We don't need a liver biopsy

We have non-invasive tests

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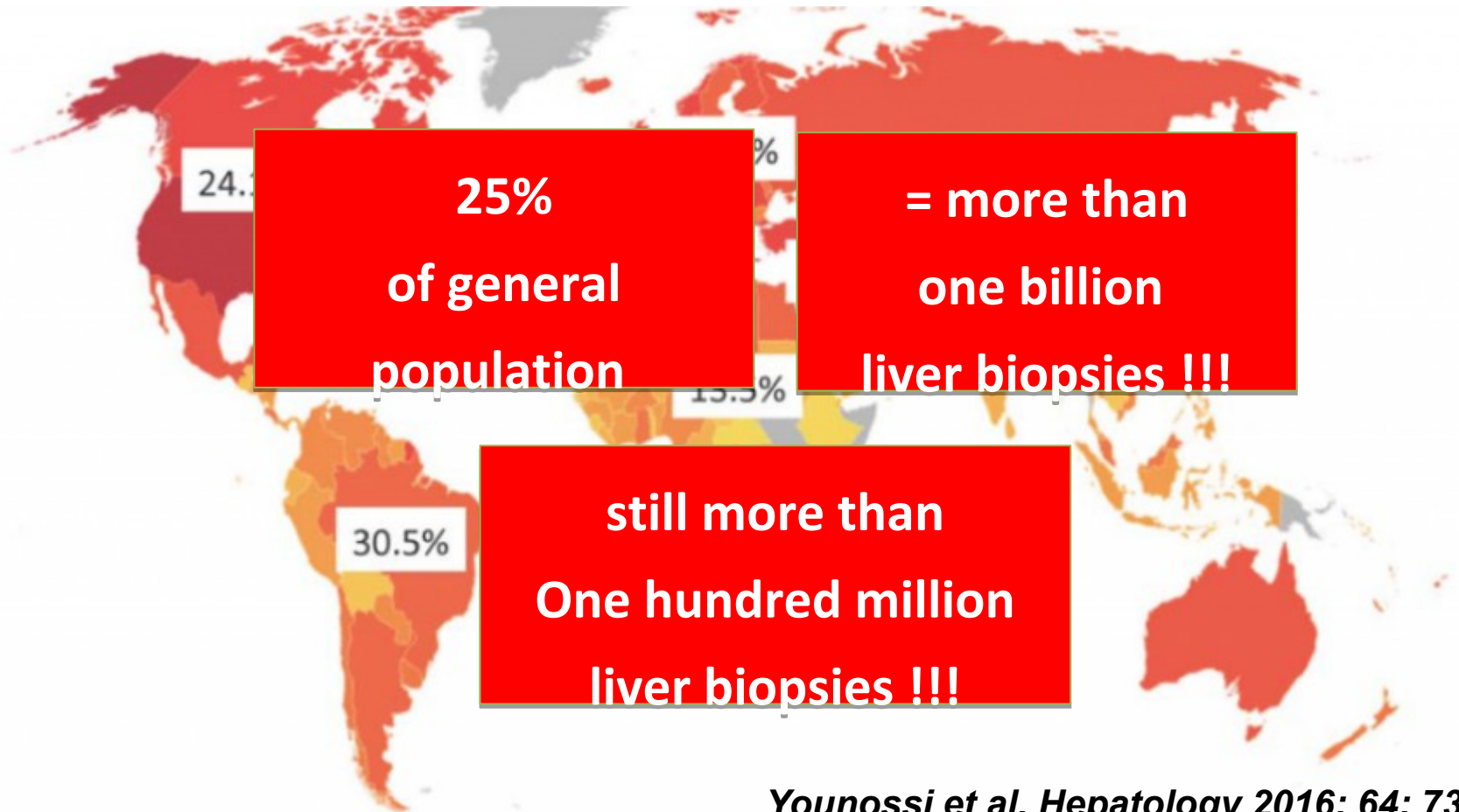*Université Paris Diderot, France*

PHC 2018 -
www.aphc.info

Liver biopsy:

an unrealistic and risky procedure

given the high prevalence of NAFLD

Diagnosing NAFLD with liver biopsy: a challenge!
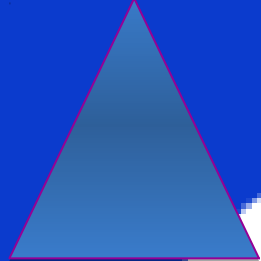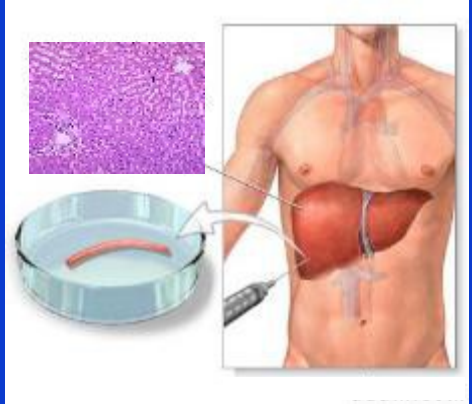
Worldwide prevalence of NAFLD

24.1%

25%

of general

population

= more than

one billion

liver biopsies !!!

13.5%

30.5%

still more than

One hundred million

liver biopsies !!!

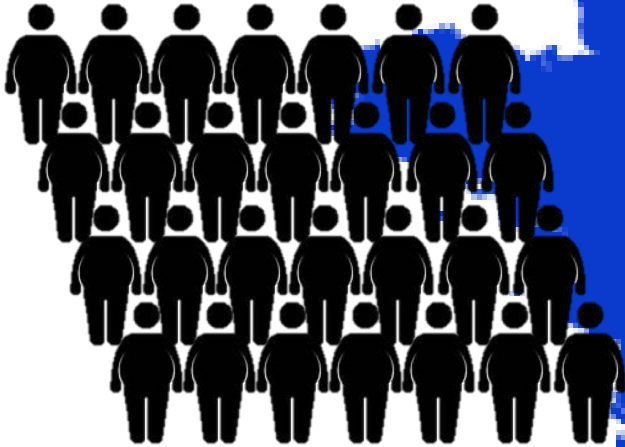*Younossi et al. Hepatology 2016; 64: 73-84*

Diagnosing NAFLD with liver biopsy: a challenge!

Patients

Hepatologists

3 - 6 million !

 # 400
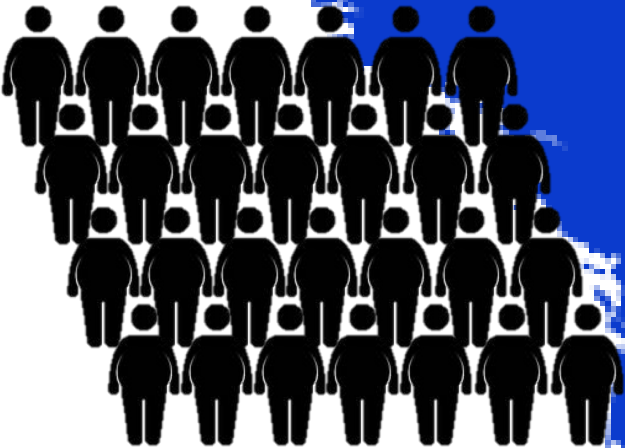
Diagnosing NAFLD with liver biopsy: a challenge!

Patients

3 - 6 million !

