



NHS

Blood and Transplant



**UNIVERSITY OF
CAMBRIDGE**

The PITHIA Trial

A stepped-wedge cluster registry randomised trial

Dominic Summers

Cambridge University Department of Surgery and NHSBT

FUNDED BY

NIHR | National Institute
for Health Research

The oracle in transplantation?

> 70% people dying
in critical care >50
years

Use of kidneys from
older donors has
increased donation

Only 28% of offered
kidneys from donors
>60 years are
transplanted

Shortage of kidneys



More than twice as
likely to lose kidney
if donor > 60 years

Primary non-
function (PNF) 4.2%
vs 1.9%

PNF mortality – 25%
at 1 year

How to sort the transplantable from the not?

Biomarkers

Machine
perfusion

Risk
modelling

Scoring system - Remuzzi

Glomerular global sclerosis

0-2%	0
2-20%	1
20-50%	2
>50%	3

Tubular atrophy

0-2%	0
<20%	1
20-50%	2
>50%	3

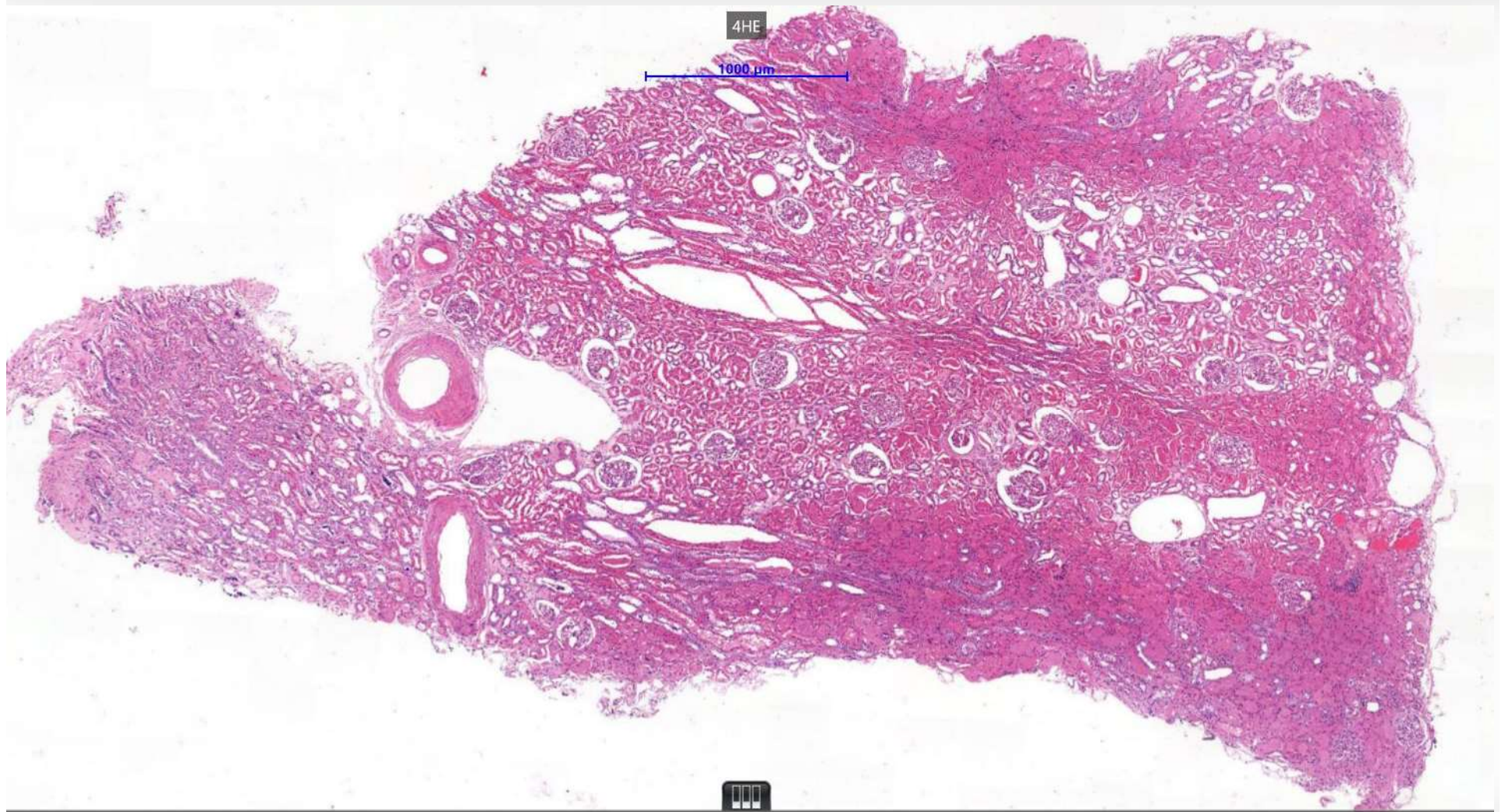
Interstitial fibrosis

0-2%	0
<20%	1
20-50%	2
>50%	3

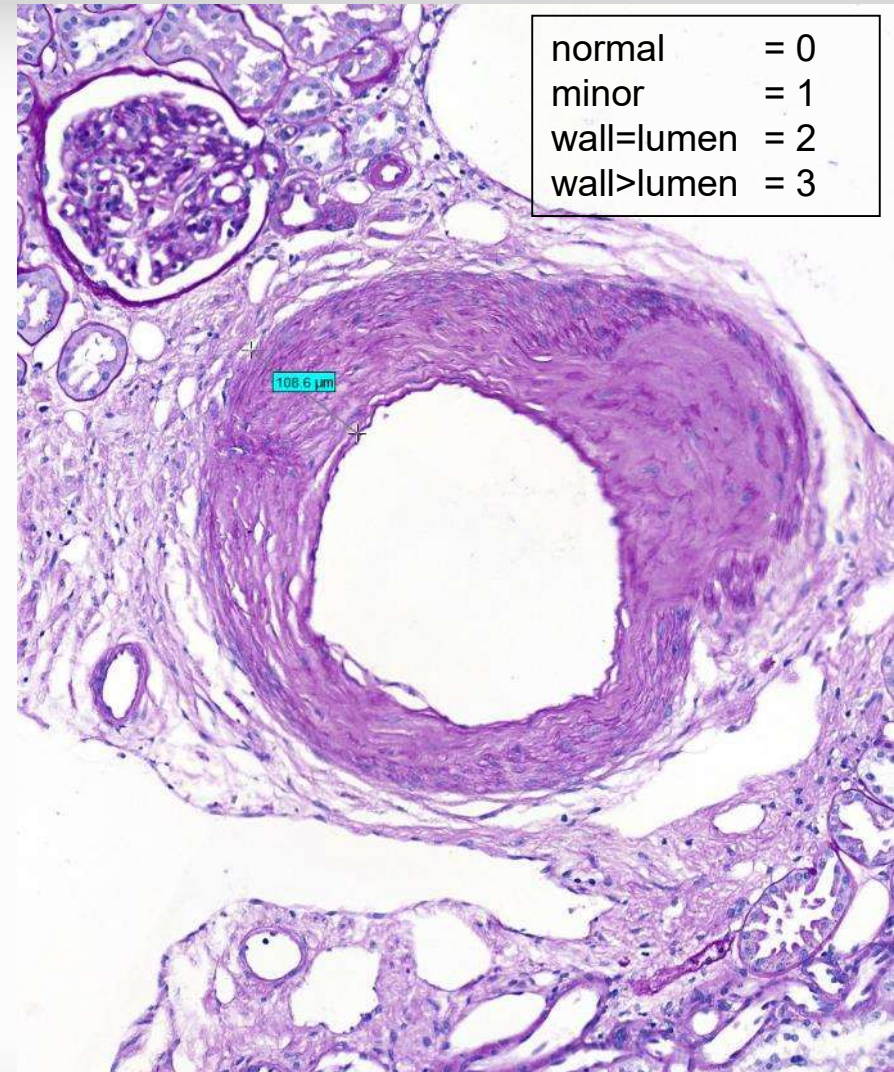
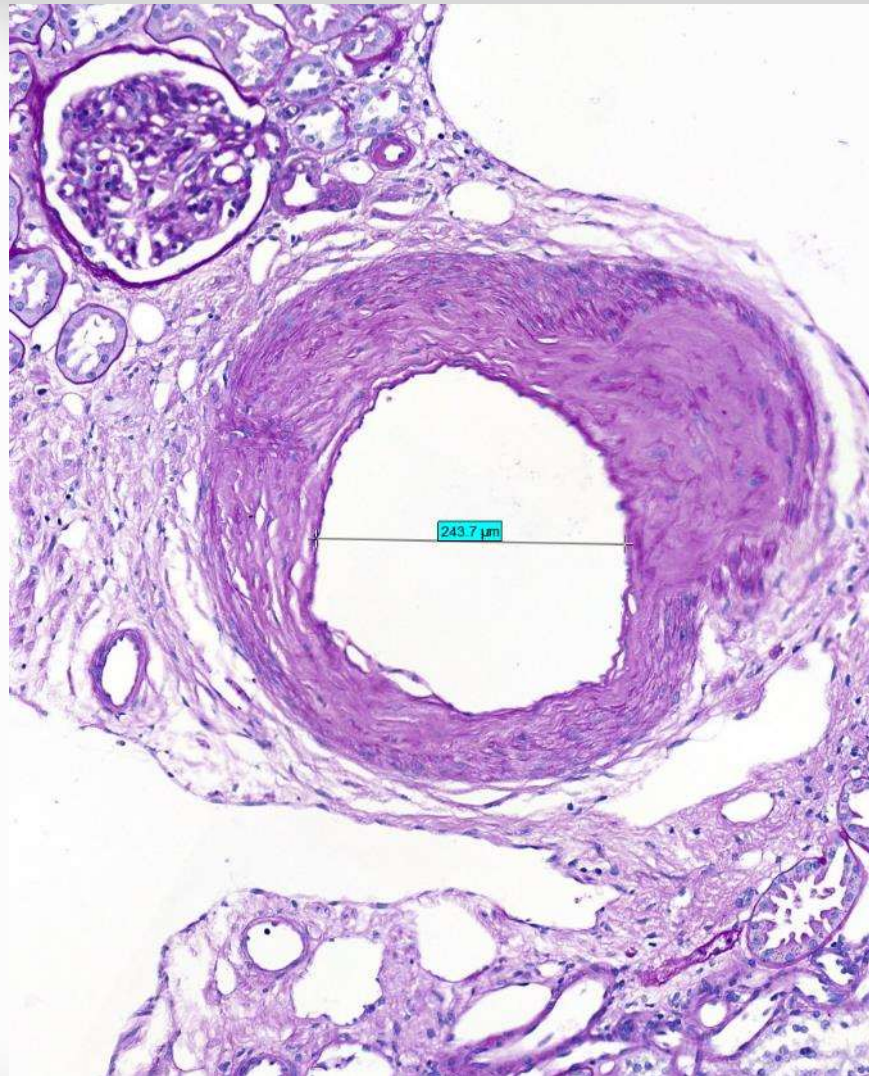
Arteries

normal	0
minor	1
wall=lumen	2
wall>lumen	3

- Measures background injury
- 4 'factors' considered important
- Each scored 0-3
- Scores are added up



