



Disparities in Test Performance:  
NITs for Risk Stratifications of NASH:  
Performance in Different Regions of the World

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# Disclosures

- Advisory board member Board/Consultant: 89BIO, Altimmune, Gilead, cohBar, Cytodyn, Intercept, Pfizer, Novo Nordisk, Blade, EchoSens, Fractyl, Madrigal, NorthSea, Prespectum, Terns, Siemens and Roche diagnostic
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# Outline

- Are there differences in NITs guidance around the world?
- Do blood-based NITs perform similarly?
  - Ethnicity/Region of the world
  - Sex
  - Age
- Do blood-based NITs monitor disease progression similarly?
- Do blood-based NITs predict outcomes similarly?

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# Cases From Around the World

Ms. Martin is a 42 yo F with history of T2DM who presents to hepatologist in London with ALT of 76 and AST 52

Ms. Vasquez is 52 yo M with history of T2DM who presents to hepatologist in Buenos Aires with ALT of 76 and AST 52

Mr. Wang is a 62 yo M with history of T2DM who presents to hepatologist in Hong Kong with ALT of 76 and AST 52

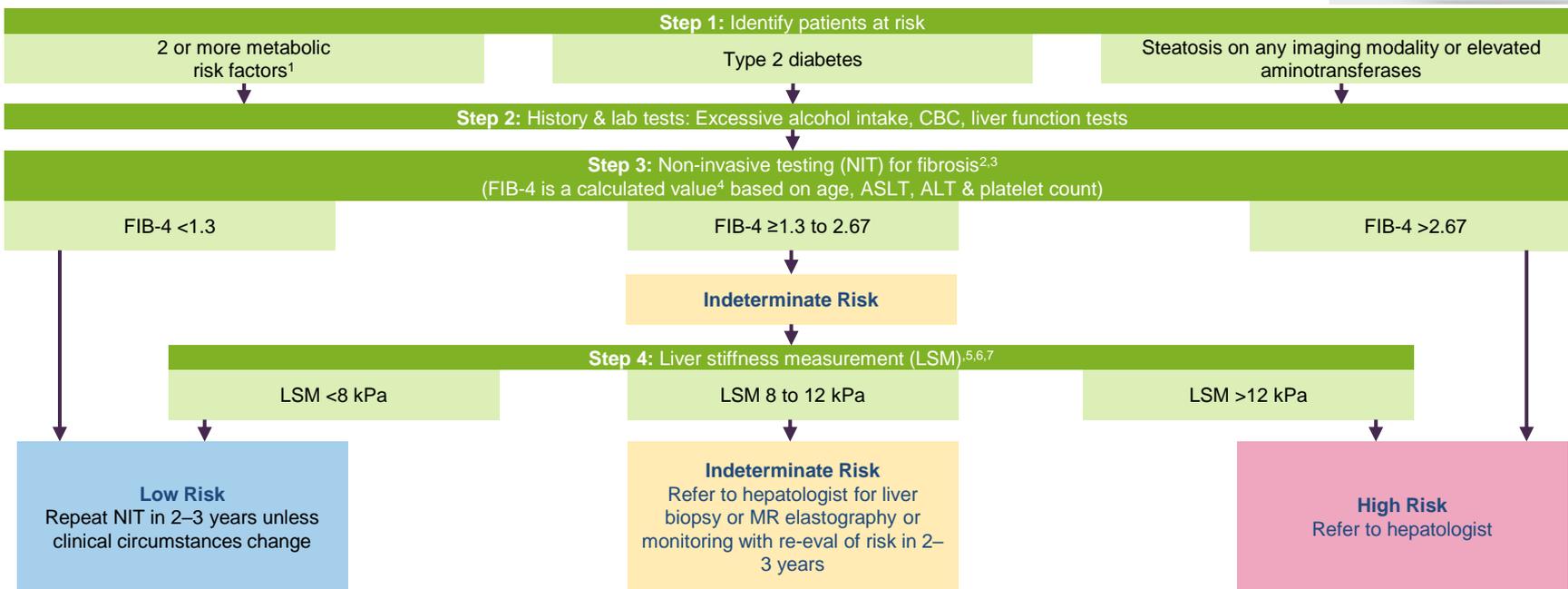
Ms. Smith is 49 yo AA F with history of T2DM who presents to hepatologist in Chicago with ALT of 76 and AST 52



# AGA 2021



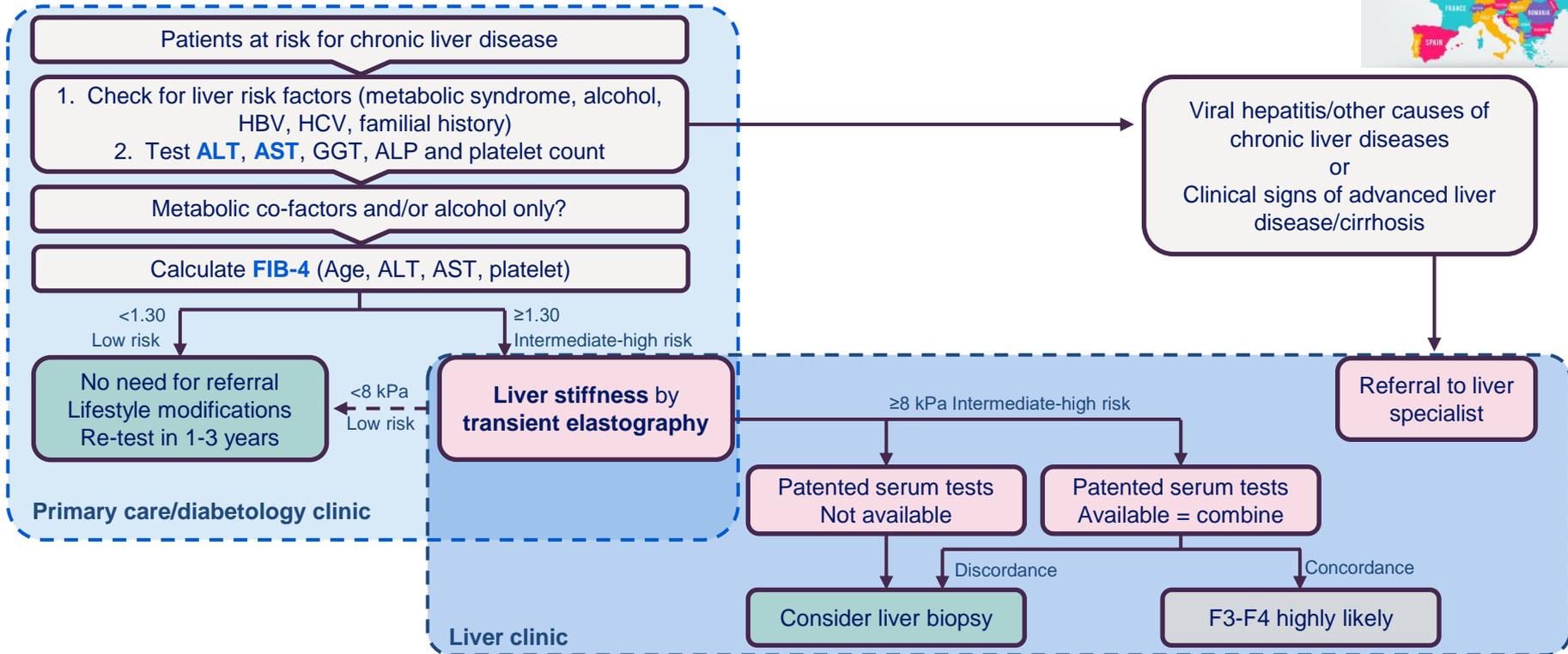
Primary care, endocrinologists, gastroenterologists and obesity specialists should screen for NAFLD with advanced fibrosis



1. Metabolic risk factors: central obesity, high triglycerides, low HDL cholesterol, hypertension, prediabetes, or insulin resistance. 2. For patients age >65, use FIB-4 <2.0 as the lower cutoff. Higher cutoff does not change. 3. Other NITs derived from routine laboratories can be used instead of FIB-4. 4. Many online FIB-4 calculators are available such as <https://www.mdcalc.com/fibrosis-4-fib-4-index-liver-fibrosis>. 5. Ultrasound acceptable if vibration-controlled transient elastography (VCTE, FibroScan<sup>®</sup>) is unavailable. Consider referral to hepatologist for patients with hepatic steatosis on ultrasound who are indeterminate or high risk based on FIB-4. 6. LSM values are for VCTE (FibroScan<sup>®</sup>). Other techniques such as bidimensional shear wave elastography or point shear wave elastography can also be used to measure LSM. Proprietary commercially available blood NITs may be considered for patients considered indeterminate or high risk based on FIB-4 or APRI, or where LSM unavailable. 7. Eddowes et al. uses 8.2 and 12.1 kPa as cutoffs for LSM using VCTE. Validation of simple (rounded) cutoffs reported by Papatheodoridi et al.

Adapted from: Kanwal F et al. *Gastroenterol.* 2021.

