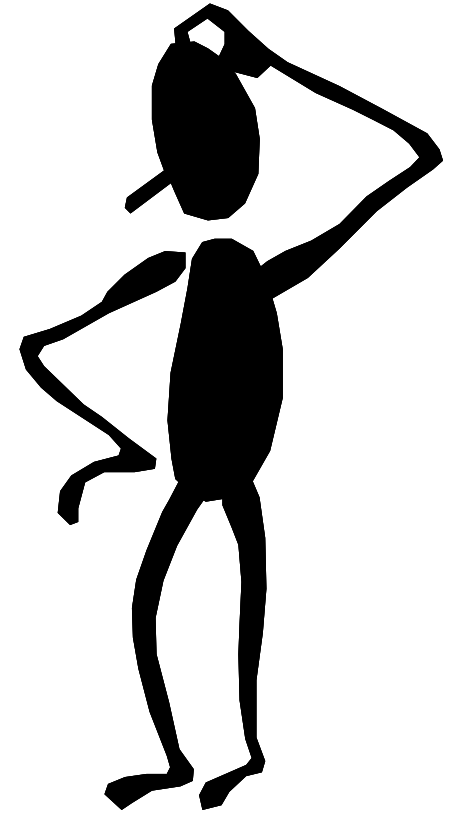
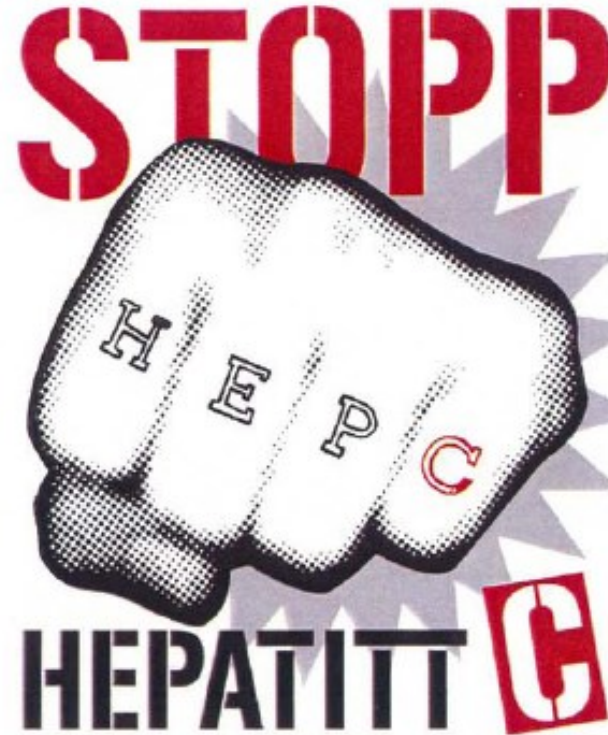


Liver Disease Assessment Among PWID: The Role of Transient Elastography



Peer Brehm Christensen,
Professor
Department of Infectious Diseases
Odense University Hospital Denmark
Peer.christensen@dadlnet.dk

