



**VCU**

Stravitz-Sanyal Institute for  
Liver Disease and Metabolic Health  
School of Medicine

# Understanding NIT to Optimize Enrollment in NASH Clinical Trials

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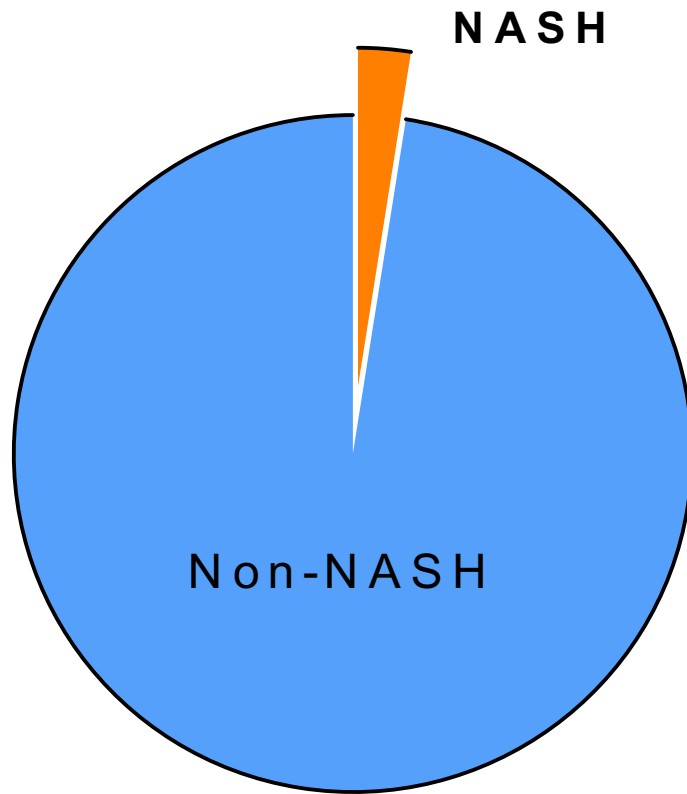
# Conflict of Interest Disclosures

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- Sagimet, AMRA

# Screening in Primary Care Setting

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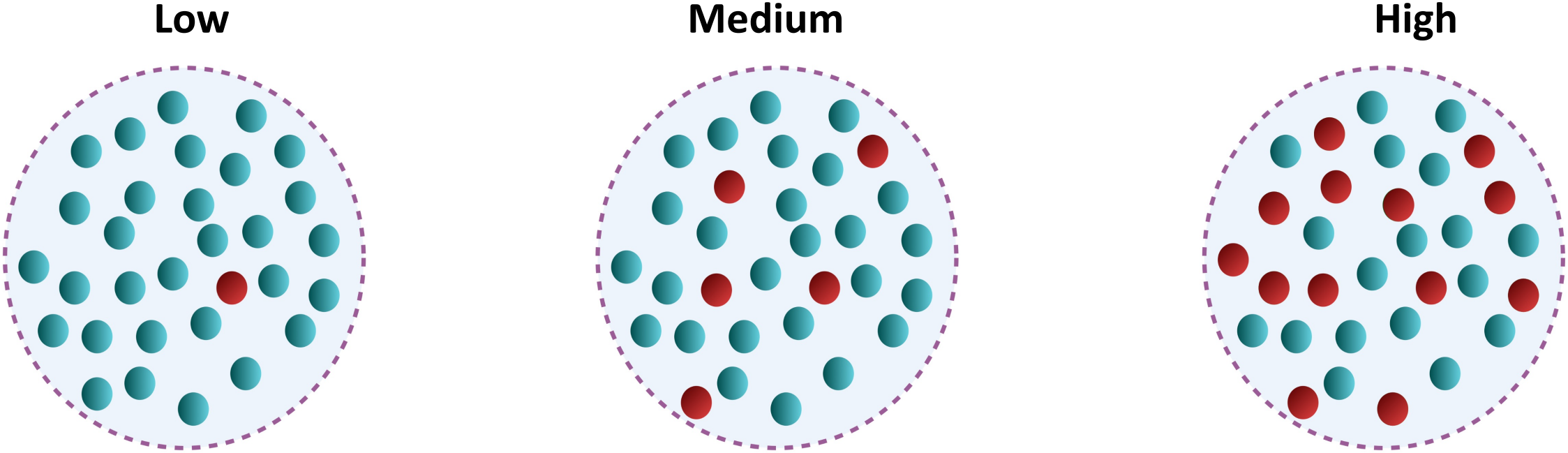


NASH Prevalence



**NASH + NAS  $\geq$  4 + Fibrosis Stage 2-3**

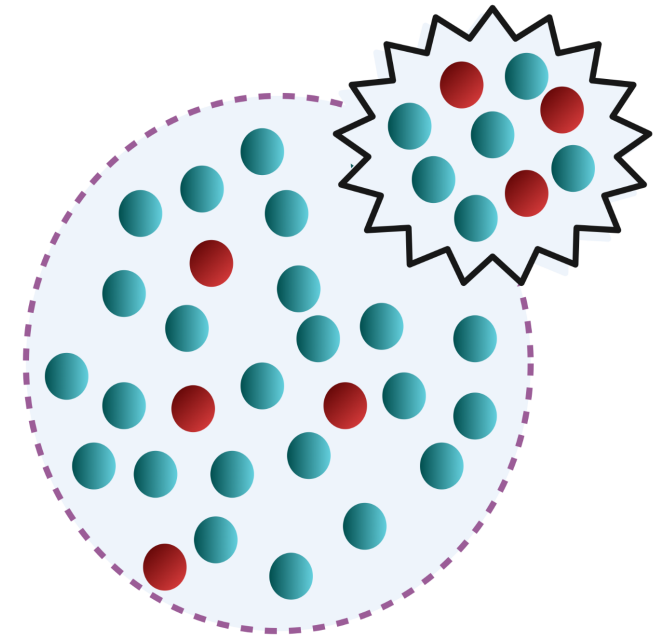
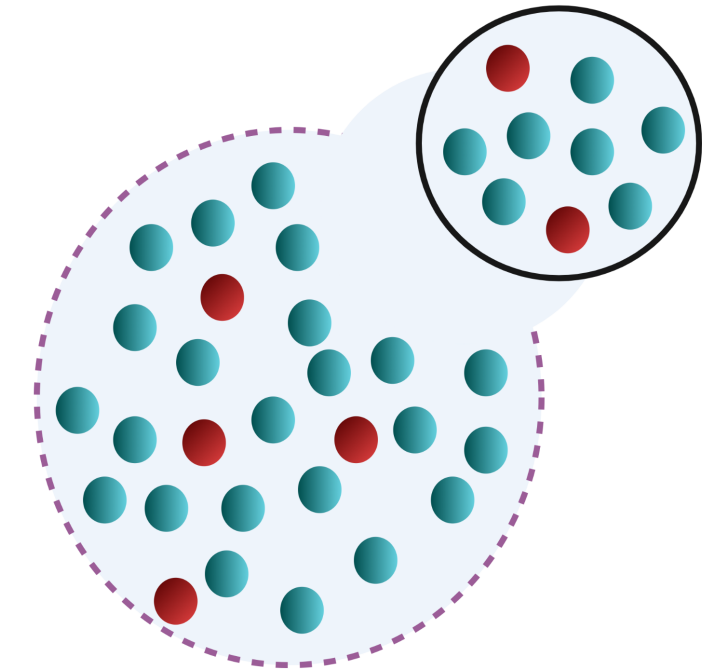
# Applying Biomarker to Different Clinical Setting