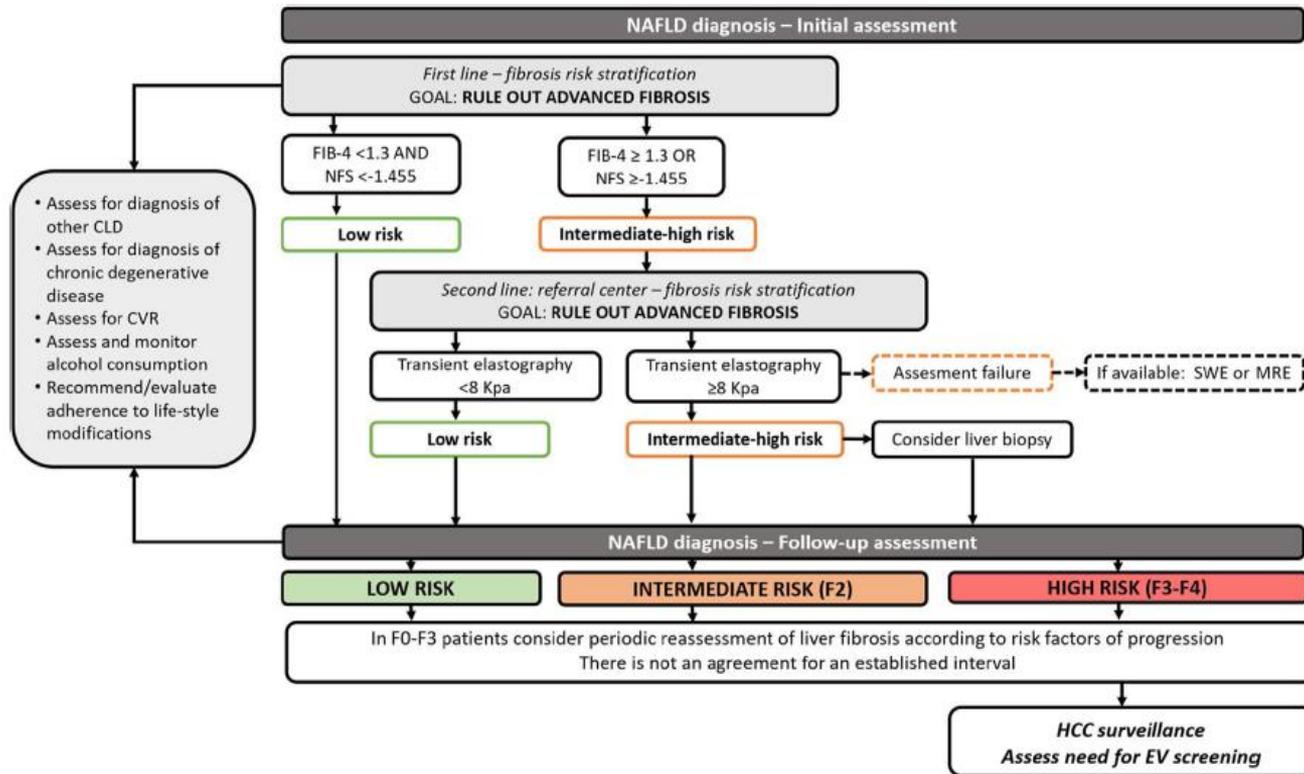
# EASL 2021



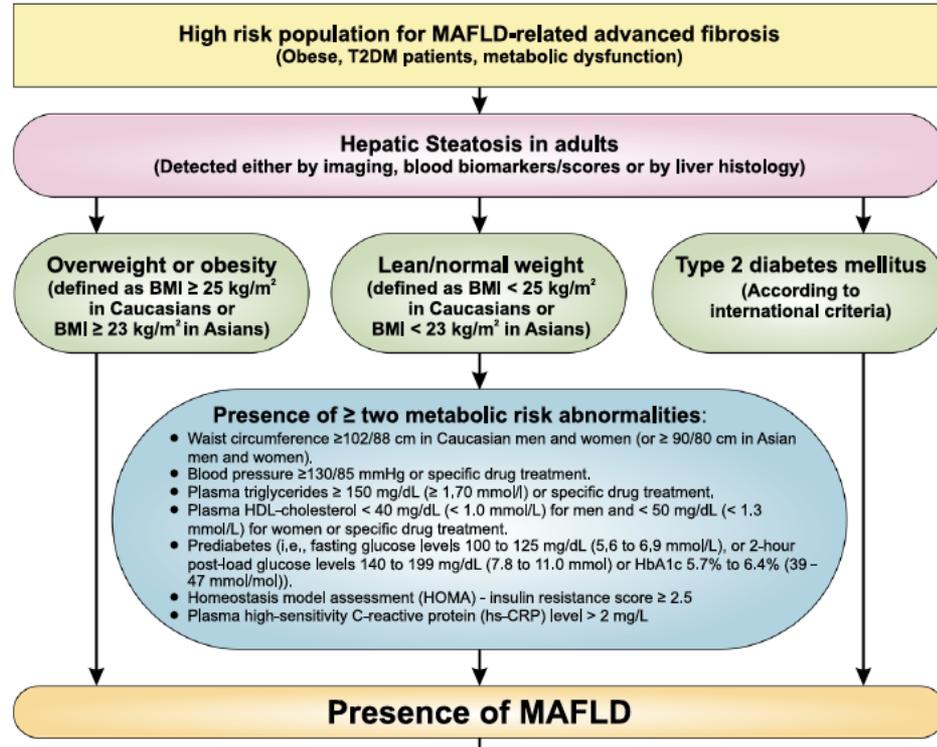
ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; EASL, European Association for the Study of the Liver; F3, advanced (bridging) fibrosis; F4, advanced liver scarring (cirrhosis); FIB-4, fibrosis-4 index; GGT, gamma-glutamyl transferase; HBV, hepatitis B virus; HCV, hepatitis C virus; kPa, kilopascal.

EASL. *J Hep.* 2021. doi:10.1016/j.jhep.2021.05.025.

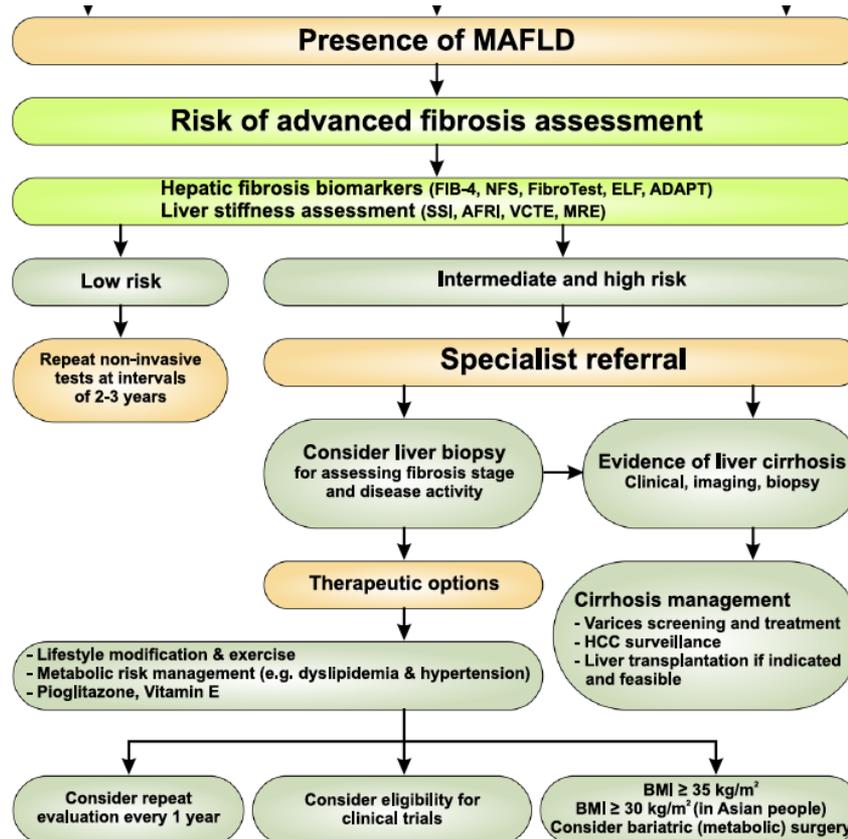
# Latin American Association for the Study of the Liver (ALEH) Practice Guidance for the Diagnosis and Treatment of NAFLD



# The Asian Pacific Association for the Study of the Liver Clinical Practice Guidelines for the Diagnosis and Management of MAFLD



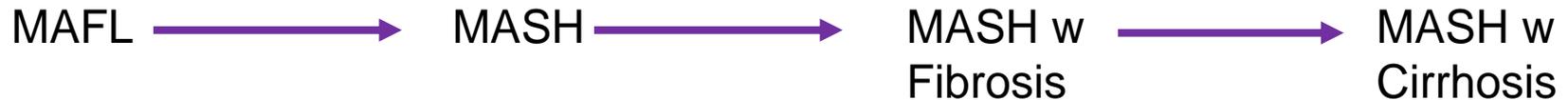
# The Asian Pacific Association for the Study of the Liver Clinical Practice Guidelines for the Diagnosis and Management of MAFLD





If MAFLD Is the Disease, then What Is  
NASH.....MASH?