Hepatologists

400

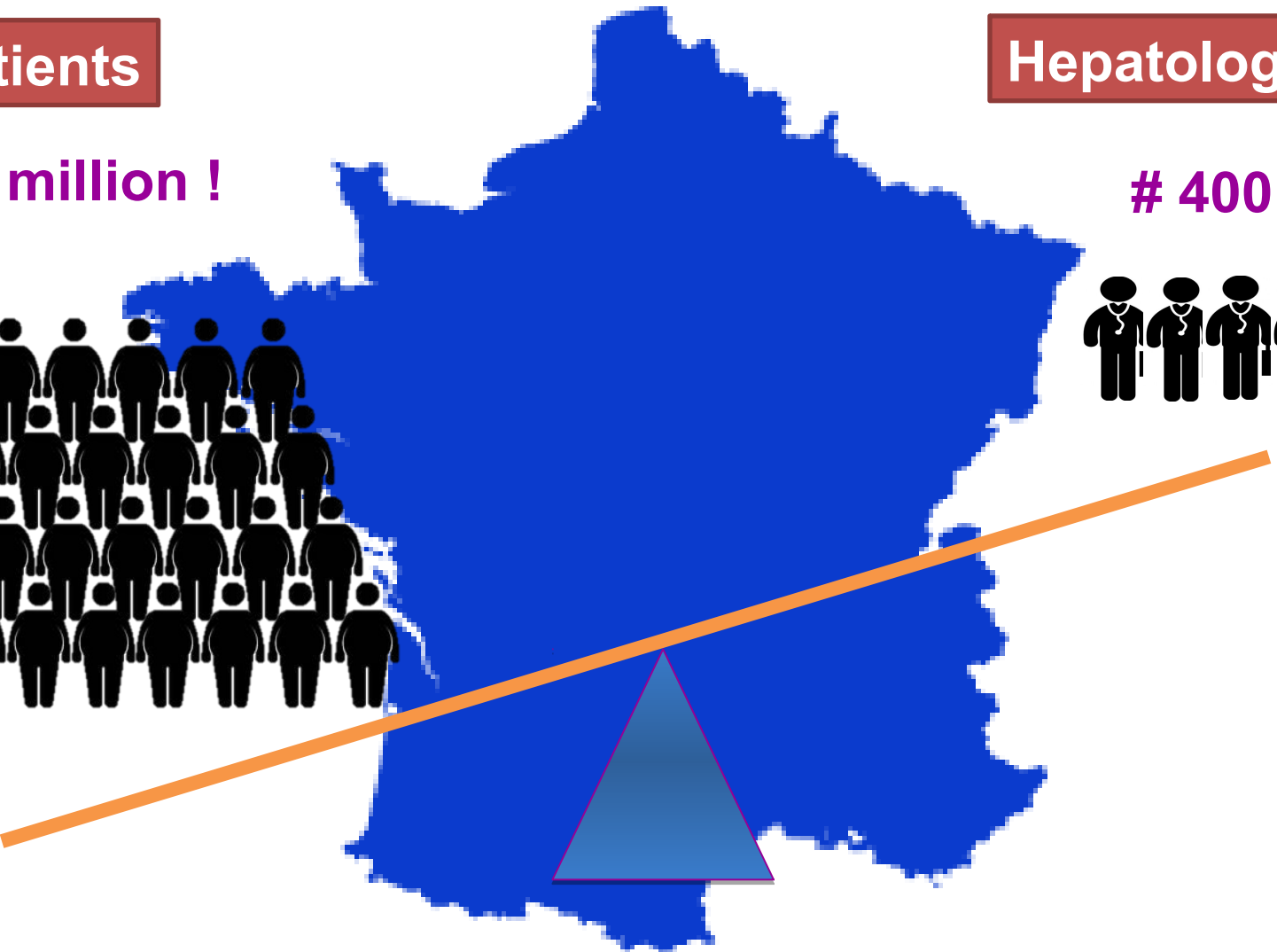# Diagnosing NAFLD with liver biopsy: a challenge!

Patients

3 - 6 million !

Pathologists

40

Inter-observer variability

Pathologist Experience

(Specialization, duration, academic practice)