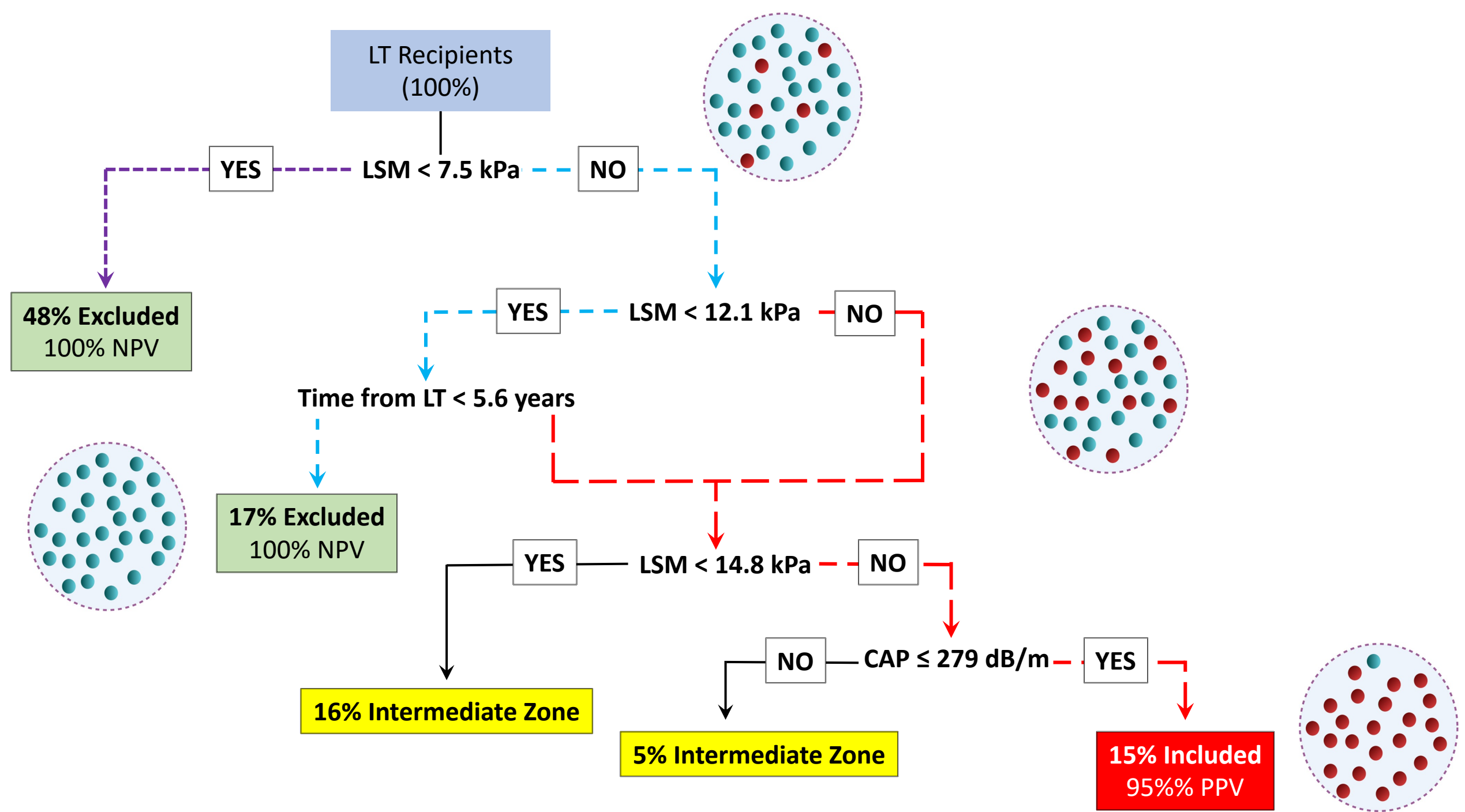


	Prevalence	AUROC	PPV
Eilenberg et. al. HBSN 2021	8%	0.79	36%
Siddiqui et. al. CGH. 2019	32%	0.94	53%
Anstee et. al. Hepatol 2019	70%	0.80	93%

# Use of Biomarker to Screen Patients

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# Impact of AASLD Practice Guidelines on NALFD on Clinical Trial Referral

## HEPATOLOGY

### PRACTICE GUIDANCE

### AASLD practice guidance on the clinical assessment and management of nonalcoholic fatty liver disease

 Rinella, Mary E.<sup>1</sup>;  Neuschwander-Tetri, Brent A.<sup>2</sup>;  Siddiqui, Mohammad Shadab<sup>3</sup>;  Abdelmalek, Manal F.<sup>4</sup>;  Caldwell, Stephen<sup>5</sup>;   
Barb, Diana<sup>6</sup>;  Kleiner, David E.<sup>7</sup>;  Loomba, Rohit<sup>8</sup>