# Noureddin's Proposal for the Spectrum of MAFLD

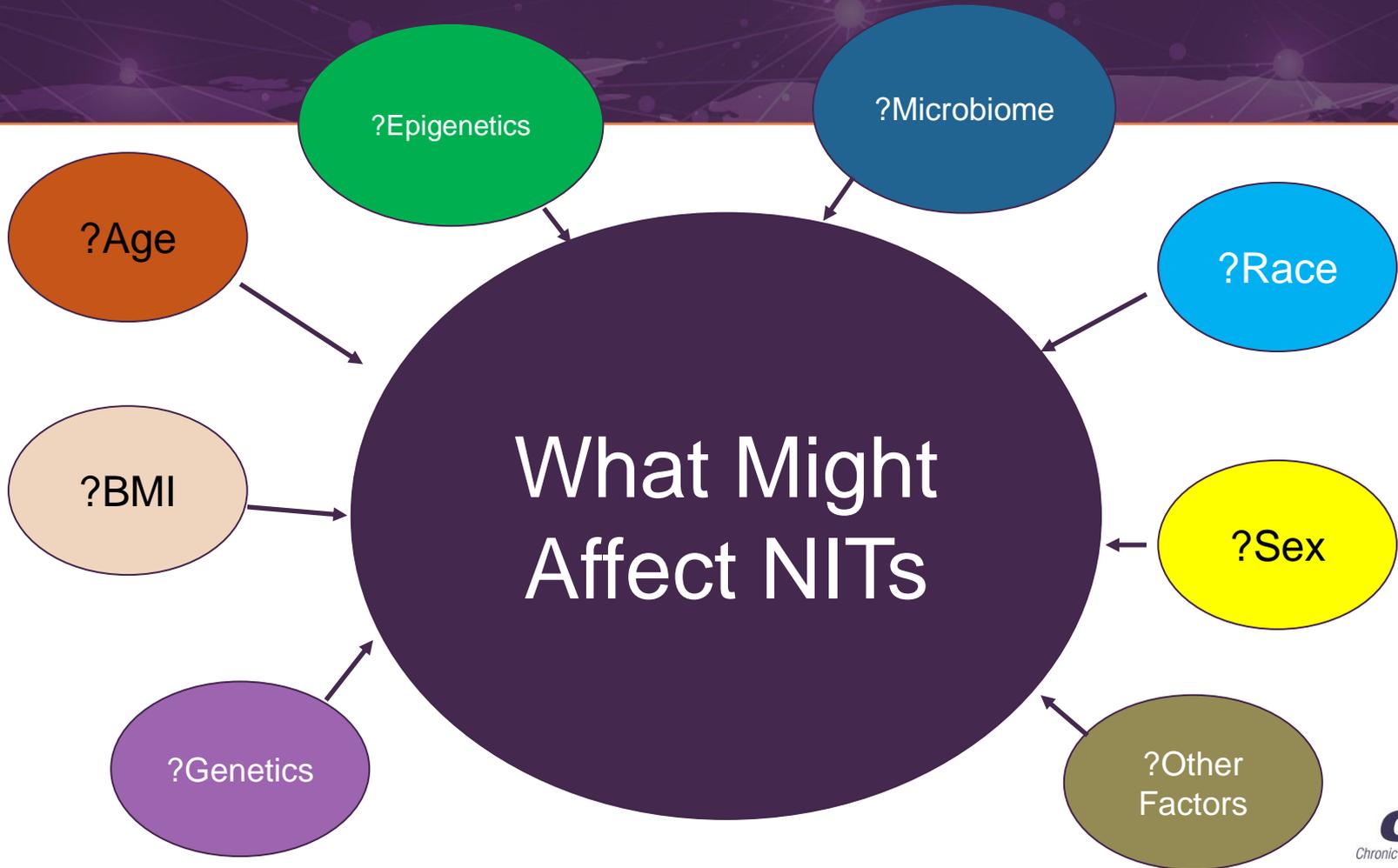


Africa?



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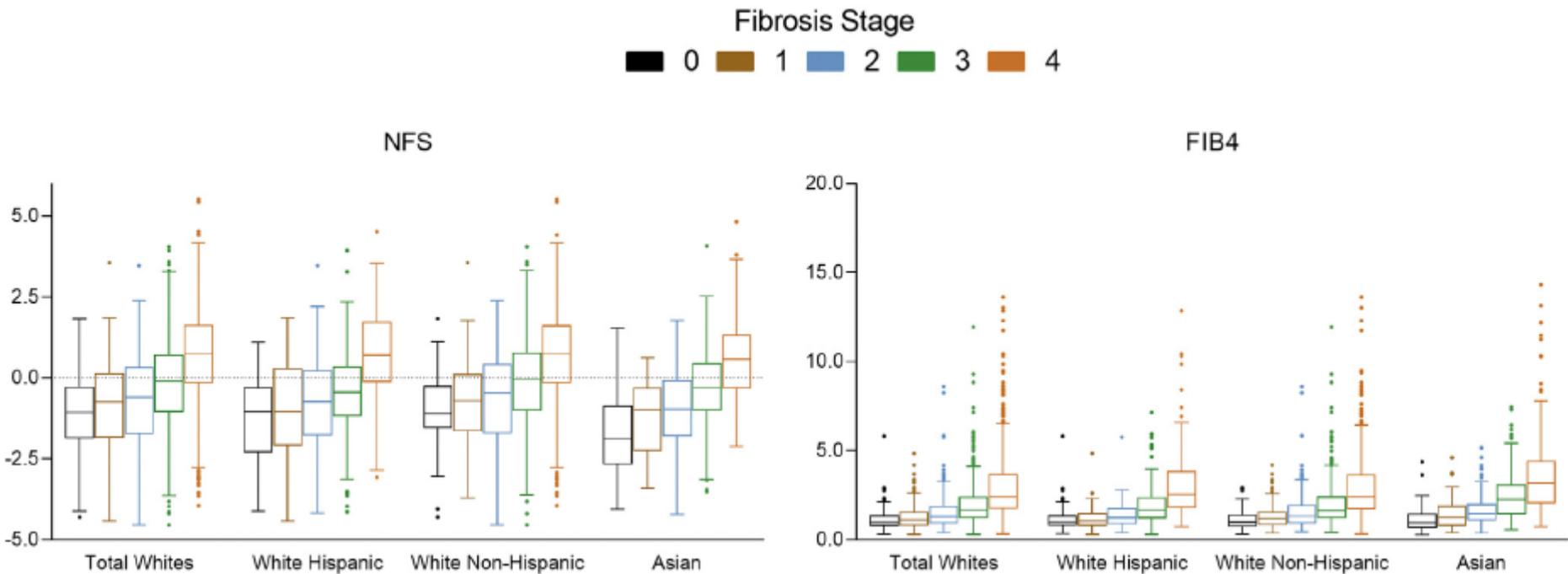
# Why Would NITs Perform Differently in Various Patients?

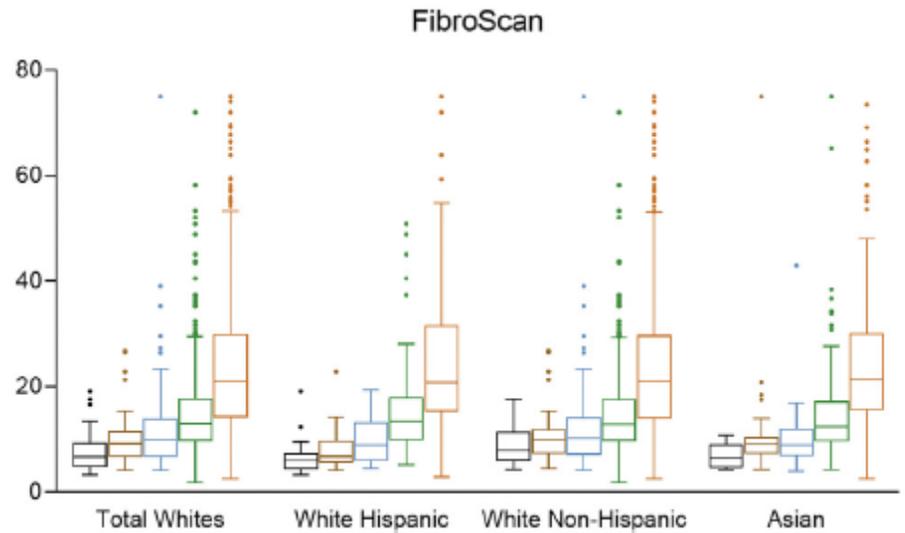
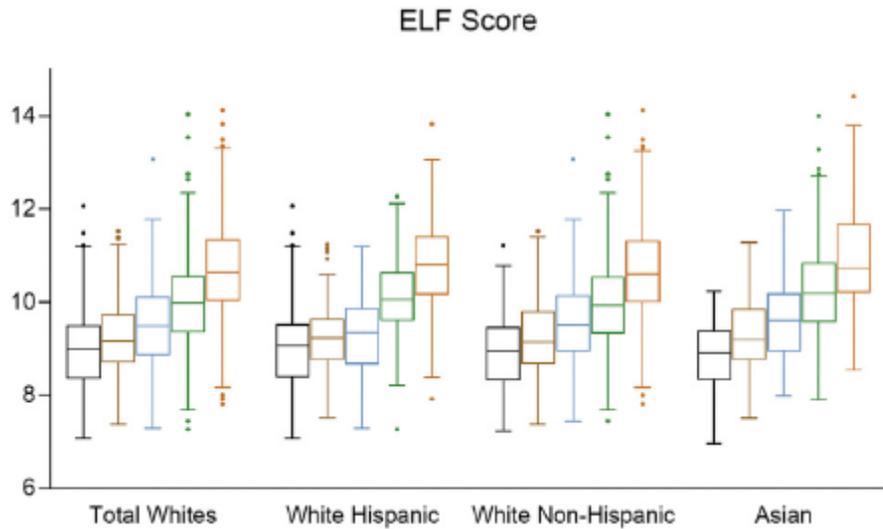
- Nonobese NAFLD was reported in ~ 40% of the global NAFLD population.
- Asians tend to develop NAFLD and metabolic complications at a lower body mass index (BMI), and lean or nonobese NAFLD is more often described in Asians.
- BMI is as a component (eg, the NAFLD fibrosis score).
- Liver stiffness measurement by VCTE might be less accurate in patients with extreme BMI
- Age has been proposed as A factor
- Genetic differences (? role in metabolomics, proteomics and microbiome as NTIs)