Specimen Characteristics

Size, fibrosis stage
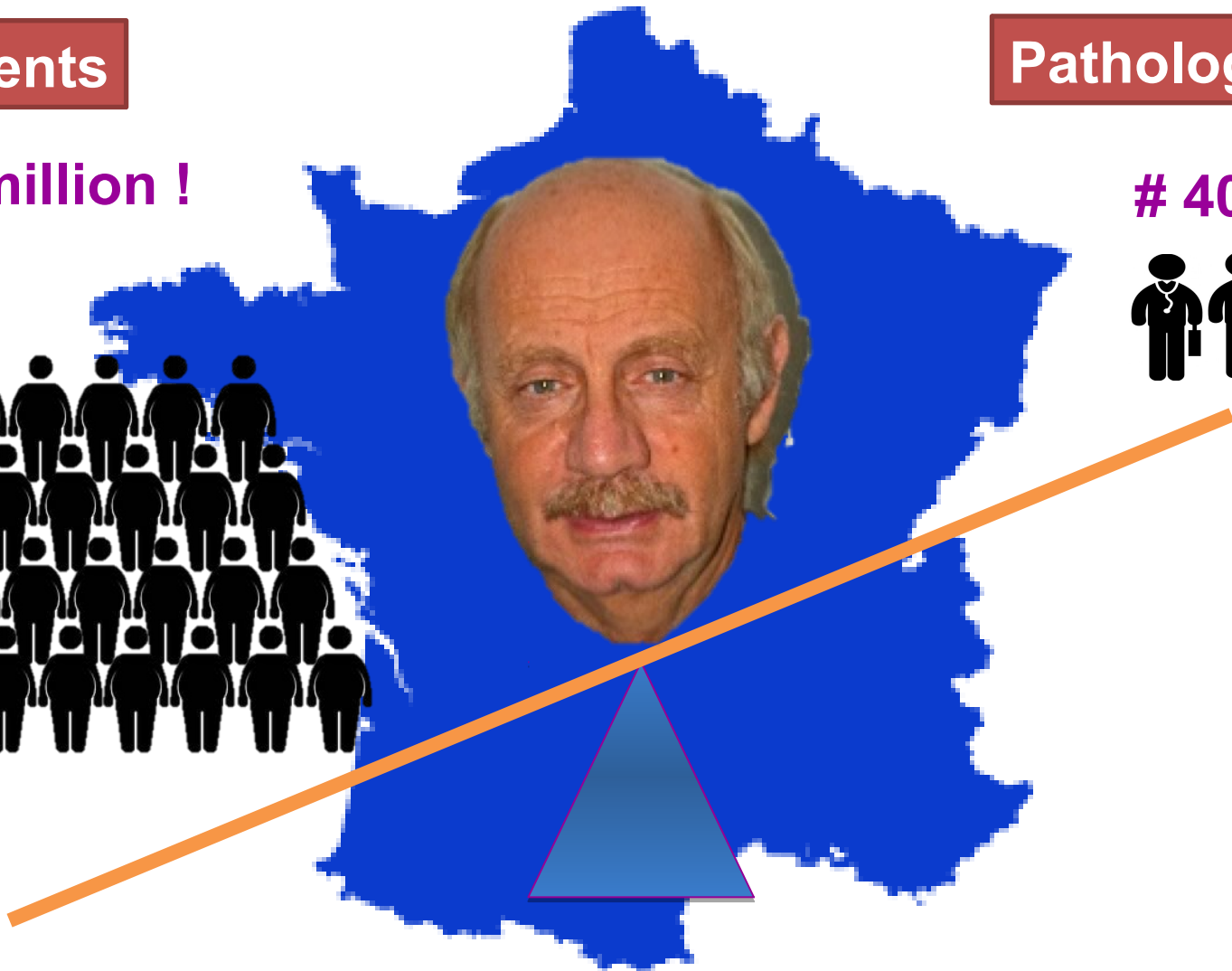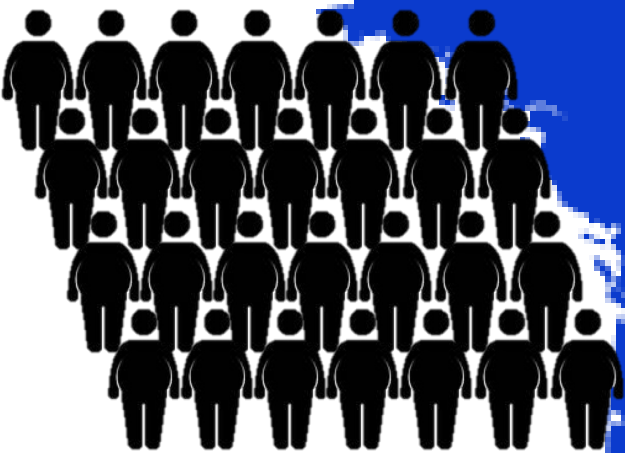
Rousselet et al. Hepatology 2005; 41: 257-64.
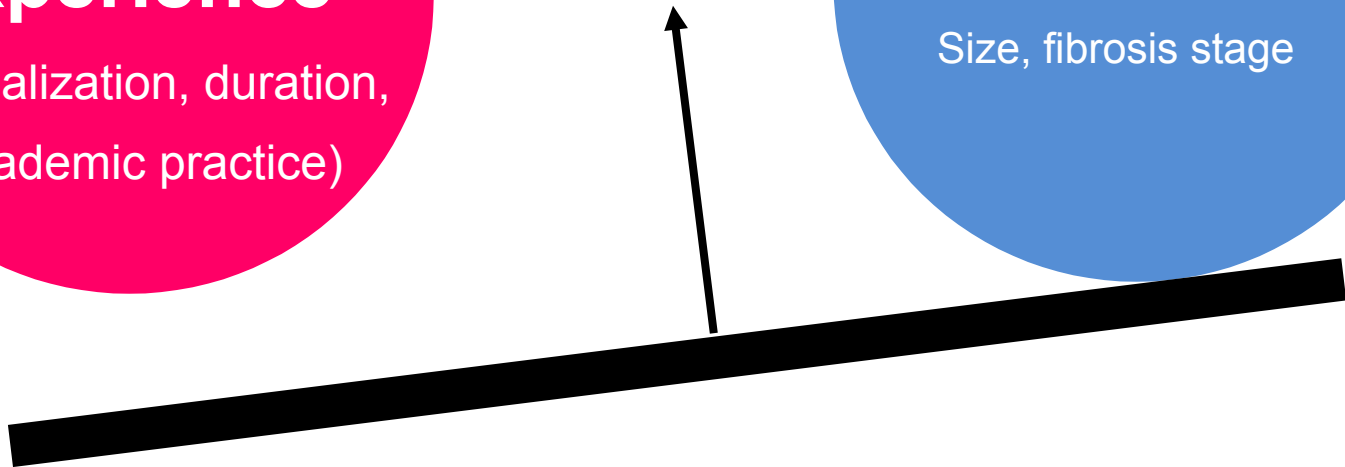
Limitations of liver biopsy

- Invasive

- Sampling error

- Interobserver variability

- Nondynamic evaluation of fibrosis

Regev et al. Am J Gastroenterol 2002; 97:2614-8
Bedossa et al. Hepatology 2003;38: 1449-57
Rousselet et al. Hepatology 2005; 41: 257-64.

The patient perspective !

Trends in liver biopsy practice:

