UNIVERSITY OF BIRMINGHAM | COLLEGE OF MEDICAL AND DENTAL SCIENCES

Performance of Non-Invasive Tests in the Staging of Fibrosis in Patients with NAFLD:

Interim Results of a Prospective Multicentre Study

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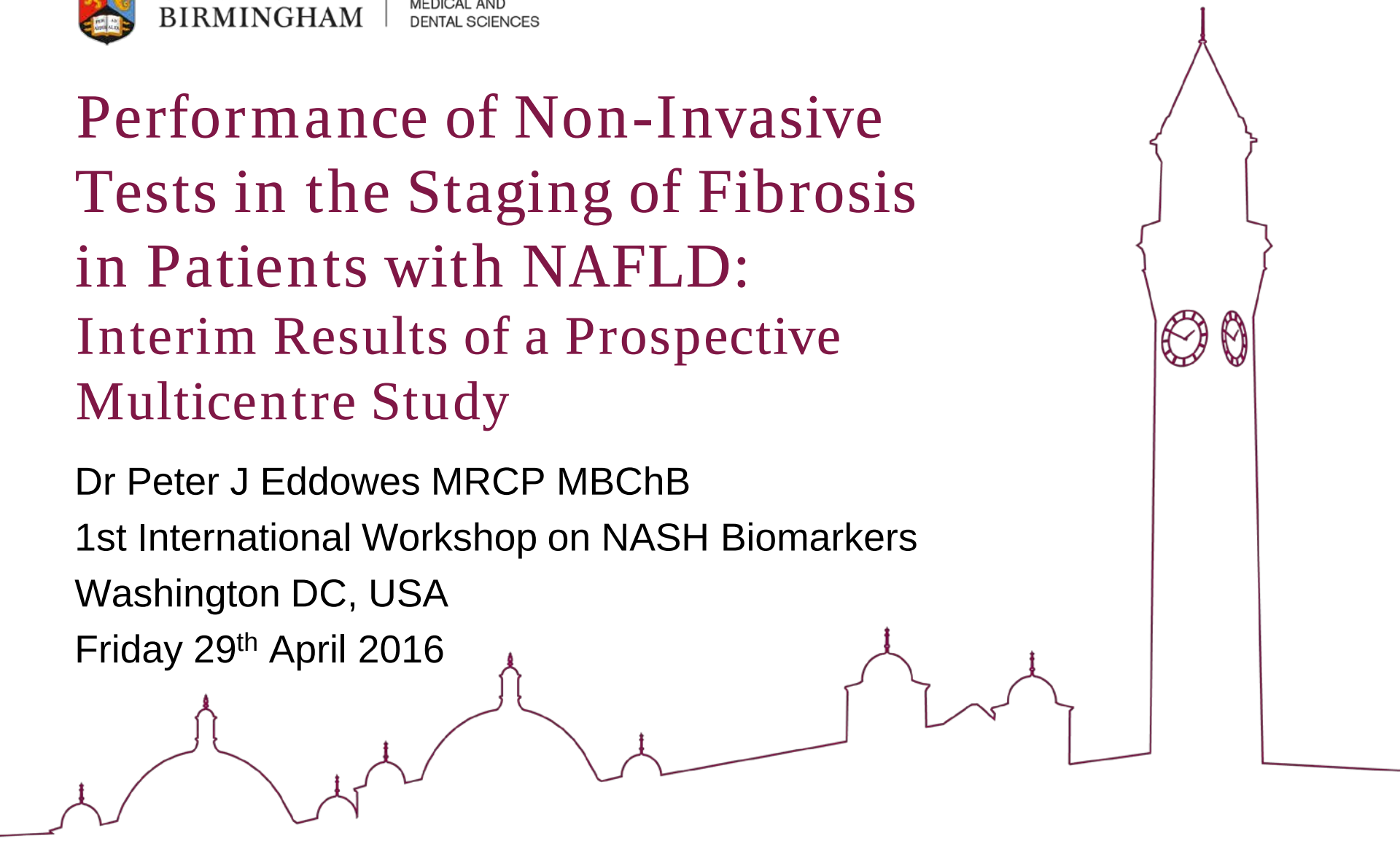
1st International Workshop on NASH Biomarkers

