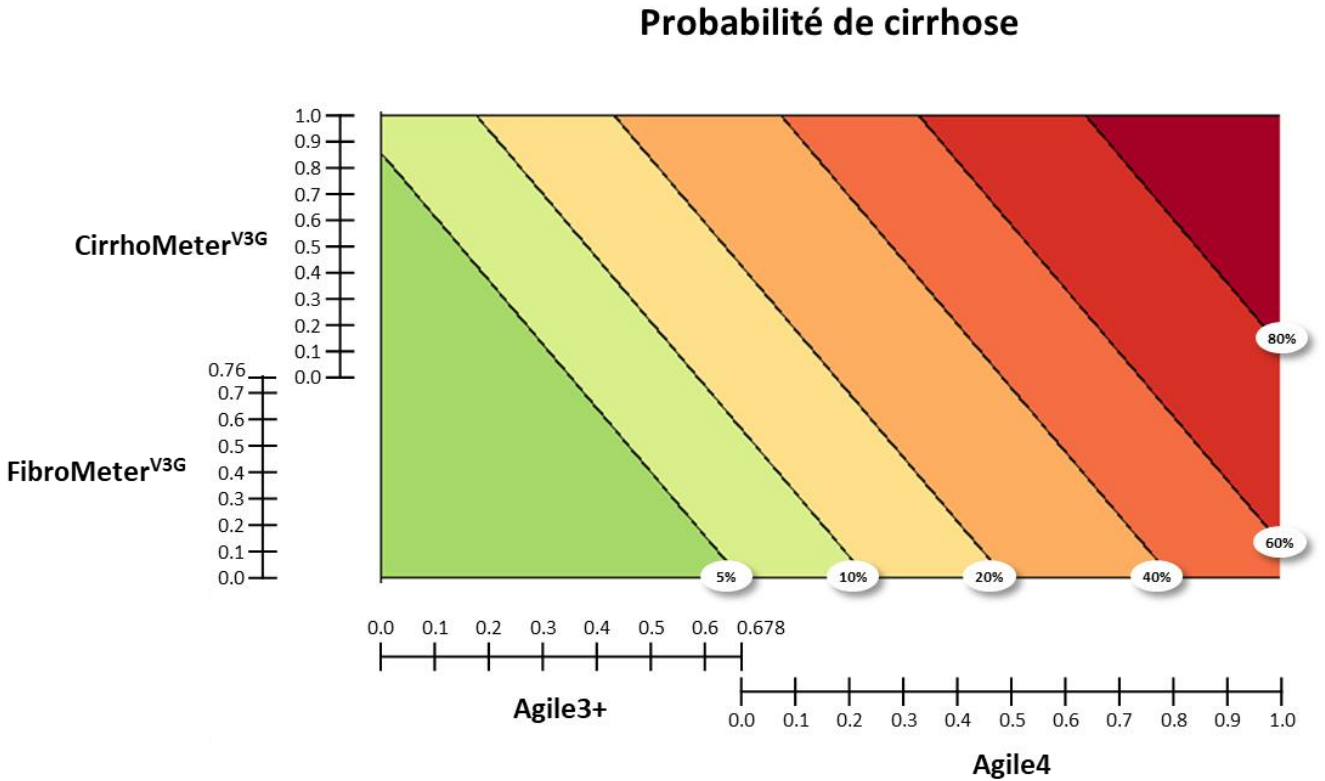
Validation in 314 NAFLD patients (Japan)



F0-1	**77**	**23**	**6**	Spe 94%
F2-4	13	52	143	Se 94%
	NPV 86%	24%	PPV 96%	

Tamaki, Hepatology 2022

Diagnostic non-invasif de cirrhose



Boursier, Nature Communications 2023

Conclusion

- Many NITs are now available for the evaluation of liver fibrosis in clinical practice.
- All guidelines are aligned on how to use them (sequence, thresholds) for the diagnosis of advanced liver fibrosis.
- NITs should be correctly performed and interpreted at each step of the diagnostic algorithms, to ensure a robust and correct diagnosis.
- Efforts should now be made to improve the diagnosis of moderate fibrosis, as a treatment is now approved for these patients.