Artery Scoring



Pre-implantation biopsy

- Results from historical Cambridge 'time-zero' biopsies
- Good independent correlation between score and outcome

Assess

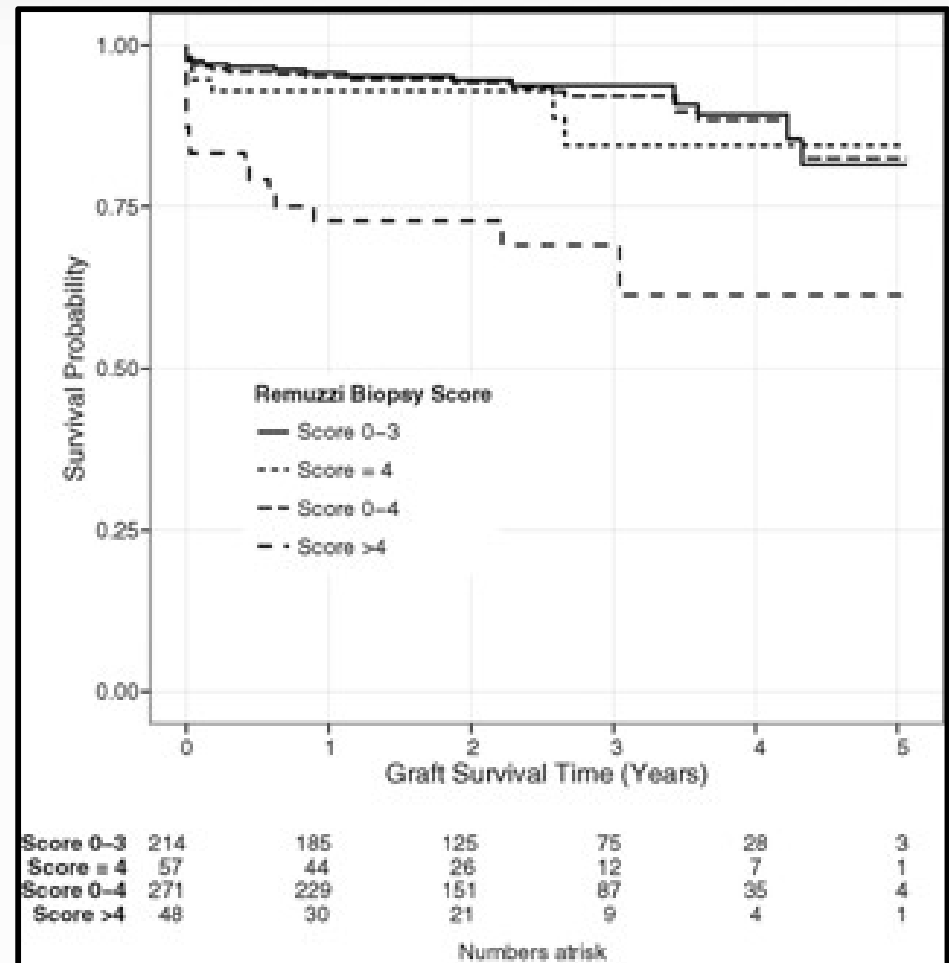
Prolong ischaemia

Increase quality

Increase discards

Increase number

Cost



Kosmoliaptsis et al AJT 2015

Current Practice

1	2
3	4

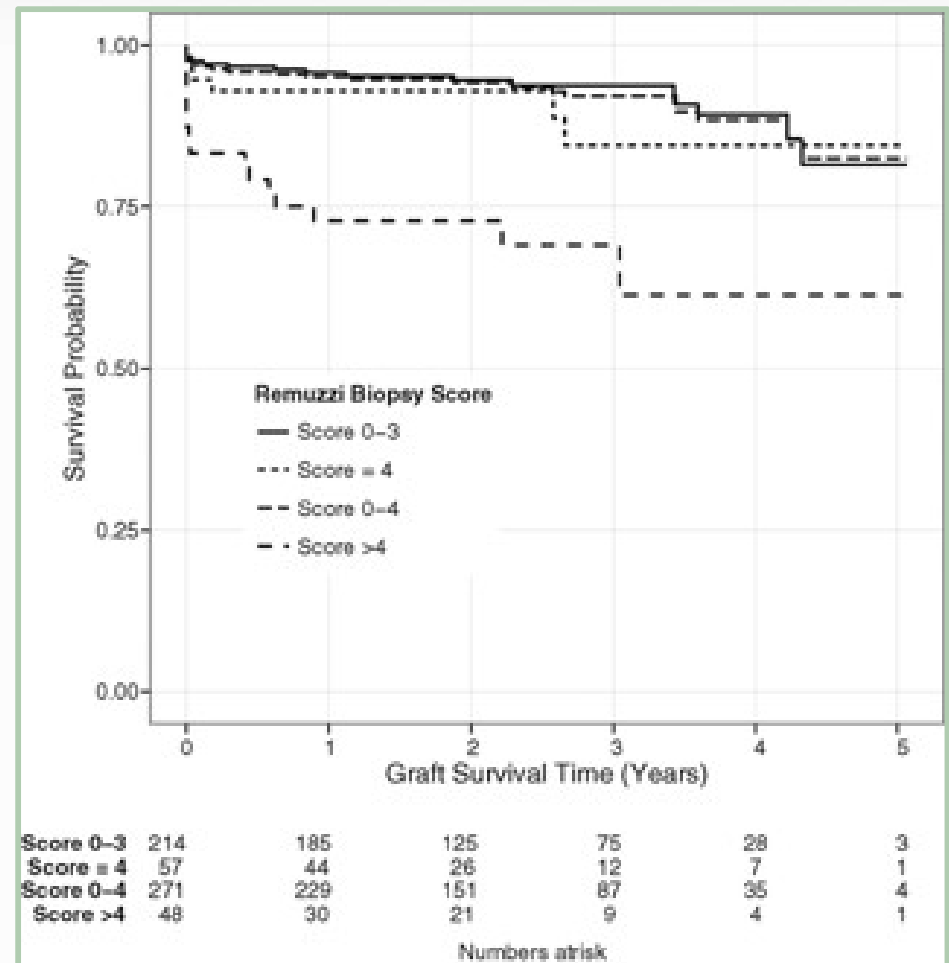
Single

5	6
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Double

7	8
9	10
11	12

Discard



Kosmoliaptsis et al AJT 2015