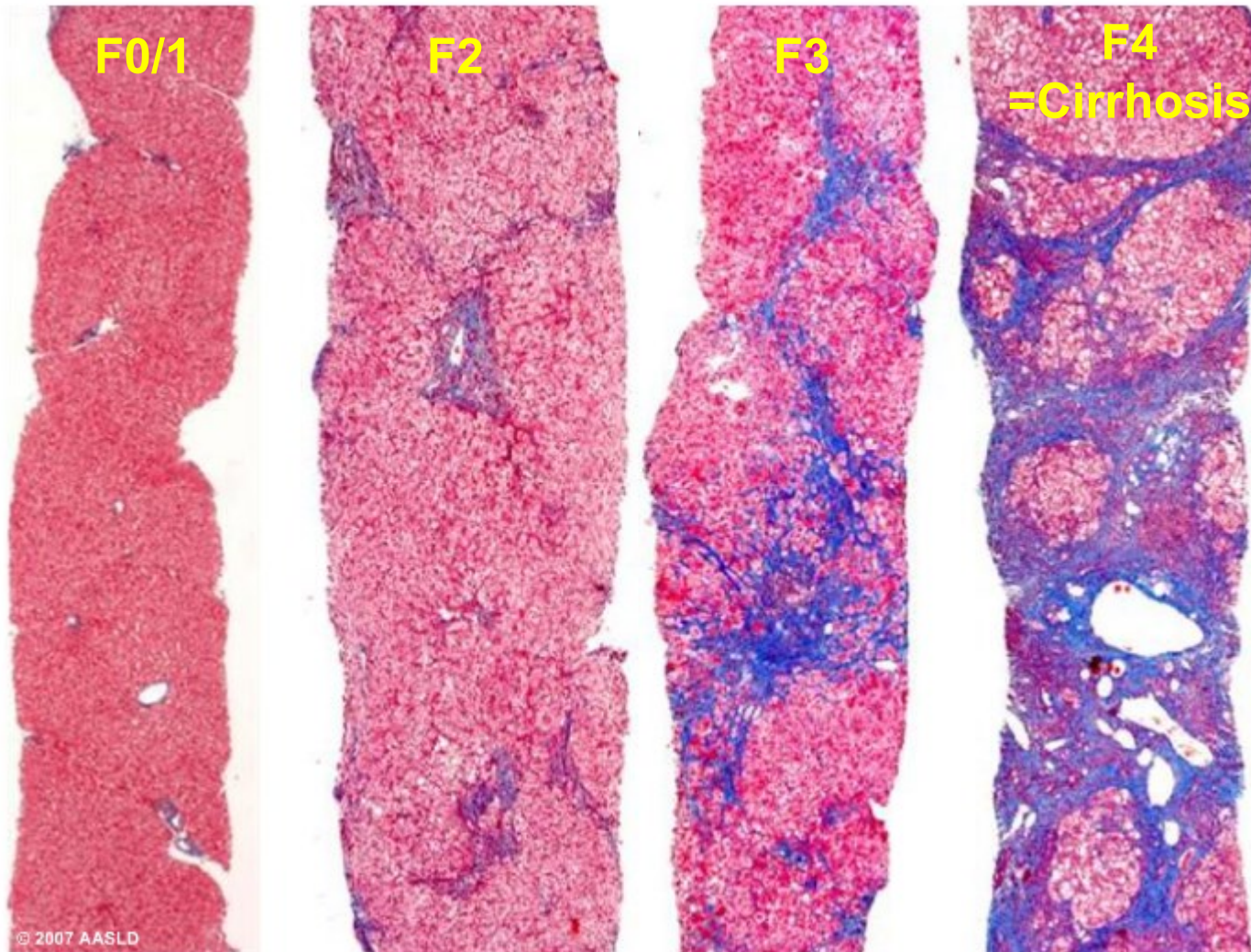
Disclosures

- I have received research grants from
 - Roche, Schering-Plough, Gilead, and Abbvie
 - Echosens have facilitated a Fibroscan device for my research

Why bother about liver fibrosis ?

- Because:
 - As long as we cannot afford to treat everyone with hepatitis C, we should at least identify and treat the patients at risk of complications
 - These patients are characterized by fibrosis of the liver.

Liver biopsy is the "gold" standard: Metavir fibrosis score



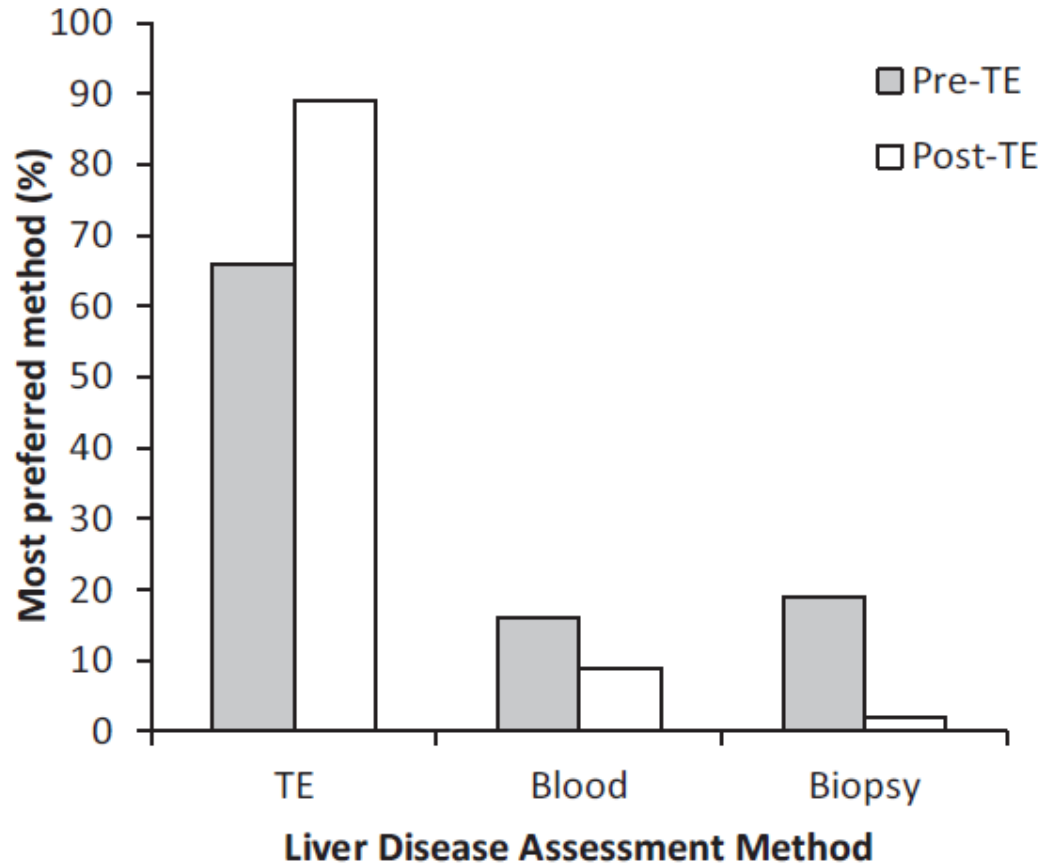
Non-invasive diagnosis of liver fibrosis

- (Clinical signs)
- Image modalities (ultrasound)
- Blood test
- Liver stiffness measurement (LSM) (transient elastography)

