

Tratamiento antirretroviral y esteatosis hepática

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Sevilla

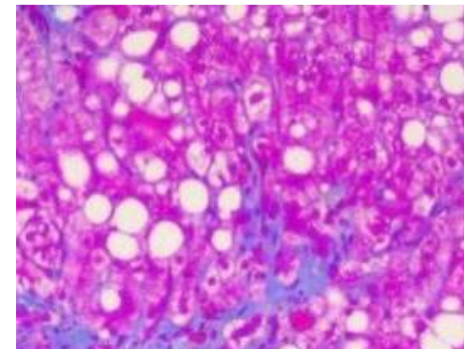
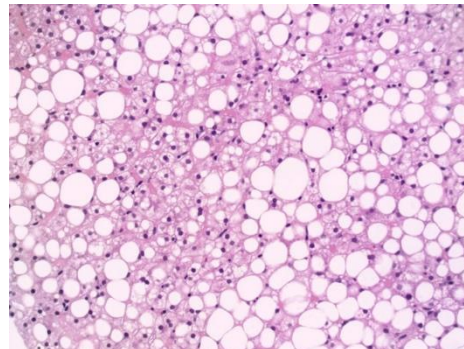
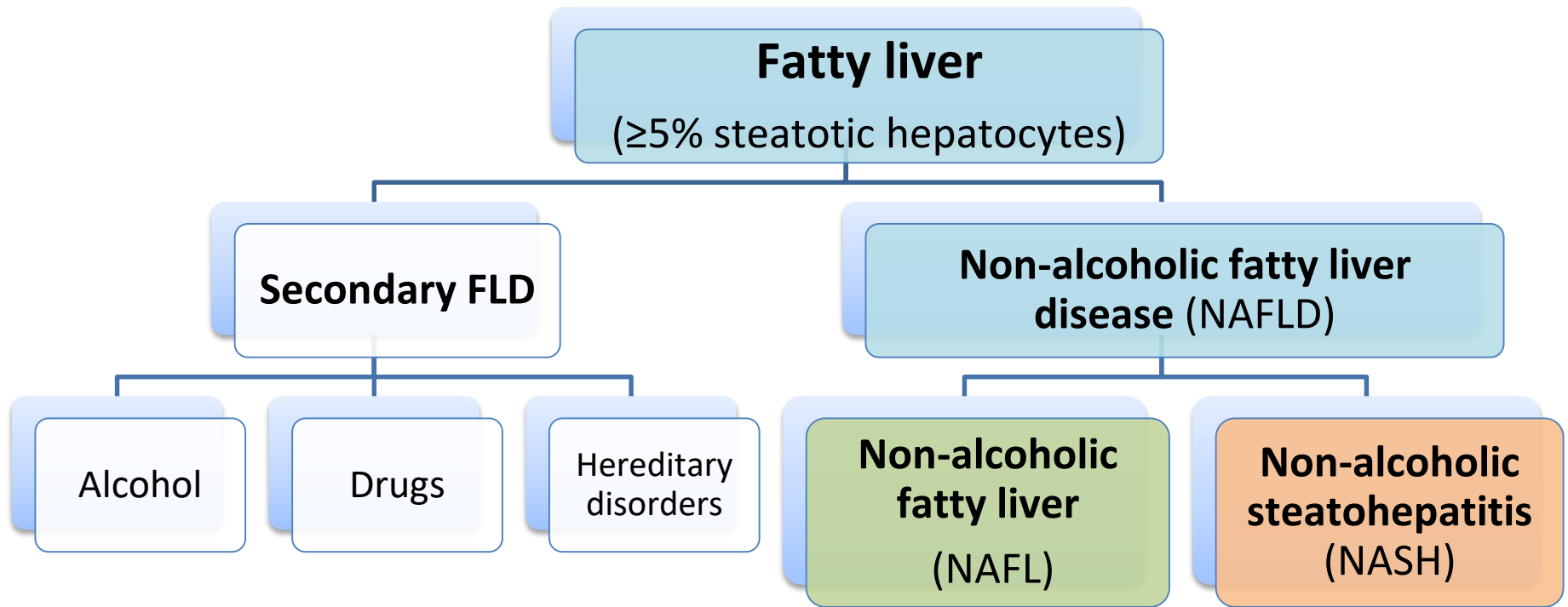
Conflictos de interés

JM ha sido investigador en ensayos clínicos apoyados por Bristol-Myers Squibb, Gilead, Merck Sharp & Dome y ViiV. Ha recibido honorarios por conferencias de Gilead, Bristol-Myers Squibb, Merck Sharp & Dome, Abbvie y ViiV, y honorarios por consultoría de Bristol Myers-Squibb, Gilead, Merck Sharp & Dome y Abbvie.

Non-alcoholic fatty liver disease (NAFLD) in HIV-infected patients

- Definition and diagnosis
- Prevalence
- Factors associated with NAFLD progression
- Management

Definition of NAFLD



MAFLD: Metabolic Associated Fatty Liver Disease



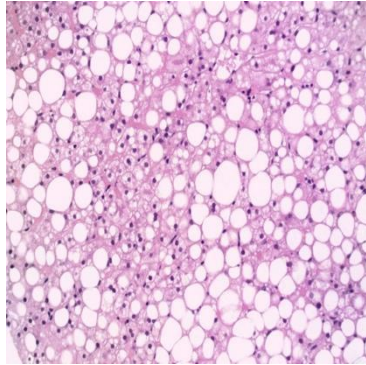
Proposed Definition¹

- Diagnosis based on presence of **hepatic steatosis** plus at least 1 of:
 - **Obesity, T2D, metabolic disease**
- Not a diagnosis of exclusion
- Acknowledges metabolic basis of disease

Considerations²

- Ambiguity about definition of “metabolic disease”
- Better nomenclature will be based on **specific underlying causes**, not associations
- Consensus needed

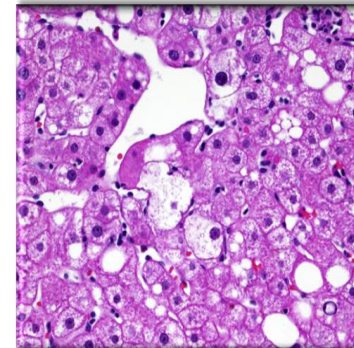
Liver biopsy: The Gold Standard



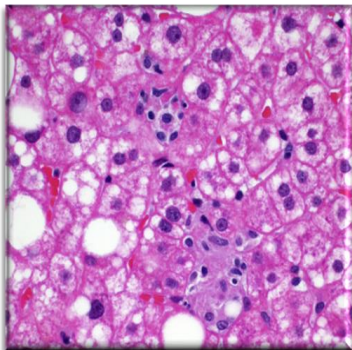
Steatosis?



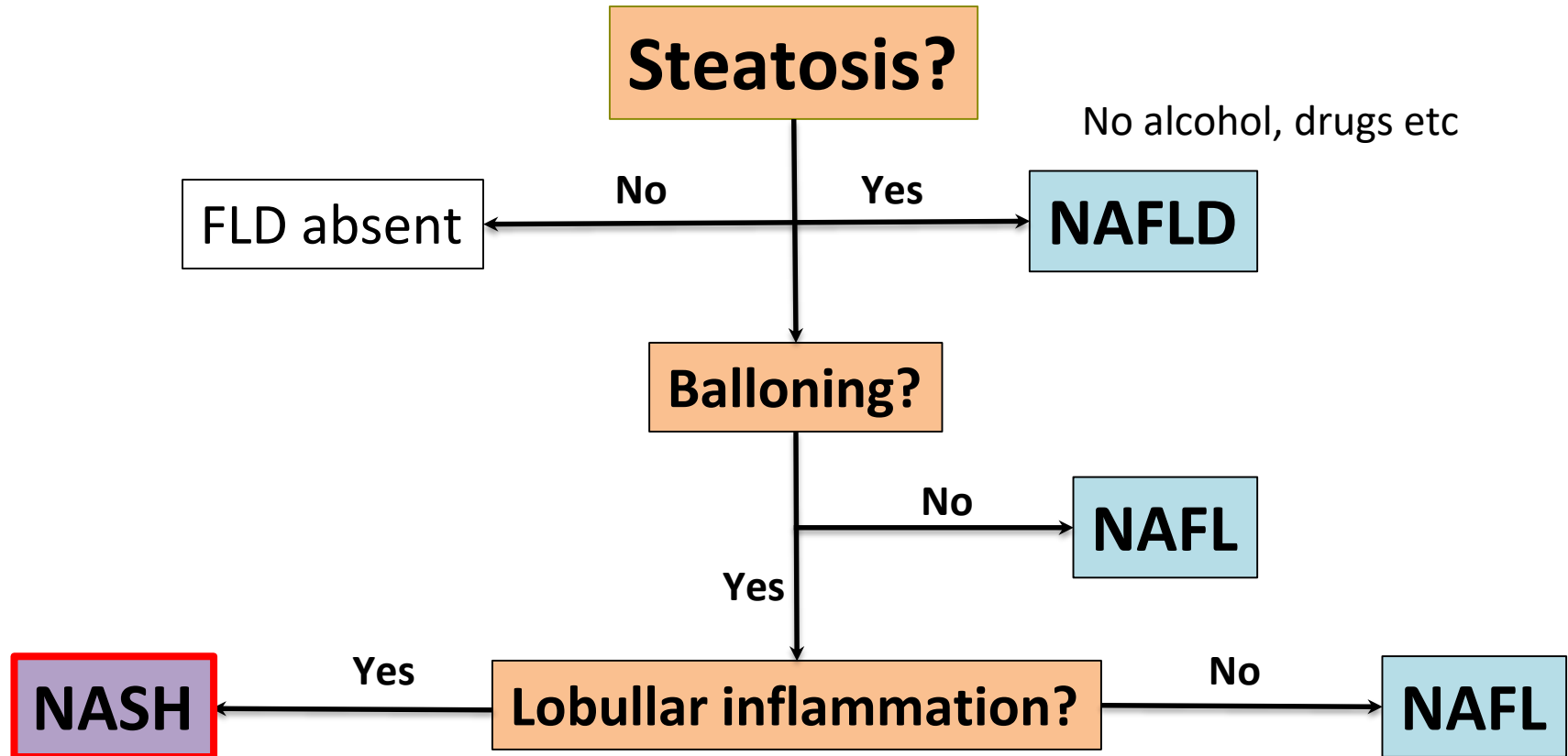
Balloning?