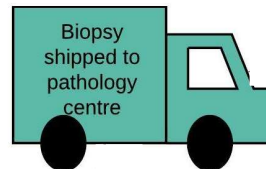
A national pathology service

Organ
Recovery

Donor aged
over 60 years

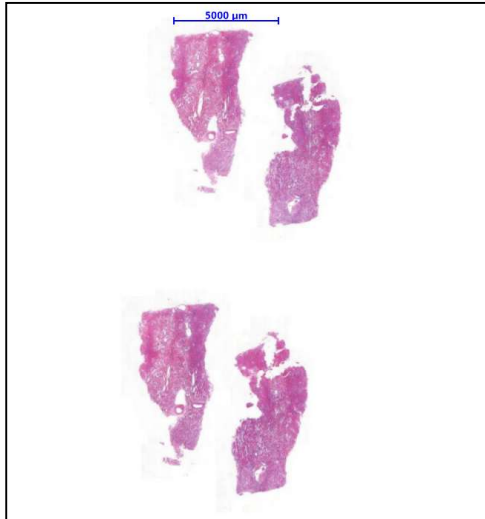
Transport

Biopsy
Processing



A national pathology service

Biopsy
Processing



Scanning



On call renal
pathologist



The PITHIA trial

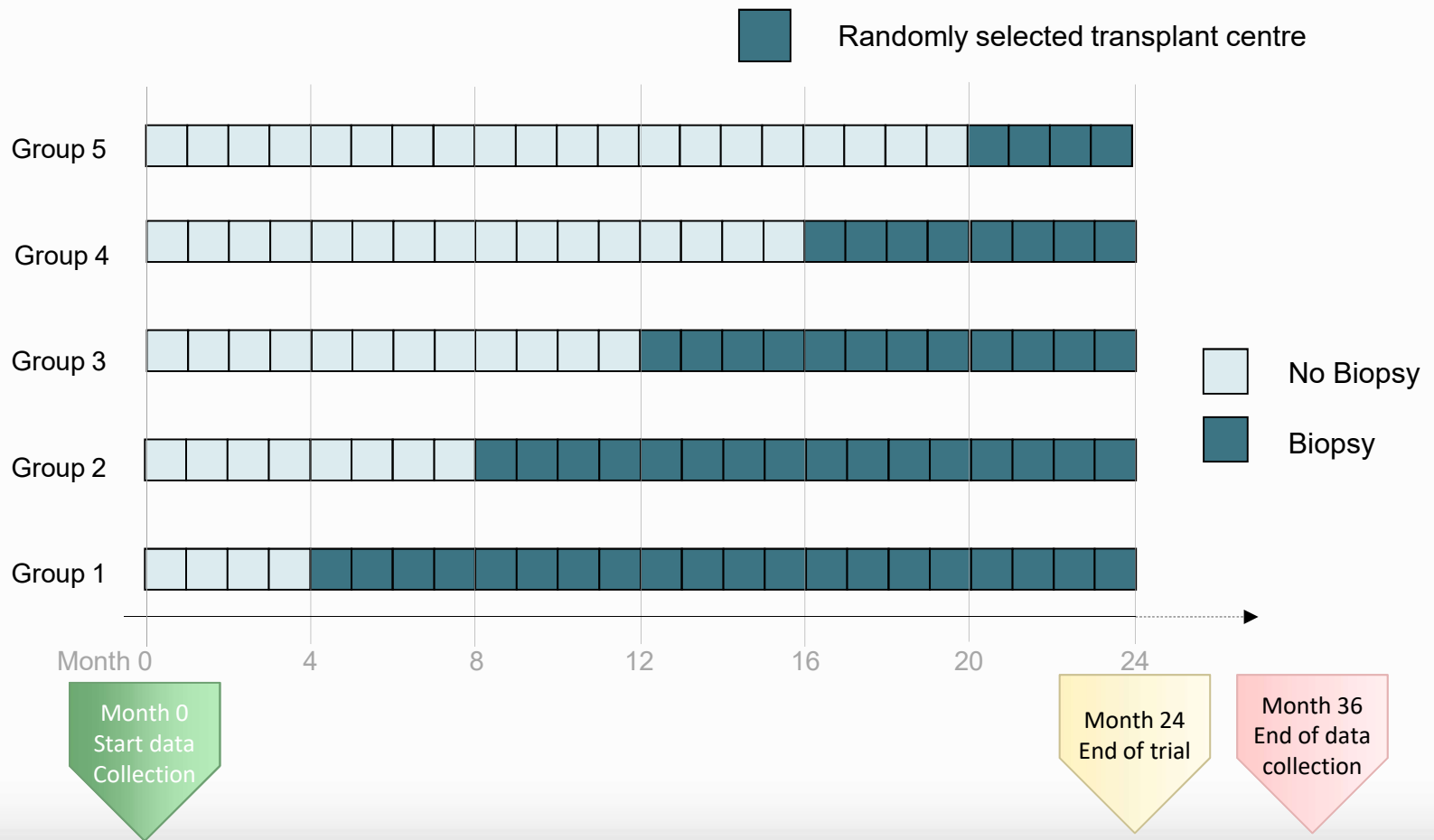
Pre-Implantation Trial of Histopathology In renal transplant Allografts
PITHIA

Does having access to a biopsy result increase the number
and quality of kidneys for transplantation?



