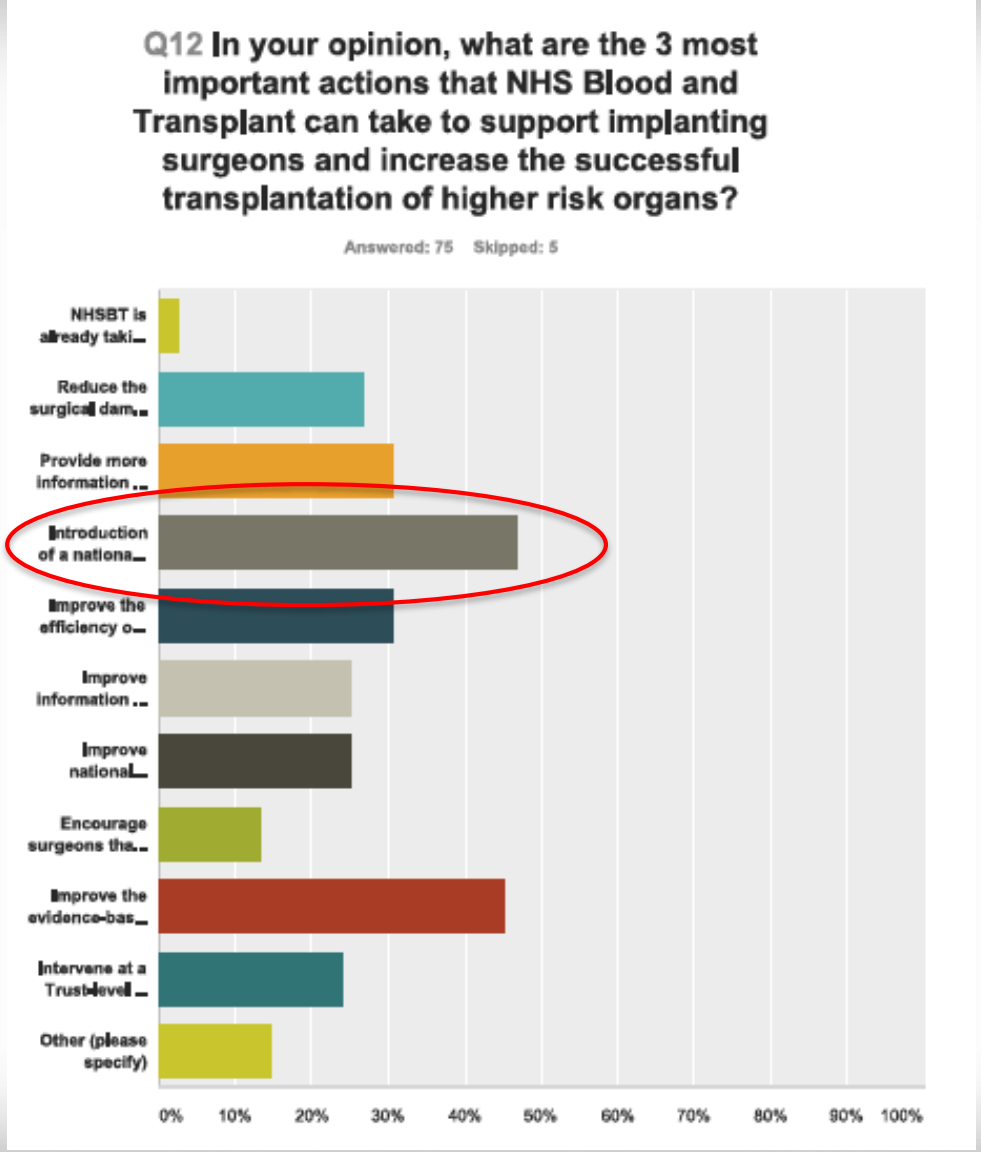
The PITHIA trial

- 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.
- Powered for an additional 150 kidney transplants.
- Stepped-wedge cluster design.
- A randomised registry trial in transplantation – relatively low cost trial design.

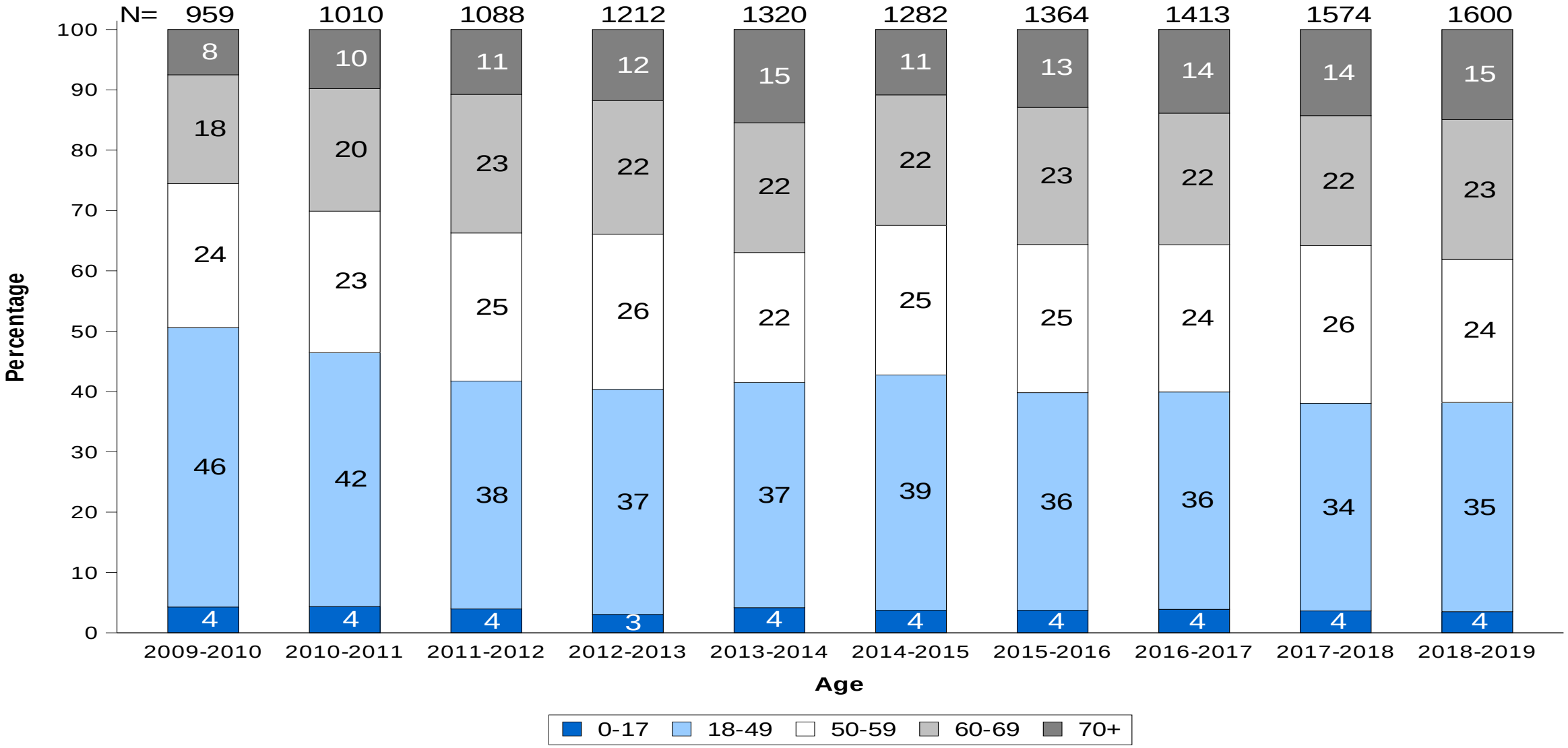
FUNDED BY
NIHR | National Institute for Health Research

Results – NHSBT actions

- Support for:
  - National 24/7 histopathology service
  - Improved evidence-base
  - Improved offering, allocation, and transport
  - More information on organ appearance