Washington DC, USA

Friday 29th April 2016



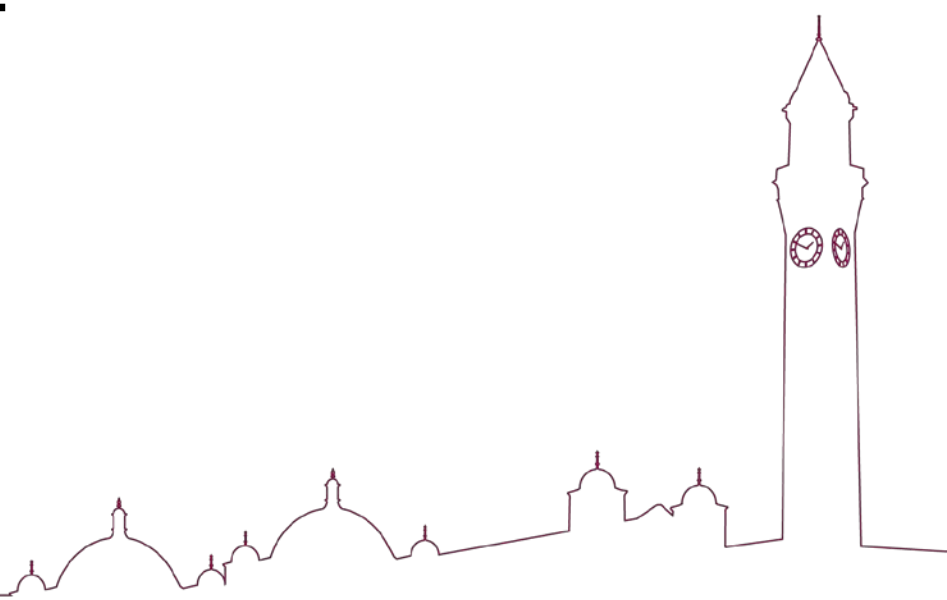
Disclosures

- This study is funded by Echosens
- I have no financial interests in Echosens

Aims

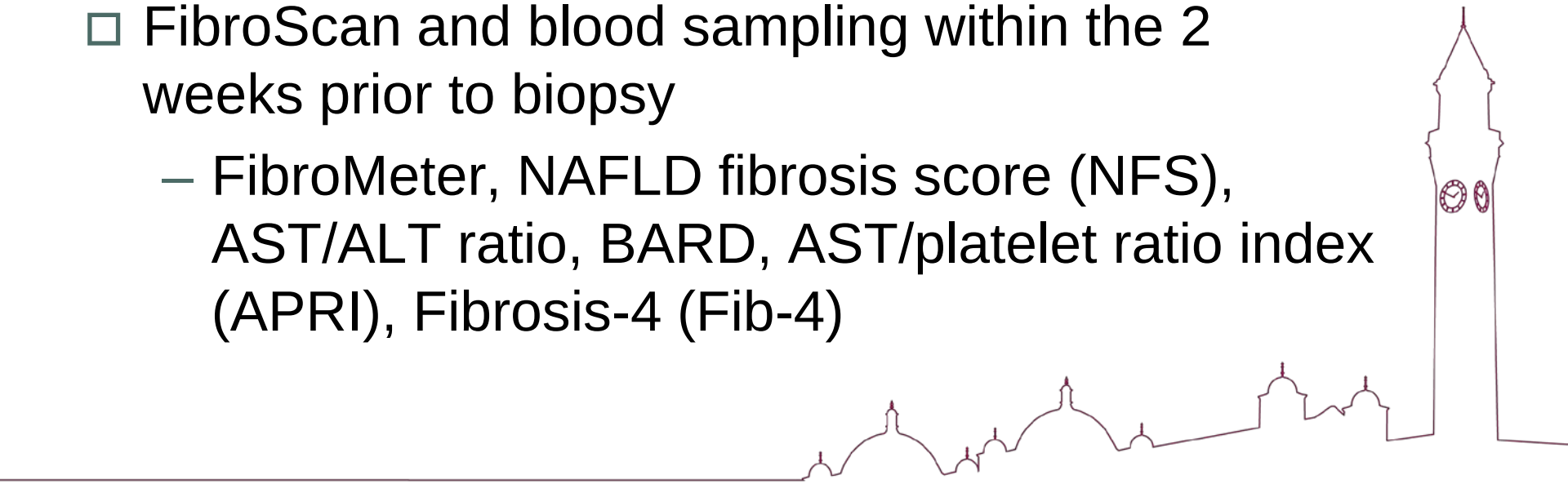
- Assess the diagnostic performance of non-invasive fibrosis tests in a population of patients with NAFLD

- Define cut-off values for:
  - FibroMeter V
  - FibroMeter NAFLD
  - FibroMeter VCTE