HCV *vs.* HBV
The Beaujon Experience 2000-2013

Courtesy of Pierre Bedossa
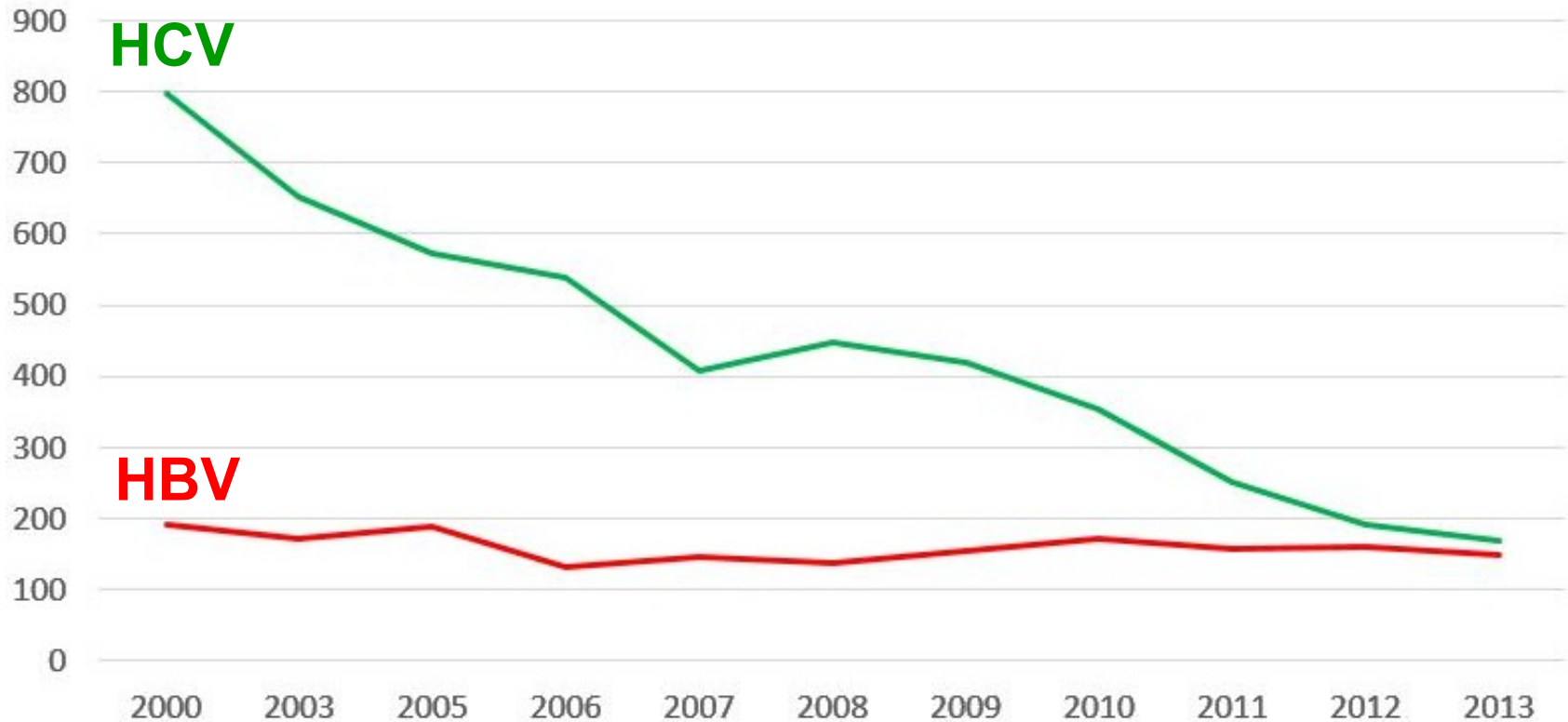
Non Invasive Tests:
An exponential increase in publications!
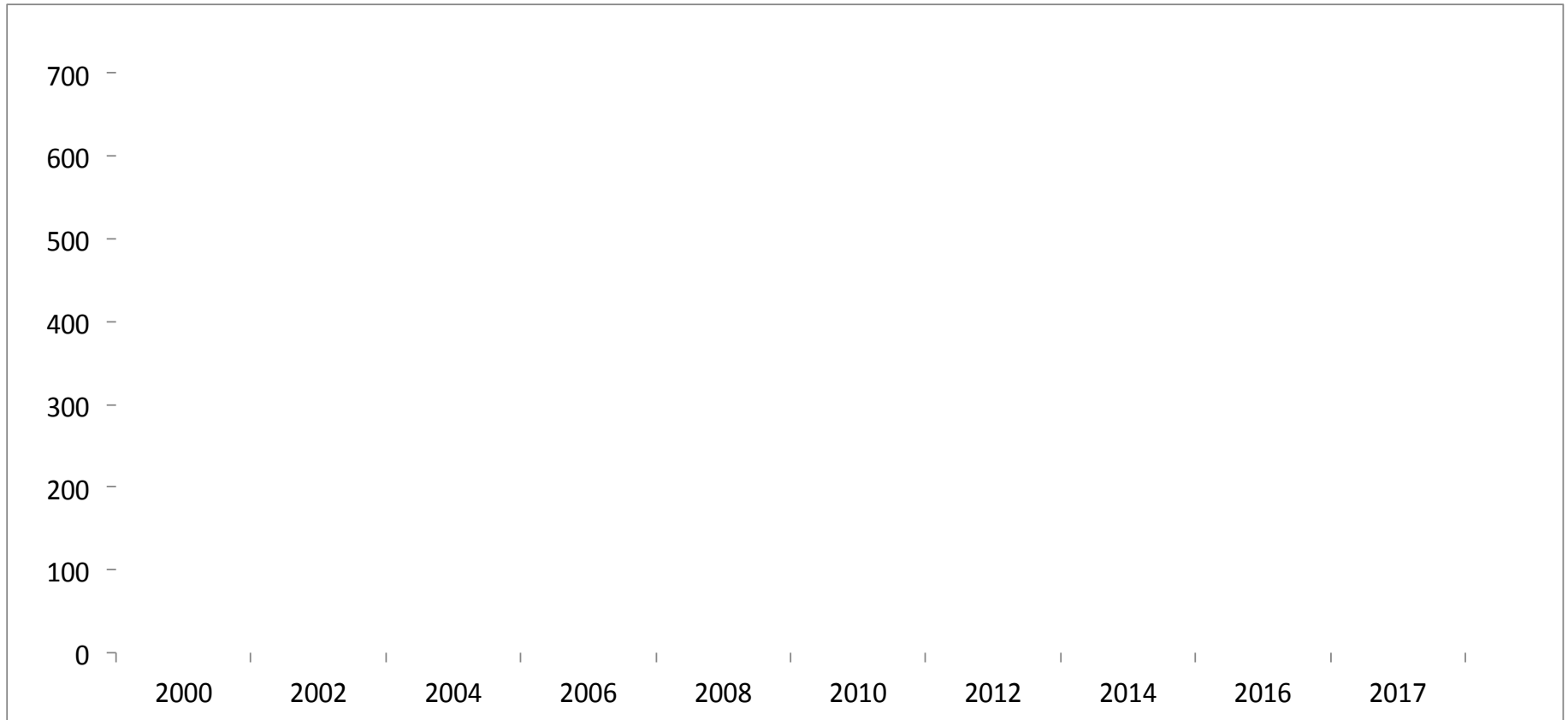
Source PubMed 2000-2017

Non-invasive tests
are ready for Prime Time

Non-Invasive Tests:
recommended by international guidelines

Recommendations for Testing, Managing, and Treating Hepatitis C

Hepatol Int (2017) 11:1–30
DOI 10.1007/s12072-016-9760-3

GUIDELINES

Asian-Pacific Association for the Study of the Liver (APASL) consensus guidelines on invasive and non-invasive assessment of hepatic fibrosis: a 2016 update

GUIDELINES FOR THE SCREENING, CARE AND TREATMENT OF PERSONS WITH HEPATITIS C INFECTION

Available non-invasive methods
2 different but complementary approaches

« Biological » approach   **« Physical » approach**

Serum Biomarkers   **CAP / TE   PDFF / MRE**

Serum Biomarkers *vs.* FibroScan
Summary

Serum biomarkers

- **Advantages**

  - Good reproducibility
  - High applicability (95%)
  - Low cost & wide availability
  (non-patented)

- **Disadvantages**

  - Non-specific for the liver
  - Performance for cirrhosis
  - Cost & availability (patented)

FibroScan

- **Advantages**

  - Genuine property of the liver
  - High performance for cirrhosis
  - User-friendly

- **Disadvantages**

  - Low applicability (80%)
  - False positive (inflammation)
  - Requires a dedicated device

Castera L. Gastroenterology 2012;142:1293-302.