Lobular inflammation?



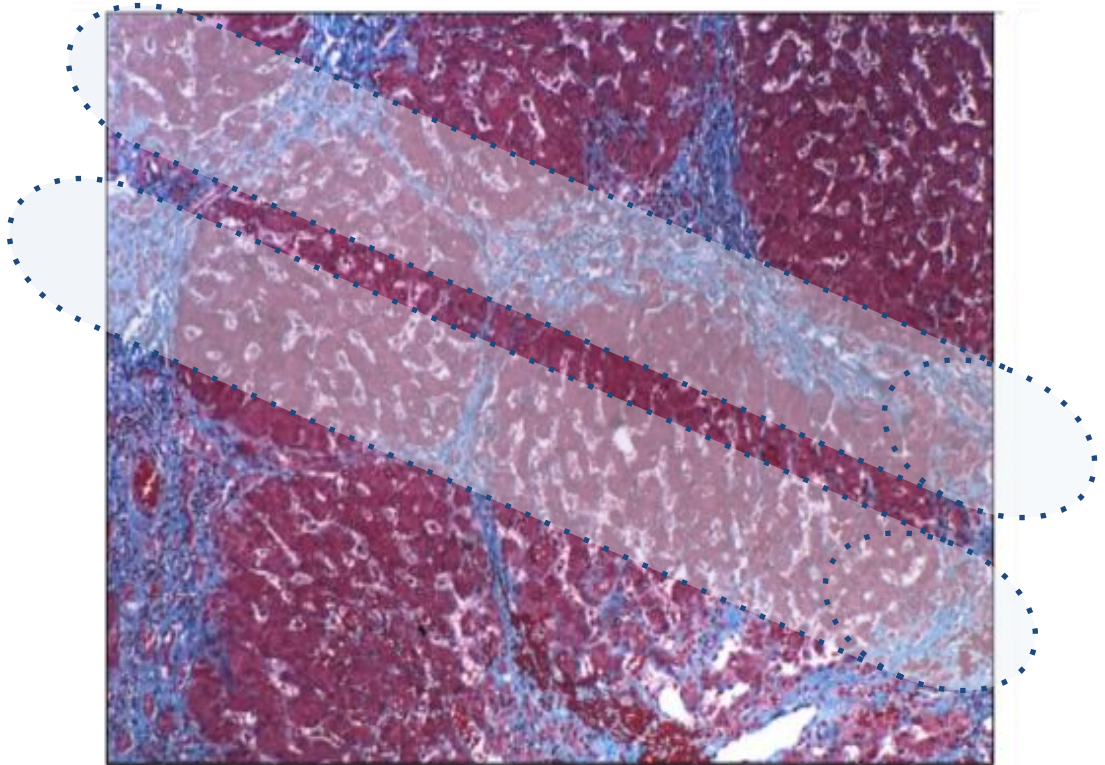
Liver biopsy: The Gold Standard



Liver biopsy: The imperfect Gold Standard

Limitations

- Invasive
- Painful
- Expensive
- Morbidity/mortality
- Sampling variability
- Observer variability
- Expertise to perform
- Impractical for population screening



Sampling variability:
Same biopsy may give
2 different grades of liver
fibrosis

Non-invasive diagnosis of NAFLD:

First detect steatosis

Imaging techniques

- *US?*
- CT
- MRI
- VCTE-CAP

Blood tests?

- **FLI:** Waist (cm), BMI, TG, GGT.

Steatosis



Balloning?

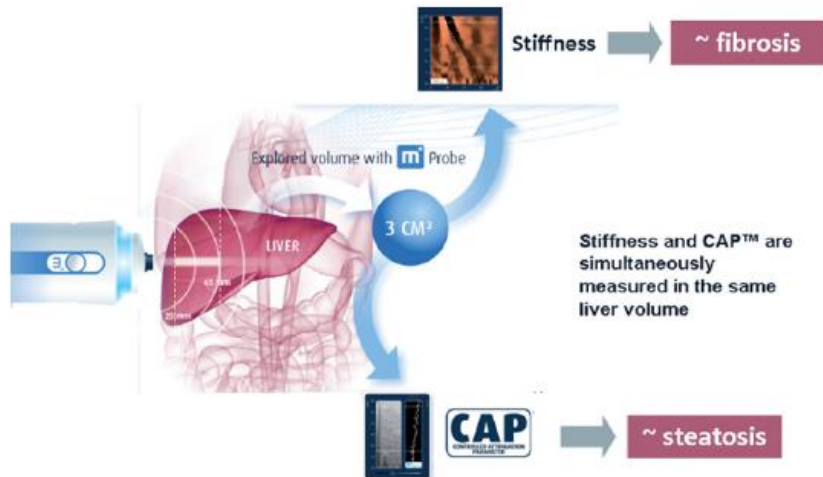


Lobullar inflammation?



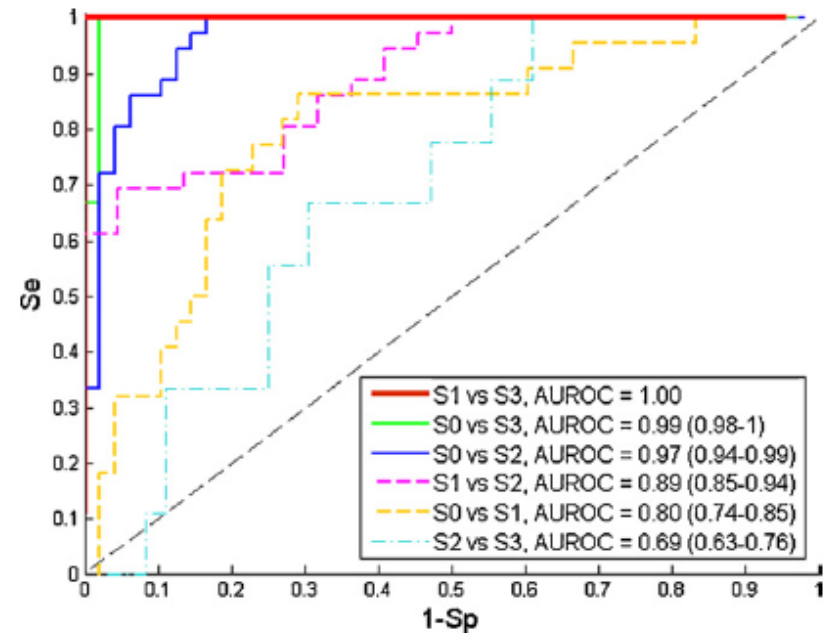
Diagnosis of steatosis with VCTE-CAP

- CAP is an estimation of the attenuation of the ultrasound wave with the M probe of Fibroscan®.
- CAP uses the same data required for liver stiffness.



Performance of CAP according to liver biopsy*

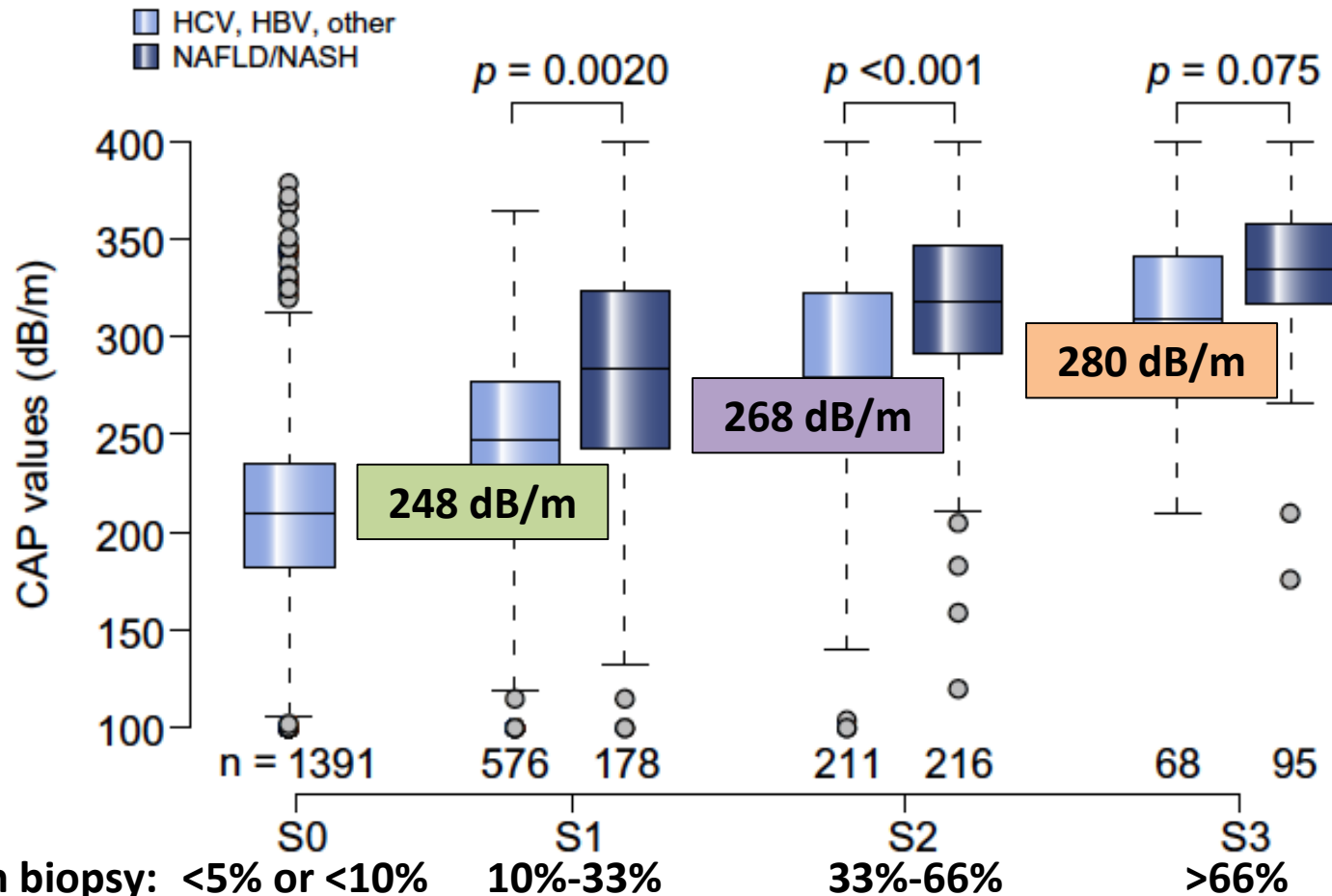
- n=115 patients: (42 HCV; 17 HBV; 39 alcohol; 17 NAFLD).
- Steatosis: (S0: < 10%, S1: 11-33%, S2: 34-66%; S3: > 67%).