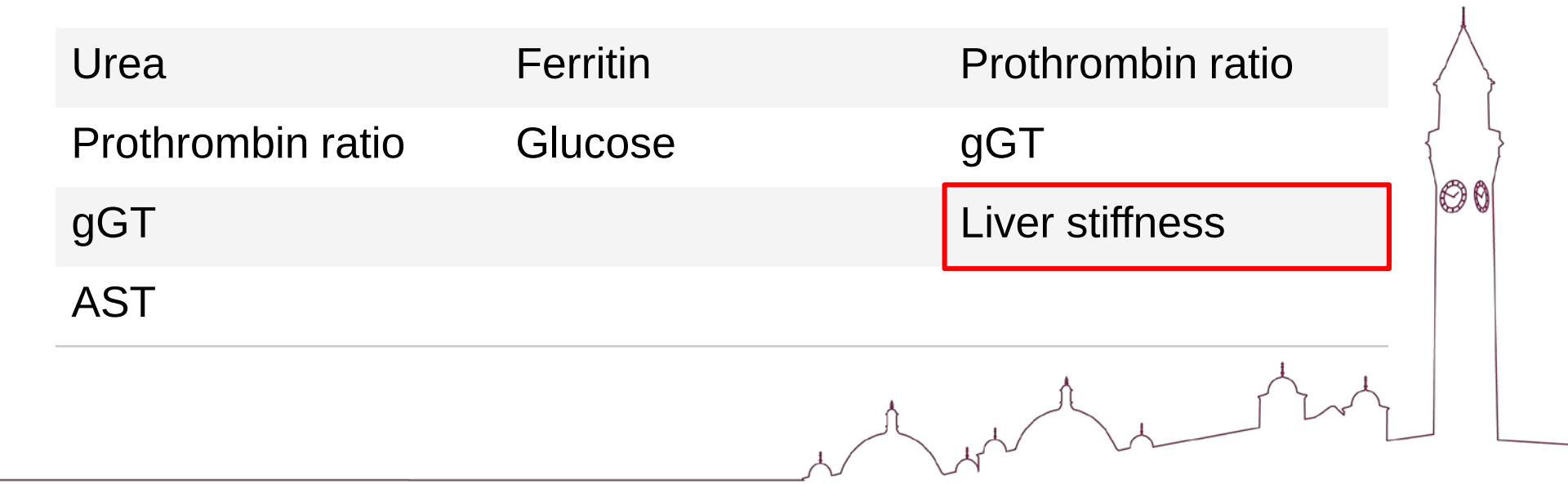
Methods

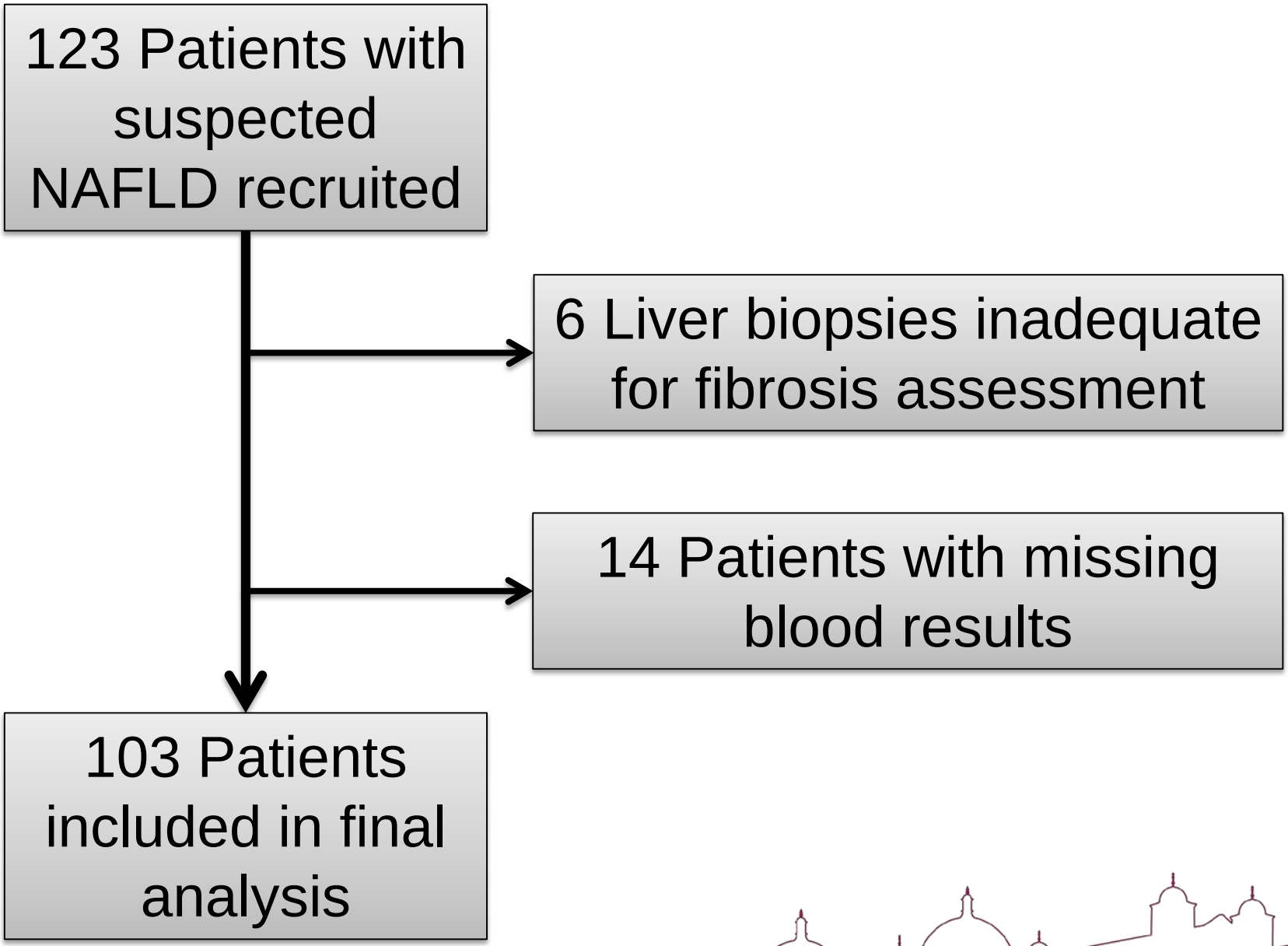
- Prospective recruitment from 4 UK sites between March 2014 and May 2015
- Standard of care liver biopsy for known or suspected NAFLD
- Histology assessed by 2 expert liver pathologists
- FibroScan and blood sampling within the 2 weeks prior to biopsy
  - FibroMeter, NAFLD fibrosis score (NFS), AST/ALT ratio, BARD, AST/platelet ratio index (APRI), Fibrosis-4 (Fib-4)



FibroMeter

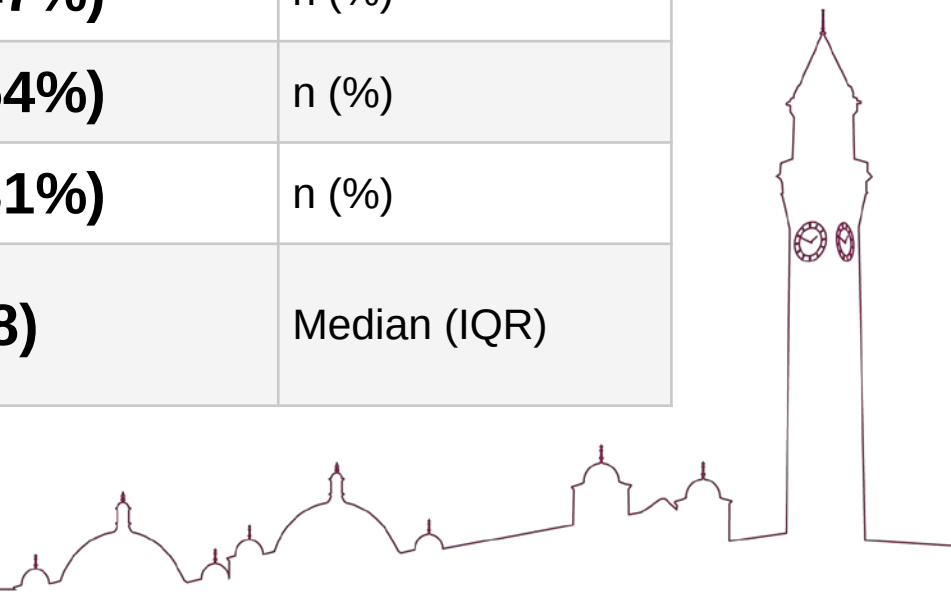
FibroMeter V	FibroMeter NAFLD	FibroMeter VCTE
age, gender	age, weight	age, gender
Platelets	Platelets	Platelets
Alpha-2-macroglobulin	AST	Alpha-2-macroglobulin
ALT	ALT	AST
Urea	Ferritin	Prothrombin ratio
Prothrombin ratio	Glucose	gGT
gGT		Liver stiffness
AST		