### Screening Recommended

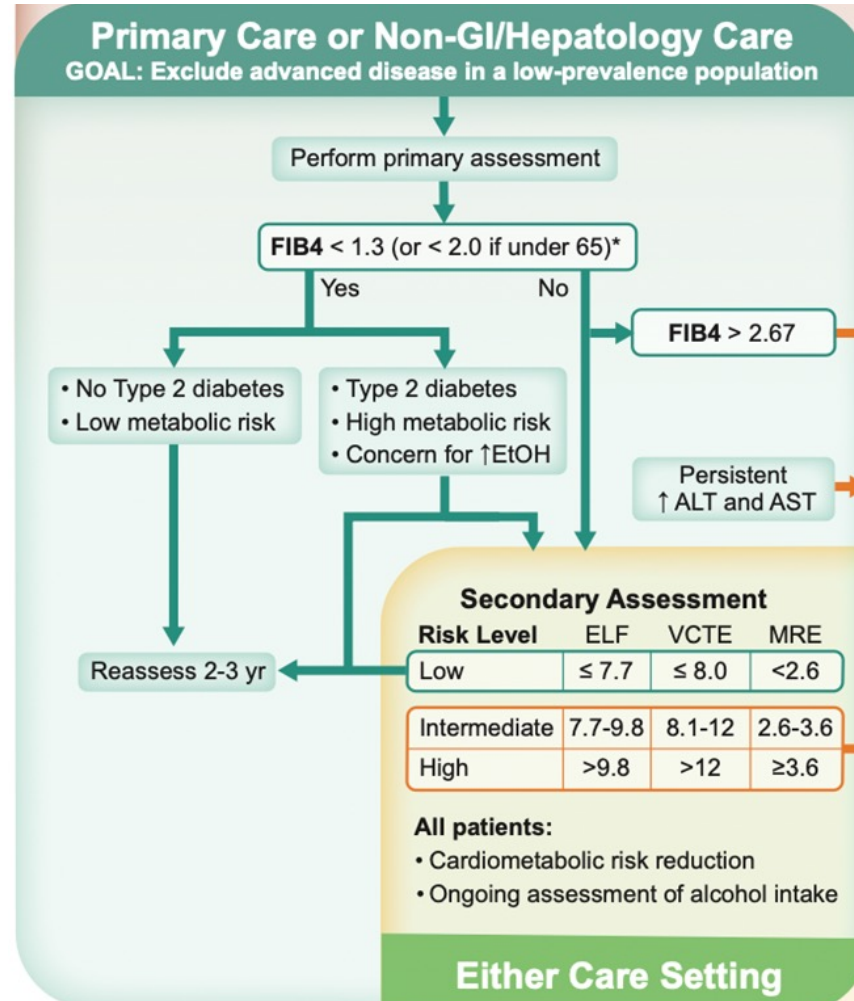
Type 2 Diabetes Mellitus

Medically Complicated Obesity

First-degree relative in patient with cirrhosis due to NASH

NAFLD in the context of moderate alcohol use

# Impact of AASLD Practice Guidelines on NALFD on Clinical Trial Referral

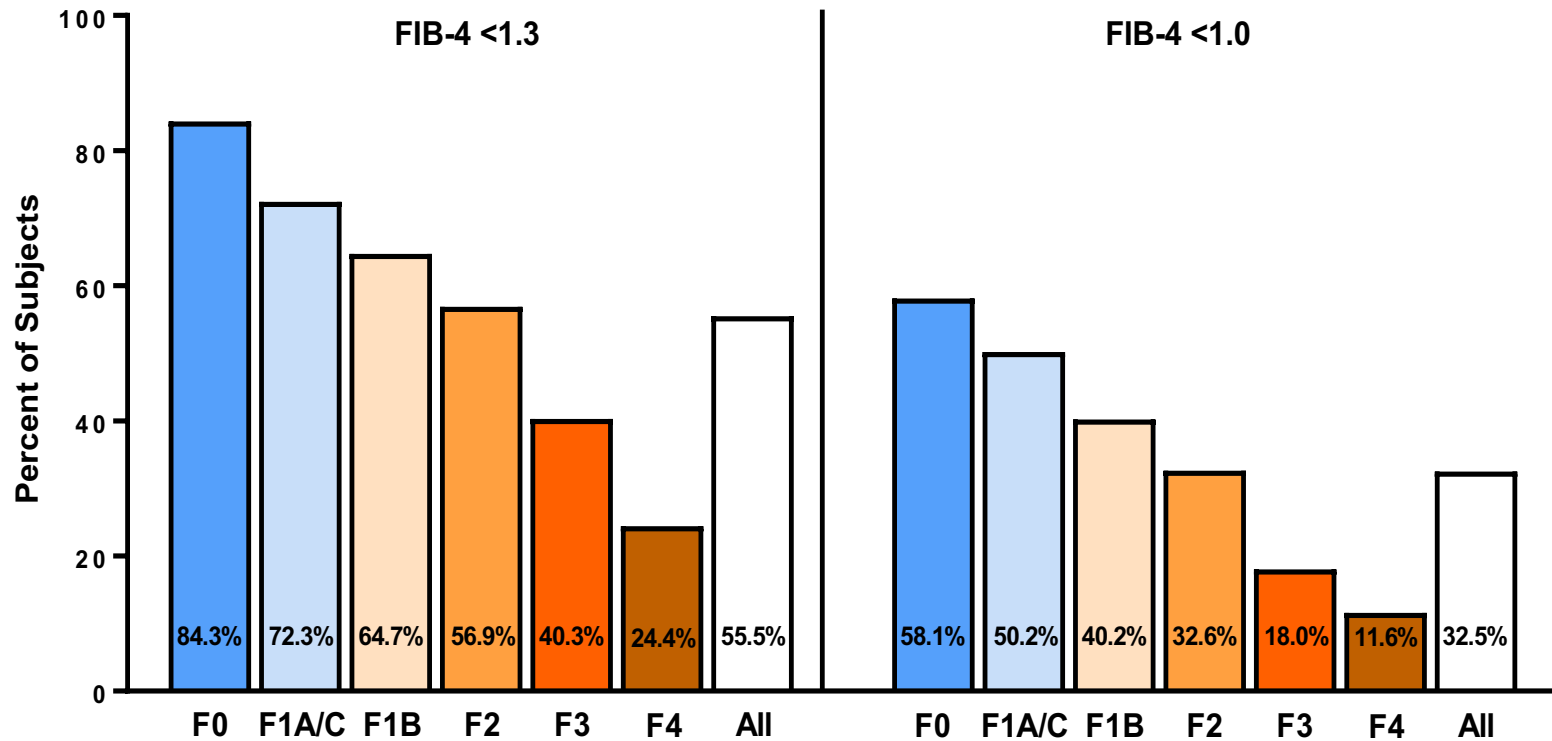


Increase number of patients who are referred for NAFLD for specialized care (i.e. Gastroenterology & Hepatology)