*Sasso M, et al. Ultrasound Med Biol 2010; 36: 1825.

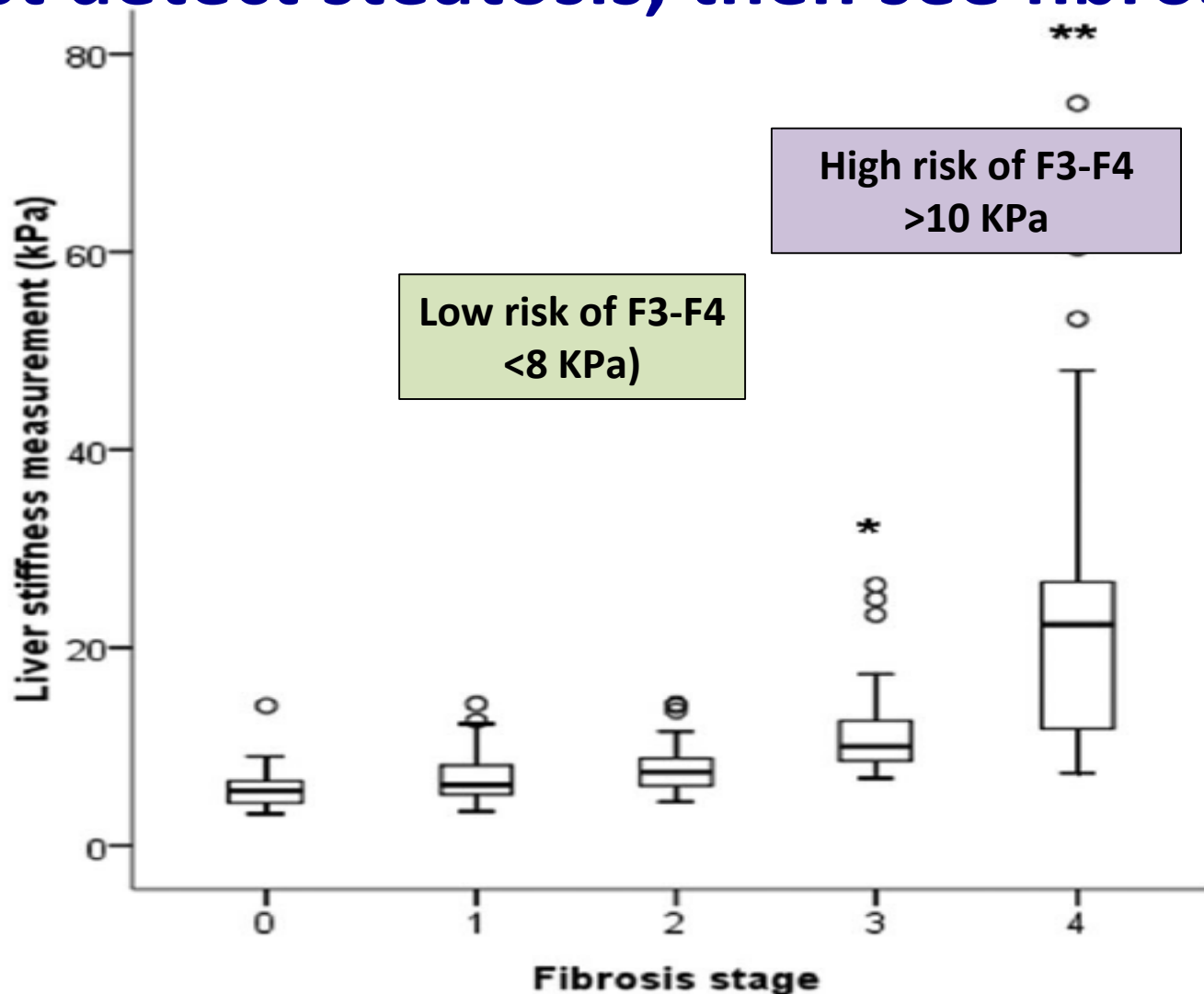
NAFLD & VCTE-CAP: Improved CAP cut-offs to predict steatosis

Meta-analysis of individual data from 19 studies (n=2735, 37% HBV, 36% HCV, 20% NAFLD/NASH, 7% other).



Non-invasive diagnosis of NAFLD

First detect steatosis, then see fibrosis



*P<0.01 compared with F0, F1, and F4, P<0.05 compared with F2;

**P<0.001 compared with all other fibrosis stages

Fibrosis and NAFLD: Blood biomarkers

Ruling out F $\geq$ 3

Panels with best diagnostic yield to predict histologic advanced fibrosis or cirrhosis in NAFLD (N = 145).

Test	AUROC (95% CI)	Cut-off	PPV	NPV
FIB-4	0.86 (0.78-0.94)	1.30 3.25	36% 75%	95% 85%
NAFLD fibrosis score	0.81 (0.71-0.91)	-1.455 0.676	30% 79%	92% 86%

Indeterminate fibrosis: FIB-4 or NAFLD fibrosis score values between cut-off points.

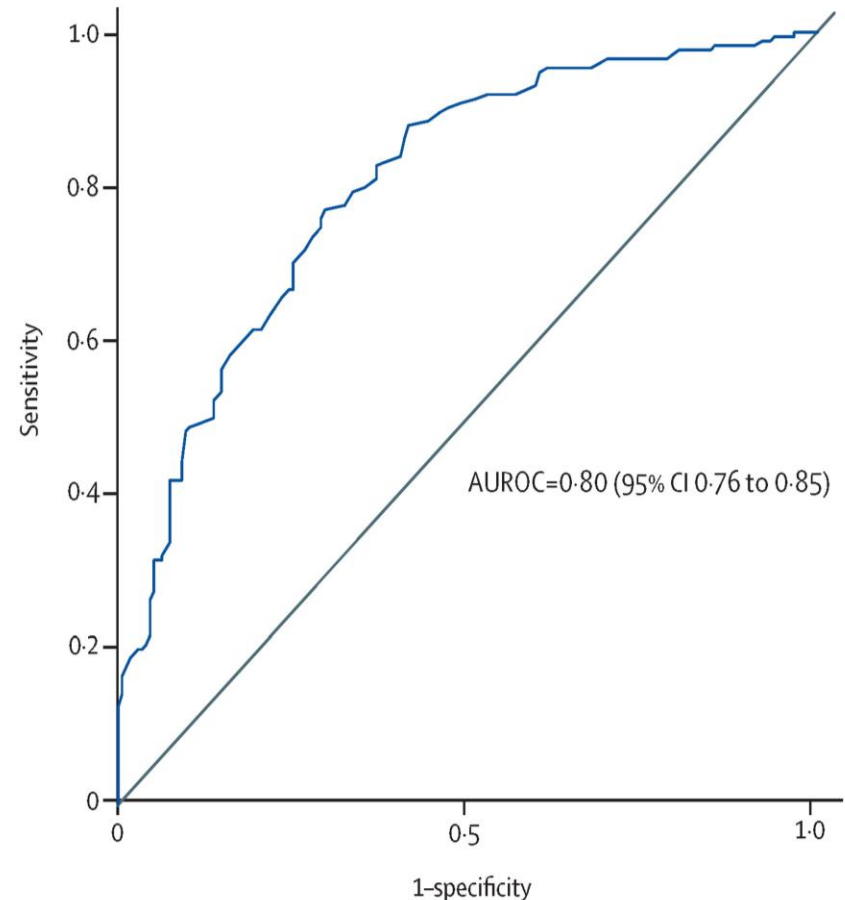
FIB-4: (Agex AST)/platelets ($10^9/L$) $\times \sqrt{ALT}$

NAFLD fibrosis score: $-1.675 + 0.037 \times \text{age} + 0.094 \times \text{BMI (Kg/m}^2\text{)} + 1.13 \times \text{abnormal FPG/DM (yes=1, no=0)} + 0.99 \times \text{AST/ALT} - 0.013 \times \text{platelets (}10^9/L\text{)} - 0.66 \times \text{albumin (g/dL)}$

AUROC: Area under the ROC curve; 95% IC: 95% confidence interval; PPV: Positive predictive value; NPV: Negative predictive value.