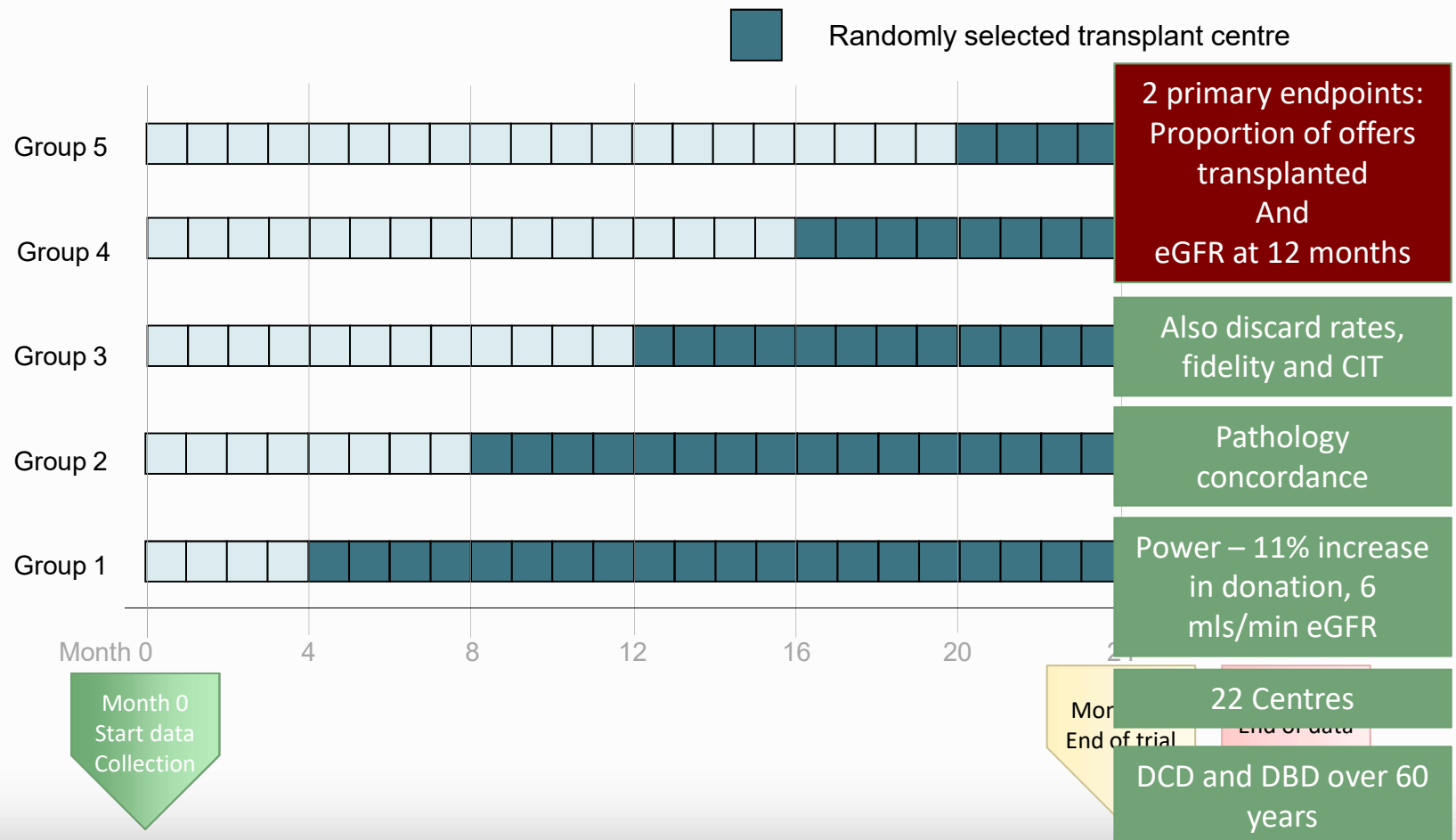
The PITHIA trial

Does having access to a biopsy result increase the number and quality of kidneys for transplantation?