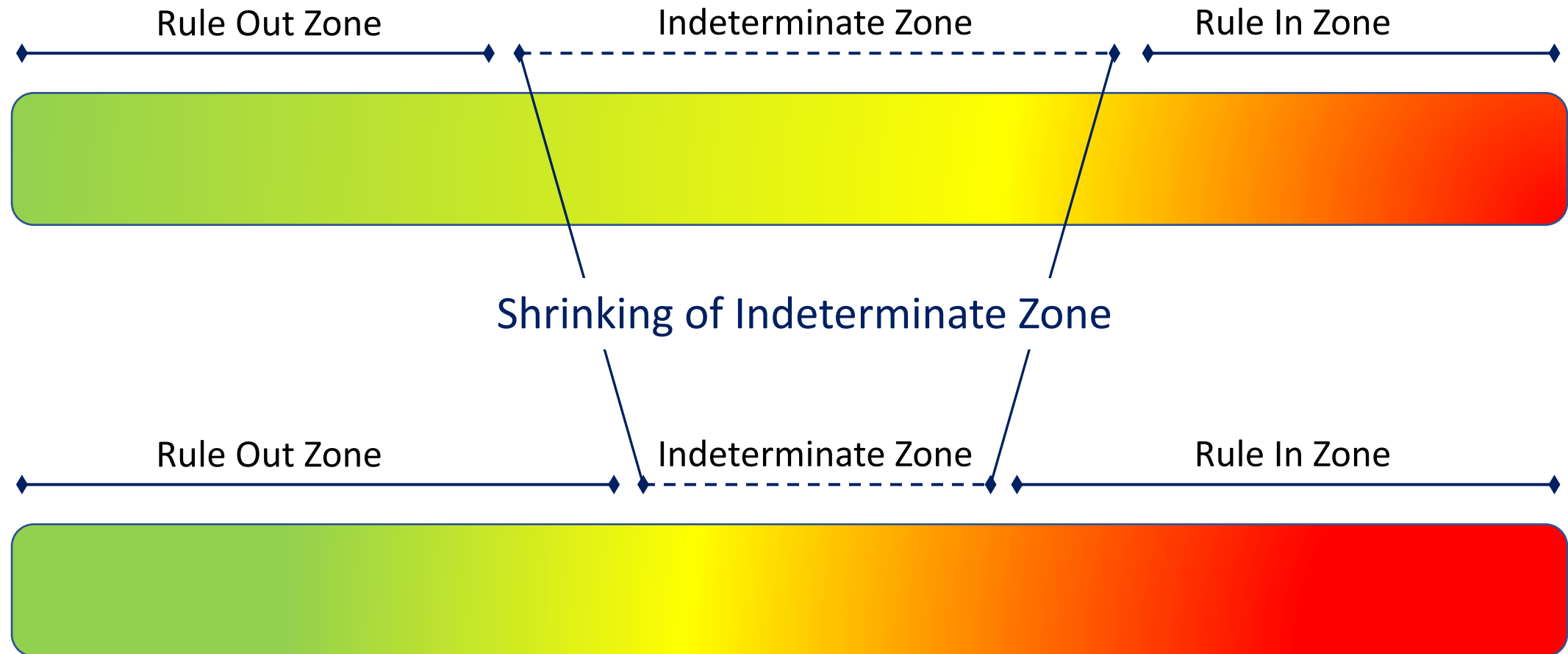
# Using FIB-4 For Screening

## Screening Data of 2000 Patients in Resmetirom Phase 3 Clinical Trial (MAESTRO-NASH)

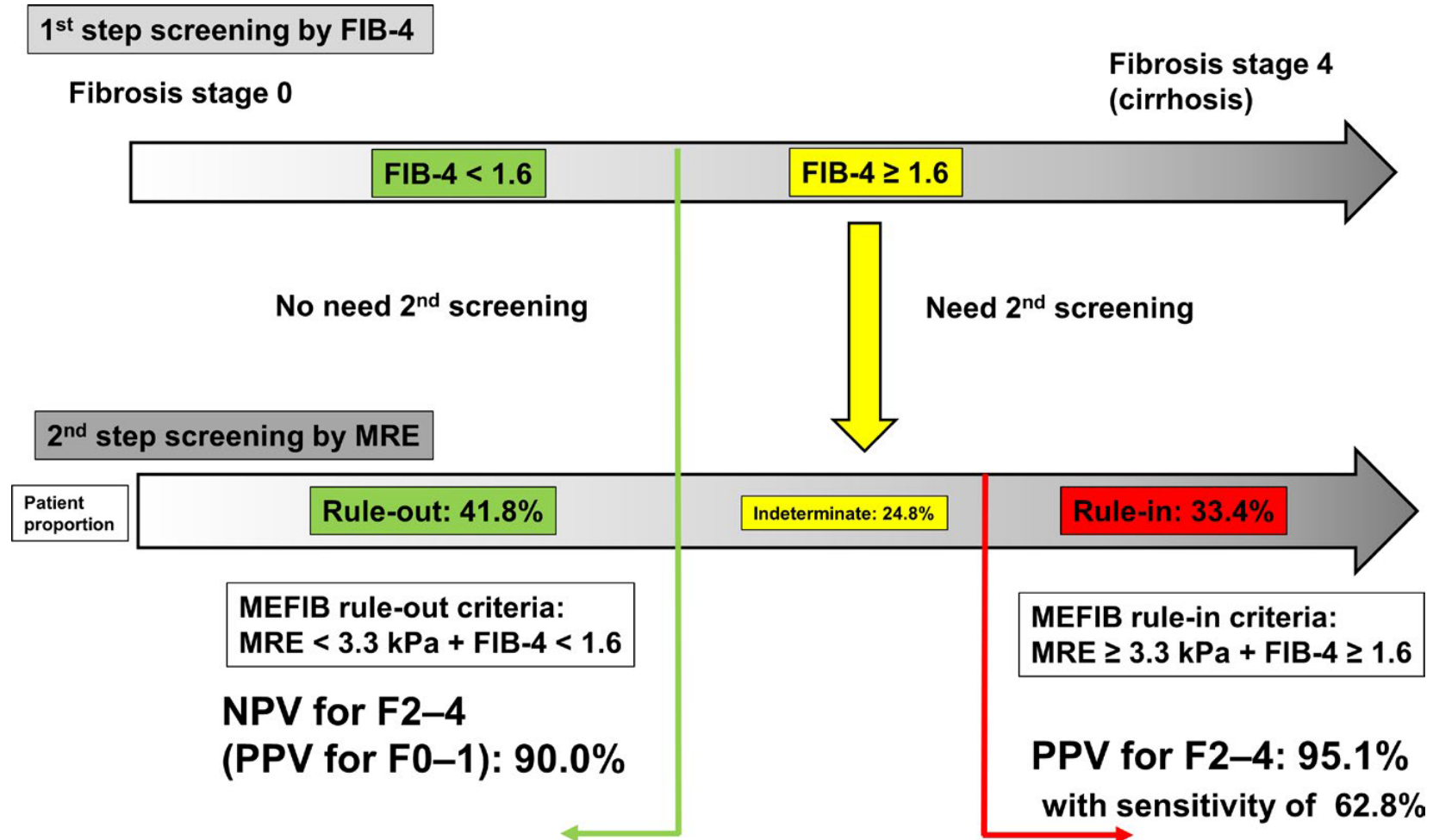


46% and 59% of patients with NASH + NAS ≥4 + stage 2-3 fibrosis had FIB-4 <1.3 and < 1.0, respectively