FAST score: NASH with activity and fibrosis

- Patients undergoing liver biopsy for suspected NASH
 - Derivation cohort: 350
 - Validation: 1026
- **FAST:**
 - LSM, CAP, AST
 - $NAS \geq 4$ and $F \geq 2$
- **Rule-out zone** ($FAST \geq 0.35$):
 - Classified: 113 (32%)
 - **NPV:** 0.85
- **Rule-in zone** ($FAST \geq 0.67$):
 - Classified: 136 (39%)
 - **PPV:** 0.83



External validation of FAST

- N = 585 adults with biopsy-confirmed NASH from the multicenter NASH CRN cohort
 - “At-risk” NASH: NASH + NAS ≥ 4 and F ≥ 2
- 38% male, 79% white; 73% obese; mean age: 51 yrs; mean ALT: 68 U/L; mean AST: 53 U/L
- Prevalence of “at-risk” NASH: 37%

	Cut-off	Sensitivity	Specificity	PPV	NPV
Rule-out	0.35	0.91	0.50	0.51	0.90
Rule-in	0.67	0.51	0.87	0.69	0.76

NAFLD in HIV-infected patients

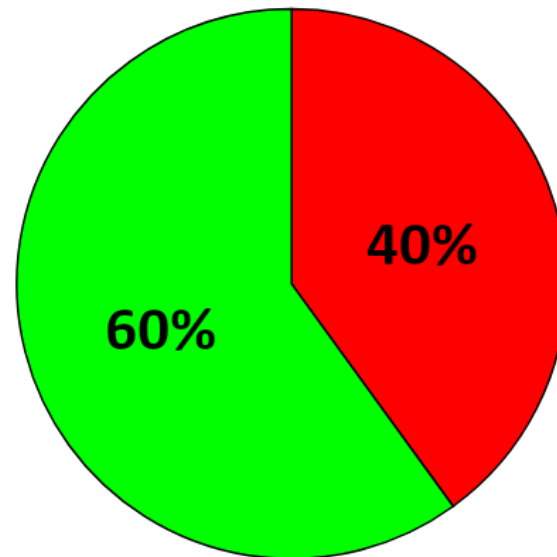
- Definition and diagnosis
- Prevalence
- Factors associated with NAFLD progression
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Prevalence of hepatic steatosis measured by CAP in HIV infection

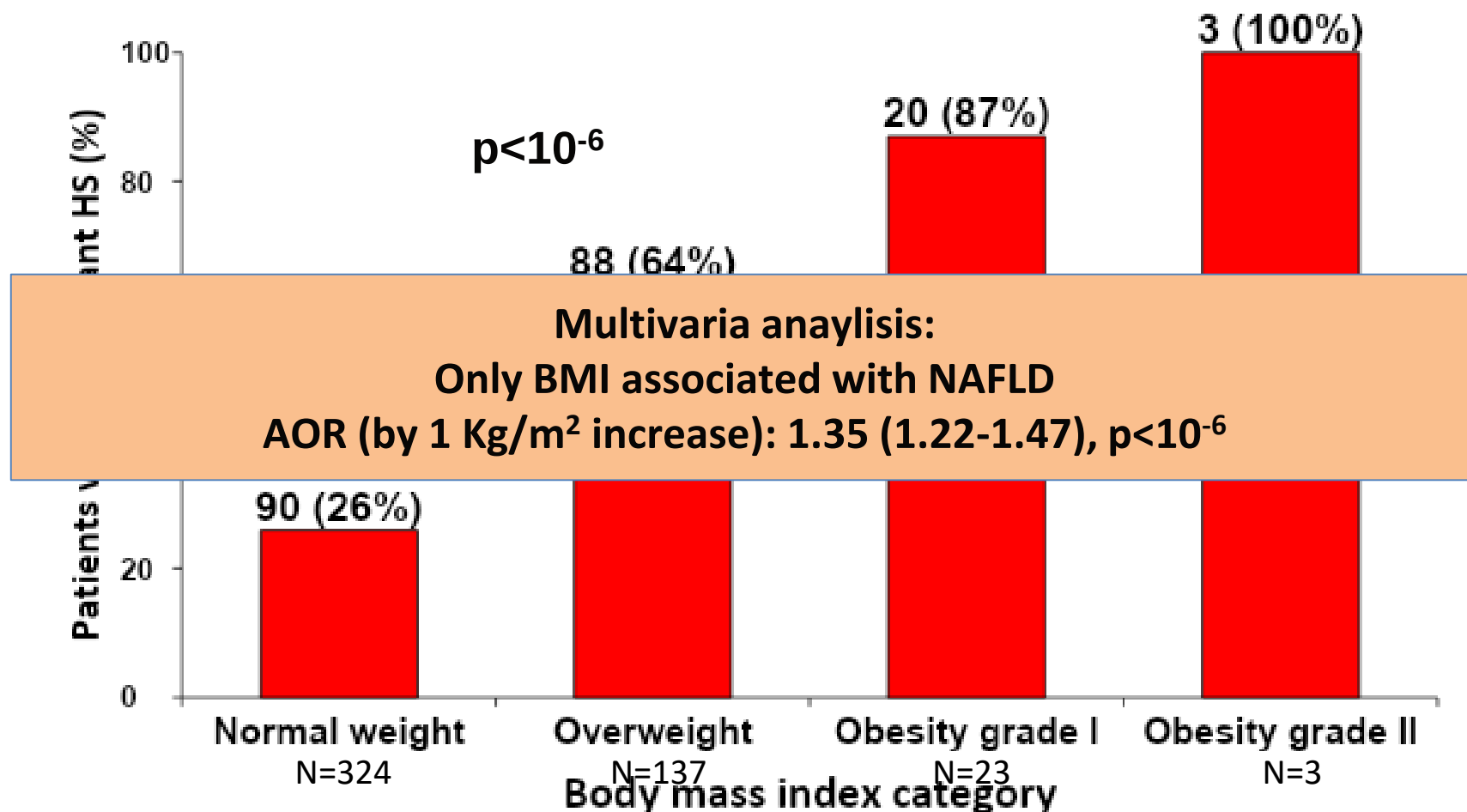
- **Design:** Prospective cross-sectional study (5 Spanish centers; Nov, 2011-Jun, 2012).
- **Patients:** Consecutive HIV-infected outpatients.
- **Methods:**
 - CAP measurements
 - Significant HS: CAP value ≥ 238 dB/m

Prevalence of HS (N=505)

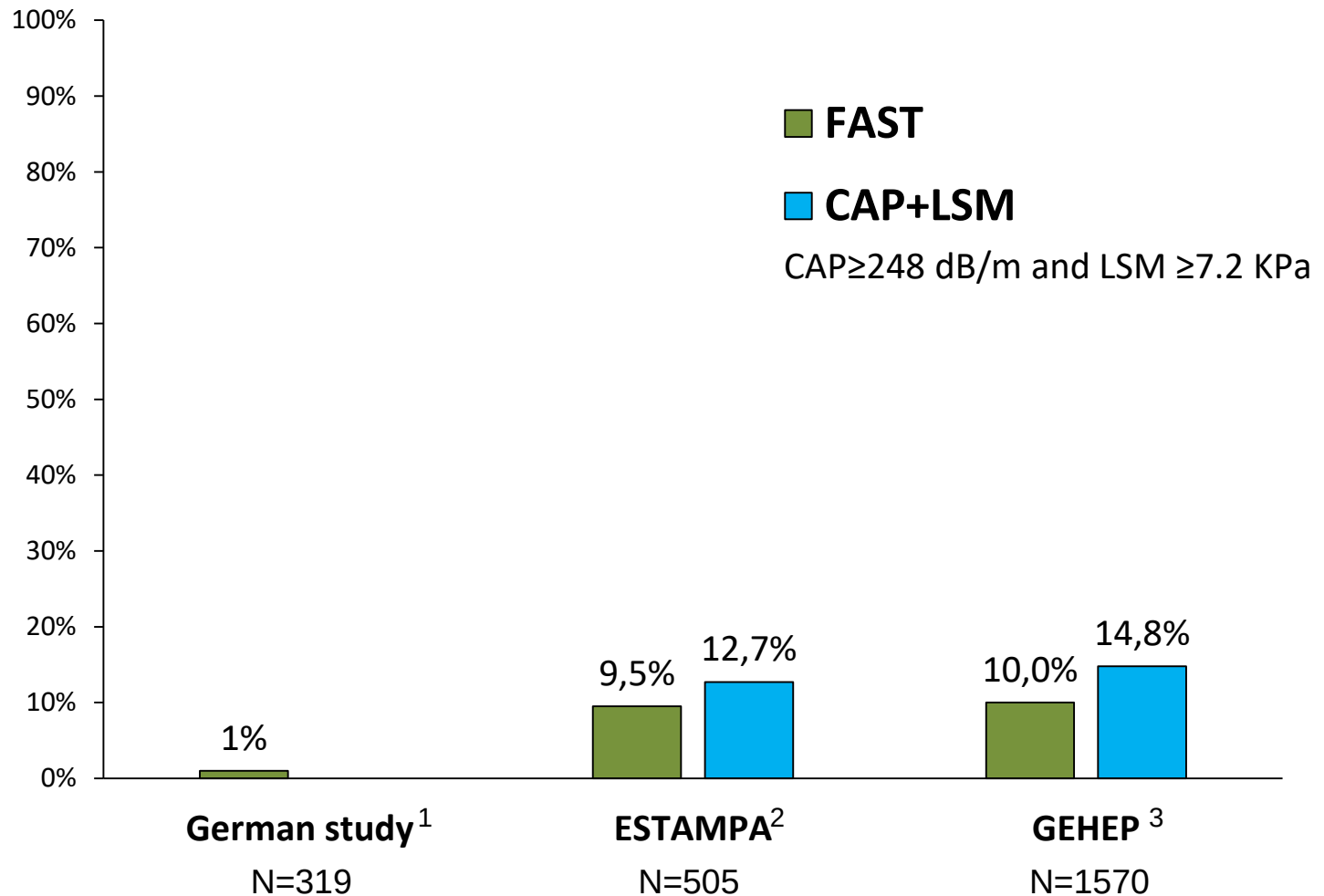
■ CAP ≥ 238 dB/m ■ CAP < 238 dB/m



Frequency of hepatic steatosis according to body mass index category (N=505)