# Assessing NITS Performance From a Large RCT (Selonsertib) and the Effect of Ethnicity, Age and BMI

- Assessed patients with NASH and F3 and F4
- 3207 patients
  - White (1742)
  - White Hispanics (539)
  - Asians (762)
- 72% of whites and 67% of Asians had advanced fibrosis
- Centrally read biopsy
- FIB-4, NFS, ELD and VCTE

		White				White and Asian (N = 3043)	White vs Asian P value	Hispanic vs non-Hispanic P value
		Hispanic (n = 539)	Non-Hispanic (n = 1734)	All white (n = 2281)	Asian (n = 762)			
Slightly lower Esp F4	NAFLD fibrosis score	-0.21 (-1.23 to 0.69)	0.26 (-0.72 to 1.15)	0.18 (-0.86 to 1.09)	-0.15 (-1.04 to 0.76)	0.1 (-0.92 to 0.98)	< .0001	< .0001
	F0	-1.04 (-2.28 to -0.4)	-1.12 (-1.52 to -0.29)	-1.07 (-1.86 to -0.29)	-1.87 (-2.62 to -0.93)	-1.22 (-2.11 to -0.45)	.129	.1201
	F1	-1.05 (-2.08 to 0.29)	-0.71 (-1.65 to 0.09)	-0.75 (-1.82 to 0.09)	-0.99 (-2.23 to -0.33)	-0.88 (-2.01 to 0.02)	.0532	.2632
	F2	-0.73 (-1.77 to 0.23)	-0.47 (-1.7 to 0.39)	-0.61 (-1.73 to 0.3)	-0.98 (-1.79 to -0.1)	-0.73 (-1.74 to 0.26)	.5721	.357
	F3	-0.44 (-1.18 to 0.34)	-0.06 (-1 to 0.77)	-0.11 (-1.04 to 0.69)	-0.3 (-1 to 0.43)	-0.18 (-1.01 to 0.6)	.0521	.0337
	F4	0.7 (-0.13 to 1.69)	0.72 (-0.16 to 1.61)	0.72 (-0.15 to 1.63)	0.57 (-0.3 to 1.3)	0.68 (-0.18 to 1.53)	.0417	.7883
Higher in Asian at F2 (P ¼ .015), F3 (P < .001), and F4 (P < .001)	FIB-4	1.58 (1.03-2.44)	1.84 (1.23-2.78)	1.78 (1.19-2.69)	2.11 (1.33-3.31)	1.85 (1.22-2.86)	< .0001	< .0001
	F0	1.03 (0.82-1.34)	1 (0.75-1.34)	1.02 (0.8-1.34)	0.97 (0.68-1.47)	1.01 (0.77-1.36)	.8487	.3447
	F1	1.05 (0.8-1.49)	1.18 (0.85-1.56)	1.12 (0.82-1.56)	1.25 (0.8-1.89)	1.18 (0.82-1.59)	.2873	.2666
	F2	1.24 (0.92-1.73)	1.31 (0.96-1.94)	1.29 (0.94-1.87)	1.46 (1.11-1.99)	1.37 (0.99-1.91)	.0151	.0983
	F3	1.66 (1.22-2.35)	1.65 (1.23-2.41)	1.65 (1.23-2.41)	2.26 (1.47-3.08)	1.76 (1.29-2.61)	< .0001	.9003
	F4	2.54 (1.82-3.83)	2.41 (1.73-3.61)	2.43 (1.75-3.66)	3.17 (2.07-4.42)	2.55 (1.8-3.84)	< .0001	.1955
Higher in Asian than in white patients at F3 (P=.002) and F4 (P = .023)	ELF	9.92 (9.07-10.8)	10.11 (9.36-10.88)	10.07 (9.3-10.86)	10.13 (9.36-10.89)	10.08 (9.32-10.87)	.1306	.0037
	F0	9.07 (8.39-9.51)	8.95 (8.32-9.45)	8.99 (8.37-9.5)	8.91 (8.35-9.34)	8.97 (8.37-9.48)	.5805	.5725
	F1	9.23 (8.77-9.62)	9.14 (8.68-9.79)	9.15 (8.7-9.73)	9.18 (8.76-9.83)	9.16 (8.72-9.75)	.7284	.7307
	F2	9.35 (8.7-9.85)	9.5 (8.94-10.15)	9.49 (8.86-10.11)	9.6 (8.94-10.18)	9.51 (8.89-10.13)	.1422	.0588
	F3	10.05 (9.62-10.63)	9.93 (9.33-10.53)	9.97 (9.36-10.56)	10.18 (9.57-10.84)	10.02 (9.42-10.63)	.0022	.1227
	F4	10.8 (10.17-11.41)	10.6 (10-11.3)	10.64 (10.04-11.34)	10.72 (10.21-11.68)	10.66 (10.07-11.39)	.0234	.0361





# Changes by Ethnicity, Any?

**Table 3.** Performance of Noninvasive Tests in Diagnosing Advanced Fibrosis (F3–F4) in White and Asian Patients (2-cutoff Model)

	Percentage of patients with F3–F4	AUROC (95% CI)	Cutoff	% (95% CI)					
				Sensitivity	Specificity	PPV	NPV	Gray zone <sup>a</sup>	Accuracy
<b>White Hispanic patients</b>									
NAFLD fibrosis score (n = 372)	66	0.73 (0.68–0.78)	<–1.455 to ≥0.676	90 (86–94)	90 (84–95)	95 (91–97)	83 (75–89)	55 (50–60)	90 (87–93)
FIB-4 (n = 528)	58	0.81 (0.78–0.85)	<1.3 to ≥2.67	81 (76–85)	97 (94–99)	97 (94–99)	78 (73–83)	42 (37–46)	88 (84–90)
ELF (n = 539)	58	0.83 (0.79–0.86)	<9.8 to ≥11.3	78 (73–83)	99 (97–100)	99 (97–100)	77 (72–82)	41 (37–45)	87 (84–90)
Liver stiffness measurement (n = 238)	76	0.87 (0.82–0.92)	<9.9 to ≥11.4 kPa	84 (78–89)	75 (62–86)	92 (86–95)	59 (47–71)	5 (2–8)	82 (76–87)
<b>White non-Hispanic patients</b>									
NAFLD fibrosis score (n = 1348)	86	0.72 (0.68–0.76)	<–1.455 to ≥0.676	89 (87–91)	85 (79–90)	97 (96–98)	56 (50–62)	49 (46–52)	88 (87–90)
FIB-4 (n = 1697)	77	0.76 (0.73–0.78)	<1.3 to ≥2.67	81 (78–83)	91 (88–94)	97 (96–98)	58 (54–62)	45 (43–48)	83 (81–85)
ELF (n = 1720)	77	0.77 (0.75–0.8)	<9.8 to ≥11.3	71 (69–74)	97 (95–99)	99 (98–99)	50 (47–54)	47 (45–50)	77 (75–79)
Liver stiffness measurement (n = 1006)	89	0.76 (0.72–0.81)	<9.9 to ≥11.4 kPa	84 (82–87)	65 (55–74)	95 (93–97)	33 (27–40)	8 (7–10)	82 (80–84)
<b>All white patients</b>									
NAFLD fibrosis score (n = 1725)	82	0.73 (0.7–0.76)	<–1.455 to ≥0.676	89 (87–91)	87 (83–91)	97 (96–98)	65 (60–69)	50 (48–53)	89 (87–90)
FIB-4 (n = 2233)	73	0.78 (0.76–0.8)	<1.3 to ≥2.67	81 (79–83)	93 (91–95)	97 (96–98)	64 (61–68)	44 (42–47)	84 (83–86)
ELF (n = 2267)	72	0.79 (0.77–0.81)	<9.8 to ≥11.3	73 (70–75)	98 (96–99)	99 (98–99)	58 (55–61)	46 (44–48)	80 (78–81)
Liver stiffness measurement (n = 1247)	87	0.8 (0.76–0.84)	<9.9 to ≥11.4 kPa	84 (82–86)	68 (61–75)	95 (93–96)	40 (34–46)	8 (6–9)	82 (80–84)
<b>Asian patients</b>									
NAFLD fibrosis score (n = 586)	78	0.75 (0.7–0.8)	<–1.455 to ≥0.676	88 (85–91)	92 (86–96)	98 (96–99)	68 (61–75)	54 (50–58)	89 (86–91)
FIB-4 (n = 735)	69	0.8 (0.76–0.83)	<1.3 to ≥2.67	88 (85–90)	90 (85–93)	95 (92–97)	77 (71–82)	40 (37–44)	88 (86–91)
ELF (n = 748)	68	0.81 (0.77–0.84)	<9.8 to ≥11.3	76 (72–80)	96 (93–98)	98 (96–99)	66 (60–70)	44 (40–47)	83 (80–85)
Liver stiffness measurement (n = 431)	76	0.83 (0.78–0.87)	<9.9 to ≥11.4 kPa	83 (78–87)	78 (68–85)	92 (88–95)	58 (50–67)	10 (7–13)	81 (77–85)