Liver fibrosis is the main prognostic factor

Loomba R et al. Gastroenterology 2015; 149: 278-81

Liver fibrosis is the main prognostic factor

Loomba R et al. Gastroenterology 2015; 149: 278-81
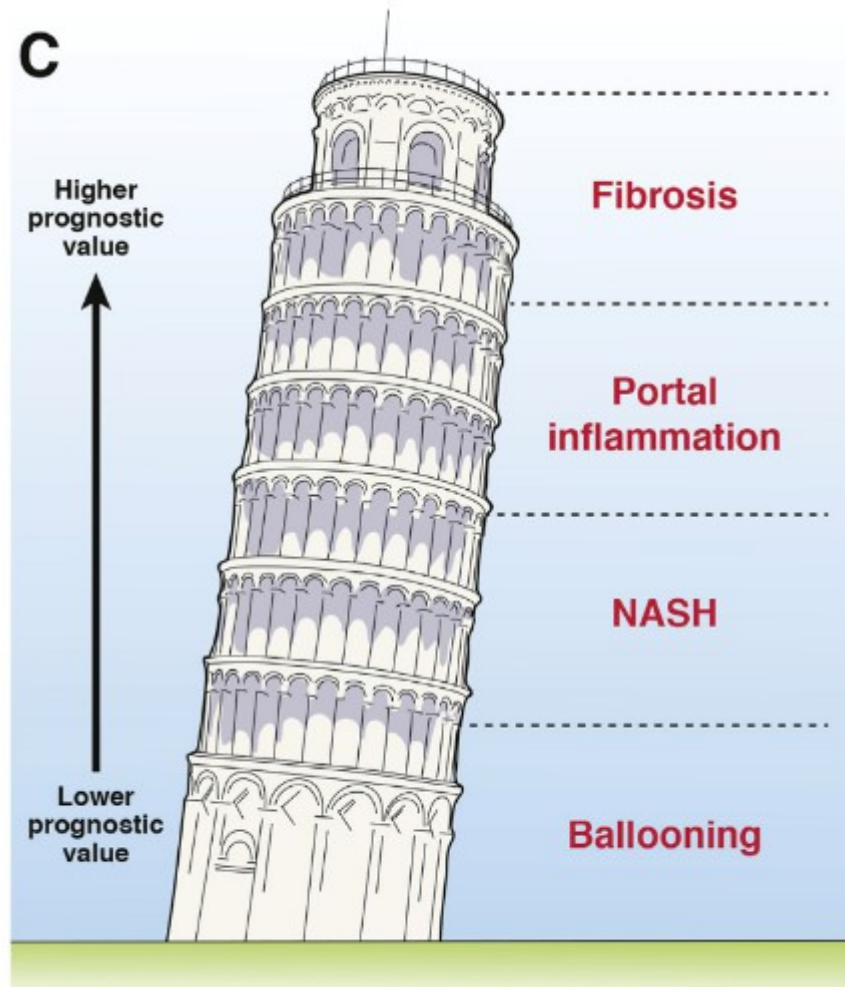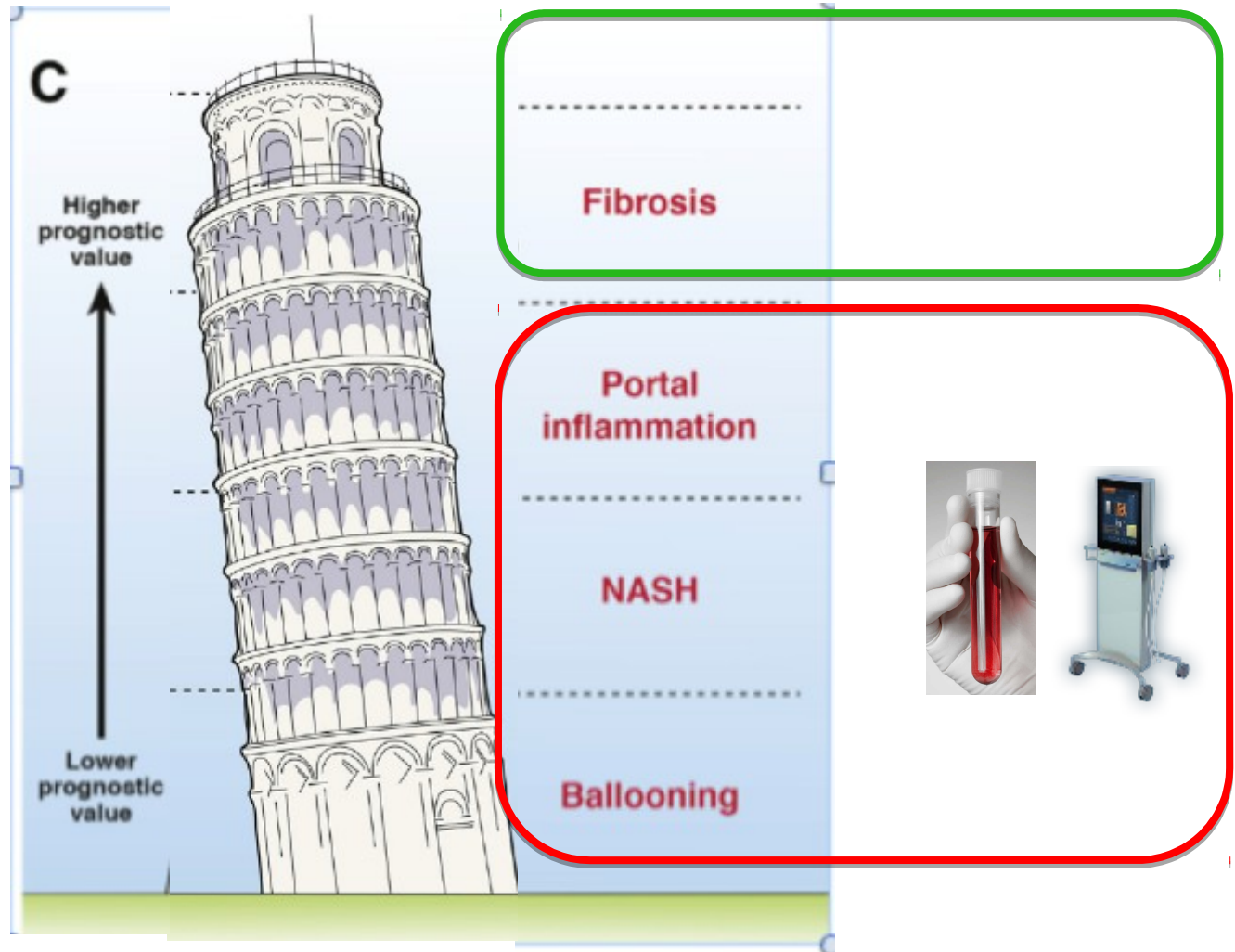
Mortality is related to cirrhosis