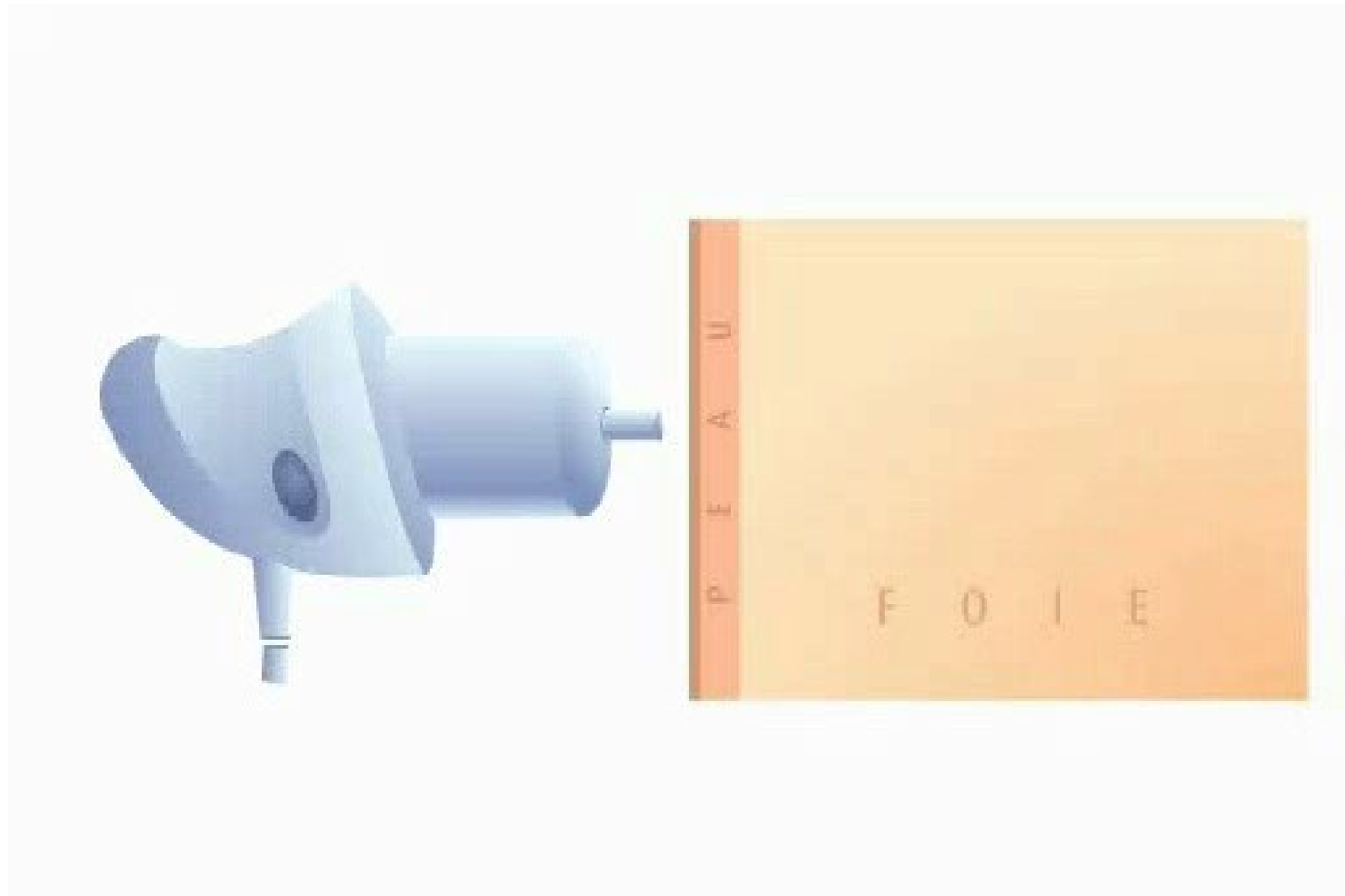
	APRI (low cut-off)	APRI (high cut-off)	FIB-4 (low cut-off)	FIB-4 (high cut-off)	Transient elastography (FibroScan®)
Significant fibrosis (METAVIR \geq F2)	0.5	1.5	1.45	3.25	7–8.5 kPa
Cirrhosis (METAVIR F4)	1.0	2.0	-	-	11–14 kPa

APRI: aminotransferase/platelet ratio index; kPa: kilopascal

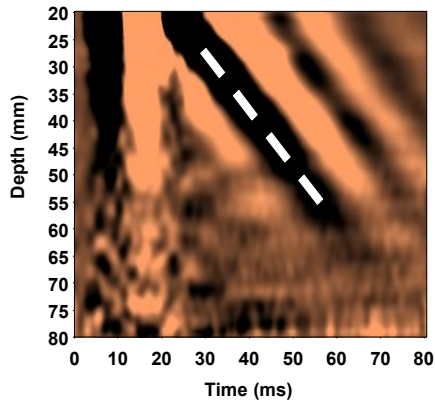
LSM is the preferred test for fibrosis among PWID



Liver stiffness measurement (Fibroscan®)



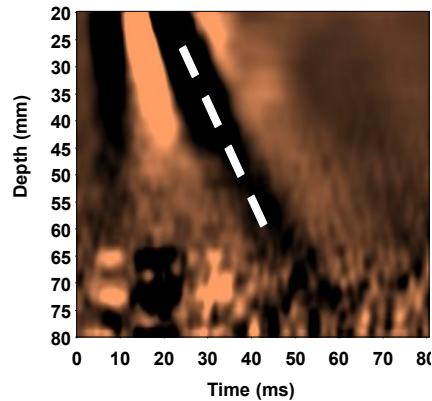
Liver stiffness varies with fibrosis



$V_s = 1.1 \text{ m/s}$
 $E \sim 3 \text{ kPa}$

F0

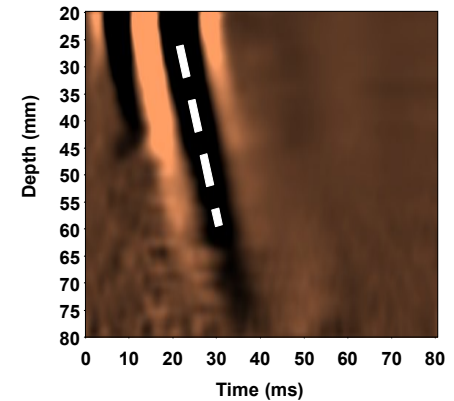
Normal liver



$V_s = 1.7 \text{ m/s}$
 $E \sim 9 \text{ kPa}$

F2

Fibrosis



$V_s = 3.6 \text{ m/s}$
 $E \sim 40 \text{ kPa}$

F4

Cirrosis

Problems with fibroscan

- **Overestimation**
 - Measurement near the liver capsule
 - Overweight
 - Narrow intercostal space
 - Post prandial examination
 - Heart failure (liver stasis)
 - Steatosis(?)
 - ALT elevation
 - Liver inflammation
 - ????
- **Invalid measurements are not rare**
 - In one out of 10 patients examination is difficult
 - With XL probe for obese patients and repeated measurement <1%