123 Patients with suspected NAFLD recruited
6 Liver biopsies inadequate for fibrosis assessment
14 Patients with missing blood results
103 Patients included in final analysis

Baseline Demographics

Male	**58 (56%)**	n (%)
Age (years)	**56 (21)**	Median (IQR)
BMI (Kg/m^2)	**31.2 (8.7)**	Median (IQR)
Type 2 diabetes	**51 (50%)**	n (%)
Hypertension	**48 (47%)**	n (%)
Hypercholesterolaemia	**56 (54%)**	n (%)
Consume alcohol	**32 (31%)**	n (%)
Alcohol intake (UK units/week)	**7 (8.8)**	Median (IQR)

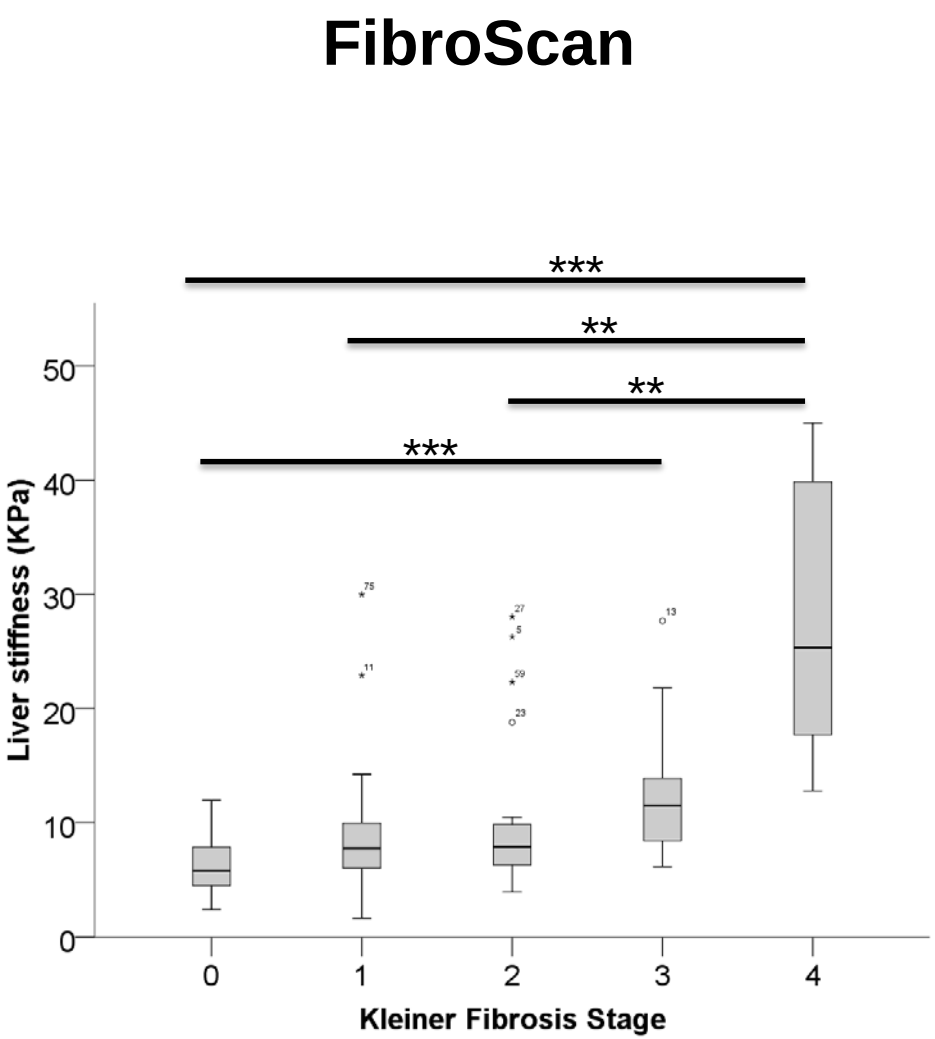


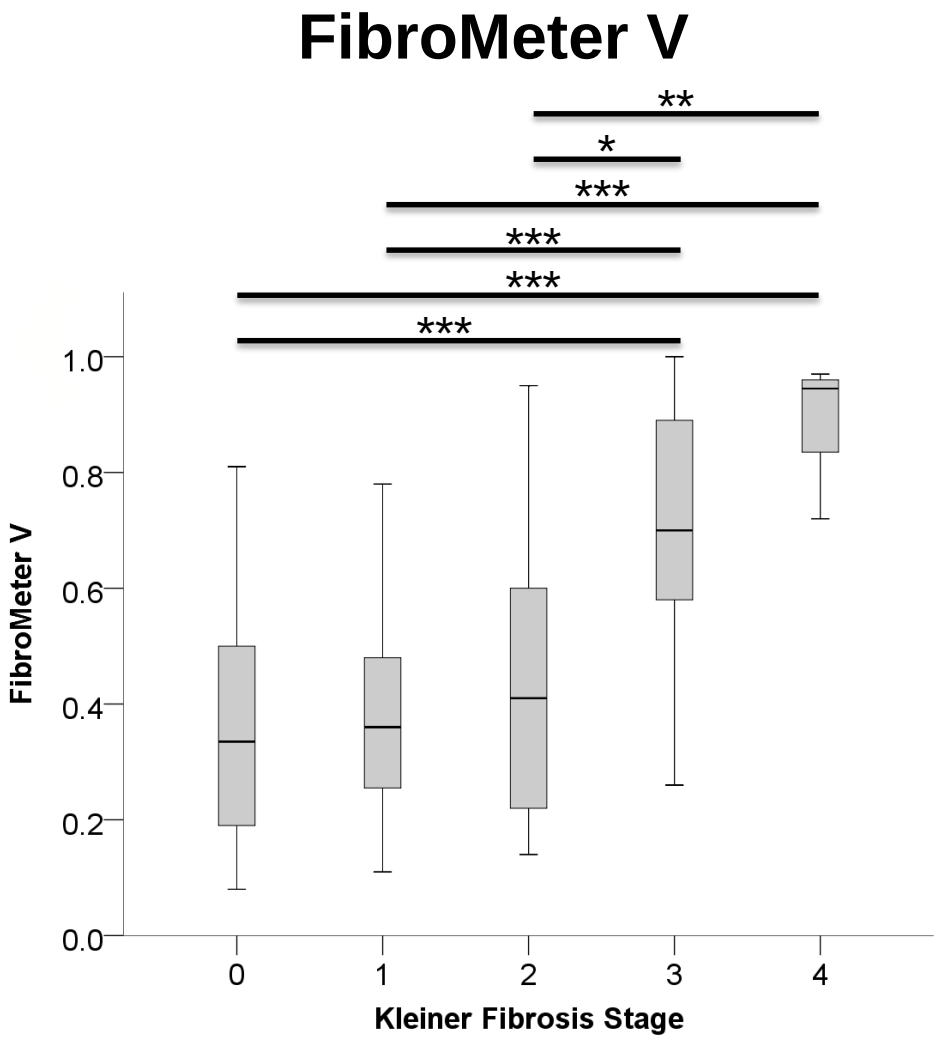
Characteristics of the Histology

Median (IQR) length of biopsies 22 (7) mm
NASH (FLIP algorithm) 54 (52%)

Kleiner Fibrosis Stage	n	%	Total NAS Score	n	%
F0	22	21%	0-2	28	27%
F1	27	26%	3-4	35	34%
F2	21	20%	5-6	37	36%
F3	25	24%	7-8	3	3%
F4	8	8%			

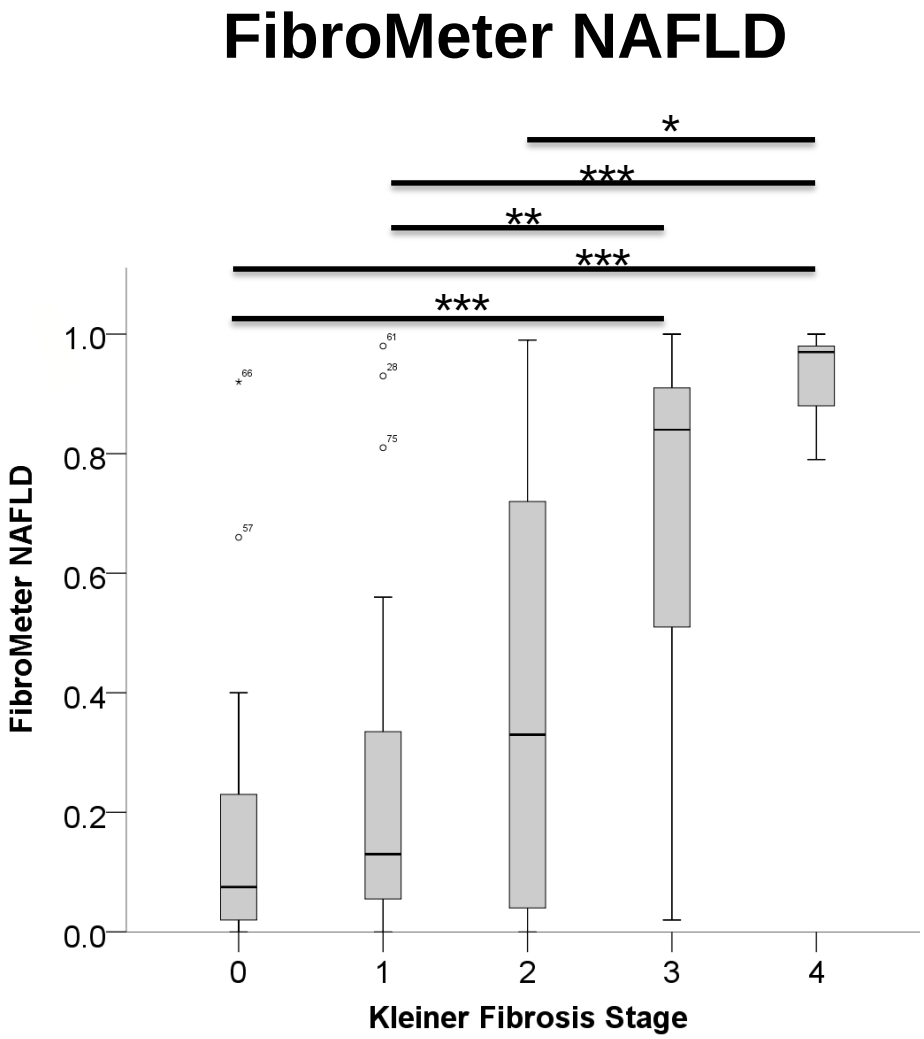
FibroScan and FibroMeter significantly associated with fibrosis