# Biomarkers in Clinical Trial Screening

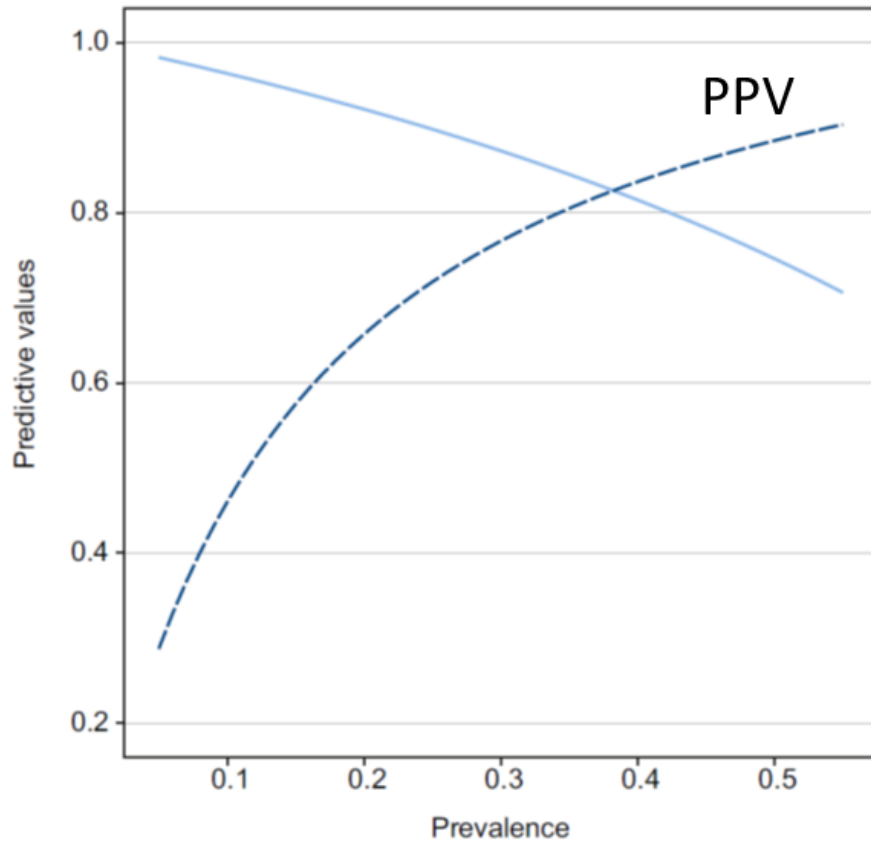


# MEFIB for Prediction of Fibrosis Stages 2-4

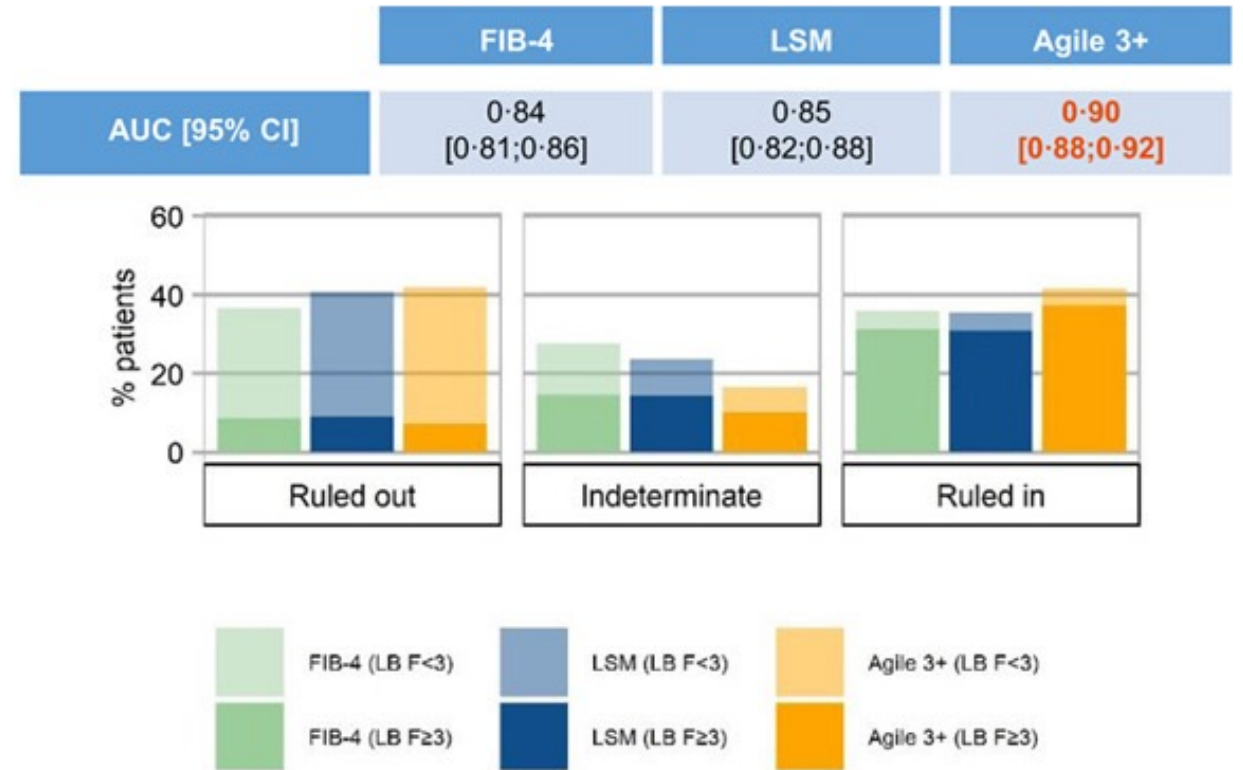


# Targeting Fibrosis to Reduce Indeterminate Range

Prevalence of Advanced Fibrosis > 50%



Rule out zone: <0.451  
Rule in zone: ≥ 0.679



# FAST Score For Diagnosis of NASH + $NAS \geq 4$ + $F \geq 2$

## FAST SCORE: LSM + CAP + AST

Pooled cohort data n= 1026



NASH CRN cohort n= 585



Validation in NASH CRN cohort

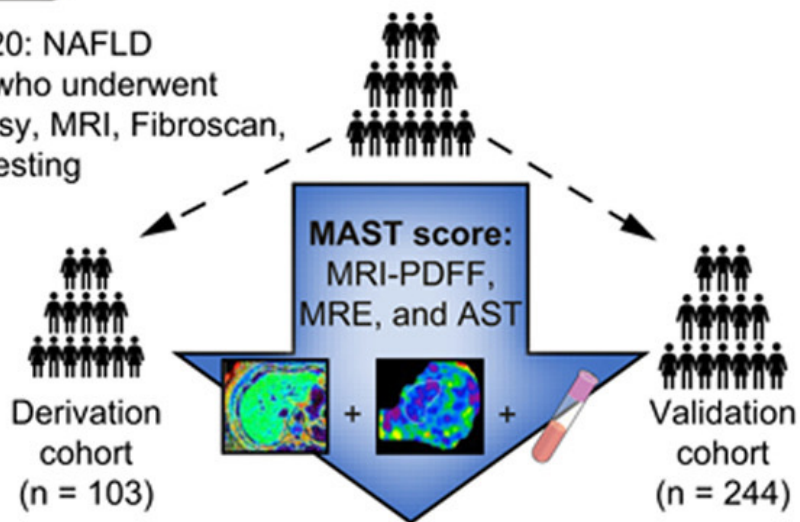
	AUROC	P-value (Comparison vs. FAST)
<b>FAST</b>	0.807	--
<b>Log LSM</b>	0.774	0.04
<b>FIB-4</b>	0.730	0.0003
<b>NFS</b>	0.668	<0.0001
<b>APRI</b>	0.739	<0.0001

Rule out zone:  $FAST \leq 0.35$   