Criteria of a valid LSM (Fibroscan) 2016

- 10 Measurements
- IQR/median $<0,30$ (if median $> 7\text{kPa}$)
- EASL guidelines
 - Fasting examination (2 hours)
 - XL probe if BMI >30 /skin capsule distance $>25\text{mm}$
 - ALT $<5 \times \text{ULN}$
 - No cholestase, heart failure / "congestive liver"
 - No ongoing alcohol abuse

Boursier. Hepatology 2013;57;1182-91

EASL Non-invasive tests J.hepatol 2015; 63:237-64

Cut-offs for fibrosis (F2+) and cirrhosis (F4) among patients with hepatitis C by LSM

- 183 HCV patients with liver biopsy and LSM
- Male 57%, Mean age 51Y
- Metavir F1 26% F2 29% F3 20% F4 25%

LSM Value	F \geq 2	F \geq 3	F = 4
Optimal cut-off ^a (kPa)	7.1	9.5	12.5
Sensitivity	.67	.73	.87
Specificity	.89	.91	.91
Positive predictive value	.95	.87	.77
Negative predictive value	.48	.81	.95

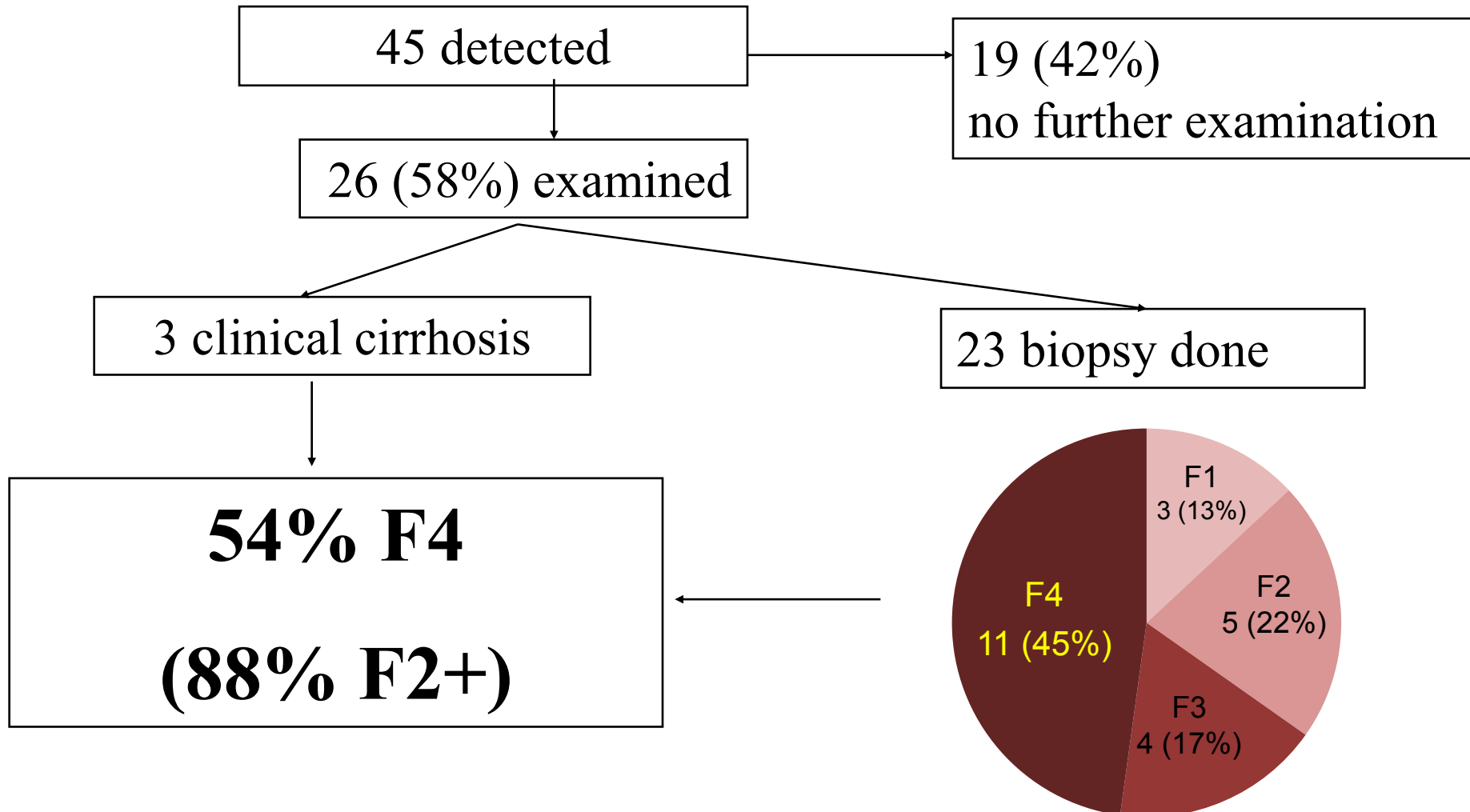
^aThe optimal cut-off values are those giving the highest sum of sensitivity + specificity.