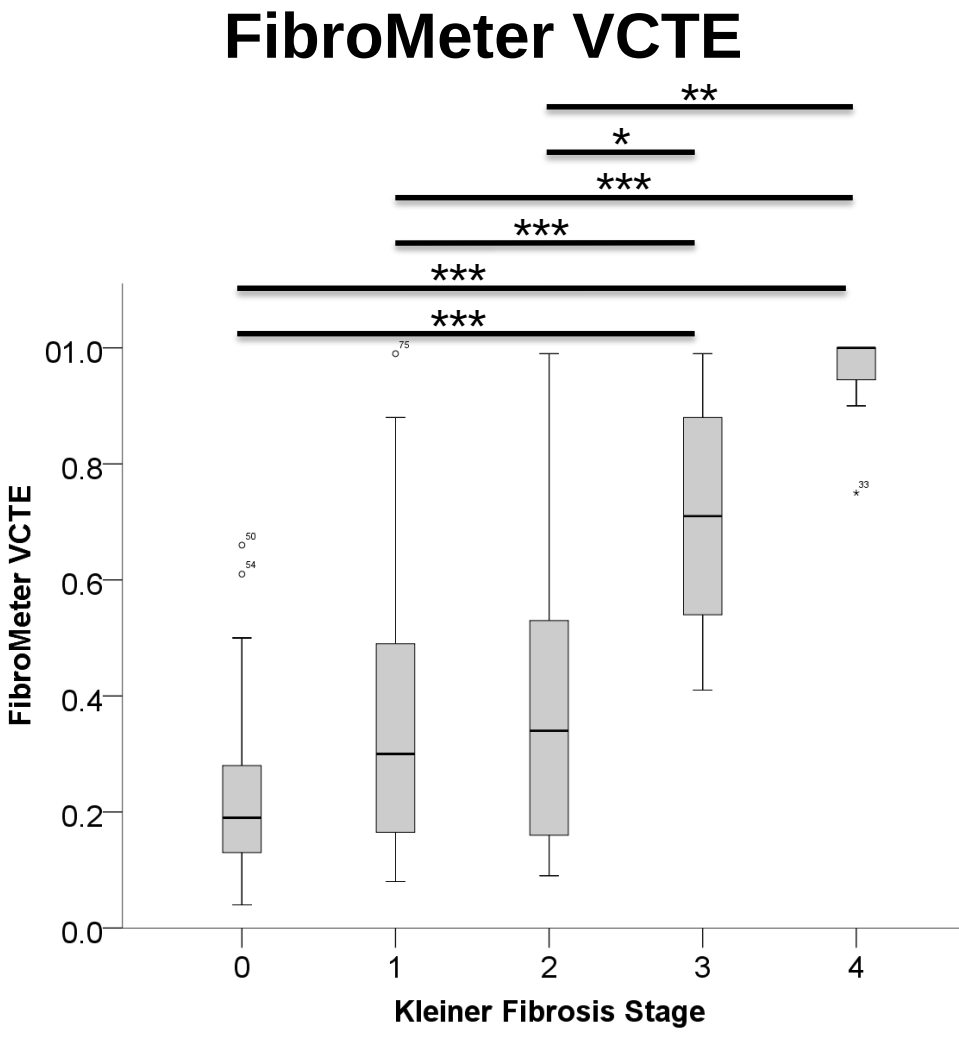




* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

FibroScan and FibroMeter significantly associated with fibrosis





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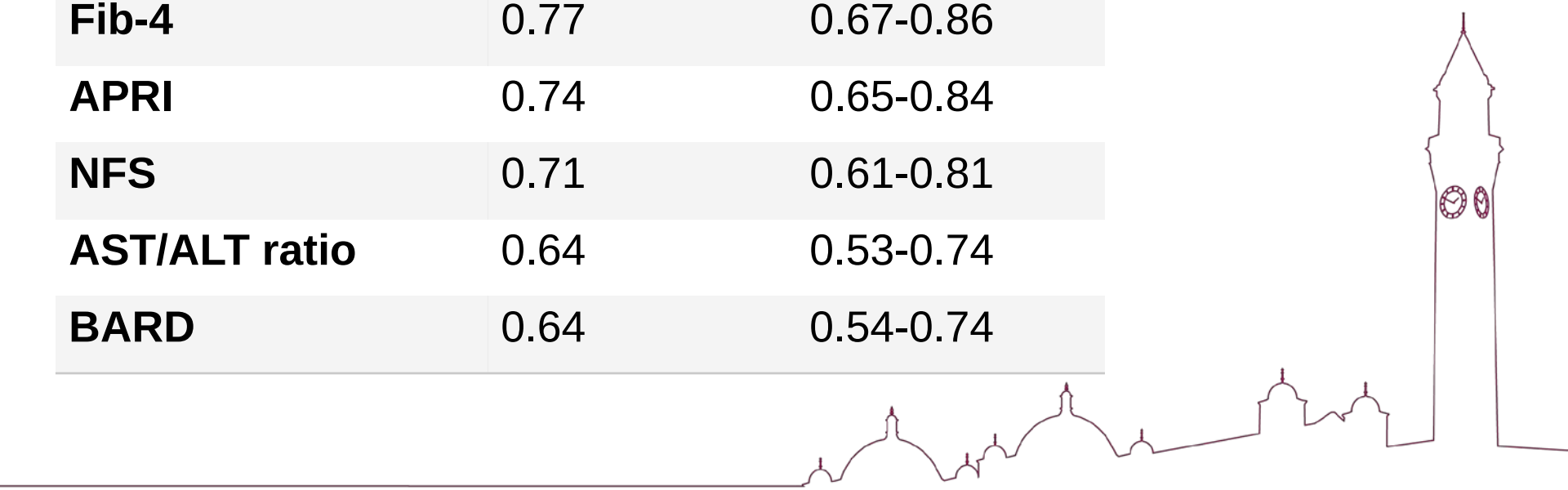
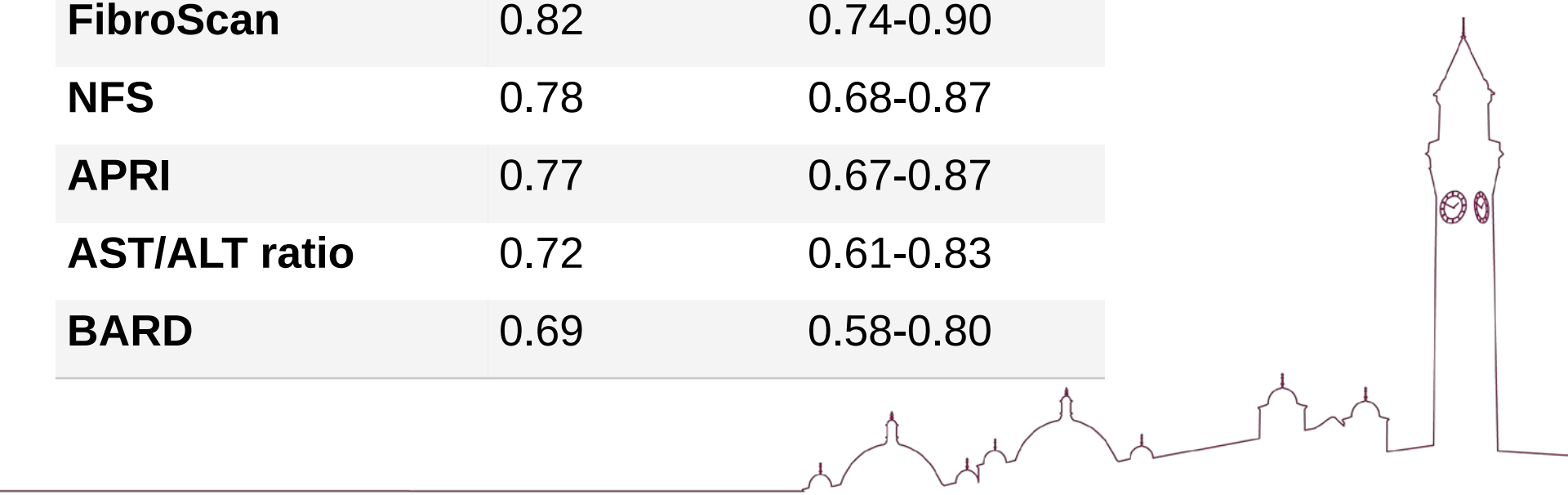
To diagnose ≥F2 fibrosis