Rule in zone:  $FAST \geq 0.67$

# MAST Score For Diagnosis of NASH + $NAS \geq 4$ + $F \geq 2$

## Methods

2016-2020: NAFLD patients who underwent liver biopsy, MRI, Fibroscan, and lab testing



**Goal:** Identify Fibro-NASH:  
NASH + NAFLD activity score  $\geq 4$   
+ significant fibrosis ( $\geq F2$ )

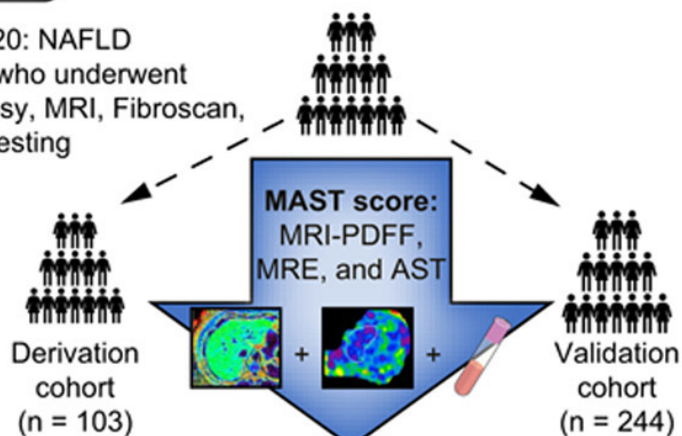
## Findings

Score	Sample	ROC area	Sensitivity	Specificity	PPV	NPV
MAST	Derivation	0.858	94.4%	72.9%	42.5%	98.4%
MAST	Validation	0.929	89.3%	73.1%	30.1%	98.1%
FAST	Validation	0.868	93.1%	64.1%	25.0%	98.6%
NAFLD (NFS)	Derivation	0.748	100.0%	52.9%	30.5%	100.0%
NAFLD (NFS)	Validation	0.689	58.6%	66.6%	18.7%	92.5%
Fib-4	Derivation	0.891	88.9%	74.7%	42.1%	97.0%
Fib-4	Validation	0.711	20.7%	95.5%	37.5%	90.2%