USA LSM validation study

- Development cohort : 188 (95%HCV)
- Validation cohort 560 (92%HCV)
- Development F0/1 56% F2/3 24% F4 20%
- Validation F0/1 33% F2/3 52% F4 15%

METAVIR LSM cutoff (kPa)		Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)		DA (%)		LR+	LR-
F _≥ 2	8.4	81.9	.042	79.0	.741	75.6	.155	84.7	.012	80.3	.012	3.91	0.23
		57.9		74.9		80.8		55.0		70.5		2.11	0.41
F _≥ 3	9.6	88.3	.192	81.9	.888	68.8	.112	93.7	.062	83.5	.075	4.71	0.14
		71.8		80.1		62.0		88.6		77.0		3.23	0.26
F4	12.8	84.2	.512	86.0	.945	60.4	.009	95.6	.245	85.6	.098	6.02	0.18
		75.9		85.1		41.6		97.6		79.8		4.09	0.14

Clinical evaluation of PWID with LSM ≥ 12 kPa



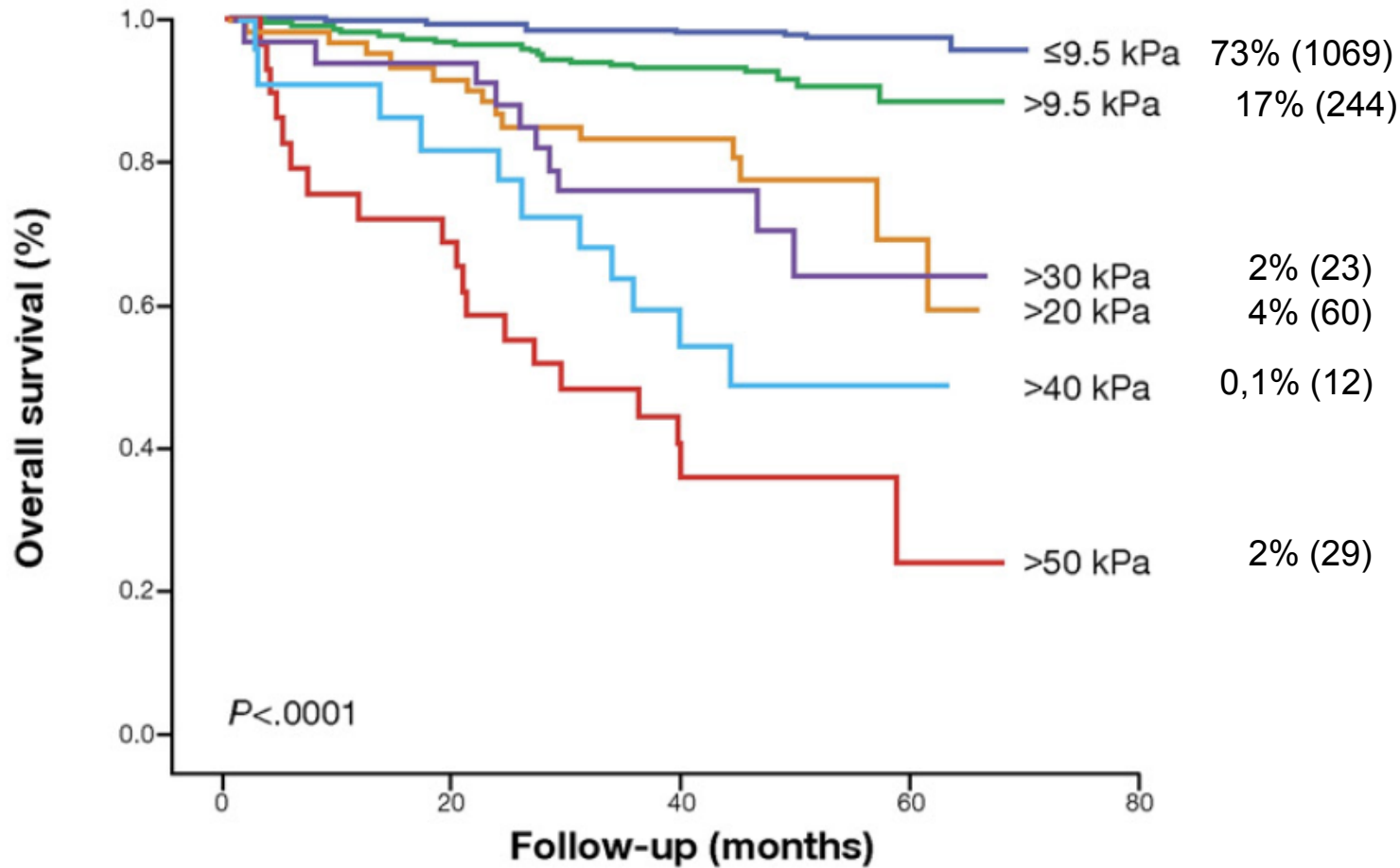
The French multicenter study (FIBROSTIC)

- N = 1307 (70% HCV)
- The diagnostic accuracy was high for cirrhosis, but poor for significant fibrosis (F2).
- A cut off of 17 kPa to rule in cirrhosis had a LR+ of 5.1 (and identified 72% of patients with cirrhosis)

	METAVIR score		Total
	= F4	< F4	
Elasticity			
≥ 12.9 kPa	127 (54%)	111	238
< 12.9 kPa	54 (5%)	1015	1069
Total	181	1126	1307