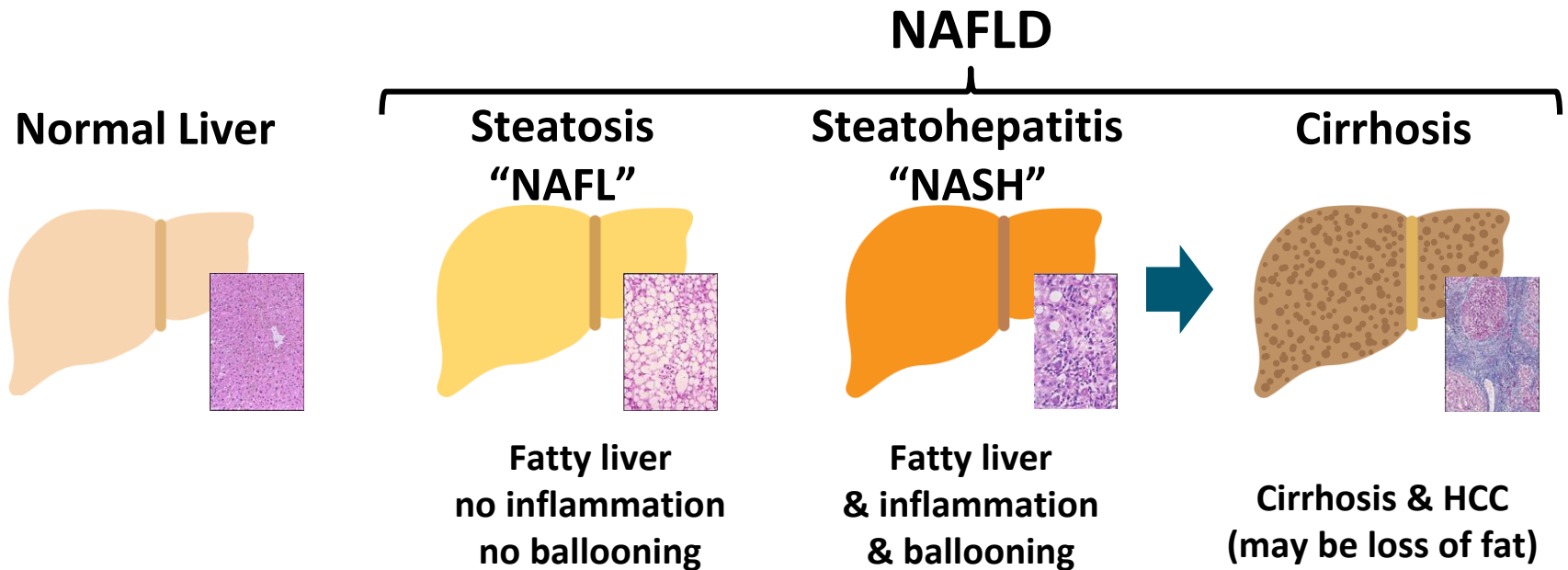
Prevalence of NASH according to FAST score or CAP + LSM



NAFLD in HIV-infected patients

- Definition and diagnosis
- Prevalence
- Natural history
- Factors associated with NAFLD progression
- Management

Natural history of NAFLD



Worldwide prevalence:

25%¹

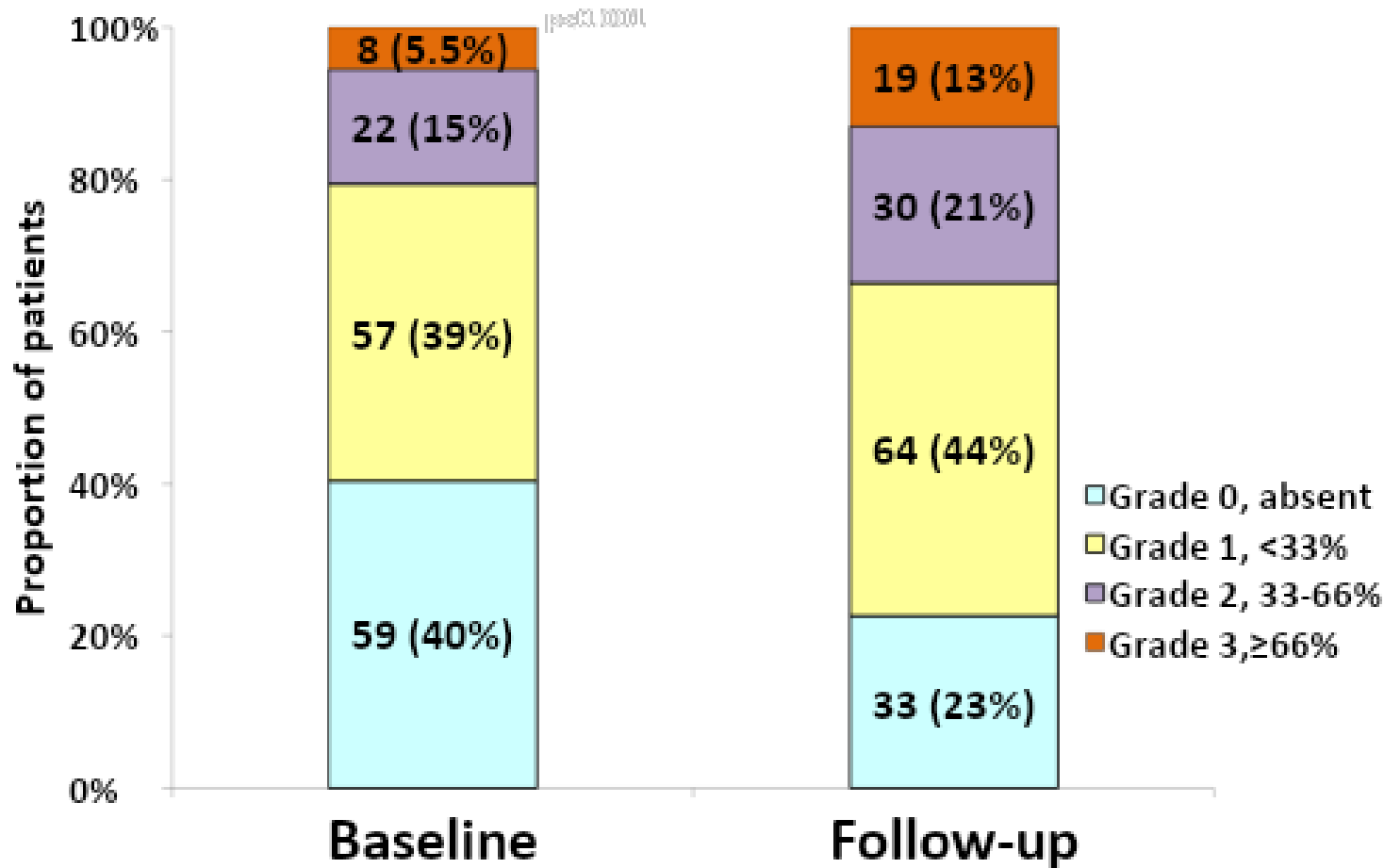
3% to 5%¹

1% to 2% at risk*

*Based on analysis of NHANES data estimating 1.74% prevalence of NASH with advanced fibrosis²

Frequency of hepatic steatosis in paired liver biopsies

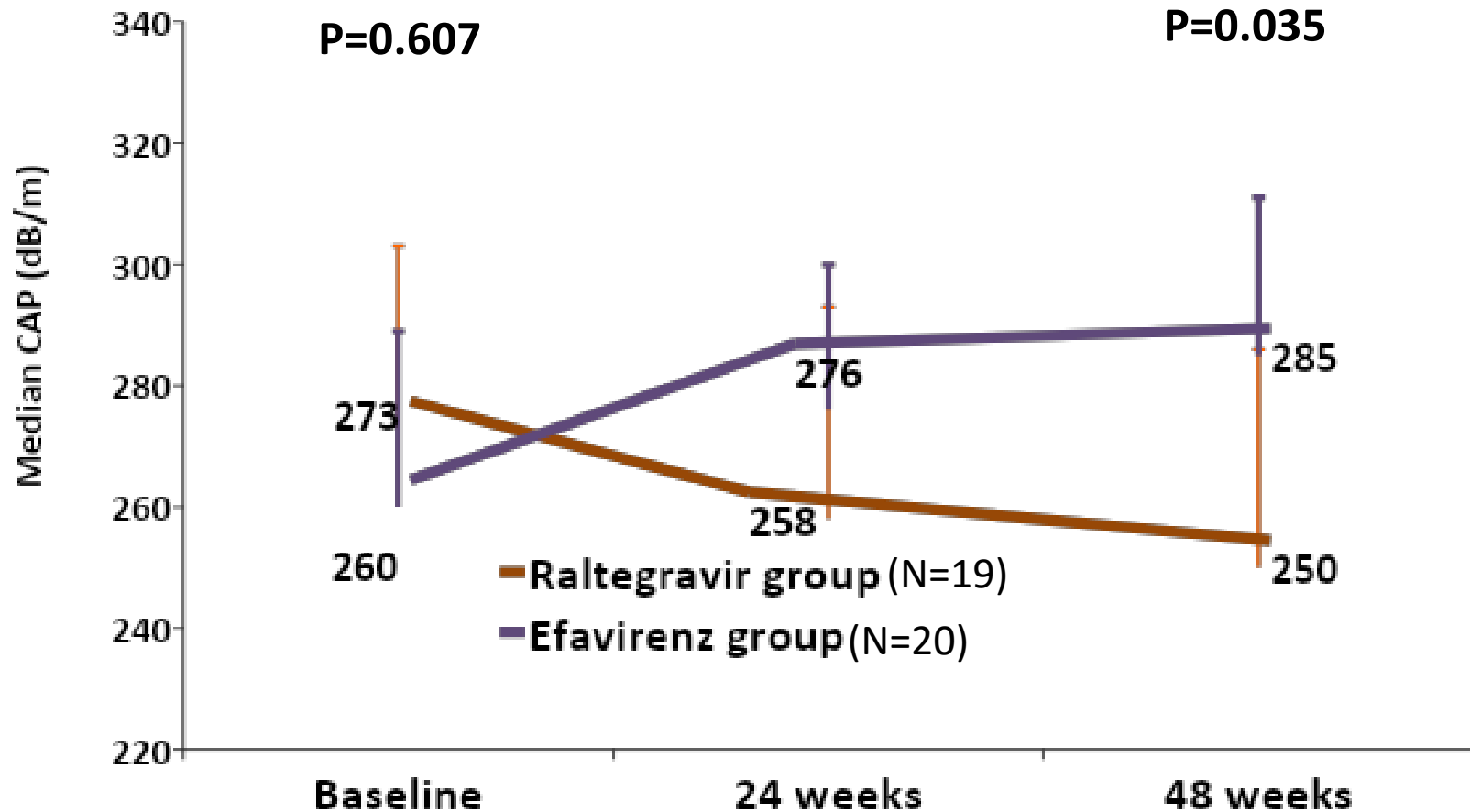
Retrospective cohort study (n=146): HIV/HCV coinfecting patients with paired biopsies



Median (Q1-Q3) time between biopsies: 3.3 (2-5.2) years

Changes in liver steatosis after switching efavirenz to raltegravir: The STERAL study