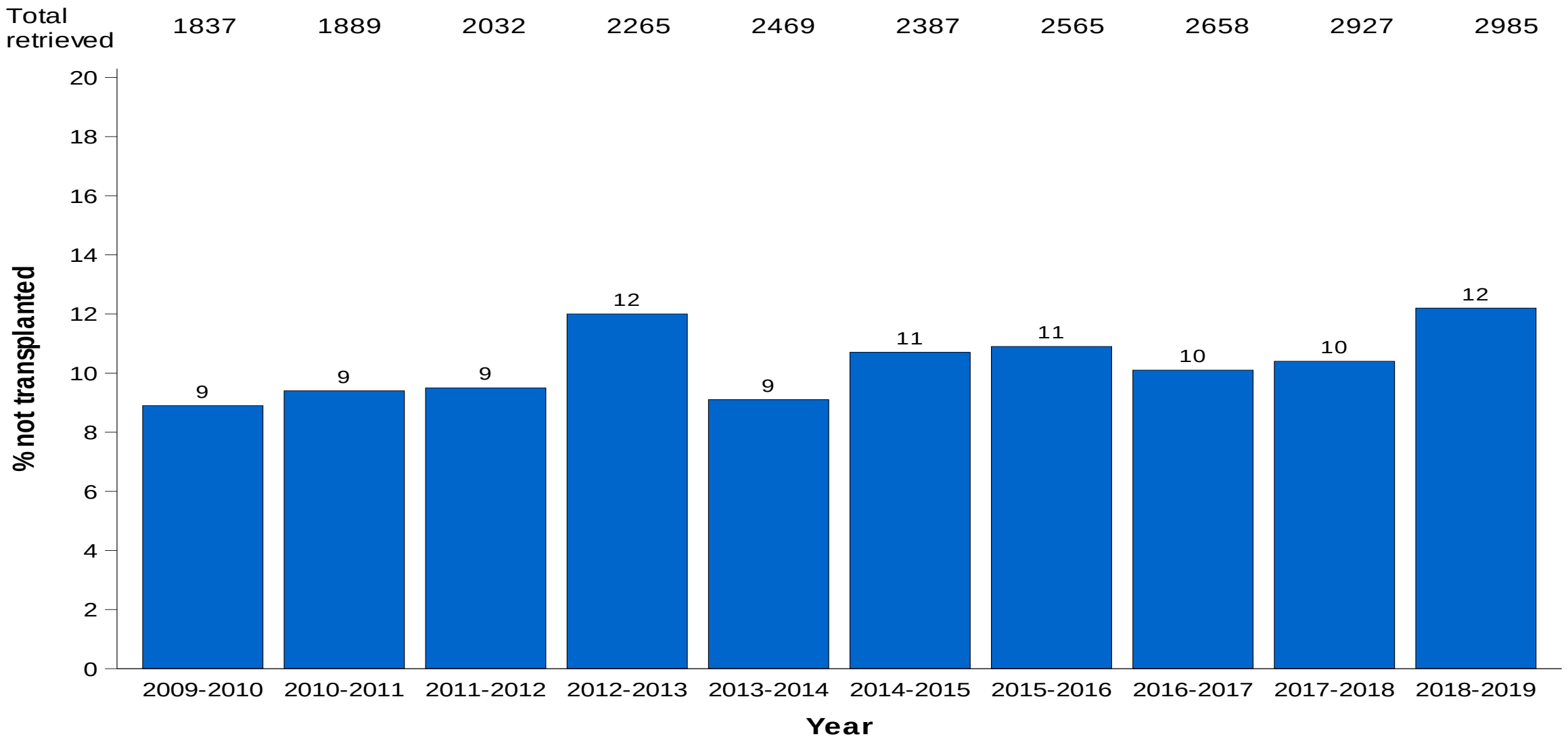


Age of deceased donors in the UK, 1 April 2009 - 31 March 2019



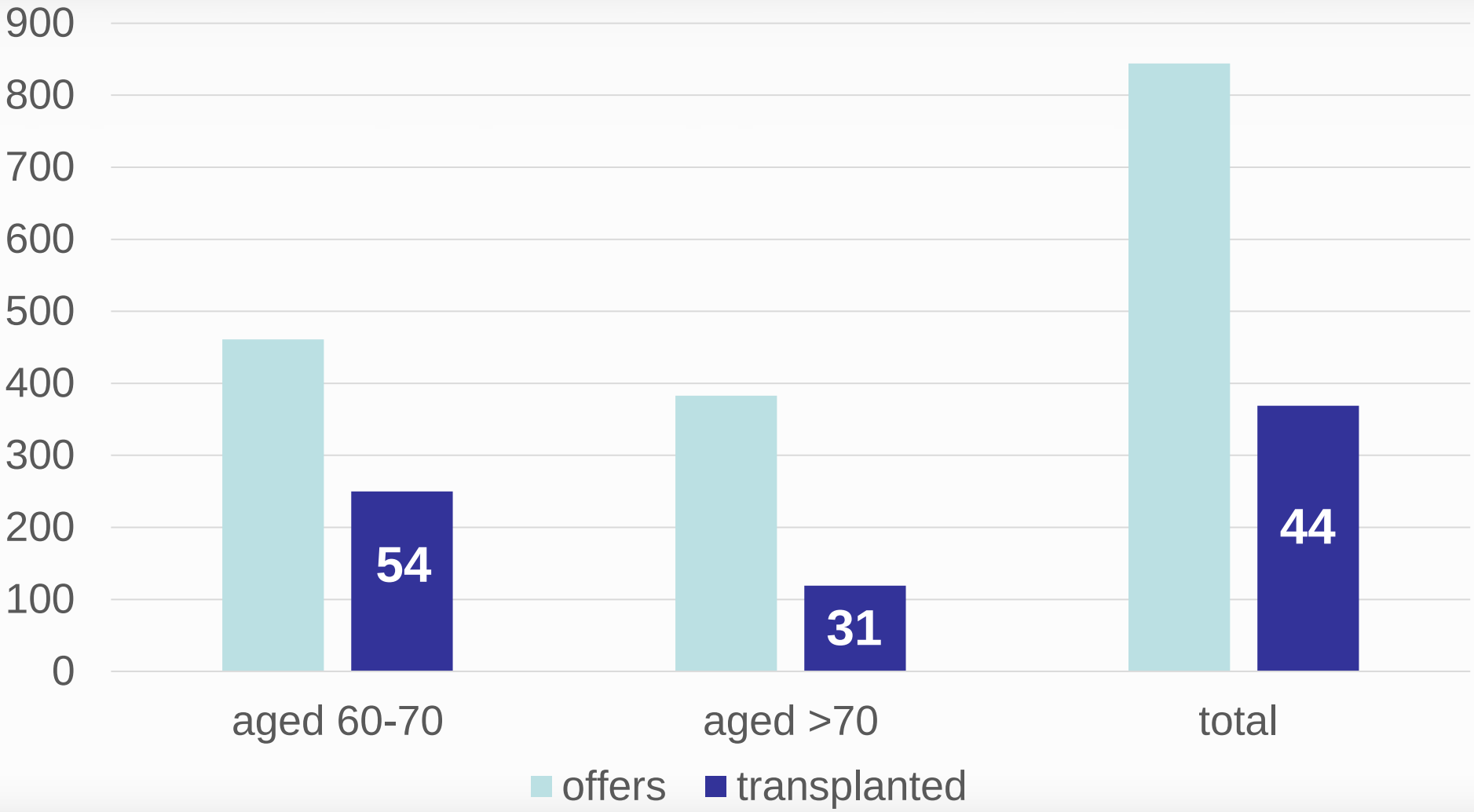
Source: Transplant activity in the UK, 2018-2019, NHS Blood and Transplant

Percentage of kidneys retrieved that were not transplanted from deceased organ donors in the UK, 1 April 2009 - 31 March 2019

