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Performance of Plasma Biomarkers and Diagnostic Panels for Nonalcoholic Steatohepatitis and Advanced Fibrosis in Patients with Type 2 Diabetes Mellitus

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List of investigators

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Supplementary Table 1. p values for the comparisons of the AUCs for the different non-invasive methods used for the diagnosis of definite NASH.

	Cohort-specific model	ALT	CK-18	HAIR	OWLiver®	NASHtest2®	BARD
Cohort-specific model		0.87	0.65	**0.034**	**0.033**	**0.016**	**<0.001**
ALT	0.87		0.76	**0.043**	**0.041**	**0.020**	**<0.001**
CK-18	0.65	0.76		0.10	0.09	**0.049**	**0.002**
HAIR	**0.034**	**0.043**	0.10		0.92	0.68	0.14
OWLiver®	**0.033**	**0.041**	0.09	0.92		0.77	0.19
NASHtest2®	**0.016**	**0.020**	**0.049**	0.68	0.77		0.32
BARD	**<0.001**	**<0.001**	**0.002**	0.14	0.19	0.32	

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Supplementary Table 2. Comparison head-to-head of the specificity of the different non-invasive methods after fixing sensitivity at 95%.

Diagnosis of definite NASH		Diagnosis of advanced fibrosis	
	Specificity (95% CI)		Specificity (95% CI)
Cohort-specific model*	28% (4-43%)	PRO-C3	71% (53-85%)
ALT	38% (16-51%)	Cohort-specific model‡	45% (10-68%)
CK-18	19% (0-37%)	APRI	57% (38-77%)
HAIR	15% (6-24%)	AST	58% (48-79%)
OWLiver®	10% (6-17%)	FIB-4	34% (16-54%)
NASHtest2®	22% (5-34%)	Fibrotest®	14% (1-34%)
BARD	7% (6-11%)	NFS	20% (8-33%)

*Model was = 0.0941 x (HOMA-IR) + 0.0039 x (CK-18) – 1.8647 ‡: Model was = 0.0034 x (CK-18) + 0.0588 x (fasting insulin) – 0.0116 x (platelets) – 1.3336 x (gender) + 0.4469 x (HbA1c) – 3.82; (where gender: 1=male and 0=female).

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Supplementary Table 3. p values for the comparisons of the AUCs for the different non-invasive methods used for the diagnosis of advanced fibrosis.

	PRO-C3	Cohort-specific model	APRI	AST	FIB-4	Fibrotest®	NAFLD fibrosis score
PRO-C3		0.32	0.13	0.12	**0.008**	**<0.001**	**<0.001**
Cohort-specific model	0.32		0.69	0.67	0.12	**0.012**	**0.001**
APRI	0.13	0.69		0.98	0.21	**0.026**	**0.004**
AST	0.12	0.67	0.98		0.21	**0.025**	**0.003**
FIB-4	**0.008**	0.12	0.21	0.21		0.30	0.11
Fibrotest®	**<0.001**	**0.012**	**0.026**	**0.025**	0.30		0.64
NAFLD fibrosis score	**<0.001**	**0.001**	**0.004**	**0.003**	0.11	0.64	

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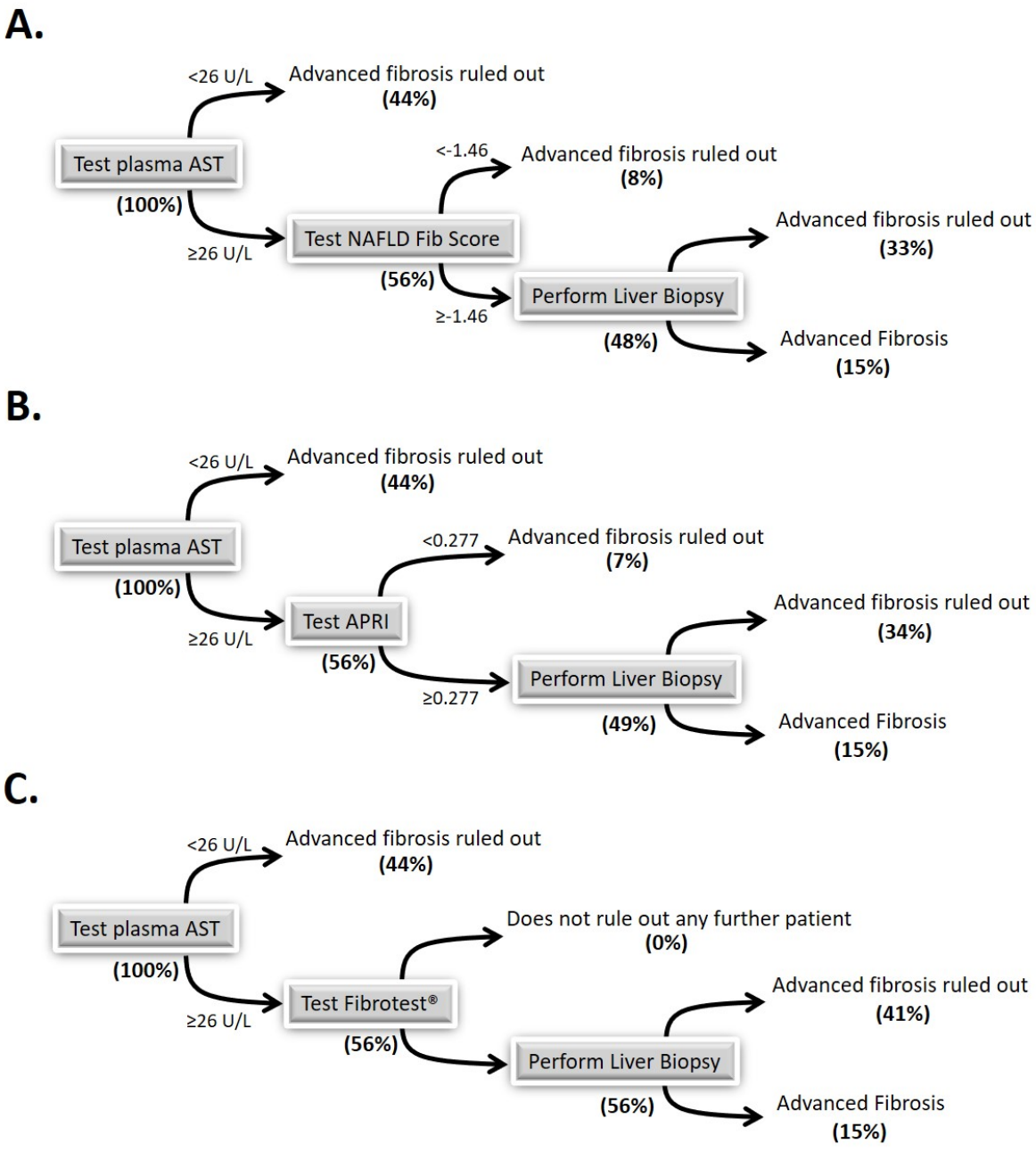
Supplementary Figure 1. Sequential testing for the diagnosis of advanced fibrosis optimized for a NPV of 100% (i.e., avoiding any false negative) assessing NAFLD fibrosis score (panel A), APRI (panel B), and FIbrotest® (panel C) after use of AST.



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Supplementary Figure 2. Parallel testing for the diagnosis of advanced fibrosis, combining the 6 models/scores (only 154 patients with complete data for all models/scores were including in this analysis). Cohort-specific cut-off points were used to determine whether tests were positive or negative (as defined in Table 3).