Test	AUROC	95% CI
FM VCTE	0.81	0.72-0.89
FM NAFLD	0.79	0.70-0.88
FM V	0.78	0.69-0.87
FibroScan	0.77	0.68-0.86
Fib-4	0.77	0.67-0.86
APRI	0.74	0.65-0.84
NFS	0.71	0.61-0.81
AST/ALT ratio	0.64	0.53-0.74
BARD	0.64	0.54-0.74



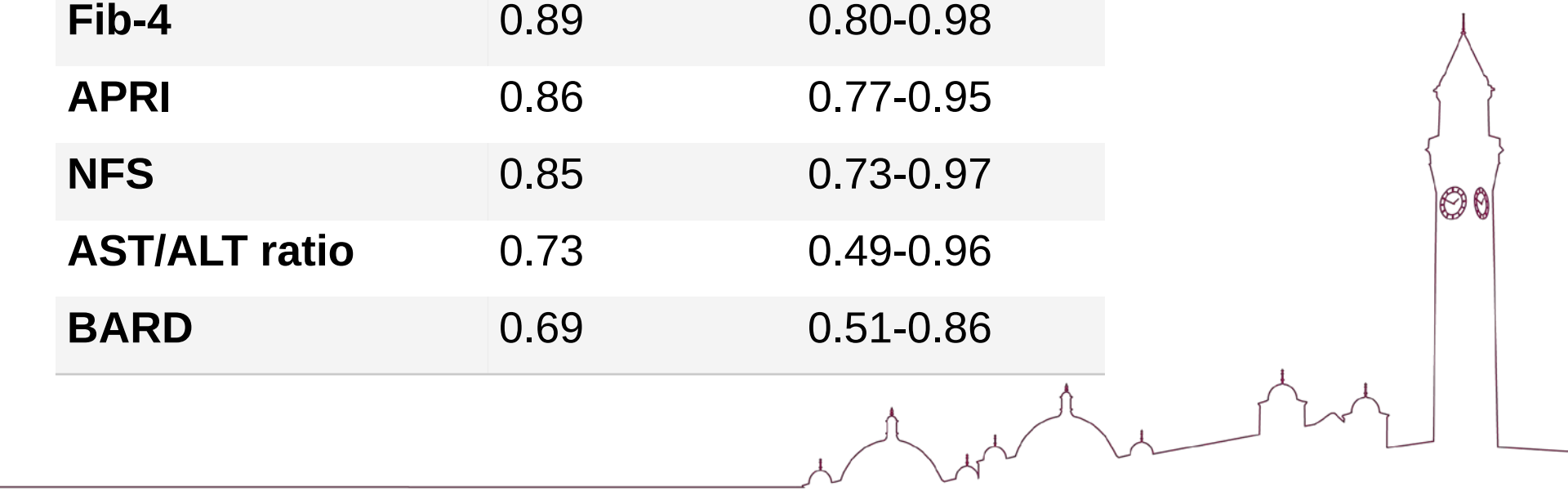
To diagnose ≥F3 fibrosis

Test	AUROC	95% CI
FM VCTE	0.90	0.84-0.96
FM V	0.87	0.80-0.94
FM NAFLD	0.85	0.77-0.93
Fib-4	0.85	0.78-0.93
FibroScan	0.82	0.74-0.90
NFS	0.78	0.68-0.87
APRI	0.77	0.67-0.87
AST/ALT ratio	0.72	0.61-0.83
BARD	0.69	0.58-0.80