Total number of deaths

Log-rank test: p<0.001

P<0.001

F1-F2

F3-F4
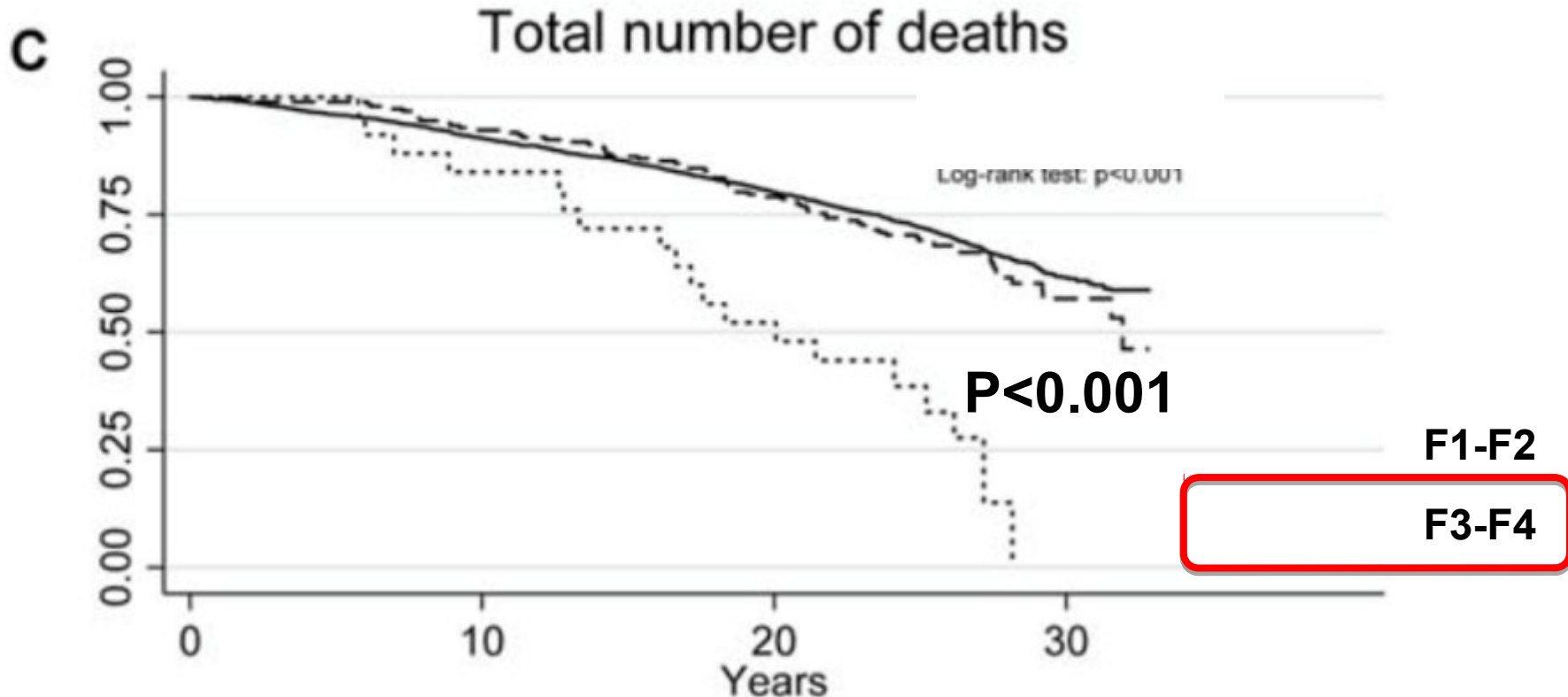
N=229 NAFLD patients ; f-up 26.4 yrs

Ekstedt M et al. Hepatology 2015: 61; 1547–54

TE has high diagnostic accuracy for viral cirrhosis

	Number of included studies	Number of included subjects for analysis	AUROC
			F4
Talwalkar[15]	<u>9</u>	<u>2,083</u>	0.957
Stebbing[16]	<u>22</u>	<u>4,760</u>	0.94
Fredrich-rust et al[17]	<u>50</u>	<u>8,206</u>	0.94
Tsochatzis et al[18]	<u>40</u>	<u>7,723</u>	N/A
Chon et al	<u>18</u>	<u>2,772</u>	**0.929**

Talwalkar et al. CGH 2007   Friedrich-Rust et al. Gastroenterology 2008
Stebbing et al. APT 2010 Tsochatzis et al. J Hepatol 2011   Chon et al. PLoS ONE 2012

TE has high diagnostic accuracy for NAFLD cirrhosis

Meta-analysis

Sum AUROCS: 0.94

Sum Se: 87%   **Sum Sp: 86%**

DOR=44.0
(C2)-FibroScan M
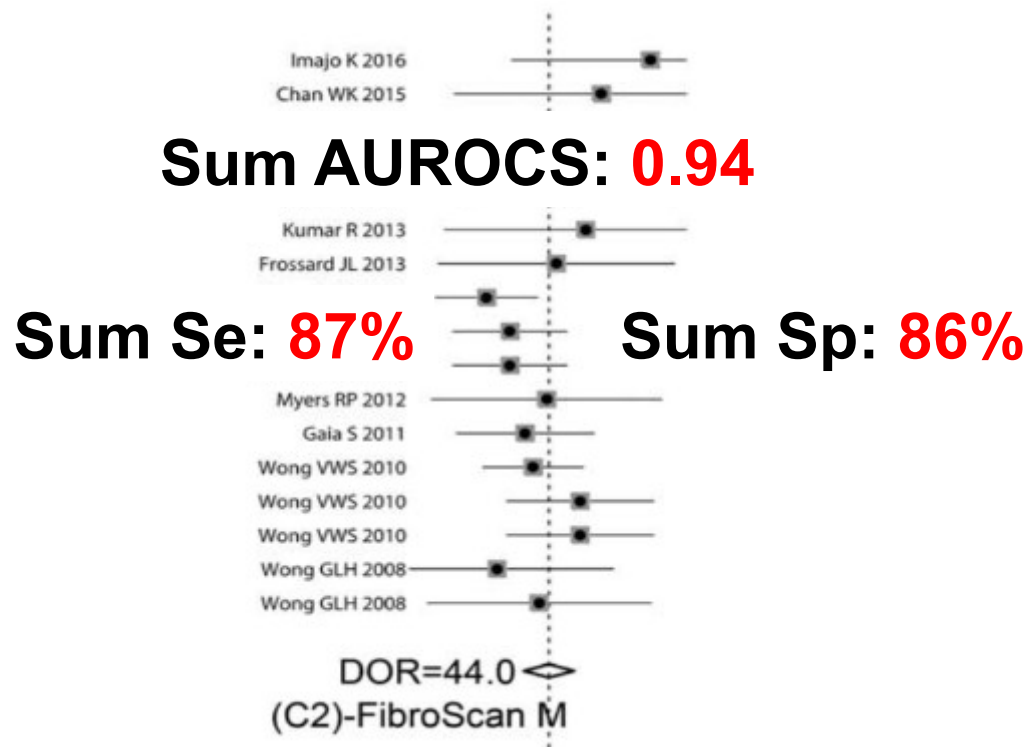
13 studies; n= 1780 patients

Xiao et al. Hepatology 2017; 66: 1486-501

Recommendations
Cirrhosis diagnosis

- TE is a reliable method for the diagnosis of cirrhosis in patients with chronic liver diseases, that generally performs better at ruling out than ruling in cirrhosis (with negative predictive value higher than 90%) (**A1**)

Use in clinical practice

Ultrasound
(steatosis biomarkers[1])/
Liver enzymes[2]

Steatosis present   **Steatosis absent**

**Normal
liver enzymes**   **Abnormal[3]
liver enzymes**   **Normal
liver enzymes**

Serum
fibrosis markers[4]

Low risk[5]   Medium/high risk[5]

Follow-up/2 years   Specialist referral   Follow-up/3-5 years

Liver enzymes,
fibrosis biomarkers   Identify other chronic liver diseases
In-depth assessment of disease
severity   Ultrasound/liver
enzymes