# Does BMI Change Things by Ethnicity?

**Table 4.** Performance of Noninvasive Tests in Diagnosing Advanced Fibrosis (F3-F4) in White and Asian Patients by BMI (2-cutoff Model)

	Percentage of patients with F3-F4	AUROC (95% CI)	Cutoff	% (95% CI)						
				Sensitivity	Specificity	PPV	NPV	Gray zone <sup>a</sup>	Accuracy	
<b>White patients, BMI &lt;30 kg/m<sup>2</sup></b>										
NAFLD fibrosis score (n = 428)	81	0.76 (0.71-0.81)	<-1.455 to ≥0.676	80 (76-84)	99 (93-100)	100 (98-100)	55 (46-63)	58 (53-62)	84 (80-87)	
FIB-4 (n = 429)	81	0.75 (0.69-0.8)	<1.3 to ≥2.67	82 (78-86)	87 (78-93)	96 (93-98)	54 (45-63)	44 (39-49)	83 (79-87)	
ELF (n = 436)	80	0.80 (0.75-0.85)	<9.8 to ≥11.3	70 (65-75)	100 (96-100)	100 (98-100)	45 (38-53)	48 (43-53)	76 (72-80)	
Liver stiffness measurement (n = 263)	81	0.79 (0.73-0.83)	<8.9 to ≥11.1 kPa	78 (73-83)	78 (56-93)	97 (94-99)	26 (16-38)	12 (8-16)	78 (73-83)	
<b>White patients, BMI ≥30 kg/m<sup>2</sup></b>										
NAFLD fibrosis score (n = 1297)	82	0.73 (0.69-0.76)	<-1.455 to ≥0.676	92 (90-94)	83 (78-88)	96 (95-97)	70 (64-75)	48 (45-50)	91 (89-92)	
FIB-4 (n = 1300)	82	0.78 (0.75-0.81)	<1.3 to ≥2.67	80 (77-82)	94 (90-97)	98 (97-99)	50 (45-55)	46 (44-49)	82 (80-84)	
ELF (n = 1310)	82	0.8 (0.76-0.83)	<9.8 to ≥11.3	73 (70-76)	97 (95-99)	99 (98-100)	45 (40-49)	49 (46-52)	78 (75-80)	
Liver stiffness measurement (n = 846)	80	0.71 (0.67-0.83)	<8.9 to ≥11.1 kPa	88 (83-93)	61 (48-73)	97 (95-98)	26 (19-33)	6 (5-8)	84 (81-86)	
<b>Asian patients, BMI &lt;30 kg/m<sup>2</sup></b>										
NAFLD fibrosis score (n = 376)	78	0.75 (0.69-0.81)	<-1.455 to ≥0.676	87 (83-91)	93 (85-97)	98 (95-99)	68 (58-76)	57 (51-62)	89 (85-92)	
FIB-4 (n = 377)	78	0.75 (0.69-0.81)	<1.3 to ≥2.67	93 (89-95)	77 (67-86)	93 (90-96)	74 (64-83)	37 (32-42)	89 (86-92)	
ELF (n = 381)	77	0.78 (0.72-0.83)	<9.8 to ≥11.3	78 (73-83)	97 (90-99)	99 (96-100)	56 (48-64)	49 (44-54)	82 (78-86)	
Liver stiffness measurement (n = 220)	87	0.8 (0.72-0.83)	<8.9 to ≥11.1 kPa	88 (71-93)	79 (59-92)	96 (92-99)	37 (25-50)	10 (7-15)	80 (74-85)	
<b>Asian patients, BMI ≥30 kg/m<sup>2</sup></b>										
NAFLD fibrosis score (n = 210)	79	0.75 (0.68-0.83)	<-1.455 to ≥0.676	90 (84-94)	91 (78-97)	97 (93-99)	70 (57-82)	50 (43-56)	90 (85-94)	
FIB-4 (n = 210)	79	0.75 (0.68-0.83)	<1.3 to ≥2.67	78 (71-84)	93 (81-99)	98 (94-100)	53 (42-65)	45 (38-52)	81 (75-86)	
ELF (n = 211)	79	0.78 (0.71-0.86)	<9.8 to ≥11.3	71 (64-78)	93 (81-99)	98 (93-99)	46 (35-57)	44 (37-51)	76 (69-81)	
Liver stiffness measurement (n = 137)	85	0.85 (0.73-0.83)	<8.9 to ≥11.1 kPa	85 (73-91)	86 (64-97)	97 (92-99)	51 (34-69)	10 (6-17)	85 (78-91)	

# Does Age Change Things by Ethnicity?

Table 5. Performance of Noninvasive Tests in Diagnosing Advanced Fibrosis (F3–F4) in White and Asian Patients by Age (2-cutoff Model)

	Percentage of patients with F3–F4	AUROC (95% CI)	Cutoff	% (95% CI)						
				Sensitivity	Specificity	PPV	NPV	Gray zone <sup>a</sup>	Accuracy	
<b>White patients, age &lt;40 years</b>										
NAFLD fibrosis score (n = 68)	69	0.7 (0.57–0.82)	<–1.455 to ≥0.676	53 (38–68)	95 (76–100)	96 (80–100)	48 (32–64)	34 (23–46)	66 (54–77)	
FIB-4 (n = 105)	53	0.71 (0.61–0.81)	<1.3 to ≥2.67	34 (22–48)	100 (93–100)	100 (82–100)	57 (46–68)	18 (11–27)	65 (55–74)	
ELF (n = 111)	51	0.75 (0.66–0.84)	<9.8 to ≥11.3	40 (28–54)	100 (93–100)	100 (85–100)	61 (50–72)	23 (16–32)	69 (60–78)	
Liver stiffness measurement (n = 51)	78	0.71 (0.55–0.86)	<9.9 to ≥11.4 kPa	80 (64–91)	81 (31–89)	89 (74–97)	47 (21–73)	6 (1–16)	76 (63–87)	
<b>White patients, age 40–64 years</b>										
NAFLD fibrosis score (n = 1261)	81	0.74 (0.7–0.77)	<–1.455 to ≥0.676	89 (86–90)	91 (87–94)	98 (96–99)	65 (60–70)	52 (49–55)	89 (87–91)	
FIB-4 (n = 1637)	72	0.77 (0.75–0.8)	<1.3 to ≥2.67	79 (77–81)	94 (91–96)	97 (96–98)	64 (60–67)	45 (43–47)	83 (81–85)	
ELF (n = 1655)	72	0.79 (0.76–0.81)	<9.8 to ≥11.3	71 (69–74)	98 (96–99)	99 (98–100)	58 (54–61)	45 (43–48)	79 (77–81)	
Liver stiffness measurement (n = 923)	86	0.82 (0.78–0.86)	<9.9 to ≥11.4 kPa	85 (82–87)	88 (62–78)	95 (93–96)	44 (37–51)	8 (6–10)	83 (80–85)	
<b>White patients, age ≥65 years</b>										
NAFLD fibrosis score (n = 396)	86	0.68 (0.6–0.75)	<–1.455 to ≥0.676	96 (94–98)	69 (55–81)	95 (92–97)	75 (60–86)	47 (42–52)	92 (89–95)	
FIB-4 (n = 491)	80	0.78 (0.73–0.83)	<1.3 to ≥2.67	92 (89–94)	88 (79–93)	97 (94–98)	73 (64–80)	48 (44–53)	91 (88–93)	
ELF (n = 501)	80	0.77 (0.72–0.82)	<9.8 to ≥11.3	81 (77–85)	96 (90–99)	99 (97–100)	57 (49–64)	53 (49–58)	84 (81–87)	
Liver stiffness measurement (n = 273)	92	0.72 (0.62–0.83)	<9.9 to ≥11.4 kPa	83 (77–87)	57 (34–78)	96 (92–98)	21 (12–34)	7 (4–11)	81 (75–85)	
<b>Asian patients, age &lt;40 years</b>										
NAFLD fibrosis score (n = 39)	59	0.83 (0.69–0.97)	<–1.455 to ≥0.676	57 (34–77)	94 (70–100)	93 (66–100)	60 (39–79)	28 (15–45)	72 (55–85)	
FIB-4 (n = 64)	38	0.76 (0.64–0.88)	<1.3 to ≥2.67	42 (22–63)	100 (91–100)	100 (69–100)	74 (60–85)	19 (10–30)	78 (66–87)	
ELF (n = 66)	36	0.76 (0.64–0.88)	<9.8 to ≥11.3	50 (29–71)	100 (92–100)	100 (74–100)	78 (64–88)	23 (13–35)	82 (70–90)	
Liver stiffness measurement (n = 35)	51	0.82 (0.69–0.96)	<9.9 to ≥11.4 kPa	94 (73–100)	65 (38–86)	74 (52–90)	92 (62–100)	17 (7–34)	80 (63–92)	
<b>Asian patients, age 40–64 years</b>										
NAFLD fibrosis score (n = 392)	79	0.76 (0.71–0.82)	<–1.455 to ≥0.676	87 (82–90)	95 (88–99)	99 (96–100)	66 (57–74)	58 (53–63)	89 (85–92)	
FIB-4 (n = 489)	68	0.8 (0.76–0.84)	<1.3 to ≥2.67	87 (83–91)	94 (89–97)	97 (94–99)	77 (71–83)	45 (41–50)	89 (86–92)	
ELF (n = 500)	67	0.8 (0.76–0.84)	<9.8 to ≥11.3	74 (69–78)	96 (91–98)	97 (94–99)	64 (57–70)	43 (38–47)	81 (77–84)	