# MAST Score For Diagnosis of NASH + NASH ≥ 4 + F ≥ 2

## Methods

2016-2020: NAFLD patients who underwent liver biopsy, MRI, Fibroscan, and lab testing

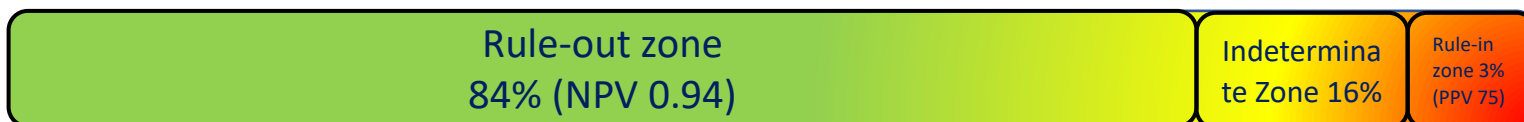


**Goal:** Identify Fibro-NASH:  
NASH + NAFLD activity score  $\geq 4$   
+ significant fibrosis ( $\geq F2$ )

## MAST



## FAST



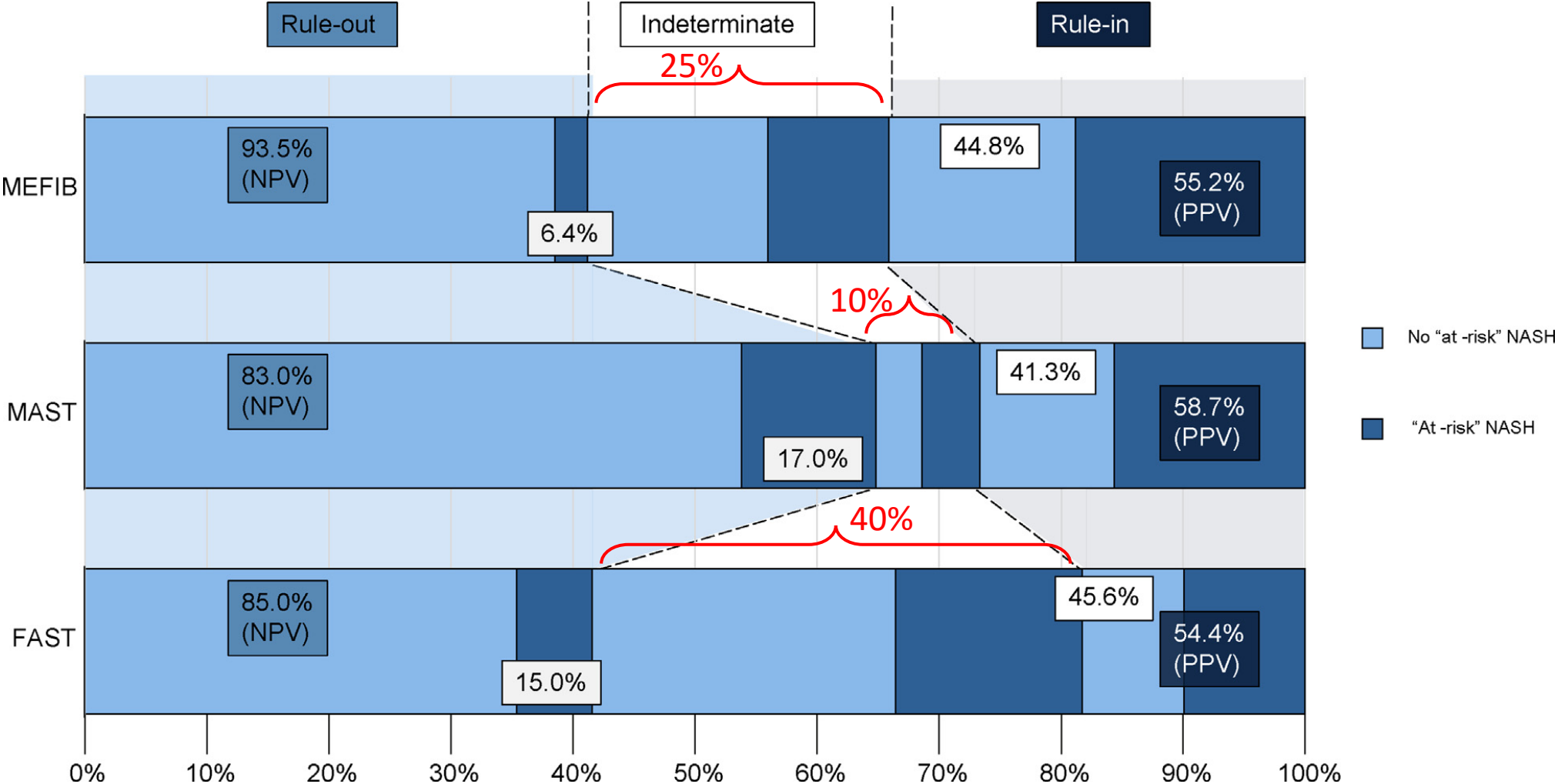
Rule out zone: FAST  $\leq 0.35$

Rule in zone: FAST  $\geq 0.67$

Rule out zone: MAST  $\leq 0.165$

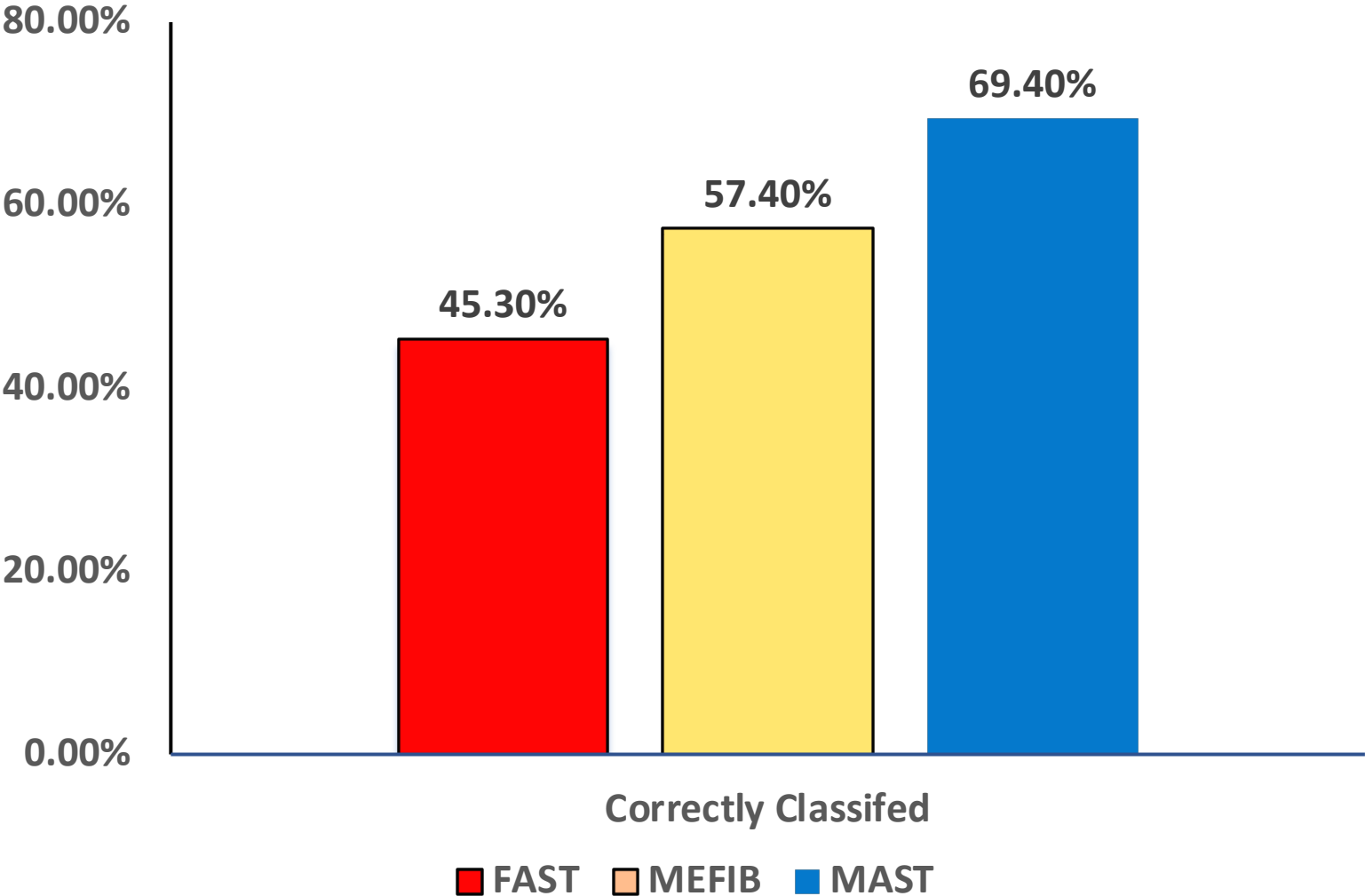
Rule in zone: MAST  $\geq 0.242$

# Comparison of Combinational Scores to Detect 'At Risk' NASH





# Comparison of Combinational Scores to Detect 'At Risk' NASH



Adapted, Courtesy of Dr. Nouredin