Decision to perform liver biopsy
Initiate monitoring/therapy

Non-invasive tests have prognostic value in NAFLD

Serum biomarkers

NFS <-1.455

NFS >0.676
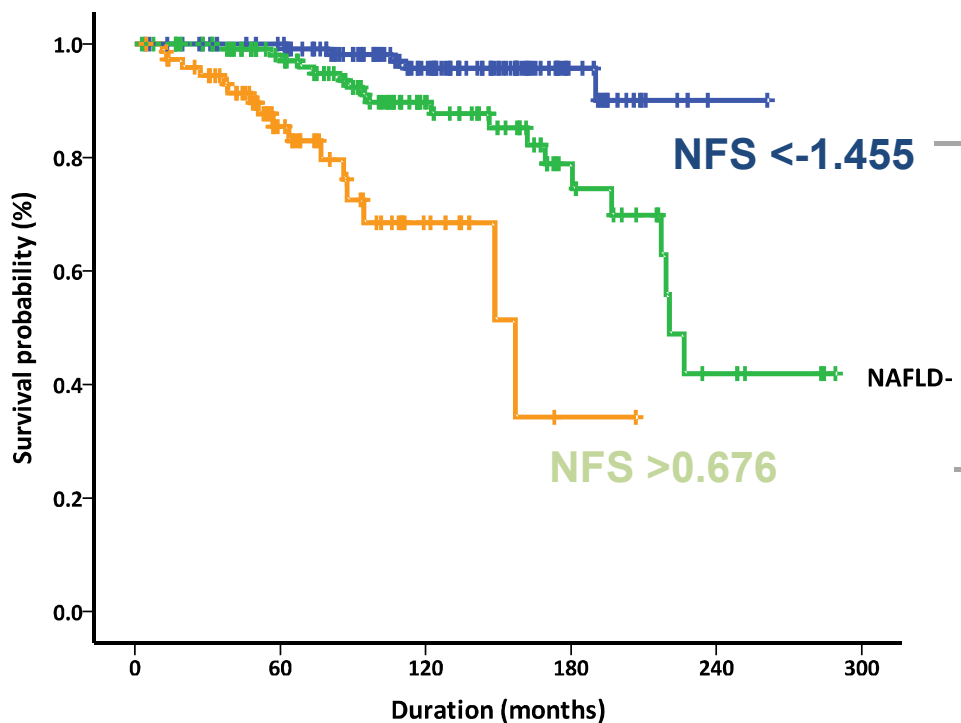
NAFLD-

N= 320 NAFLD patients ; F-up 105 mo

Angulo et al. Gastroenterology 2013; 145: 782-9

Liver stiffness

F0-2
8.8
F2/3
12.0
F3/4
38.6
F4

p <0.001
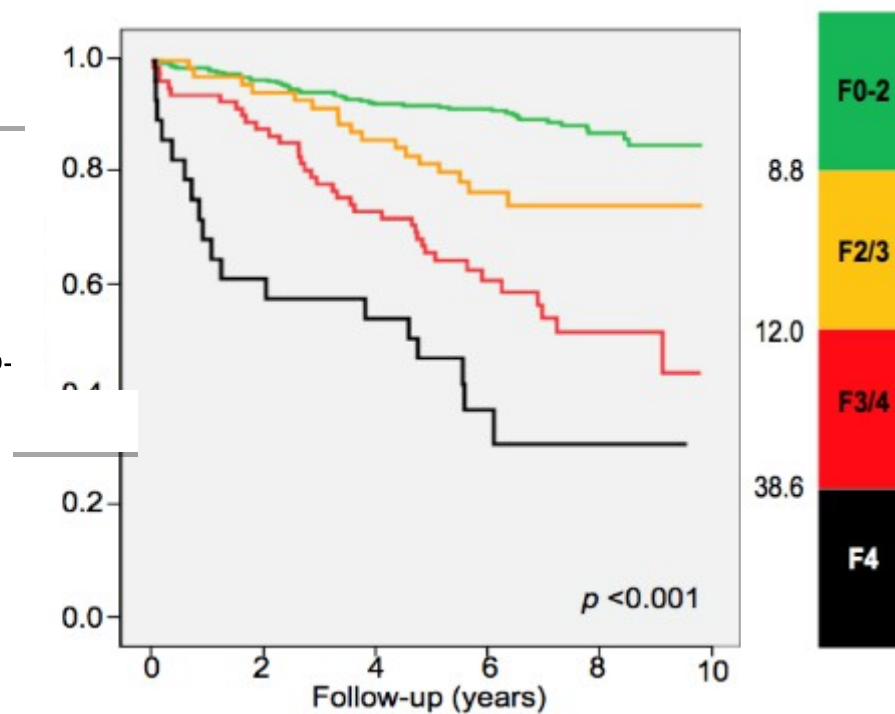
N= 360 NAFLD patients; f-up 6 yrs

Boursier et al. J Hepatol 2016; 65: 570-78

Screening the general population

for NAFLD

using non-invasive tests

Screening general population for NAFLD

The typical NAFLD patient

- Asymptomatic

- Low awareness

- Low risk-perception

- No approved treatment

Tru MP et al. J Fake News 2017; in press

Screening General population
FibroScan

1 335 subjects

58 ans
%
26.5 kg/m2

LSM failure
(n=51)

Unreliable LSM
(n=94)

1 190 subjects

1 101 subjects with
LSM < 8.0 kPa

80 subjects with
8.0 ≤ LSM ≤ 13.0 kPa

9 subjects with
LSM > 13.0 kPa

F>2 7.5%

F4 0.7%

Roulot et al. Gut 2011; 60: 977-84

Scre...n

7554 Subjects pre-included
Consultation and serum

33 (0.4%) FibroTest not interpretable

7521 (99.6%) FibroTest Interpretable

57 ans

kg/m2

16 Refused protocol

13 Subjects duplicate

10 Younger t...

7521 (99.6%) FibroTest Interpretable

7482 Included

19 With previous history Of liver disease

7463 Without previous history Of liver disease

Fibrosis (≥2)   2.8 %

Cirrhosis   0.3%

Screening General population
MRI-Spectroscopy/ FibroScan

3000 invitations sent

1069 responded

52 had contraindications to magnetic resonance imaging
1 failed magnetic resonance spectroscopy
91 had hepatitis B infection
3 had hepatitis C infection

922 underwent proton-magnetic resonance spectroscopy

NAFLD 29%

264 had intrahepatic triglyceride content ≥5.0%

658 had intrahepatic triglyceride content <5.0%

217 had valid liver stiffness measurement by transient elastography

542 had valid liver stiffness measurement by transient elastography

F3-F4 1%

8 had liver stiffness ≥9.6 kPa

7 had liver stiffness ≥9.6 kPa

Age   48 ans
H   42 %
BMI   23 kg/m2

Wong V et al. Gut 2012; 61: 409-15
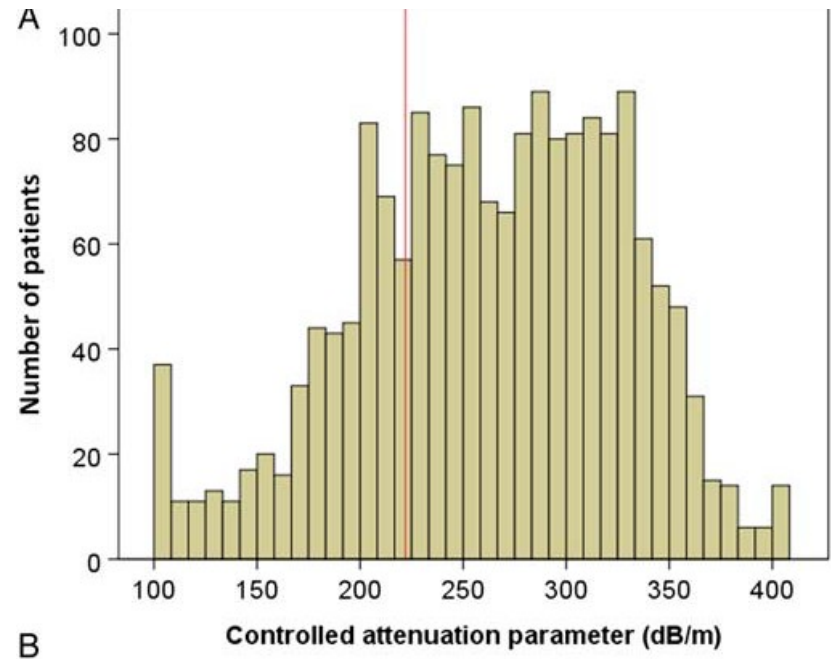
Screening Diabetics
CAP/ FibroScan