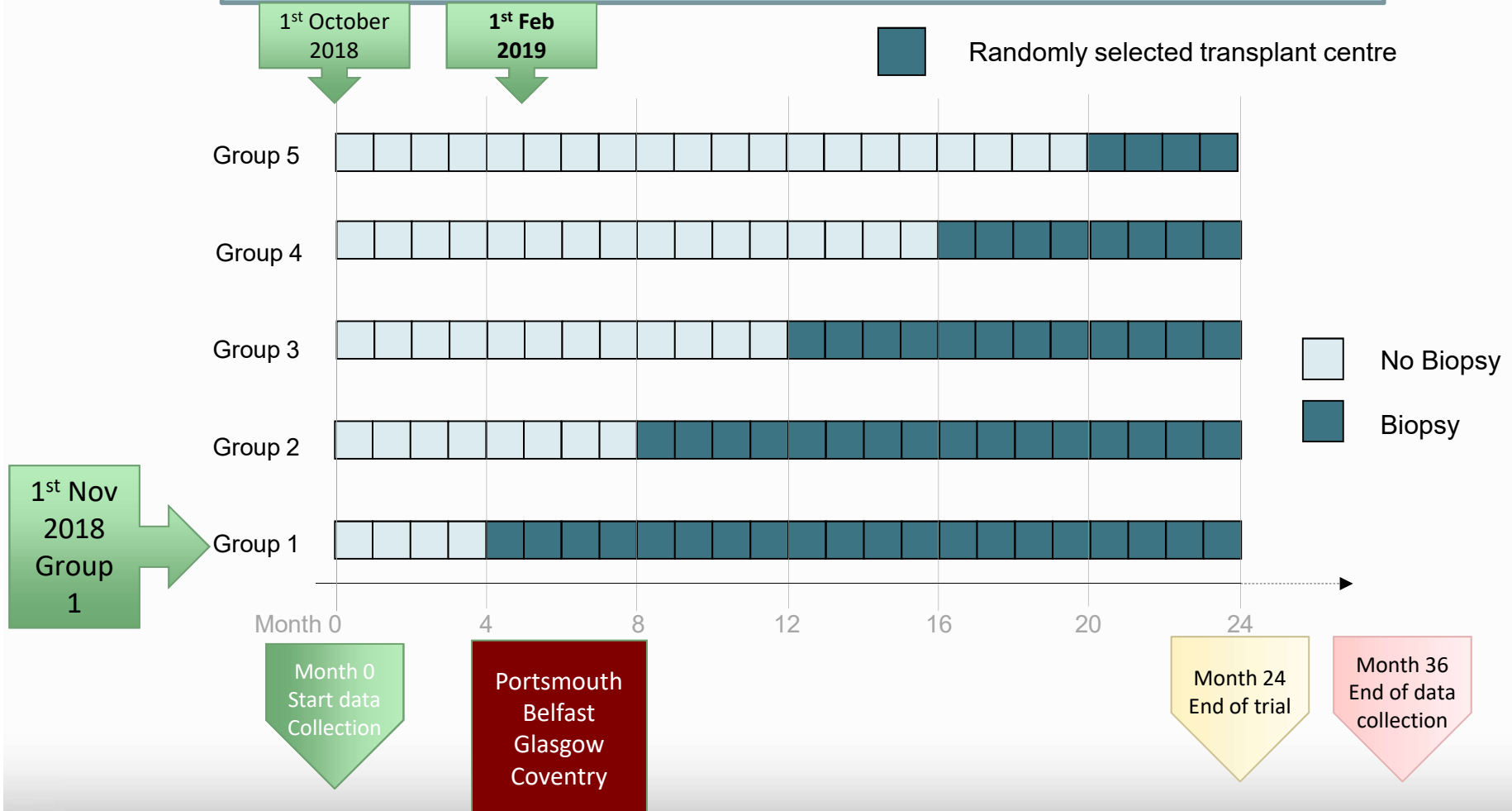
The PITHIA trial

Does having access to a biopsy result increase the number and quality of kidneys for transplantation?



The PITHIA trial

Does having access to a biopsy result increase the number and quality of kidneys for transplantation?