# Comparison of Combinational Scores to Detect 'At Risk' NASH

## MAST



## FAST



## MEFIB



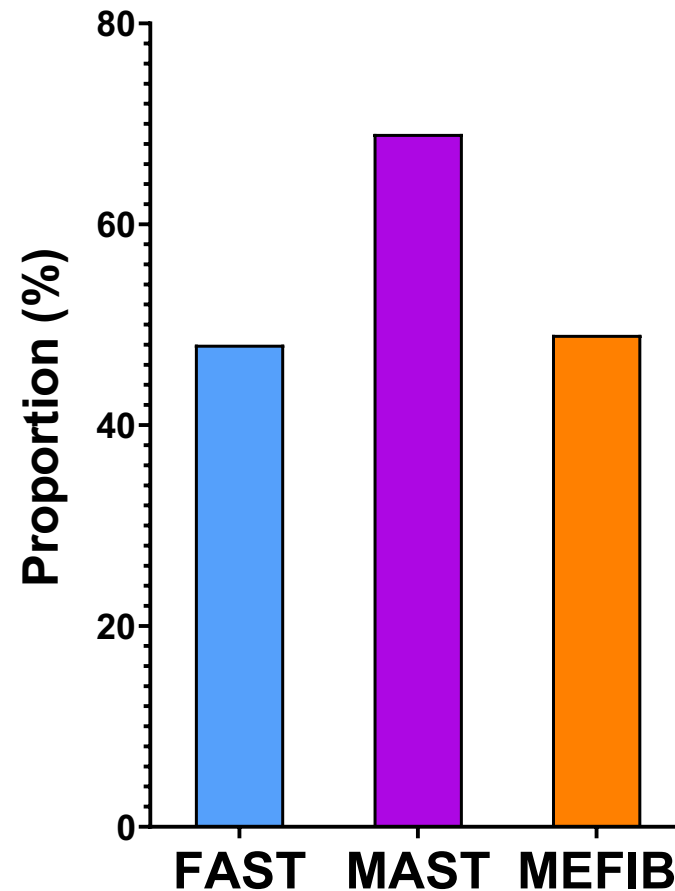
## FIB-4



# Comparison of Combinational Scores to Detect 'At Risk' NASH

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## % of Patients Correctly Classified



# Location of Screening Matters

	<u>Cost</u>	<u>Availability</u>	<u>Patient Burden</u>	<u>Biomarker</u>
Primary Care	0	+++	None	FIB-4
Endocrinology	+	++	Low	FIB-4, ELF, NIS34, VCTE
Community Based Gastroenterology	++	+	Med-High	ELF, NIS2/4, VCTE, MRI/MRE
Specialized NAFLD Practice	+++	++	Med-High	VCTE-based, MRI/MRE-based metabolomics, proteomics
				Fibro-NASH

# Thank You for Your Attention

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