Baseline LSM and survival among patients with HCV

N =1457
Males 53%
Age
51Y(mean)
F4 18%
HIV 10%



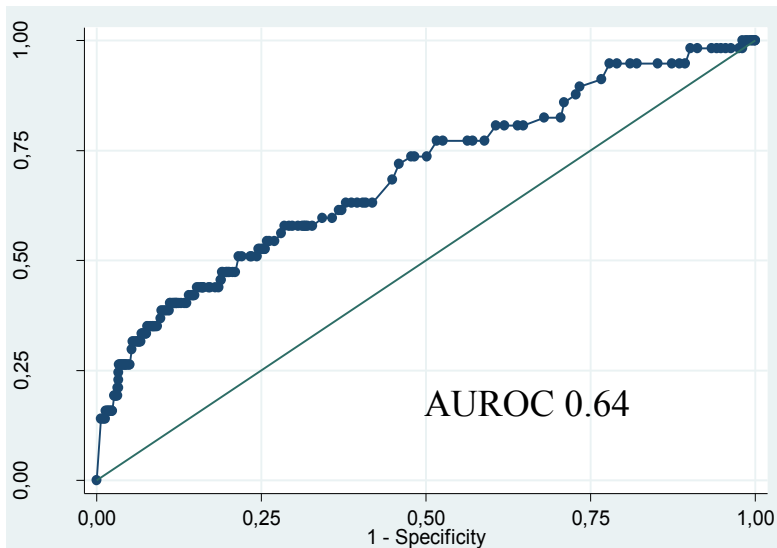
Overall mortality:
6.6% (93) ~ 1.6/100py

Liverrelated mortality
3.6%(53) ~ 0.9/100py

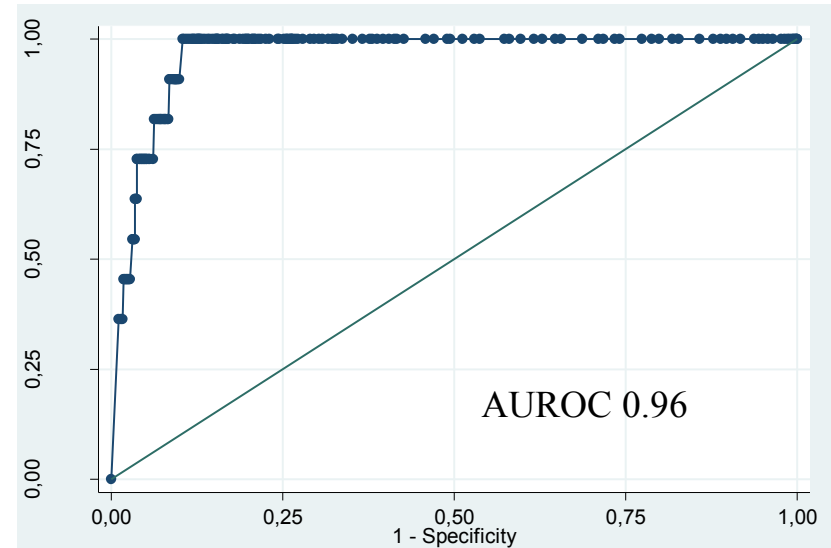
Mortality among HCV infected

- Crude mortality 2.4/100py (51/587)
 - Liver related 0.6/100py
 - Drug related causes. 0.5/100py

Overall mortality



Liver related death



- No liver related deaths below 17.6 kPa at first LSM (median 65 kPa, iqr 27-75)

LSM instead of gastroscopy can be used as screening for varices

Baveno VI recommendation

- If a patients with cirrhosis has LSM $<20\text{kPa}$ and platelets >150
 - Gastroscopy is not indicated as the risk of significant varices is $<2\%$
 - These patients can be screened by yearly LSM

LSM to rule in and rule out liver fibrosis

- 7 kPa is safe
- 10 kPa is trouble
- 17 kPa is cirrhosis

- But what about the grey zone (7-10kPa)?

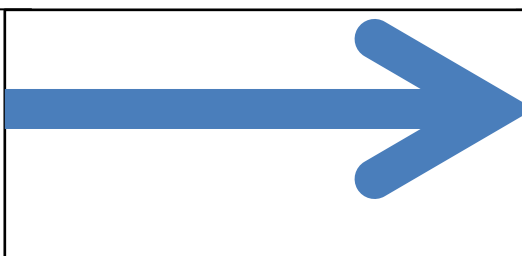
HCV 396 untreated during median 36 month of follow-up

Baseline
distribution

End of FU
distribution

51%

Baseline
<7 kPa
203 (100%)



End of follow-up
<7 kPa
214 (105%)

54%

19%

Baseline
7.0-9.9 kPa
75 (100%)



End of follow-up
7.0-9.9 kPa
69 (92%)

17%

18%

Baseline
10.0 -16.9 kPa
73 (100%)

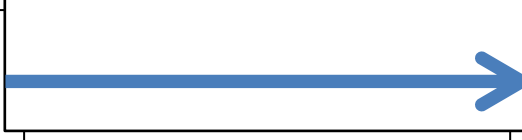


End of follow-up
10.0 -16.9 kPa
70 (96%)