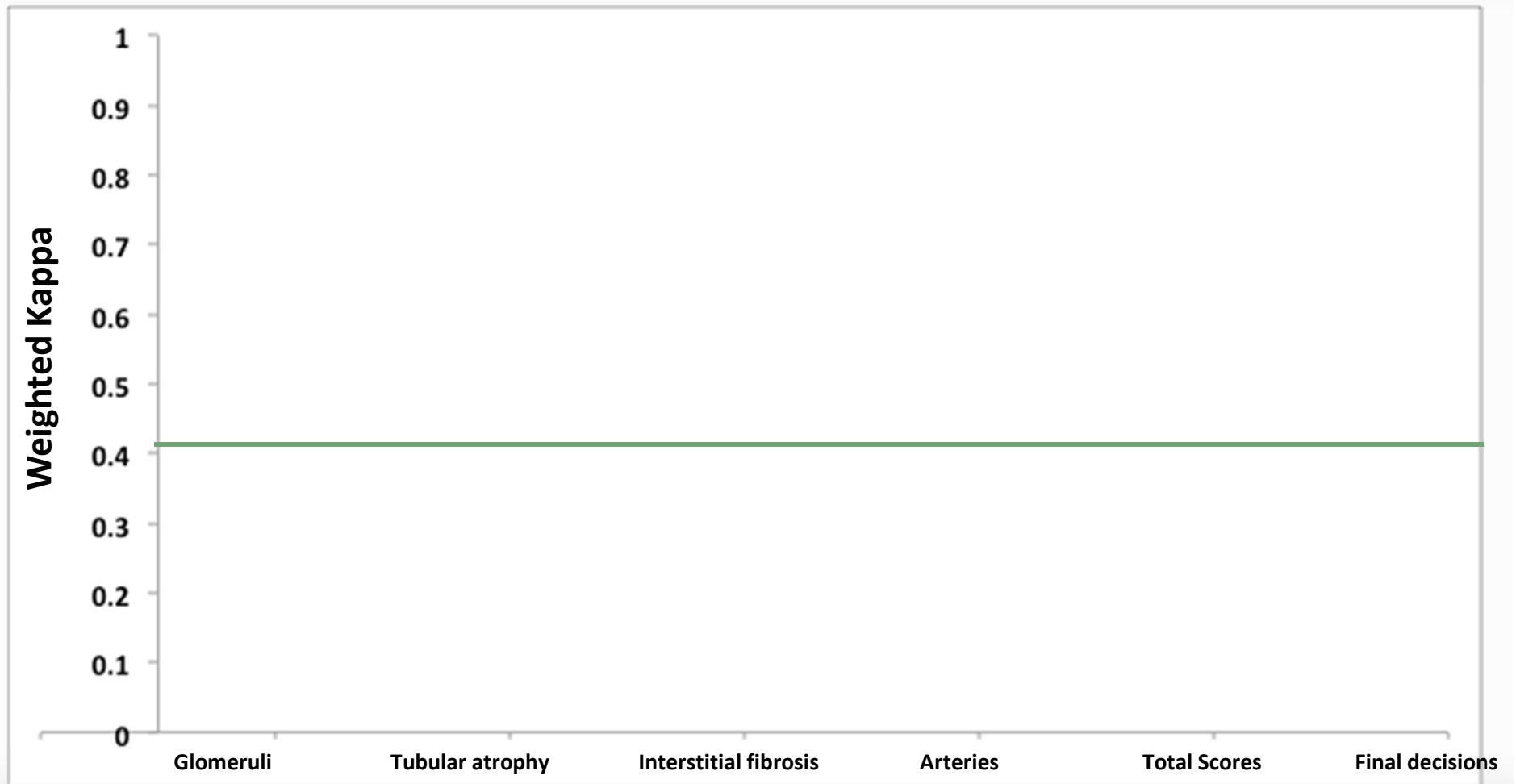


Pathology Concordance

- Critical for the trial (and histopathology service) that biopsies are reported consistently.
- 21 pathologists involved in the trial from around the UK
- Initial training with example slides and other visual aids
- Each pathologist asked to score 30 slides and scores compared to core group of pathologists who decided the 'true scores'