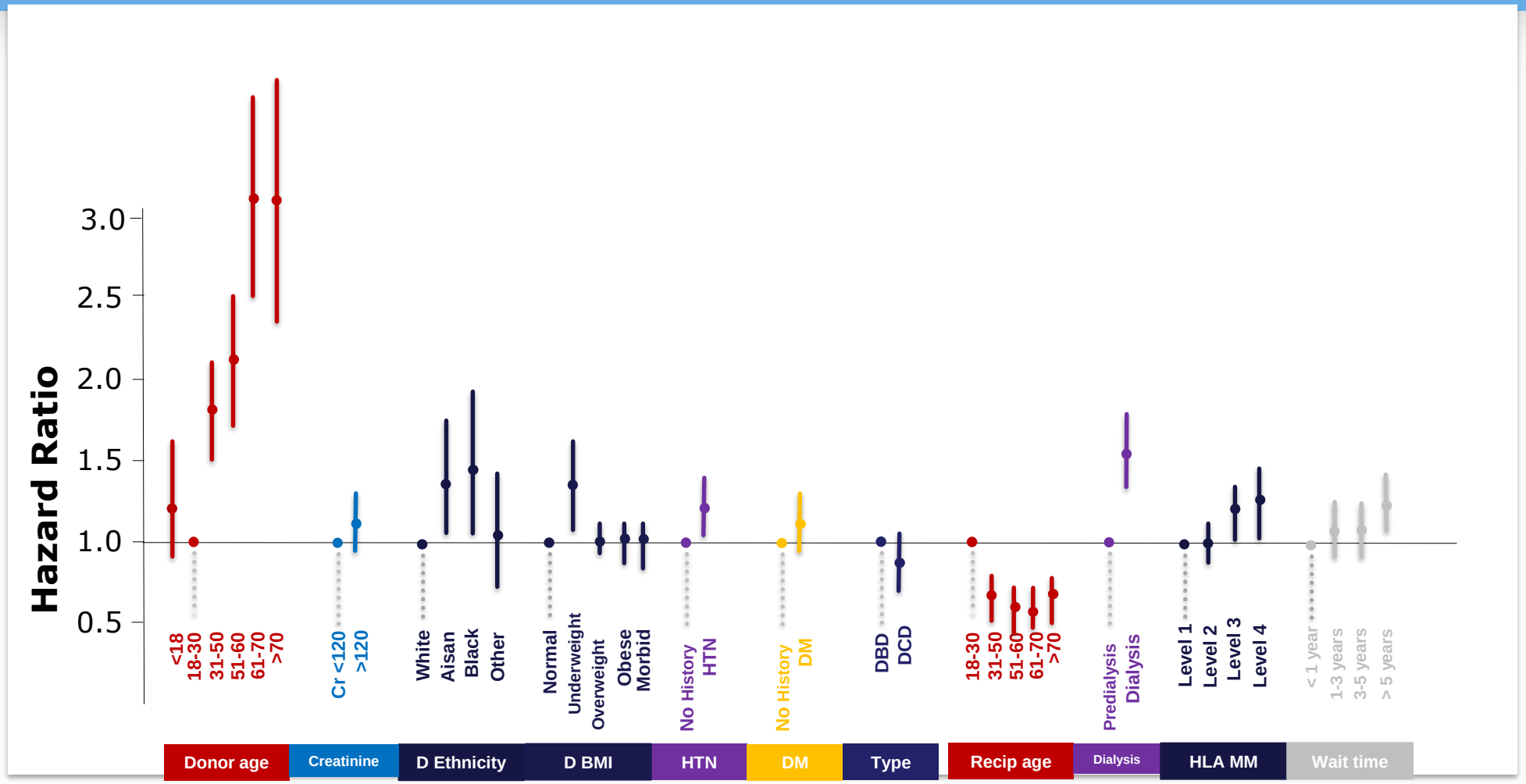


Source: Transplant activity in the UK, 2018-2019, NHS Blood and Transplant

Transplants from elderly deceased donors 1st May to 31st October 2019



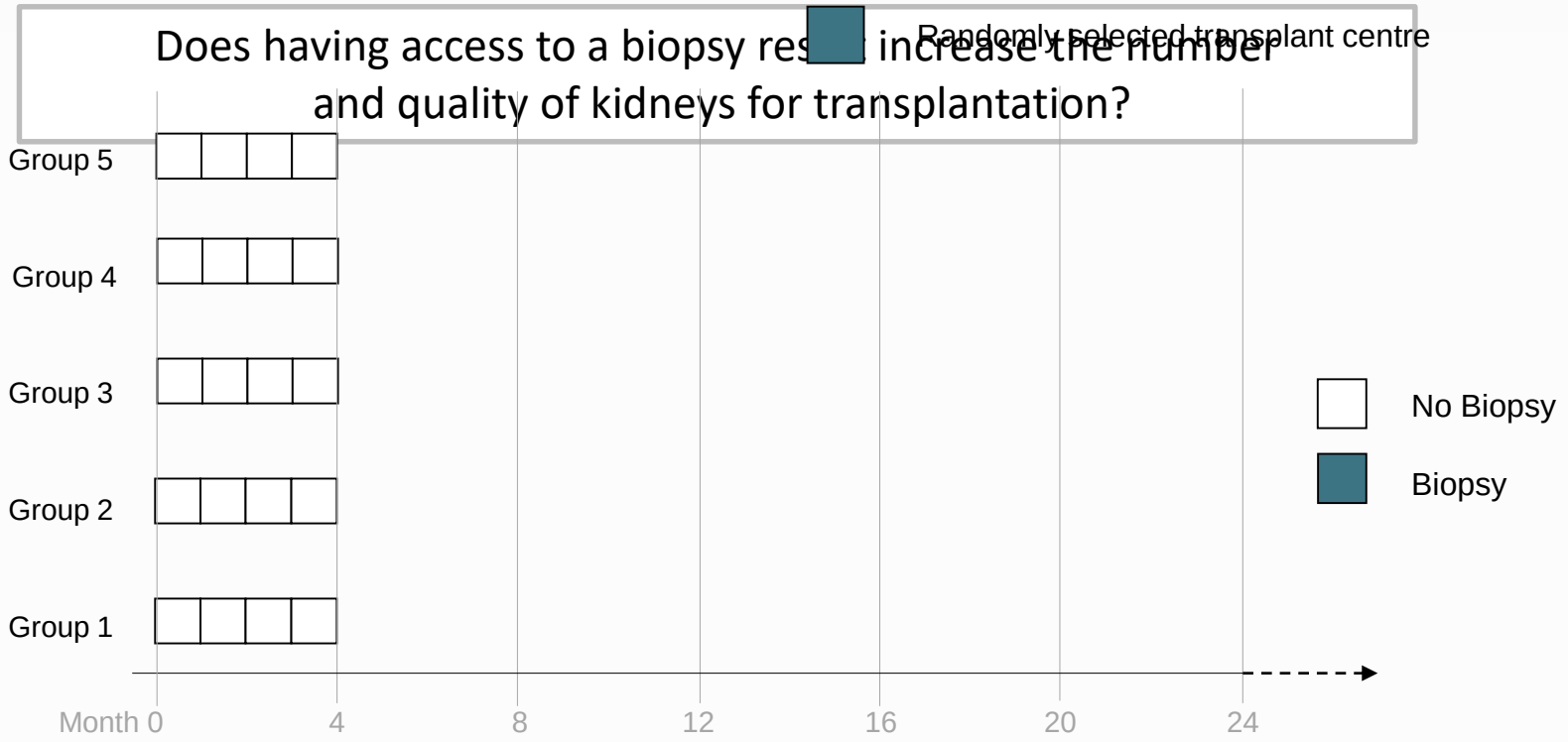
10 year death-censored graft survival model



The PITHIA trial

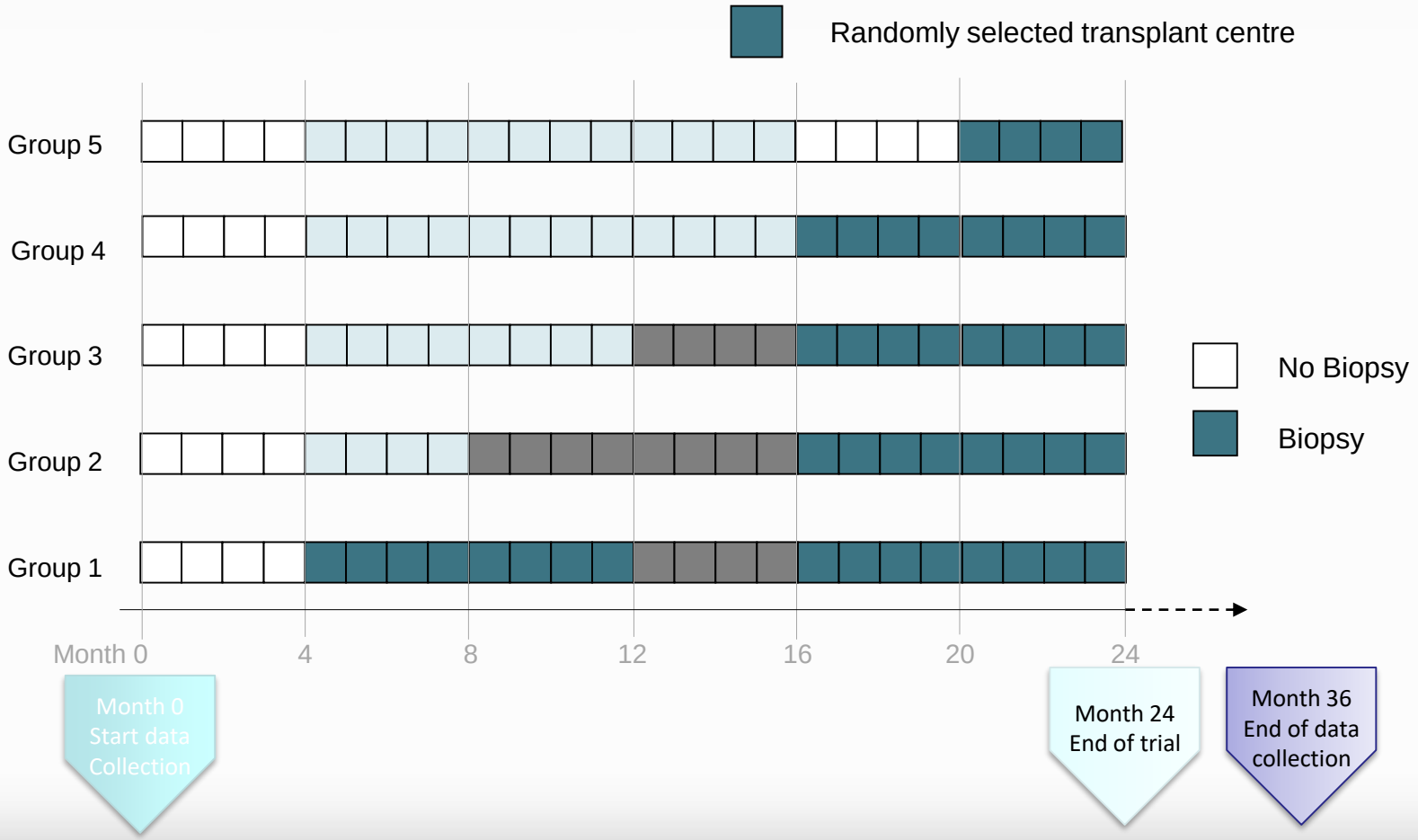
Pre-Implantation Trial of Histopathology In renal transplant Allografts
PITHIA