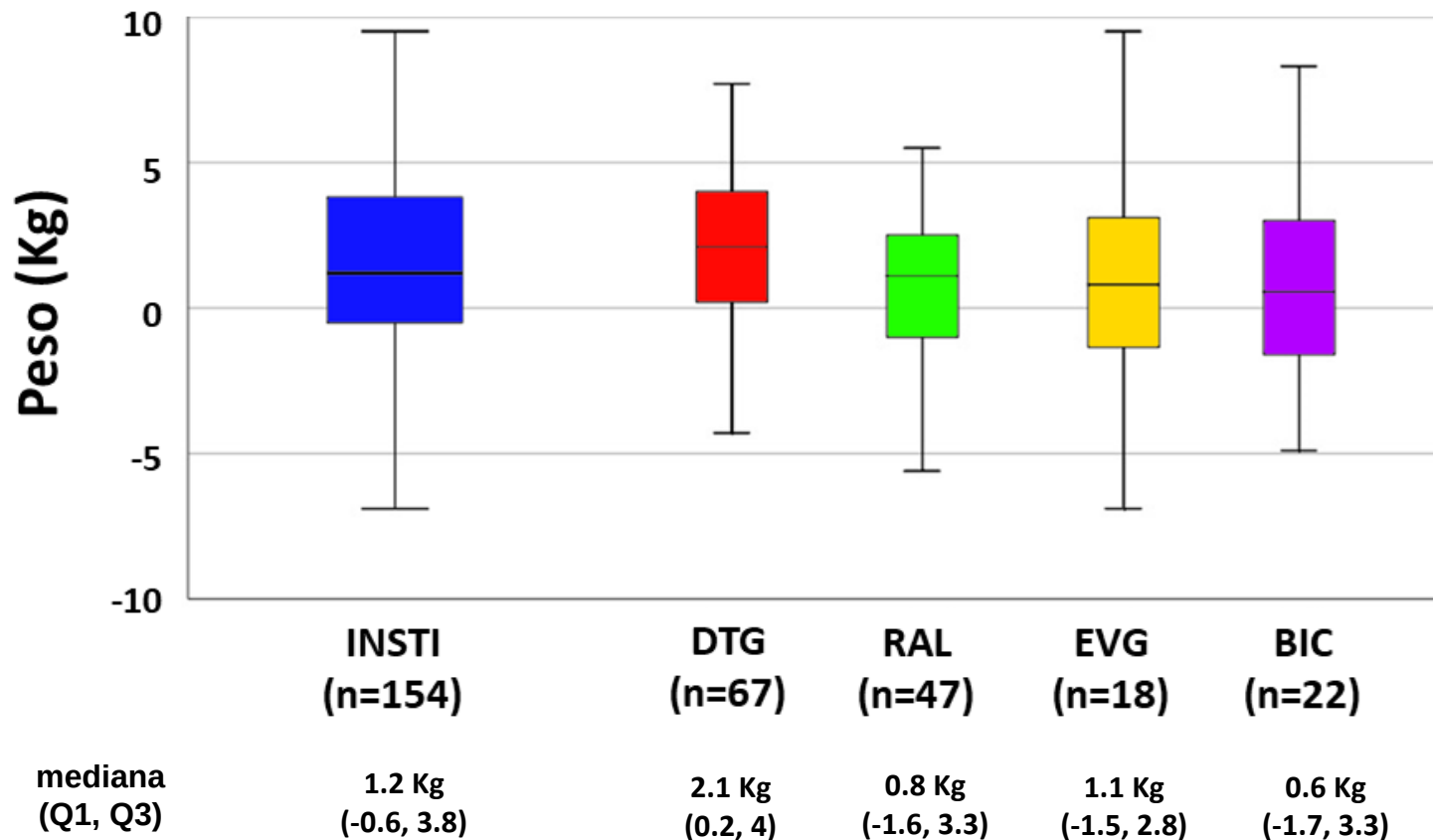
Median CAP values during the follow-up by treatment group



Weight gain after 48 wk of switching to INSTI

(n=154)

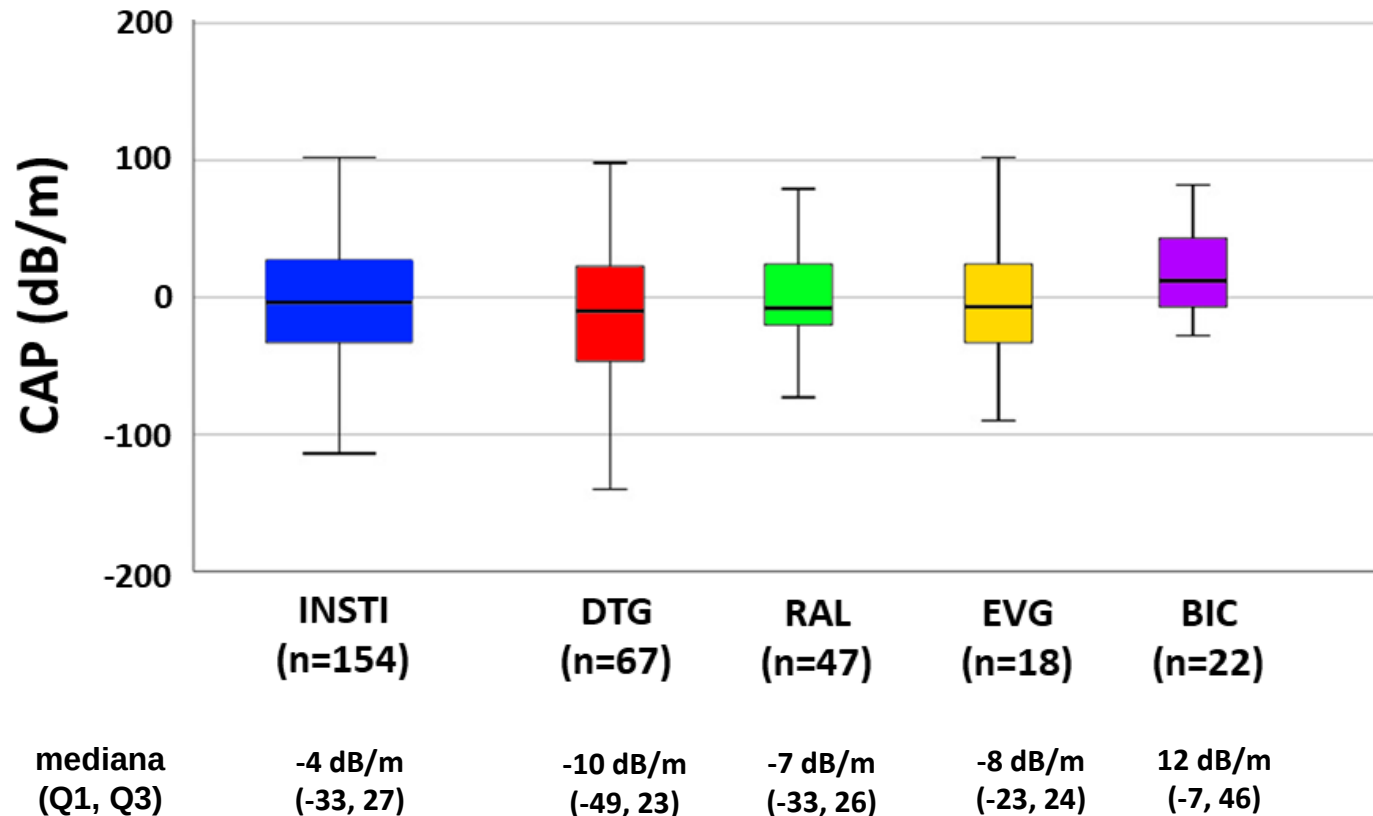
Mediana (IC 95%) de ganancia de peso en 48 semanas



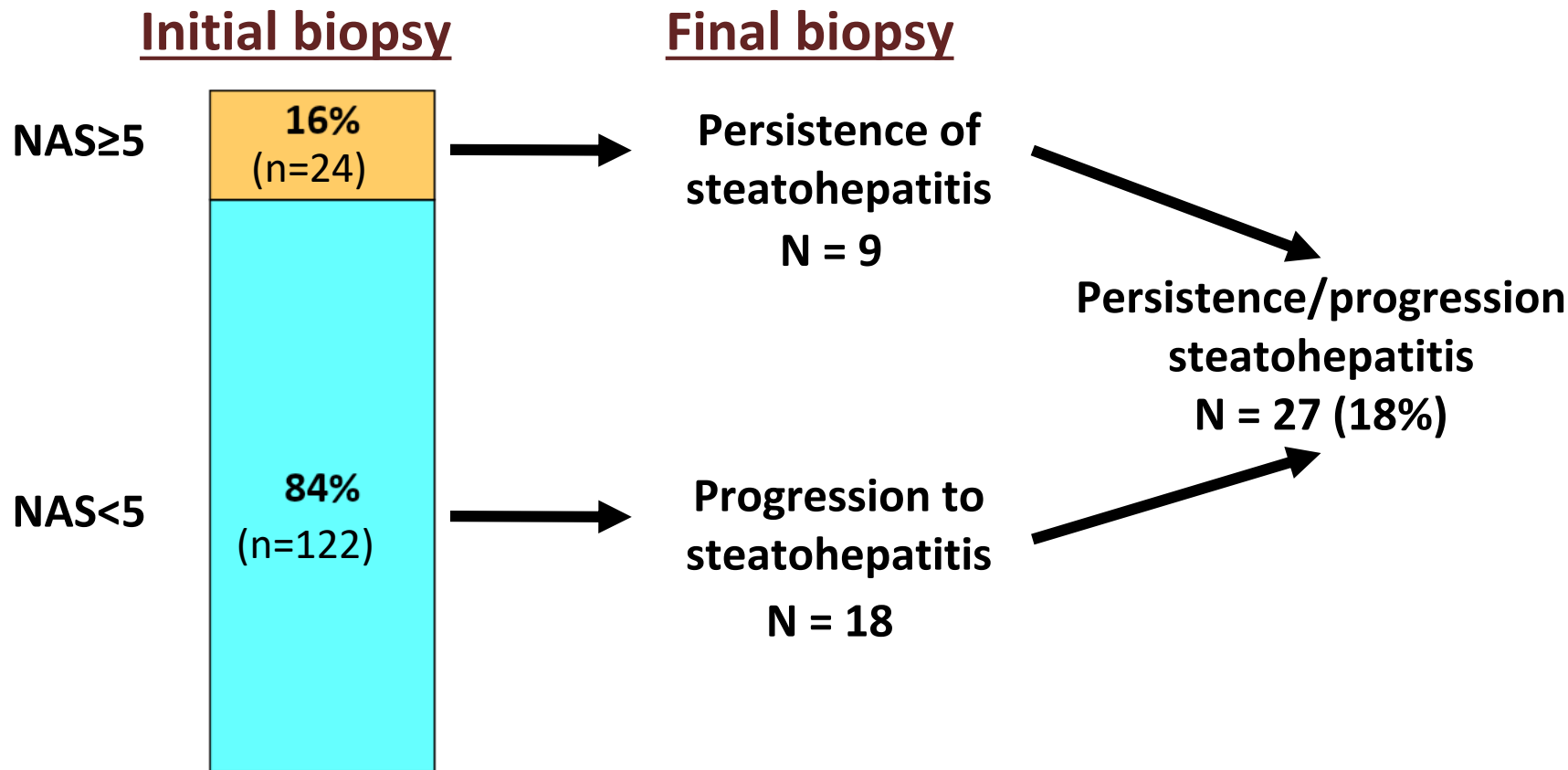
CAP changes gain after 48 wk of switching to INSTI