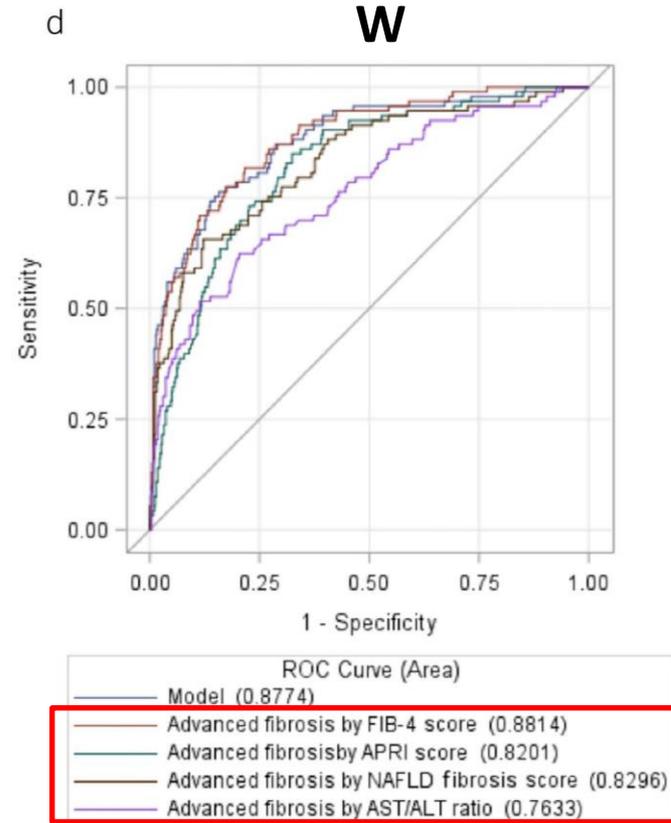
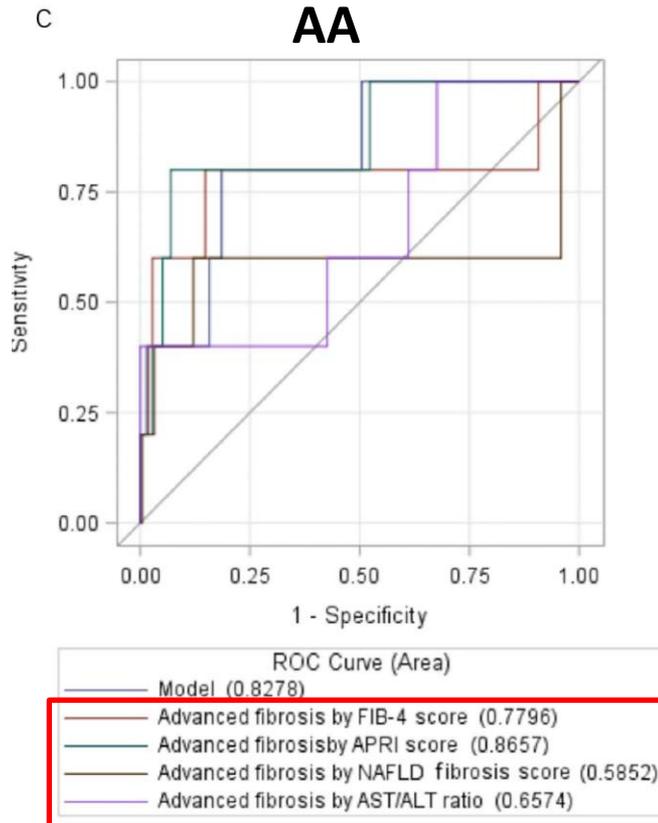
# Does Age Change Things by Ethnicity? Cont

	Percentage of patients with F3-F4	AUROC (95% CI)	Cutoff	% (95% CI)					
				Sensitivity	Specificity	PPV	NPV	Gray zone <sup>a</sup>	Accuracy
Liver stiffness measurement (n = 291)	75	0.85 (0.79-0.9)	<9.9 to ≥11.4 kPa	82 (76-87)	82 (71-90)	93 (89-96)	60 (49-69)	10 (7-14)	82 (77-86)
Asian patients, age ≥65 years									
NAPLD fibrosis score (n = 155)	83	0.68 (0.57-0.79)	<-1.455 to ≥0.676	98 (93-100)	81 (62-94)	96 (91-99)	88 (69-97)	52 (43-60)	95 (90-98)
FIB-4 (n = 182)	81	0.64 (0.54-0.74)	<1.3 to ≥2.67	97 (92-99)	56 (38-73)	91 (85-95)	79 (58-93)	35 (28-42)	89 (84-93)
ELF (n = 182)	81	0.76 (0.67-0.84)	<9.8 to ≥11.3	86 (80-92)	94 (80-99)	98 (95-100)	62 (47-75)	54 (47-62)	88 (82-92)
Liver stiffness measurement (n = 105)	87	0.78 (0.68-0.89)	<9.9 to ≥11.4 kPa	82 (73-90)	71 (42-92)	95 (88-99)	38 (20-59)	8 (3-14)	81 (72-88)

# Summary

- Sensitivities and specificities of the tests were reasonable when the original published cutoffs were applied to other ethnicities
- Currently available noninvasive tests can be used in Asians and white Hispanics without further calibration or adjustment of cutoffs
- However, the sensitivities of NFS, FIB-4, and ELF were low in both white and Asian patients younger than 40 years

# Performance of NITs in African Americans vs White



# Performance of NITs in African Americans vs White

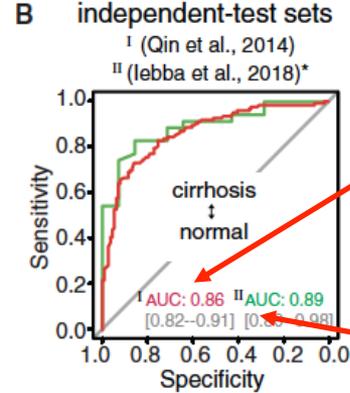
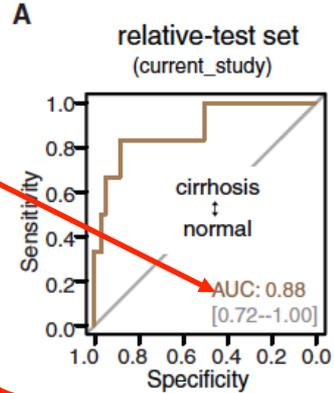
	Sensitivity	Specificity	PPV	NPV
Nonbariatric surgery group				
APRI > 1.5	15 (8–22)	95 (92–97)	46 (28–62)	78 (74–82)
NFS > 0.675	60 (50–69)	79 (74–83)	47 (38–55)	86 (82–90)
FIB-4 score > 2.67	31 (22–40)	96 (94–98)	71 (58–84)	82 (78–86)
Nonbariatric surgery Group—AA				
APRI > 1.5	40 (0–82)	87 (78–96)	22 (0–49)	94 (87–100)
NFS > 0.675	40 (0–83)	78 (67–89)	14 (0–37)	93 (86–100)
FIB-4 score > 2.67	20 (0–55)	96 (91–100)	33 (0–87)	93 (86–100)
Nonbariatric surgery group—White				
APRI > 1.5	13 (7–20)	96 (94–98)	54 (34–74)	76 (71–80)
NFS > 0.675	51 (61–71)	79 (74–84)	50 (42–59)	85 (81–89)
FIB-4 score > 2.67	32 (23–41)	96 (94–98)	74 (61–87)	80 (76–84)
Bariatric surgery group				