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



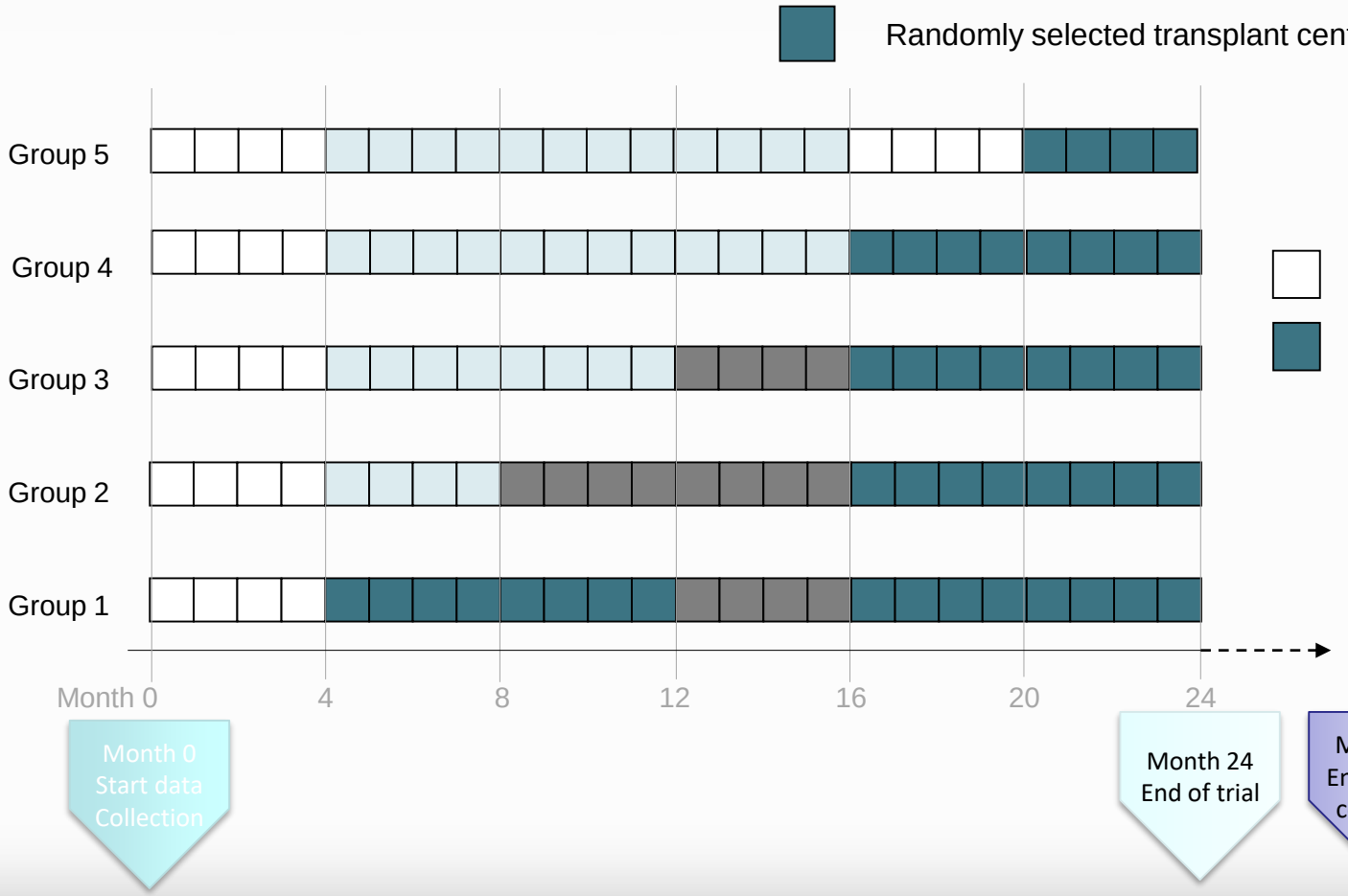
The PITHIA trial

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?



2 primary endpoints:
Proportion of offers transplanted
And
eGFR at 12 months

Also discard rates, fidelity and CIT

Pathology concordance

Power – 11% increase in donation, 6 mls/min eGFR

22 Centres

DCD and DBD over 60 years

Trial Process

Participating centre requests PITHIA sample → NORS team takes biopsy → Biopsy processed, scanned and uploaded → Histo-pathologist reviews and completes Remuzzi score → Report sent to transplant centre

sysmex

Logistics

Organ Recovery

Donor aged over 60 years

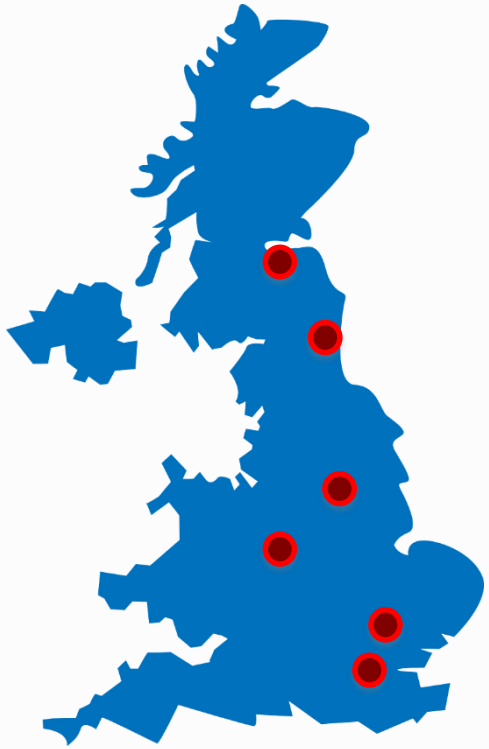
Transport

Sample accompanies NORS team to base

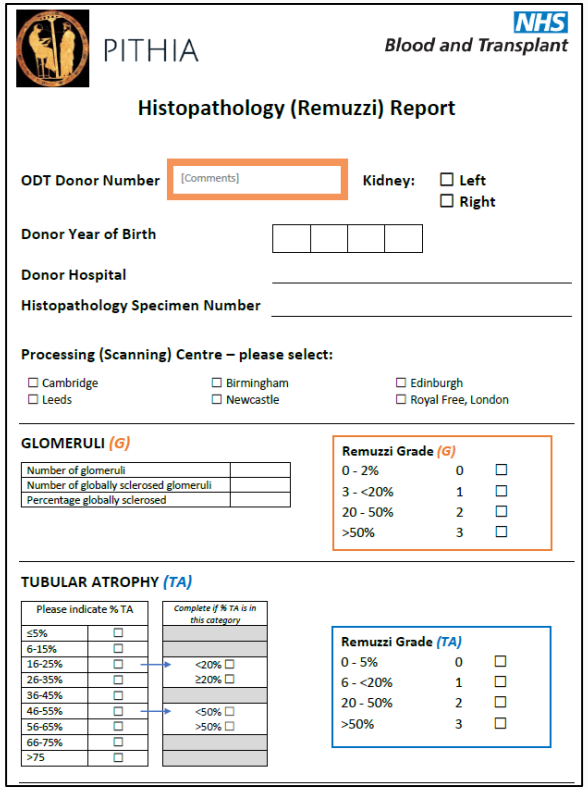
Sample accompanies an organ

Sample travels separately

Biopsy Processing



Histopathology Report



PITHIA

NHS Blood and Transplant

Histopathology (Remuzzi) Report

ODT Donor Number [Comments] **Kidney:** ☐ Left ☐ Right

Donor Year of Birth ☐☐☐☐

Donor Hospital _____

Histopathology Specimen Number _____

Processing (Scanning) Centre – please select:

☐ Cambridge ☐ Birmingham ☐ Edinburgh
☐ Leeds ☐ Newcastle ☐ Royal Free, London

GLOMERULI *(G)*

Number of glomeruli	
Number of globally sclerosed glomeruli	
Percentage globally sclerosed	

Remuzzi Grade *(G)*

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

TUBULAR ATROPHY *(TA)*

Please indicate % TA		*Complete if % TA is in this category*
≤5%	☐	
6-15%	☐	
16-25%	☐	<20% ☐ ≥20% ☐
26-35%	☐	
36-45%	☐	
46-55%	☐	<50% ☐ >50% ☐
56-65%	☐	
66-75%	☐	
>75	☐	

Remuzzi Grade *(TA)*

0 - 5%	0	☐
6 - <20%	1	☐
20 - 50%	2	☐
>50%	3	☐

INTERSTITIAL FIBROSIS *(IF)*

Please indicate % IF		*Complete if % IF is in this category*
≤5%	☐	
6-15%	☐	
16-25%	☐	<20% ☐ ≥20% ☐
26-35%	☐	
36-45%	☐	
46-55%	☐	<50% ☐ >50% ☐
56-65%	☐	
66-75%	☐	
>75	☐	

Remuzzi Grade *(IF)*

0 - 5%	0	☐
6 - <20%	1	☐
20 - 50%	2	☐
>50%	3	☐

ARTERIES *(A)*

Number of arteries	

NOTE: Score based on arteries only. If severe arteriolar changes then mention as other adverse feature in comments.

Remuzzi Grade *(A)*

Normal	0	☐
Wall thickness less than (<) lumen diameter	1	☐
Wall thickness equal or slightly greater than (>) lumen diameter	2	☐
Wall thickness much greater than (>) lumen diameter	3	☐

REMUZZI SCORE
(*G* + *TA* + *IF* + *A*) = / 12

ADEQUACY

Is the biopsy adequate (≥ 25 glomeruli AND > 1 artery)?