18%

11%

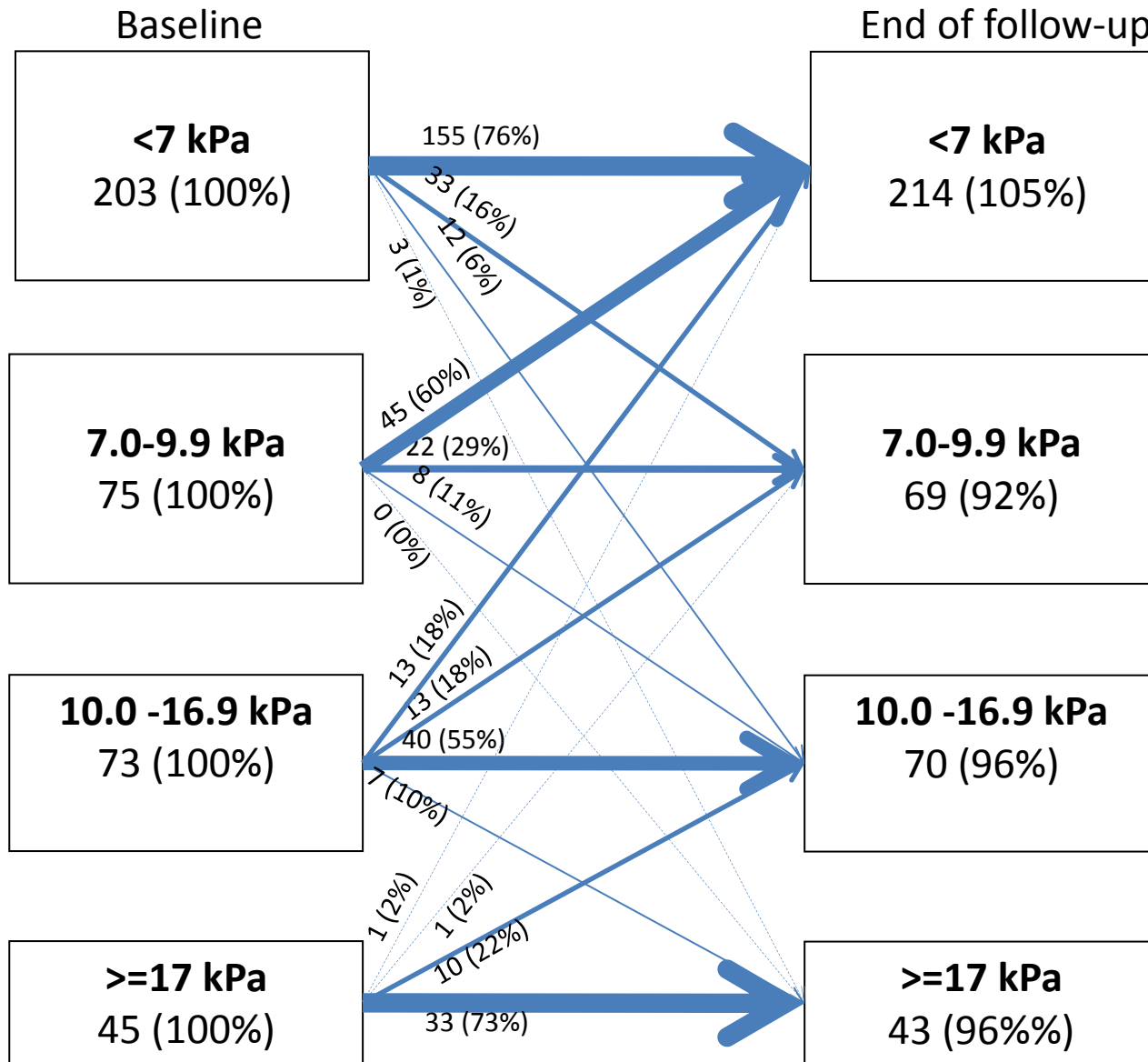
Baseline
>=17 kPa
45 (100%)



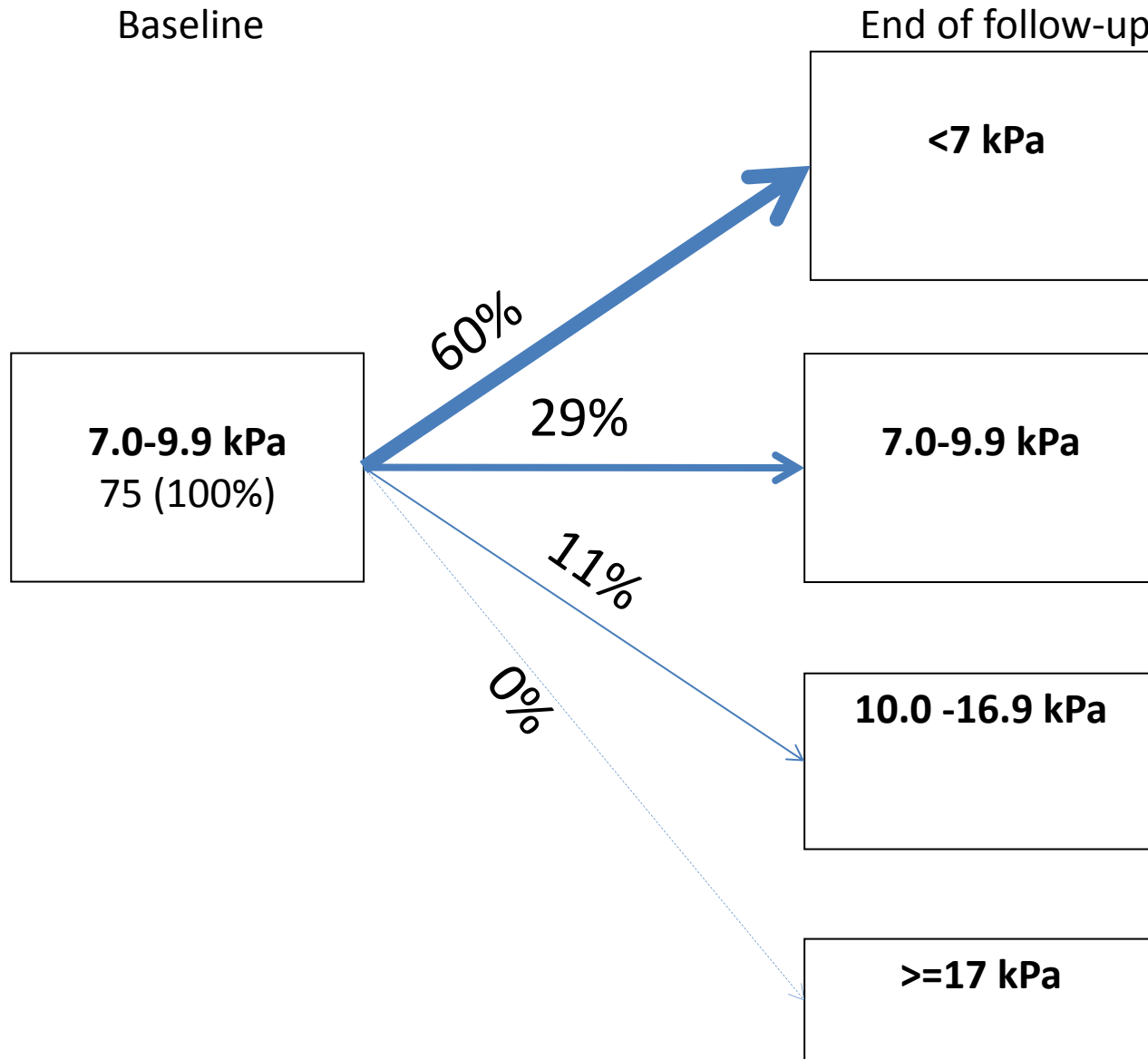
End of follow-up
>=17 kPa
43 (96%%)