(n=154)

Mediana (IC 95%) de ganancia de CAP en 48 semanas



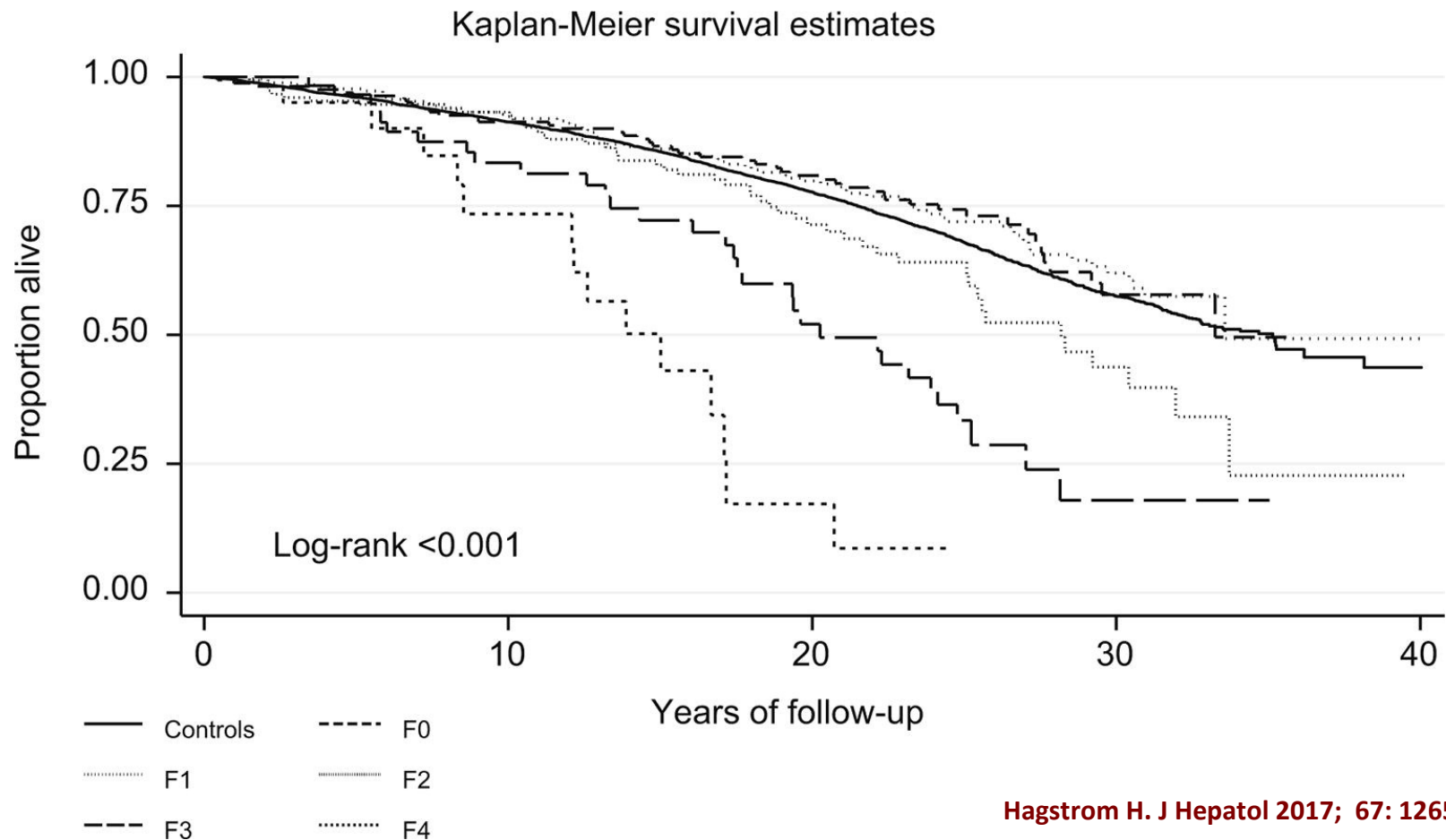
Persistence of or progression to NASH (NAS score ≥ 5)



Fibrosis progression ≥ 1 stages was associated with persistence/progression to steatohepatitis (AOR [95% CI]=2.4 [1.01-5.7], $p=0.047$)

NAFLD and fibrosis: Survival in general population

- Retrospective study (N=646) in Sweden
- NAFLD diagnosis over 40 years. 10 controls matched by each case.
- Median follow-up: 20 (0-40) years: 139.163 persons-year



NAFLD and survival in PLWH

Design: Prospective cohort

Patients: All PLWH con VCTE

Baseline: First VCTE

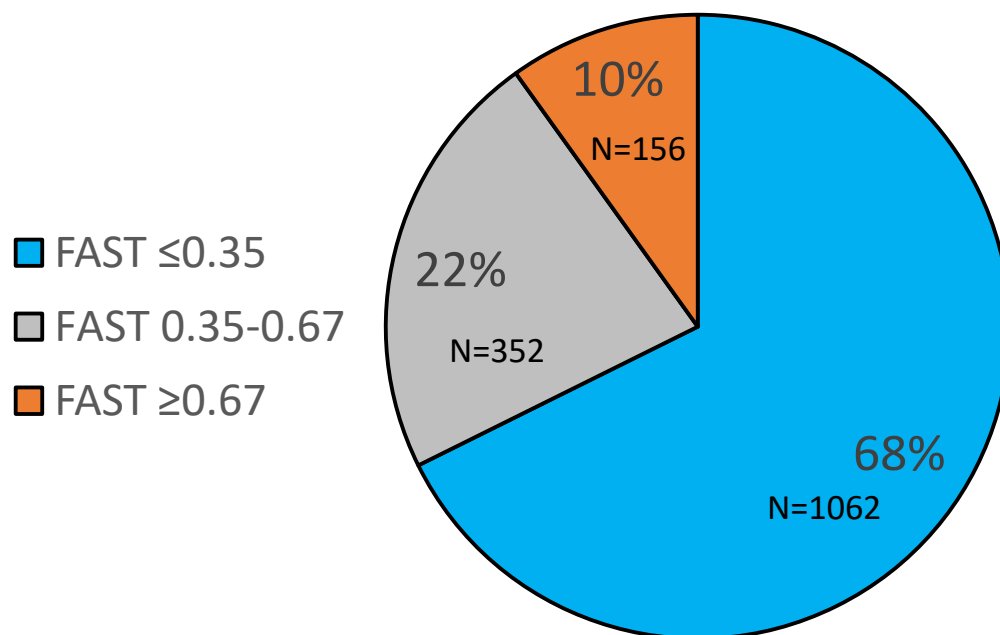
Risk of all-cause of death:

Time-to-event analyses.

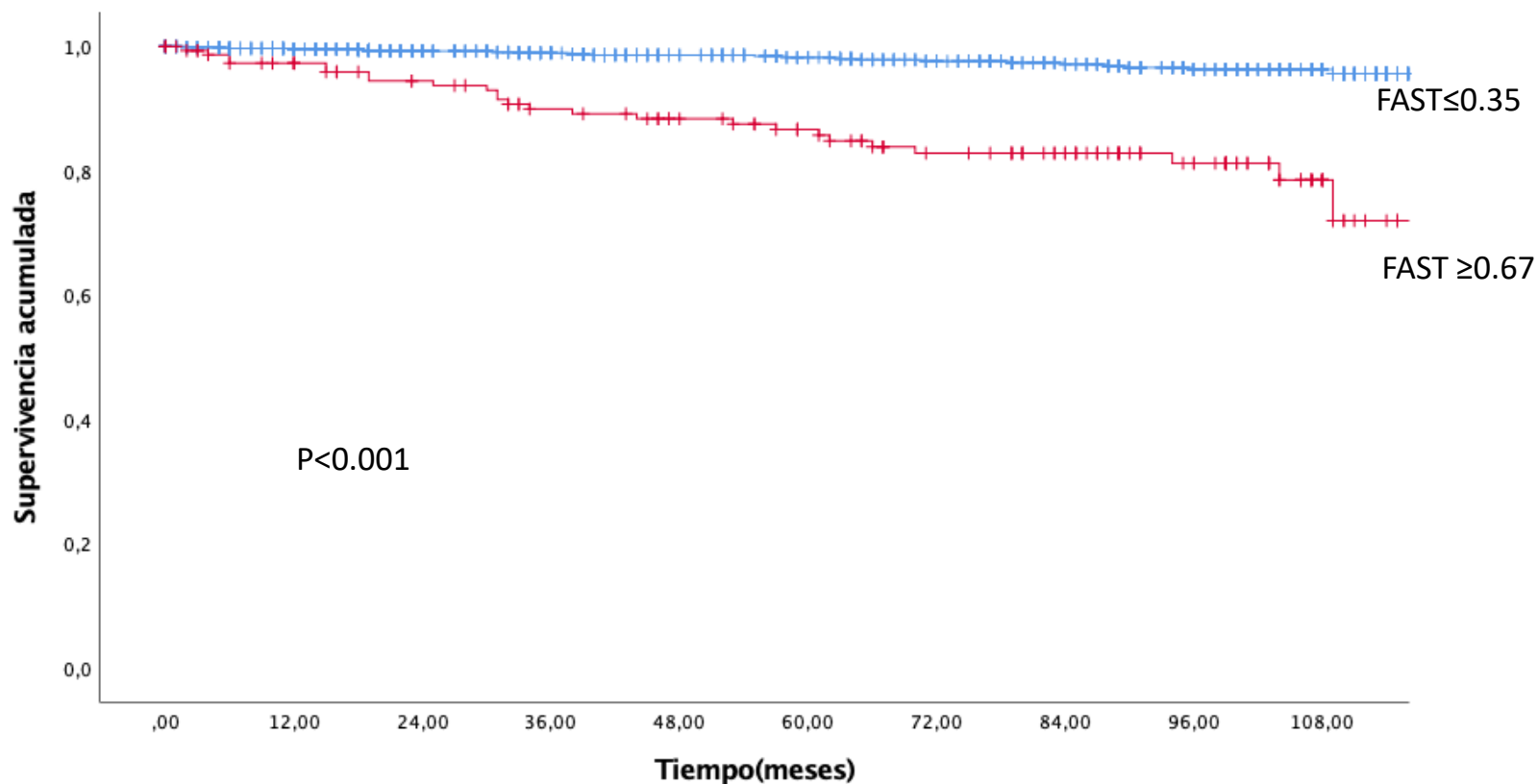
NAFLD defined as steatosis
(CAP ≥ 248 dB/m) without any
other liver disease.