☐ Yes

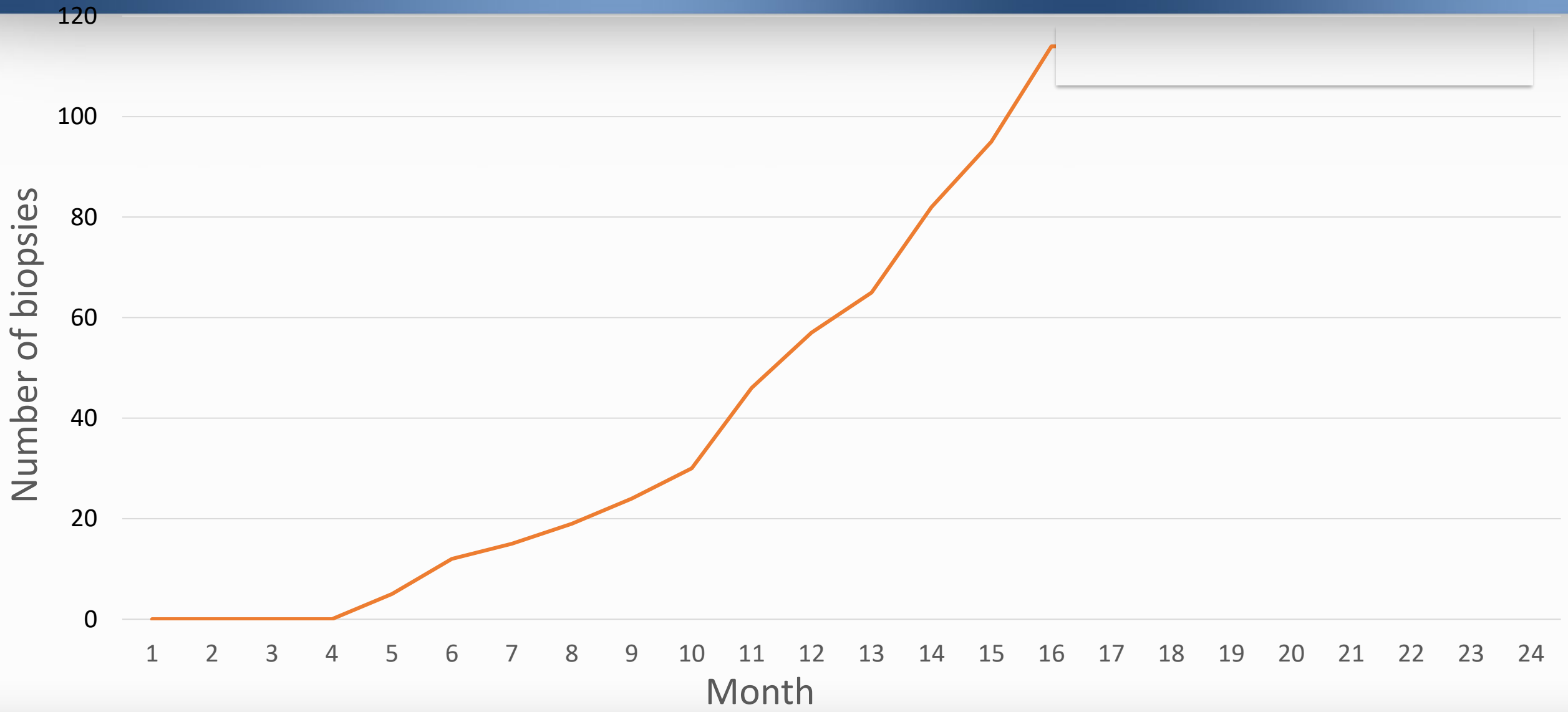
☐ No

You will also be given the contact number for the Histopathologist, who you can contact for additional information or queries.

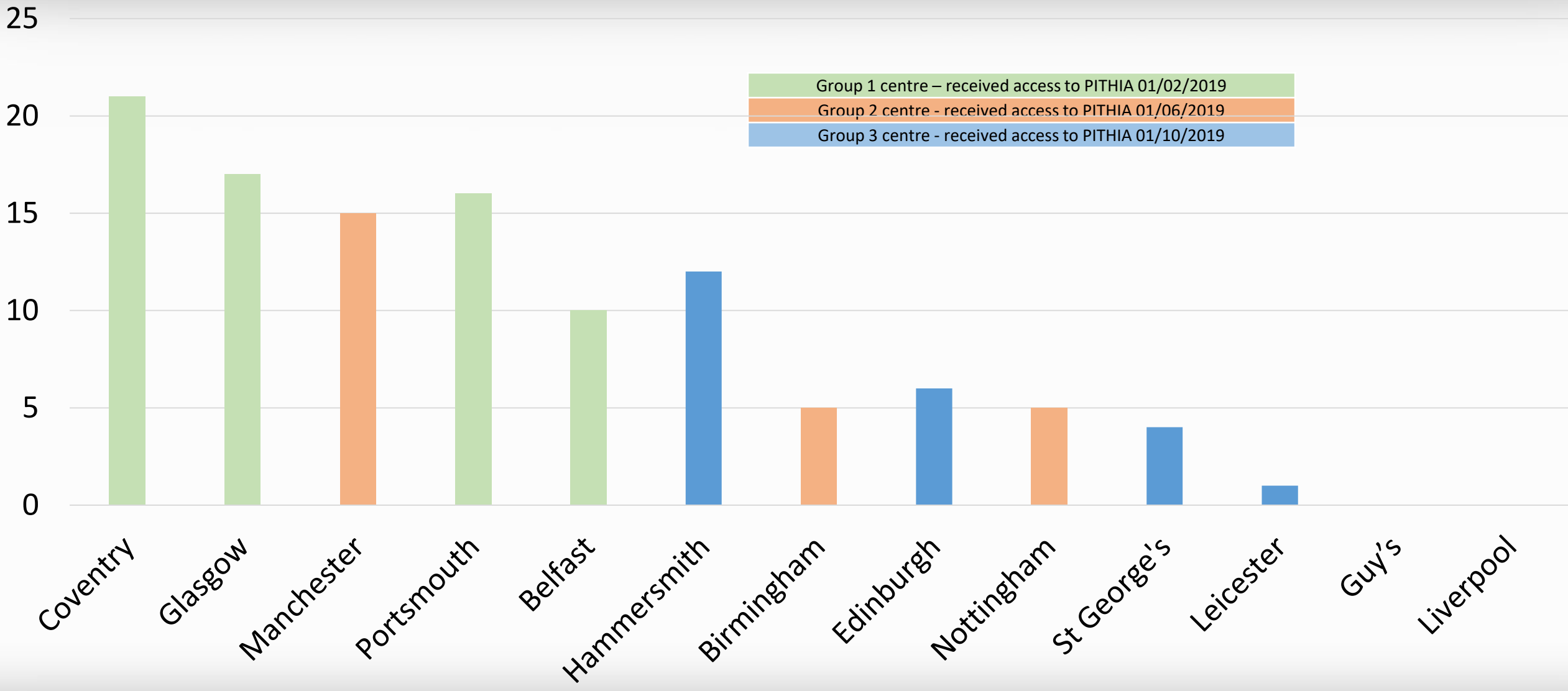
Practical Aspects

- Once a centre is enrolled – request biopsy as clinically indicated
- No mandatory component
- Biopsy result available in 4-5 hours – discussion with on-call pathologist
- Trial will run for next two years
- Around 2500 kidneys offers will be monitored during the trial
- Review meeting with centre 1 month after access.