11%

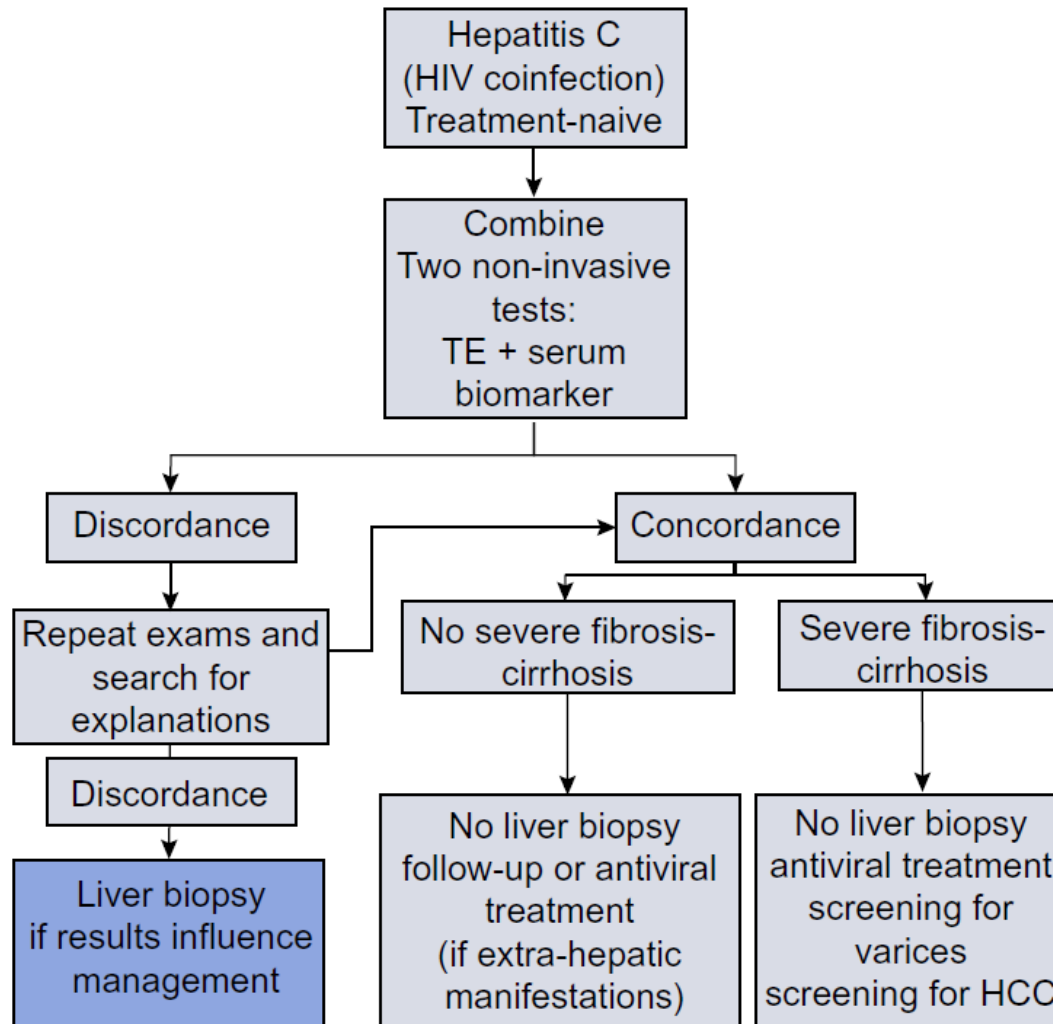
HCV 396 untreated during median 36 month of follow-up



HCV 396 untreated during median 36 month of follow-up



EASL HCV fibrose algoritme



Take home messages

- A LSM >7 kPa should be repeated in the fasting state after (1)-3 months
- A LSM of 7-10 kPa is likely to decrease over time
- A repeated LSM > 10 kPa indicates significant fibrosis
- A repeated LSM > 17 kPa indicates cirrhosis. It is associated with adverse outcome
These patients should enter a screening program for complications

Thanks to the OUH Fibrosis group:

Belinda Klemmensen Mössner

Karin Christiansen

Janne Fuglsang Hansen

Merete Skamling

Inge Birkemose

Annelise Davidsen

Tina Riis Jørgensen

Erik Jarbjerg

Benjamin Storgaard

Trine Bager