# Microbiome

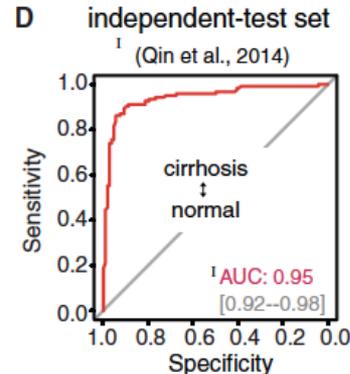
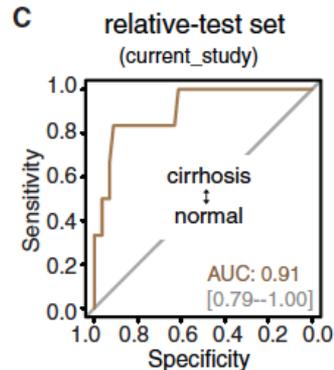


## Validation in relatives and external cohorts

model: [19 species + age]



model: [19 species + age] + Albumin



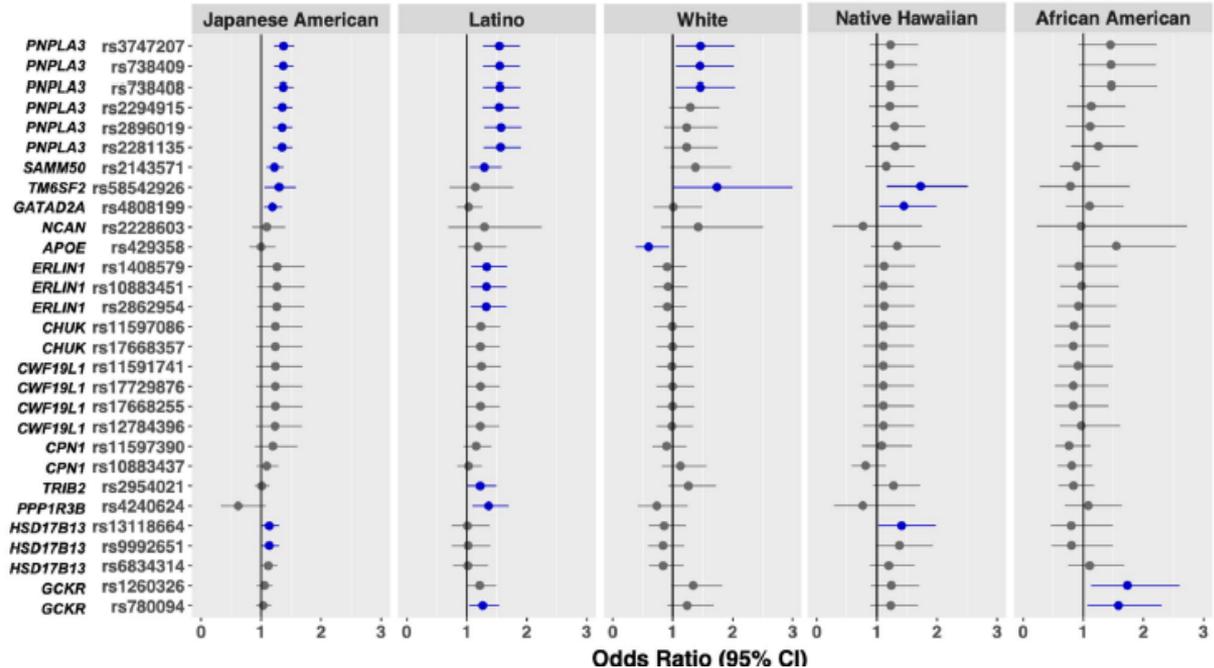
# Genetic Risk Scores

1448 cases/8,444 controls) in this multi- ethnic cohort study.

Of the 30 GWAS SNPs, 20 (67%) were replicated ( $P < 0.05$ ) in the pooled multi- ethnic population.

The highest percentage of replication was seen in Latinos (43%), followed by Japanese Americans (37%), Whites (17%), and Native Hawaiians and African Americans ( $\leq 10\%$ )

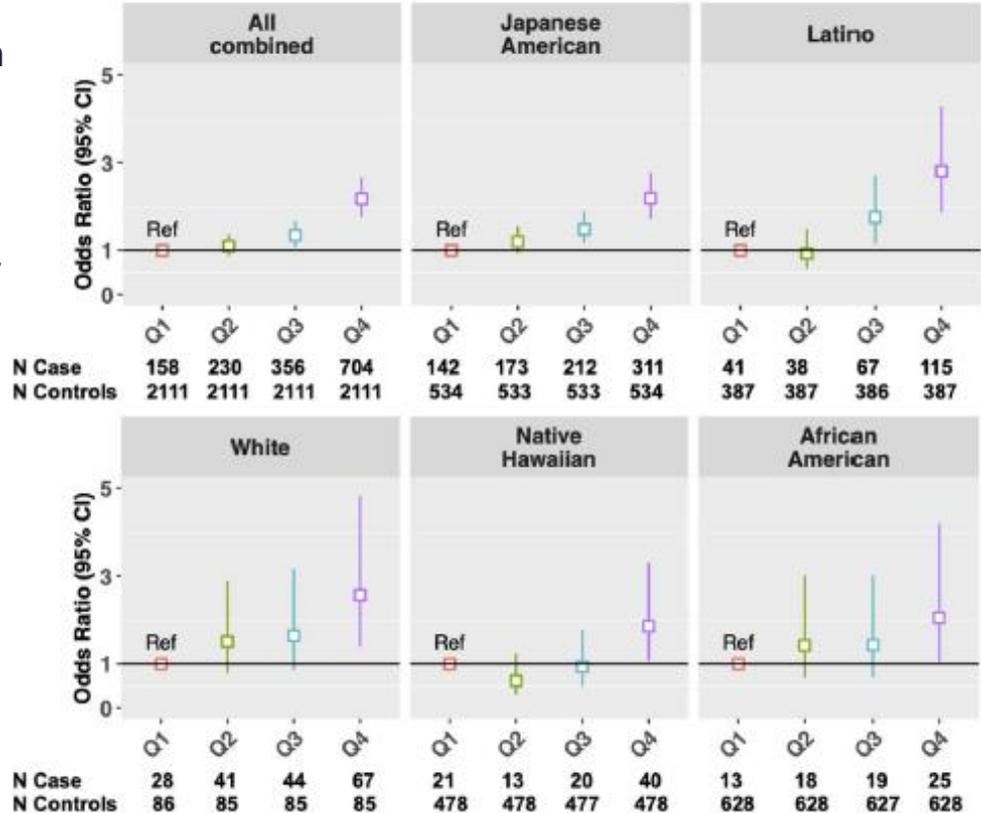
PNPLA3, HSD17B13 , TM6SF2 , GATAD2A, GCKR, SUGP1, MBOAT7, TRIB1, SAMM50, and ERLIN1– CHUK– CWF19L1 gene cluster, were replicated in at least two ethnic groups



# Genetic Risk Scores

An 11- SNP weighted GRS was associated with NAFLD risk in the multi-ethnic population as well as in each ethnic group (OR ranged from 1.30 in African Americans to 1.52 in Latinos).

The GRS– NAFLD association was stronger for NAFLD with cirrhosis (OR = 1.67; 95% CI = 1.46- 1.92) compared to NAFLD without cirrhosis (OR = 1.37; 95% CI = 1.28- 1.46) (Pheterogeneity = 0.003)



# Outline

- Are there differences in NITs guidance around the world?
- Do blood-based NITs perform similarly?
  - Ethnicity/Region of the world
  - Sex
  - Age
- Do blood-based NITs monitor disease progression similarly?
- Do blood-based NITs predict outcomes similarly?