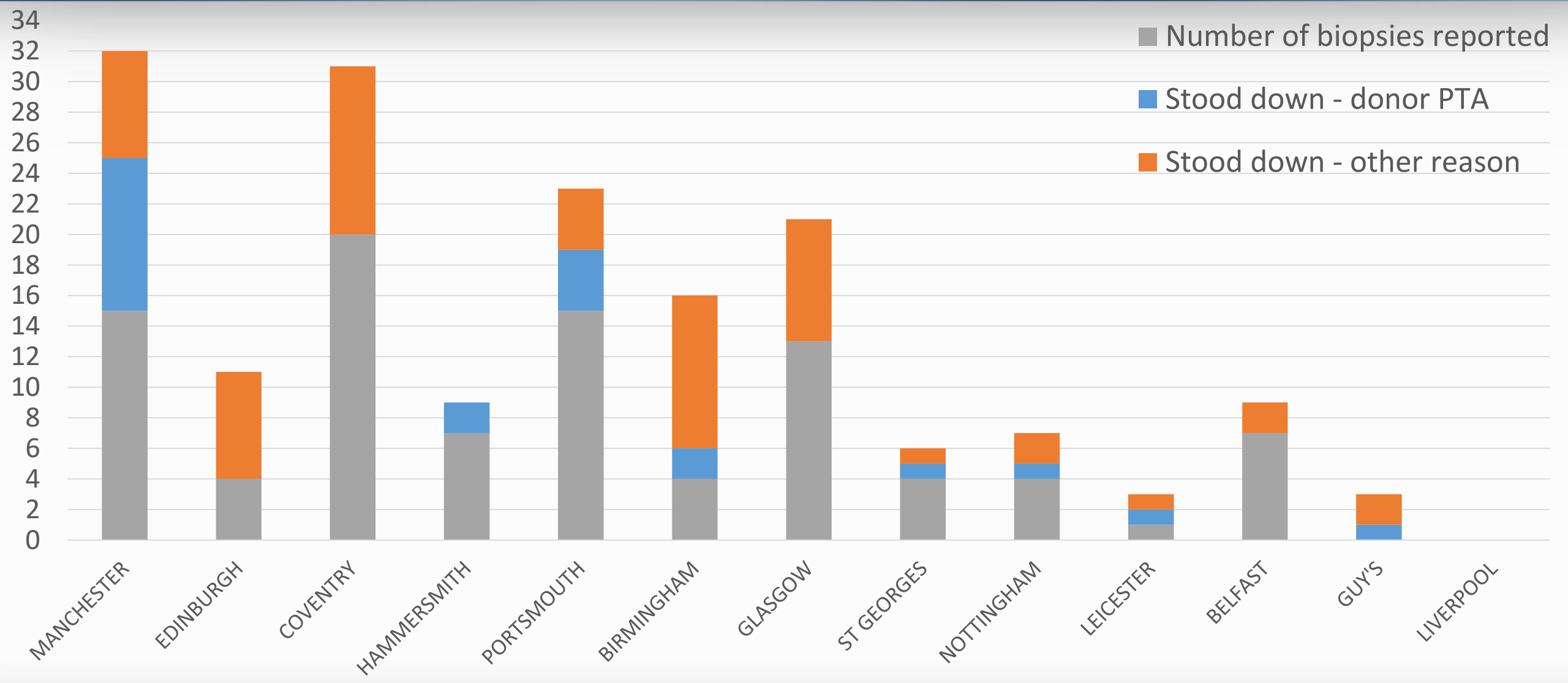
Number of PITHIA biopsies to date: 120



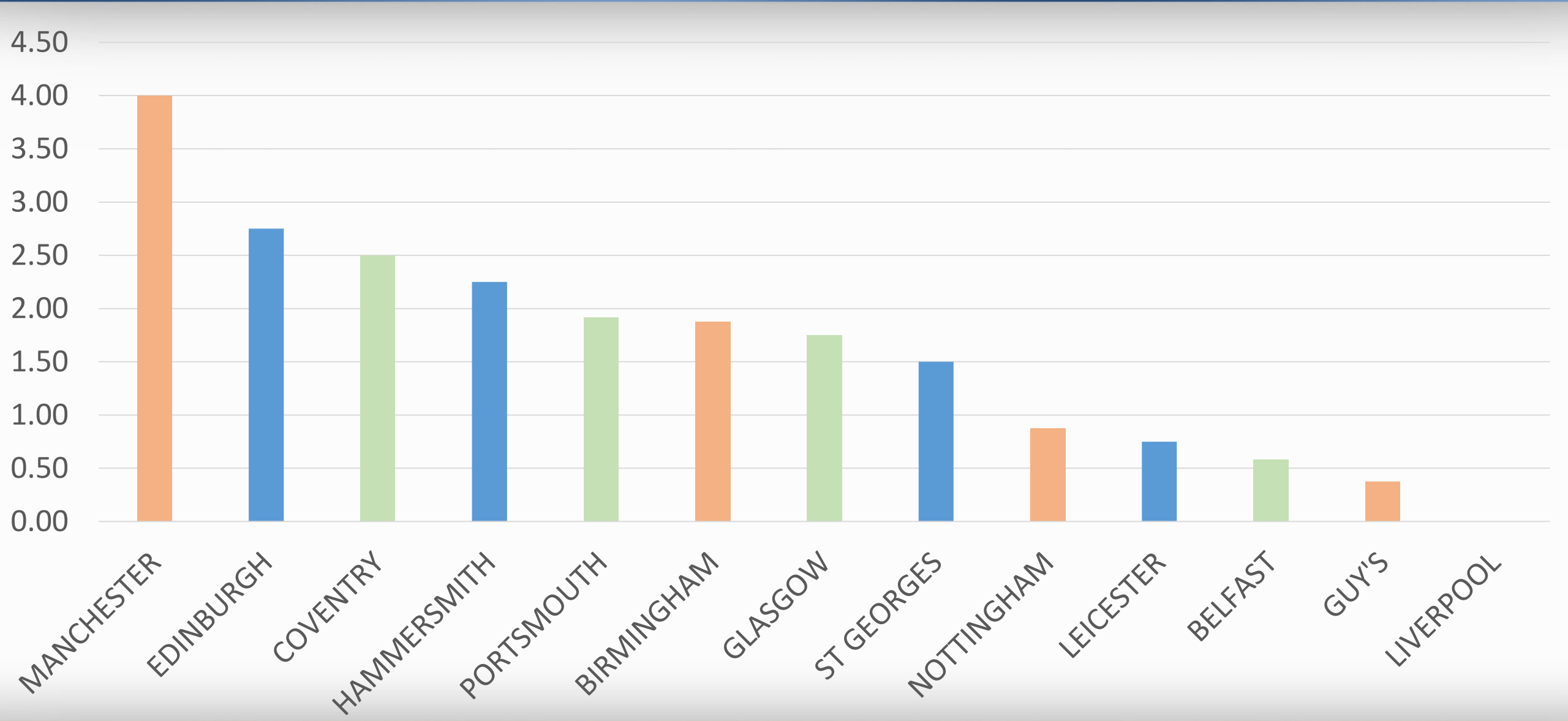
Biopsy Reports to Date



Biopsy Requests to Date



Biopsy Requests Per Month Per Centre



Why Engage in the trial?

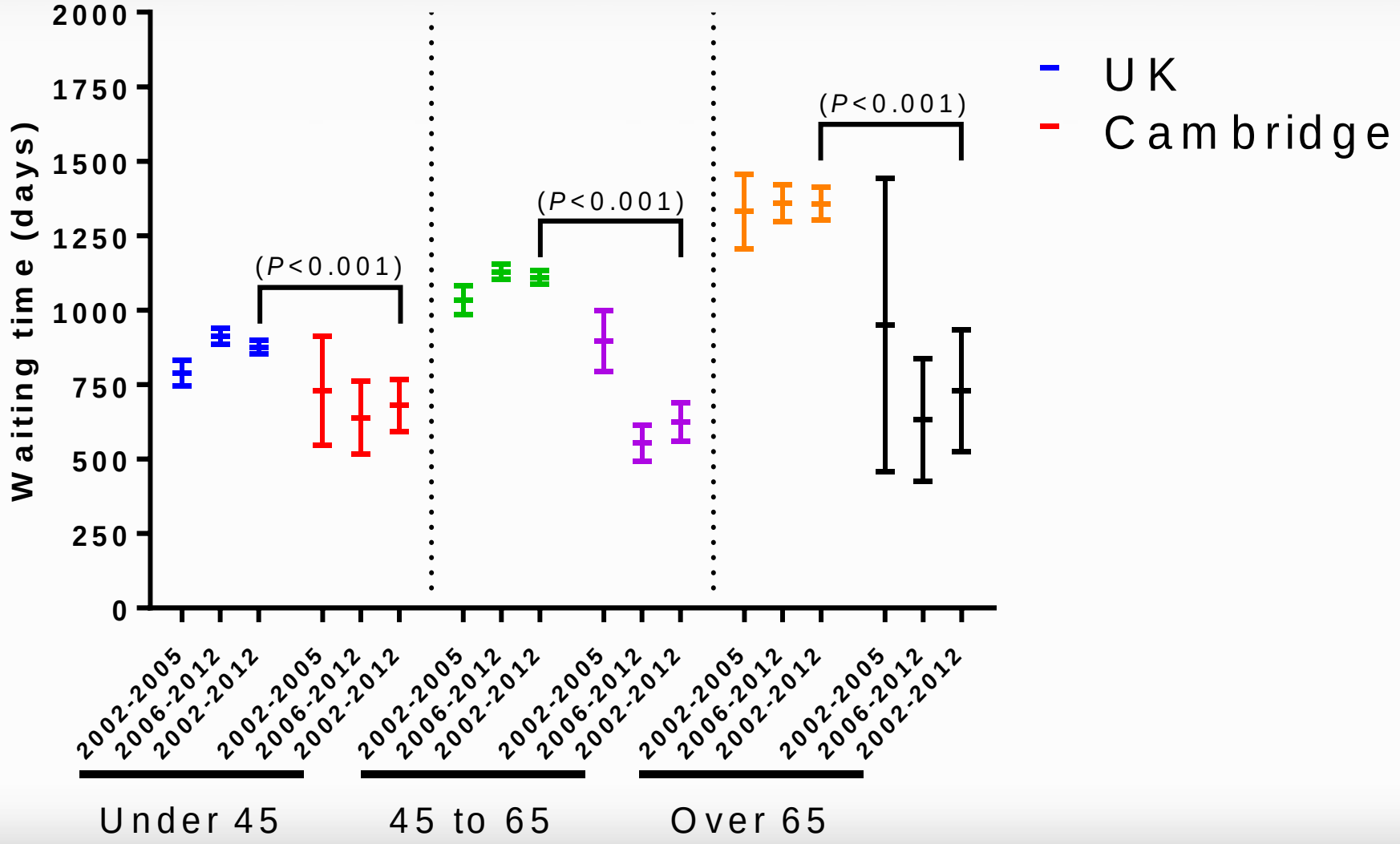
- Provide greater confidence in selection of ‘marginal’ donors
- Opportunity to further expand donor selection

Long-term outcome of renal transplantation from octogenarian donors: A multicenter controlled study