FibroScan-AST (FAST) score,
which includes AST, CAP and
LSM was calculated.

FAST score distribution (n=1570)



Survival of PLWH according to FAST (n=1214)

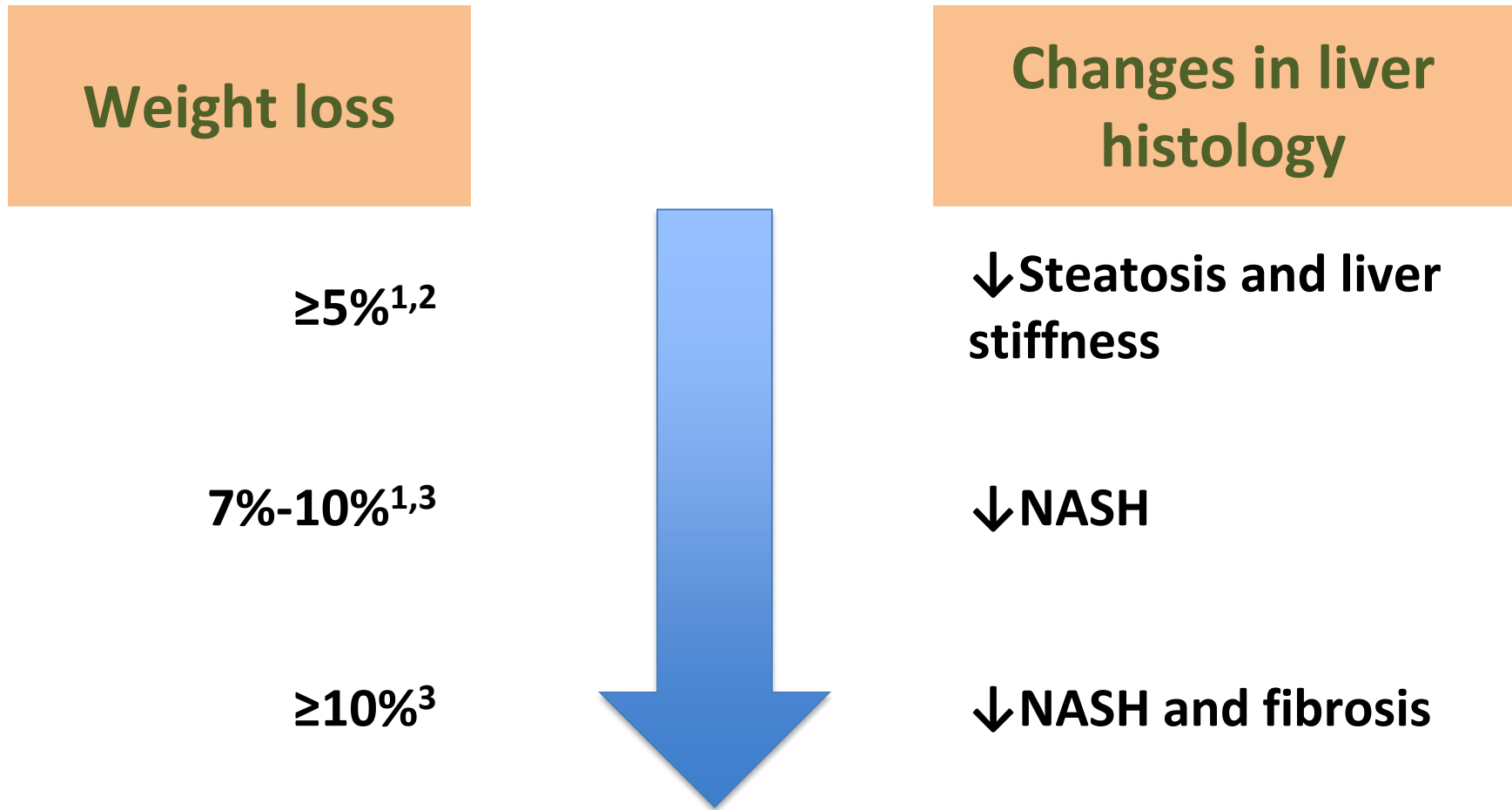


NAFLD in HIV- infected patients

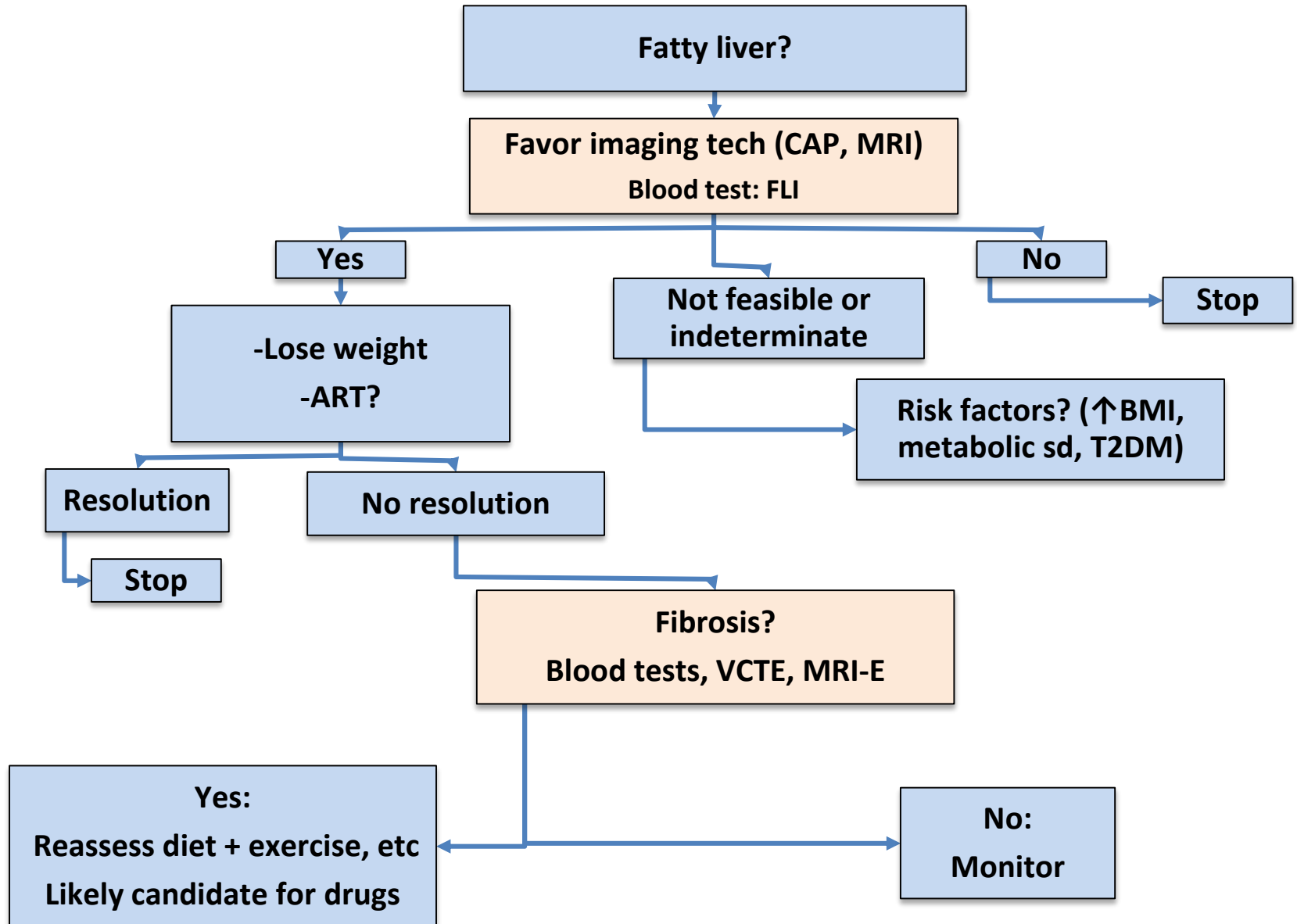
- Definition and diagnosis
- Prevalence
- Natural history
- Factors associated with NAFLD progression:
- **Management**

Treatment of NAFLD

Lose weight!!!



NAFLD screening and management: PLWH



Summary

- Steatosis, mainly NAFLD, is frequent in HIV infection and can induce fibrosis progression.
 - NASH (and fibrosis) prevalence <15%
- Factors associated with hepatic steatosis in HIV infection:
 - Metabolic factors: **TRUE NAFLD**
 - Antiretroviral drugs: Keep in mind
 - EFV, switching to RAL can induce regression
 - Other INSTI: Steatosis does not parallel weight gain
- Management = HIV-negative + Review ART



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Hospital Universitario Virgen de Valme