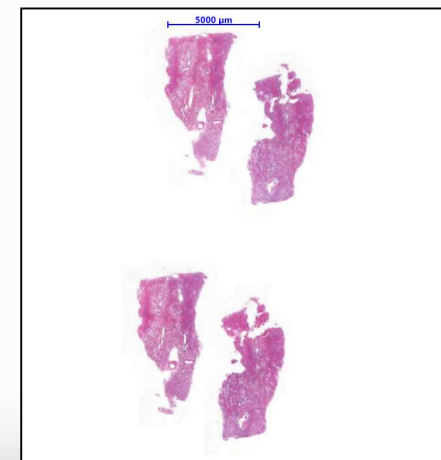


Results – concordance



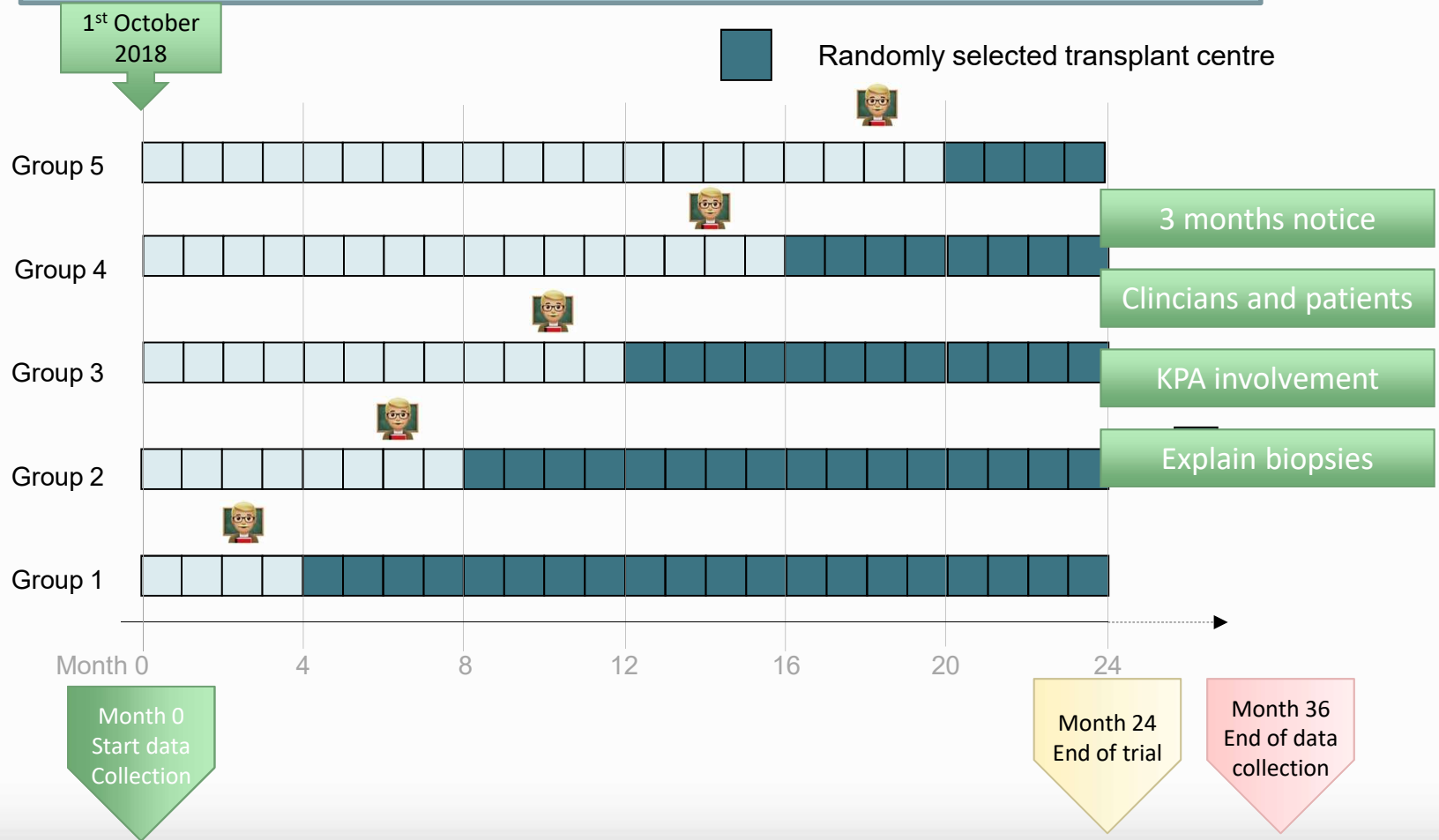
Pathology follow up

- Further discussion and retraining
- A further 20 cases were used to reassess
- Currently 12 Histopathologists signed off and on the rota
- (all voluntary)
- Over the course of the first year 100 cases will be selected and reassessed by the central team



Education Days

Does having access to a biopsy result increase the number and quality of kidneys for transplantation?



On the Night...

- Your surgeon will discuss the offered kidney as before:

- Donor age
- Other known risks

1	2
3	4

Single

- But a biopsy result may also be available or awaited

5	6
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Double

- *Biopsies are for guidance only – you have final say*

7	8
9	10
11	12

Discard

The PITHIA trial

- Pre-Implantation Trial of Histopathology In renal transplant Allografts – PITHIA
- Trial will demonstrate the value of pre-implantation histopathology in increasing number and quality of transplants
- Modest increase in acceptance rates of 10% equates to additional 150 transplants over the course of the trial
- The biopsies are for guidance only – you still have the final say
- PITHIA is a national trial with 2500 patients for only £500 000
- Stepped-wedge and randomised registry trials are both relatively novel designs, but well suited for transplantation
- The trial has started...

Surgeons	Patient Reps	Nephrologists	Statisticians	Pathologists	NHSBT
<ul style="list-style-type: none"> • Gavin Pettigrew • Dominic Summers • Tobi Ayorinde • Roberto Cacciola • Rutger Ploeg • Simon Knight • Chris Callaghan 	<ul style="list-style-type: none"> • Fiona Loud • Stewart Powell • Keith Pennington • Richard Jarvis 	<ul style="list-style-type: none"> • Nick Torpey 	<ul style="list-style-type: none"> • Karla Hemming • Laura Pankhurst • Ed Wilson • Helen Thomas 	<ul style="list-style-type: none"> • Desley Neil • Sathia Thiru • Vicky Bardsley • Meryl Griffiths • Sandrine Rendel 	<ul style="list-style-type: none"> • Emma Laing • Alison Deary • Anna Mora • Claire Williment • Maggie Stevens • Mick Stokes • Tanya Partridge

Principal Investigators

Belfast	James McDaid	Hammersmith Hospital	Frank Dor	Oxford	Simon Knight
Birmingham	Adnan Sharif	Leeds	Adam Barlow	Plymouth	Peter Rowe
Bristol	Samuel Turner	Leicester	Atul Bagul	Portsmouth	Paul Gibbs
Cardiff	Laszlo Szabo	Liverpool	Adham El-Bakry	Royal Free Hospital	Gareth Jones
Coventry	Dababrata Roy	Manchester	Titus Augustine	Royal London	Rajesh Sivaprakasam
Edinburgh	John Terrace	Newcastle	Colin Wilson	Sheffield	Badri Shrestha
Glasgow	Karen Stevenson	Nottingham	Sam Dutta	St George's Hospital	Abbas Ghazanfar
Guy's Hospital	Chris Callaghan				

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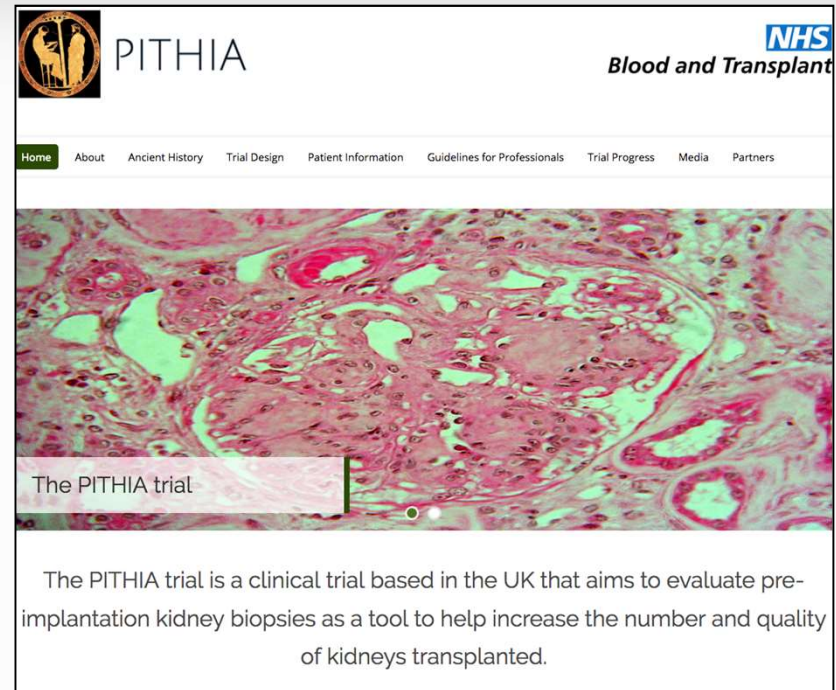


PITHIA



More information

WWW.PITHIA.ORG.UK



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