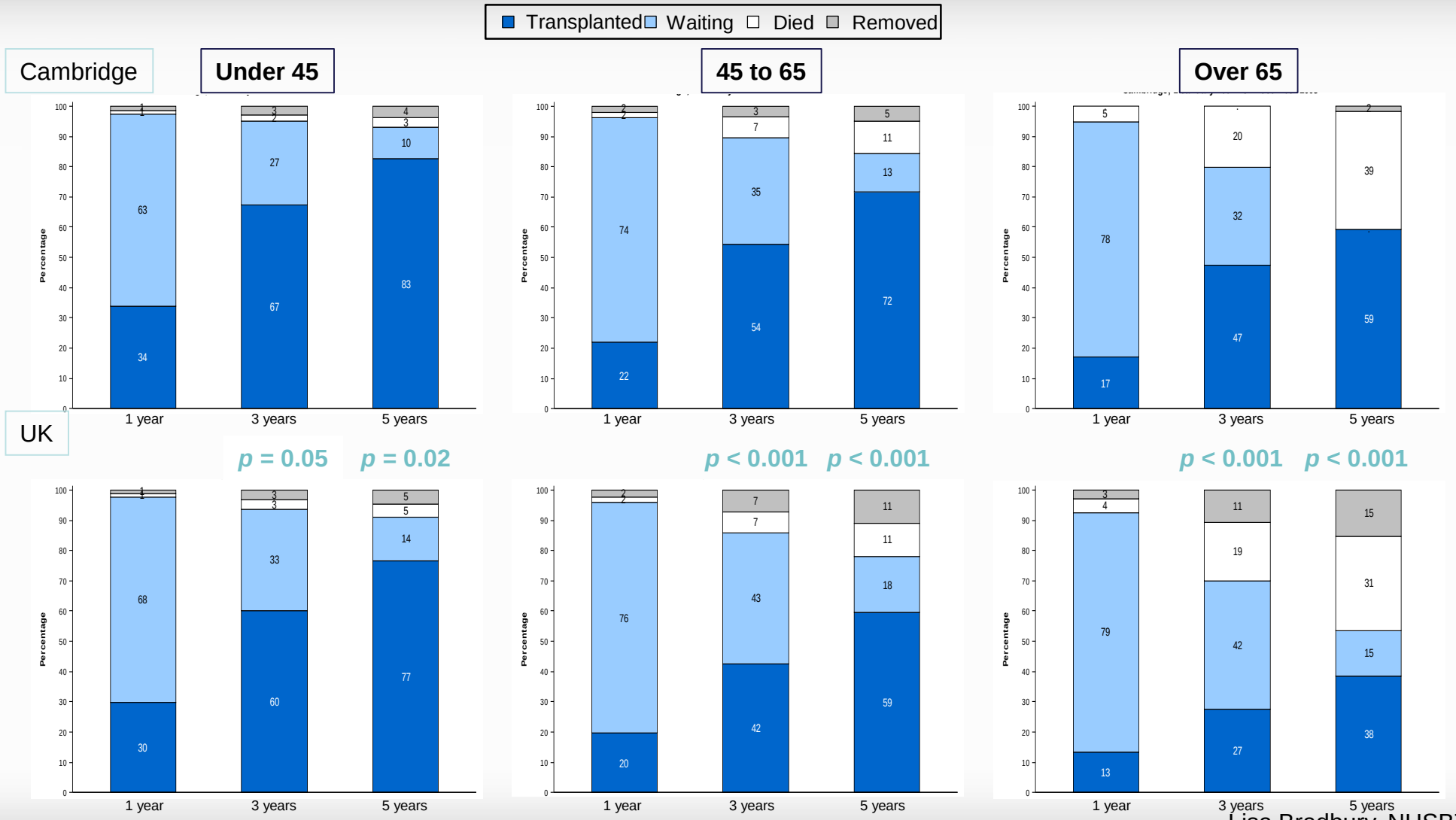
Piero Ruggenenti, Cristina Silvestre, Luigino Boschiero, Giovanni Rota, Lucrezia Furian, Annalisa Perna, Giuseppe Rossini, Giuseppe Remuzzi ✉, Paolo Rigotti

- Use the pool of underutilised elderly donors to address the inequity of transplant for elderly listed patients
- Particularly useful in conjunction with new KAS