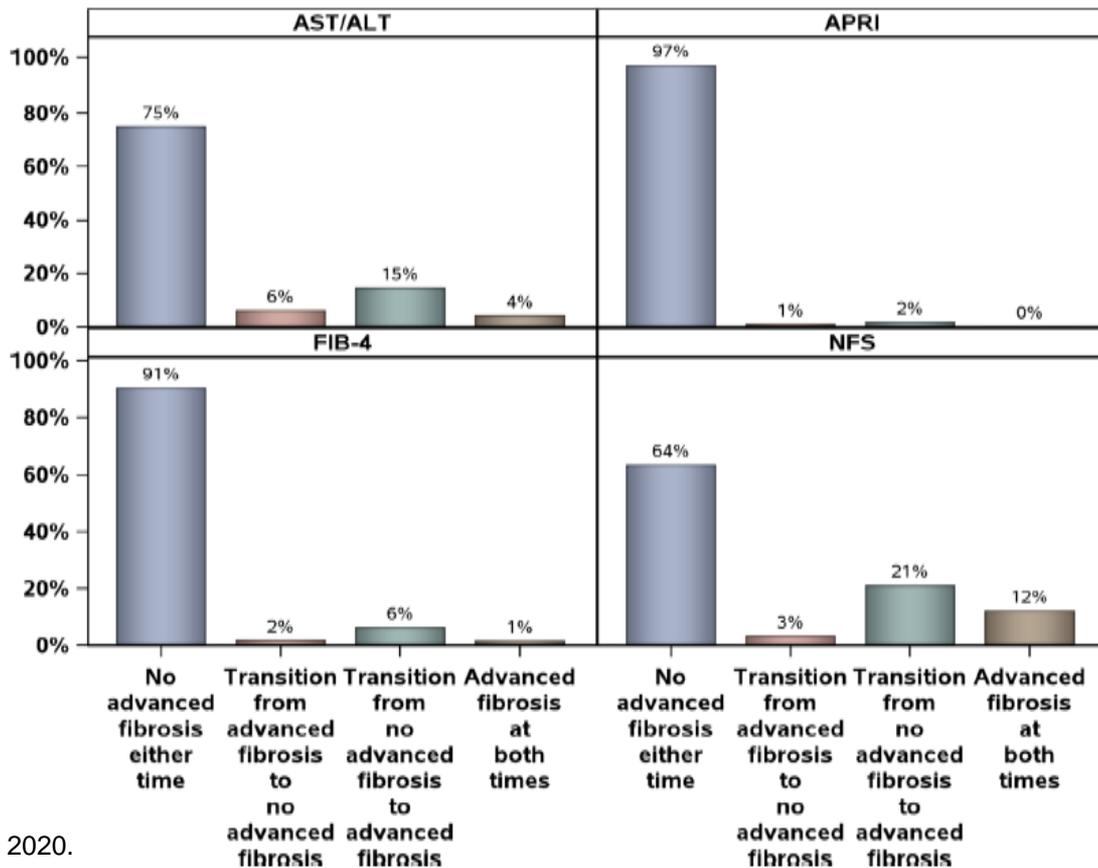
# Progression of NAFLD-Associated Fibrosis in a Large Cohort of Patients With Type 2 Diabetes

- 50,695 diabetics with NAFLD
- Median follow-up of 84.4 months
  - 25.8% transitioned from no advanced fibrosis to advanced fibrosis (progression)
  - 6.4% transitioned from advanced fibrosis to no advanced fibrosis (regression)
  - Rest remained stable

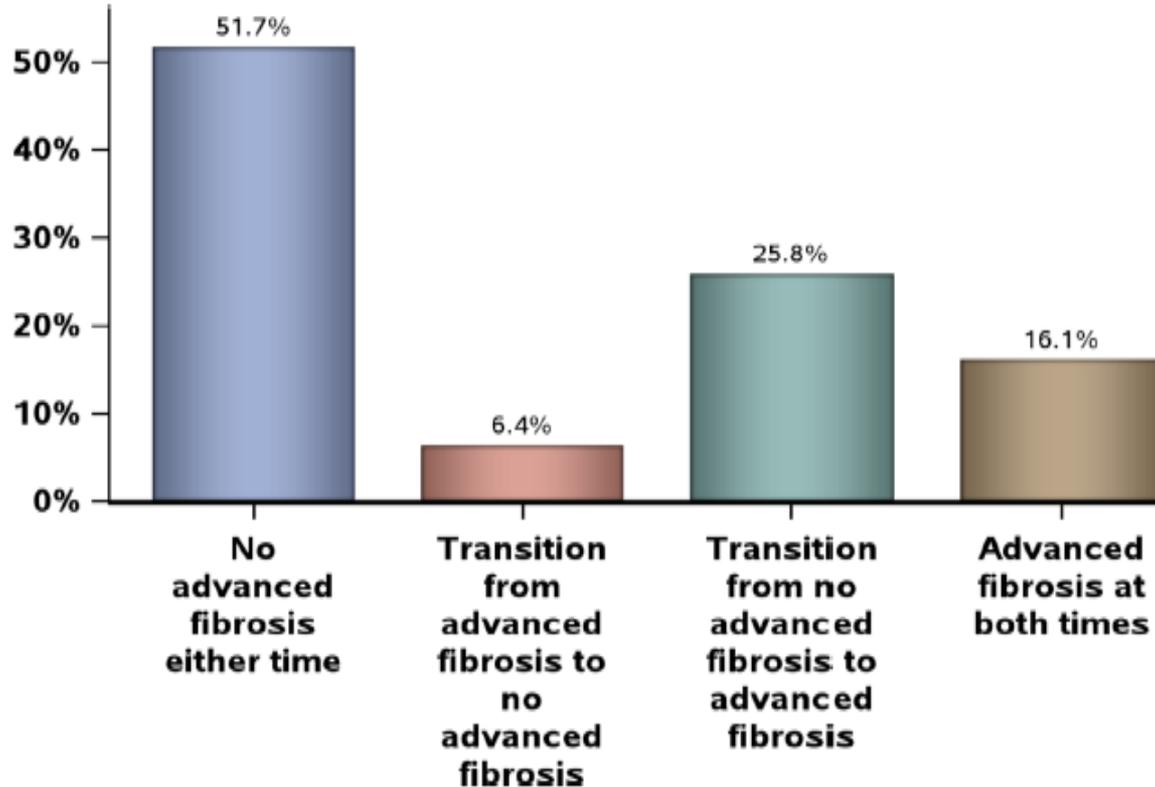
# Progression of NAFLD-Associated Fibrosis in a Large Cohort of Patients With Type 2 Diabetes

- Factors associated with transition to advanced fibrosis
  - Female sex
  - older age at first evaluation
  - African-Americans
  - Obesity, chronic kidney disease, or coronary artery disease.
  - Use of insulin increased the risk of progression
  - Use of oral hypoglycemic agents, angiotensin 2 receptor blockers, and fibrates was associated with reduced risk

# Progression of NAFLD-Associated Fibrosis in a Large Cohort of Patients With Type 2 Diabetes



# Progression of NAFLD-Associated Fibrosis in a Large Cohort of Patients With Type 2 Diabetes

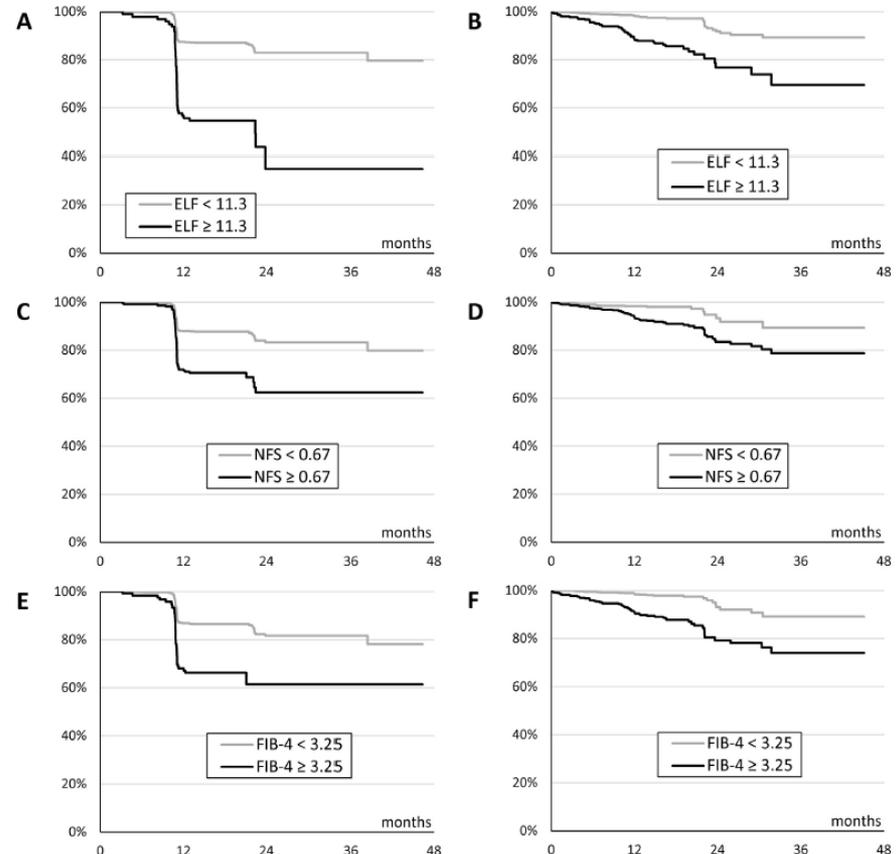


# Outline

- Are there differences in NITs guidance around the world?
- Do blood-based NITs perform similarly?
  - Ethnicity/Region of the world
  - Sex
  - Age
- Do blood-based NITs monitor disease progression similarly?
- Do blood-based NITs predict outcomes similarly?

# Association of NITS With Adverse Clinical in Patients With Advanced Fibrosis Due to NASH

- No data on ethnicity, sex or other parameters of disparities
- 2154 Patients from the simtuzumab and selonsertib trials
- F3 disease, 16.7% experienced disease progression to cirrhosis,
- F4 disease, 7.3% experienced clinical events (39% ascites, 24%hepatic encephalopathy)



# Conclusions

- Overall data suggest that wet biomarkers differ minimally in patients from various ethnicities
- Some consistency in international guidelines
- NITs could differ by Age: More data
- No clear data on the performance of wet biomarkers in women vs men
- More data is needed on NITs and disparities in terms of disease monitoring and predicting hard outcomes