N= 1918 Chinese diabetics patients

NAFLD (CAP >222 dB/m) **73%**   **F3-F4** (LSM >9.6 kPa) **18%**

Kwok et al. Gut 2016; 65: 1359-65
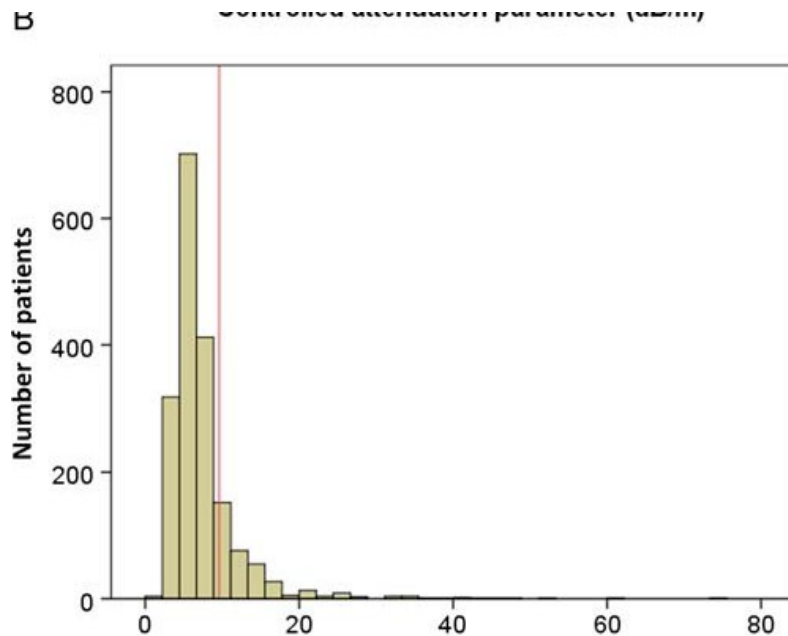
Screening Diabetics
CAP/ FibroScan

N= **435** French diabetics patients

NAFLD (CAP >236 dB/m) **75%**   **F3-F4** (LSM >9.6 kPa) **7.3%**

Roulot et al. Liver Int 2017; 37: 1897-06
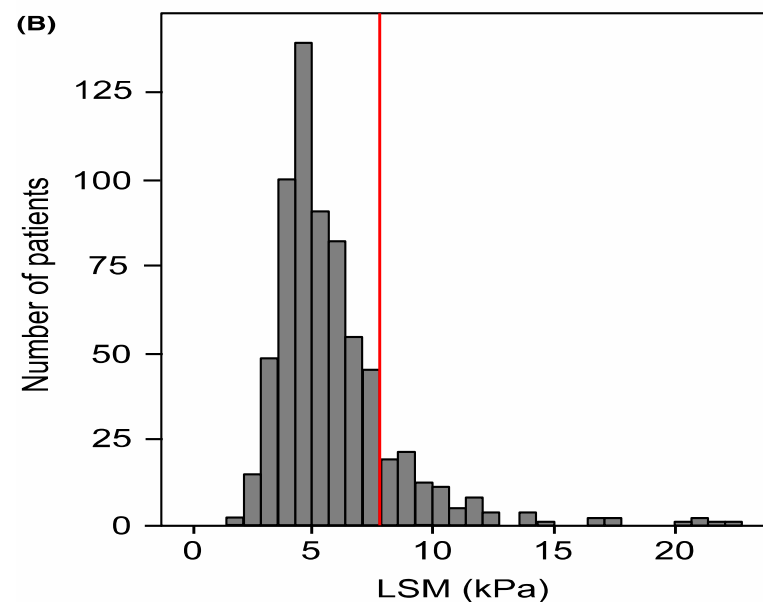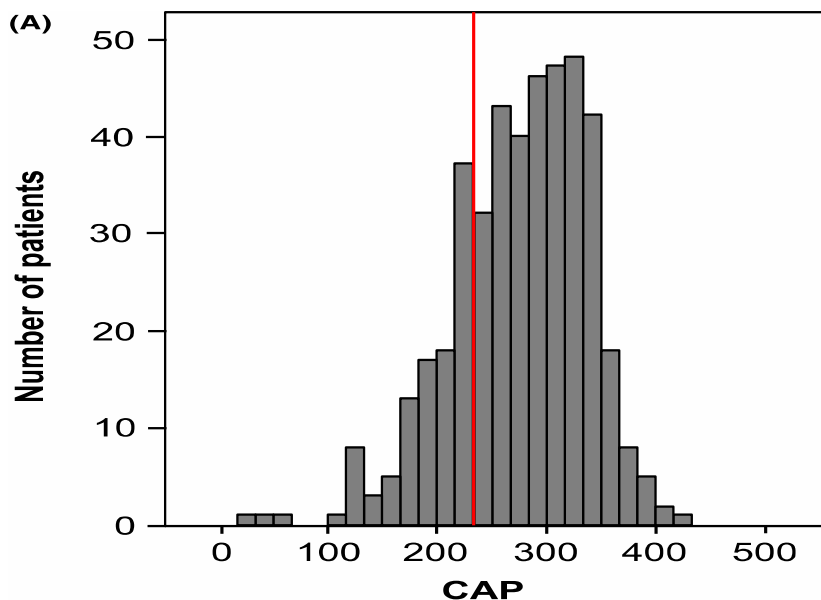
Summary

Methods for fibrosis assessment	Prevalence of fibrosis ≥F2 (result of test)	Prevalence of cirrhosis (result of test)	Common causes
FibroTest	2·8% (>0·48)	0·3% (>0·75)	NAFLD
Transient elastography	7·5% (>8 kPa)	0·6% (>13 kPa)	NAFLD
Transient elastography	5·6% (>8 kPa)	0·7% (>13 kPa)	NAFLD
Transient elastography	18% (>9·6 kPa)*	11% (>11·5 kPa)	NAFLD
Transient elastography	27% (>8 kPa)	..	NAFLD, alcoholic liver disease

Gines P ... Castera L. Lancet Gastroenterol Hepatol 2016; 1: 256-60

Take Home Message

NIT

Triage
in large
unselected
populations

Liver biopsy

Assessment
in selected
populations or
in clinical
trials

**Best used as an integrated system
to allow more efficient evaluation
of patients with NAFLD**