Waiting times by recipient age



Patient outcomes from listing

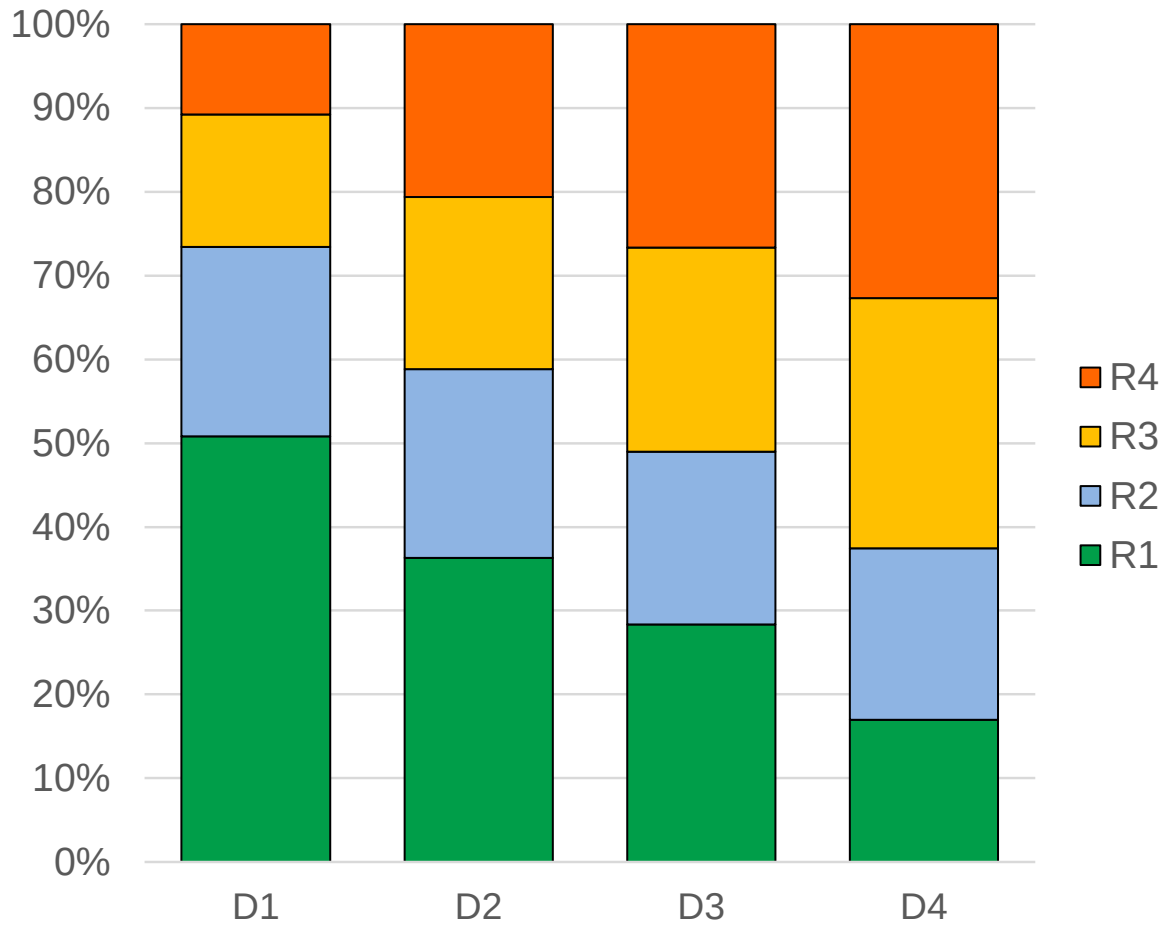


Lisa Bradbury, NHSBT

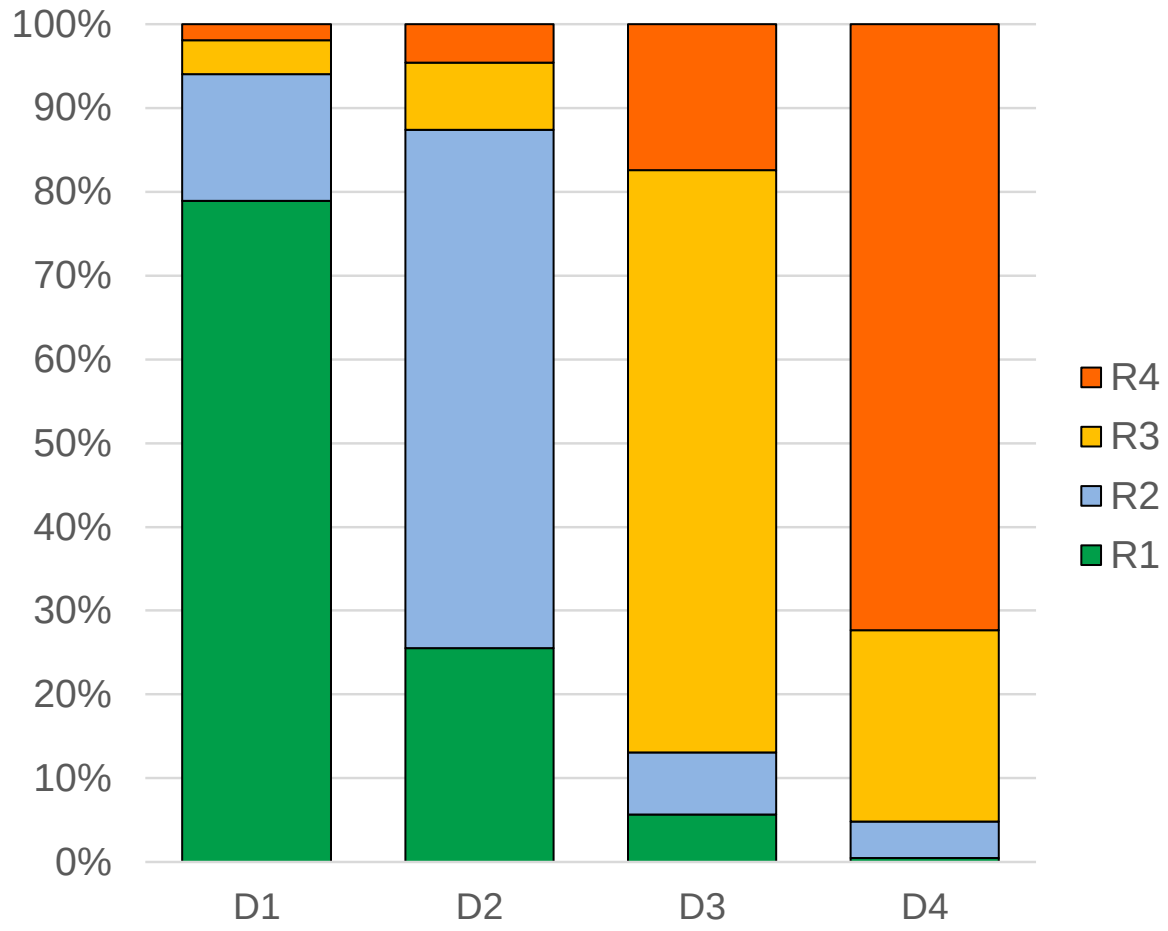
‘Quality’ matching donor to recipient

NHS Blood and Transplant

Current scheme

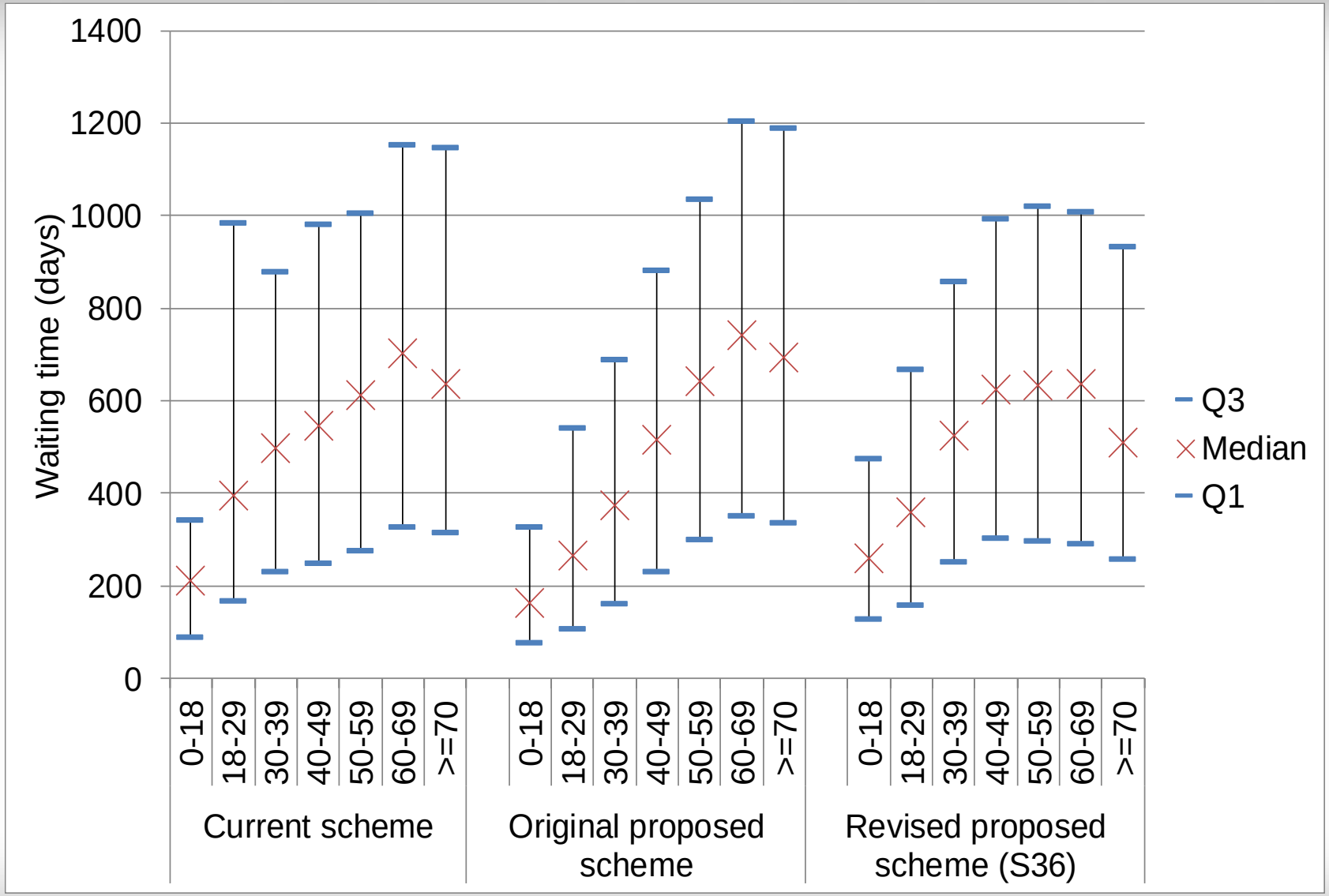


Proposed scheme

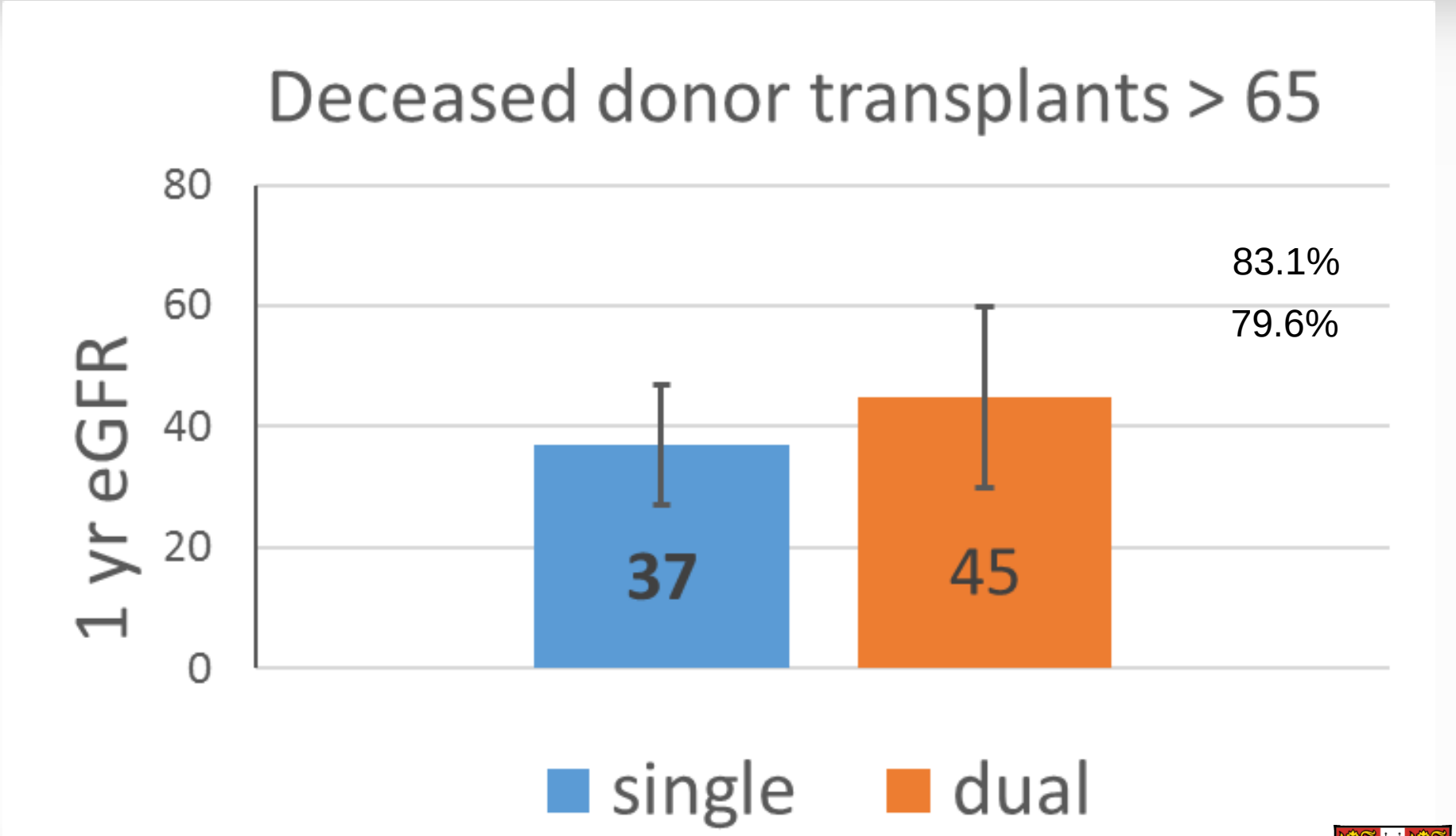


Proposed Kidney Allocation System

NHS Blood and Transplant



National Outcomes for dual transplants from donors aged over 65 years



Final word…

- This is a **trial**!
- **Persisting uncertainty over use of elderly deceased donor kidneys –**
  The trial will help decide whether preimplantation biopsy helps.
- If centres don't order biopsies in the trial then we will **never know** the answer to this question.
- The aim is to see whether biopsies will help you **select**, and **transplant**, kidneys that you normally have declined

http://www.pithia.org.uk/ **@PITHIA_trial**

And thank you!