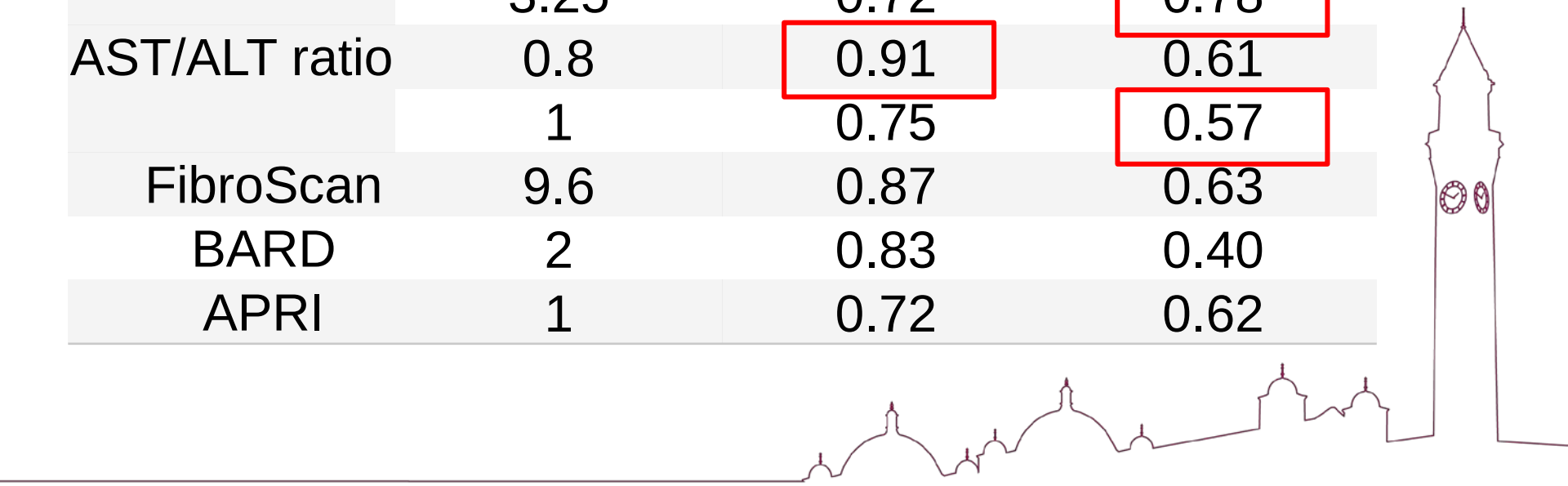
To diagnose F4 fibrosis

Test	AUROC	95% CI
FM VCTE	0.96	0.91-1
FibroScan	0.94	0.89-1
FM V	0.94	0.88-1
FM NAFLD	0.90	0.83-0.97
Fib-4	0.89	0.80-0.98
APRI	0.86	0.77-0.95
NFS	0.85	0.73-0.97
AST/ALT ratio	0.73	0.49-0.96
BARD	0.69	0.51-0.86



Published cut off values have high negative predictive value for the exclusion of advanced (≥F3) fibrosis

	Cut off value	NPV	PPV
NFS	-1.445	0.93	0.51
	0.676	0.72	0.62
Fib-4	1.3	0.91	0.61
	3.25	0.72	0.78
AST/ALT ratio	0.8	0.91	0.61
	1	0.75	0.57
FibroScan	9.6	0.87	0.63
BARD	2	0.83	0.40
APRI	1	0.72	0.62

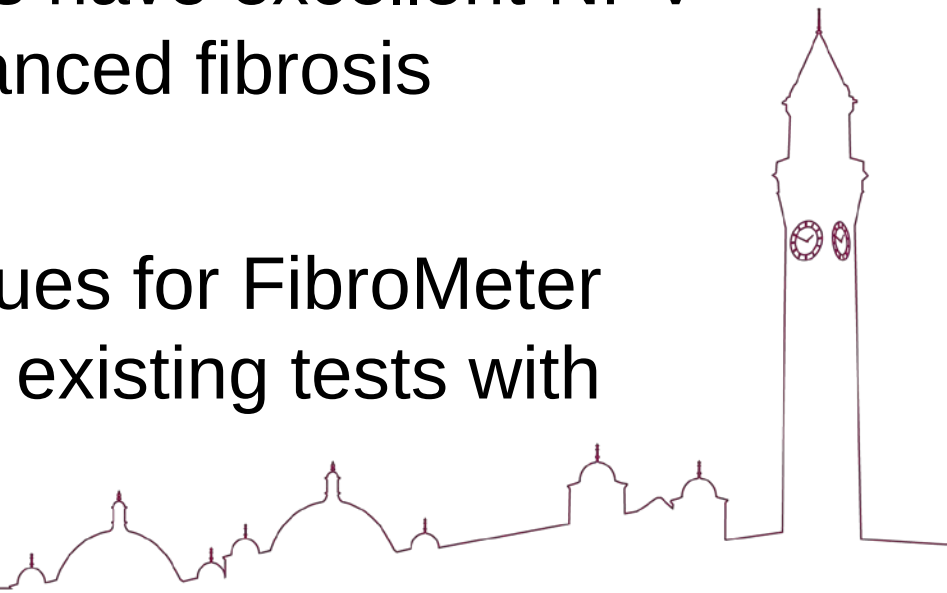


Cut off values for ≥F3 fibrosis defined for FibroMeter

Test	Cut off value	NPV	PPV
FibroMeter VCTE	0.54	0.94	0.73
FibroMeter V	0.58	0.92	0.68
FibroMeter NAFLD	0.42	0.92	0.64

Conclusion

- Of the assessed non-invasive tests, FibroMeter VTCE has the greatest diagnostic performance for all stages of fibrosis
- Simple blood biomarkers have excellent NPV for the exclusion of advanced fibrosis
- Newly defined cutoff values for FibroMeter show equivalent NPV to existing tests with improvement in PPV



Acknowledgements and Thanks

- Co-authors:
  - University of Birmingham – P.N. Newsome
  - Newcastle University – Q.M. Anstee
  - University of Nottingham – I.N. Guha
  - University College London – E. Tsochatzis
  - Beaujon Hospital Paris - V. Paradis, P. Bedossa
- Thanks to:
  - Magali Sasso
  - Céline Fournier
  - Saliha Haddag
  - Khalide Seddik

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Dr Peter Eddowes is supported by the National Institute for Health Research Birmingham Liver Biomedical Research Unit. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Supported by NHS National Institute for Health Research

Questions?