



**UK national biobank and scientific platform
with integrated clinical data
in organ donation & transplantation**

Why QUOD ?

The increase in organ donation
is in older and higher risk donors:
unstable DBD, ECD & DCD

The challenge = to improve utilisation and
reduce discard transplanting greater numbers
of organs without compromising outcome

Uncertainty !

Many organs are not retrieved or transplanted



Working in partnership with

Quality of donor organs: what do we know?



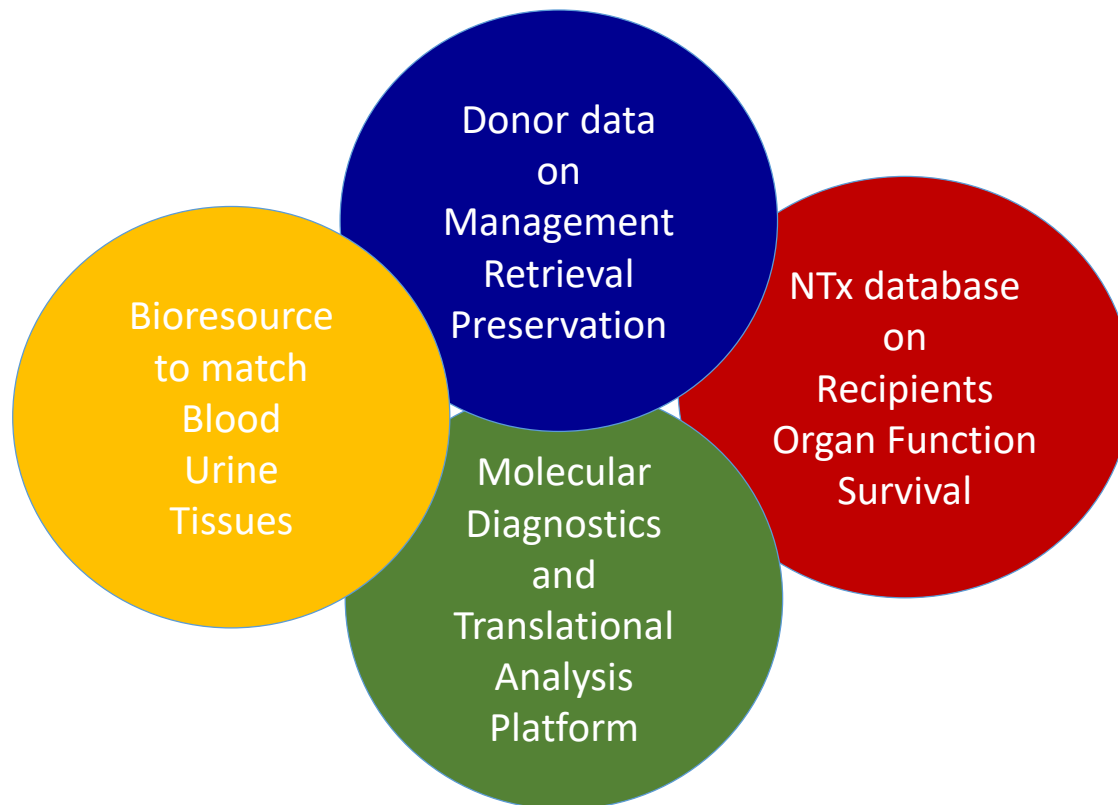
We recognise a footprint

... but need a fingerprint !

Objectives

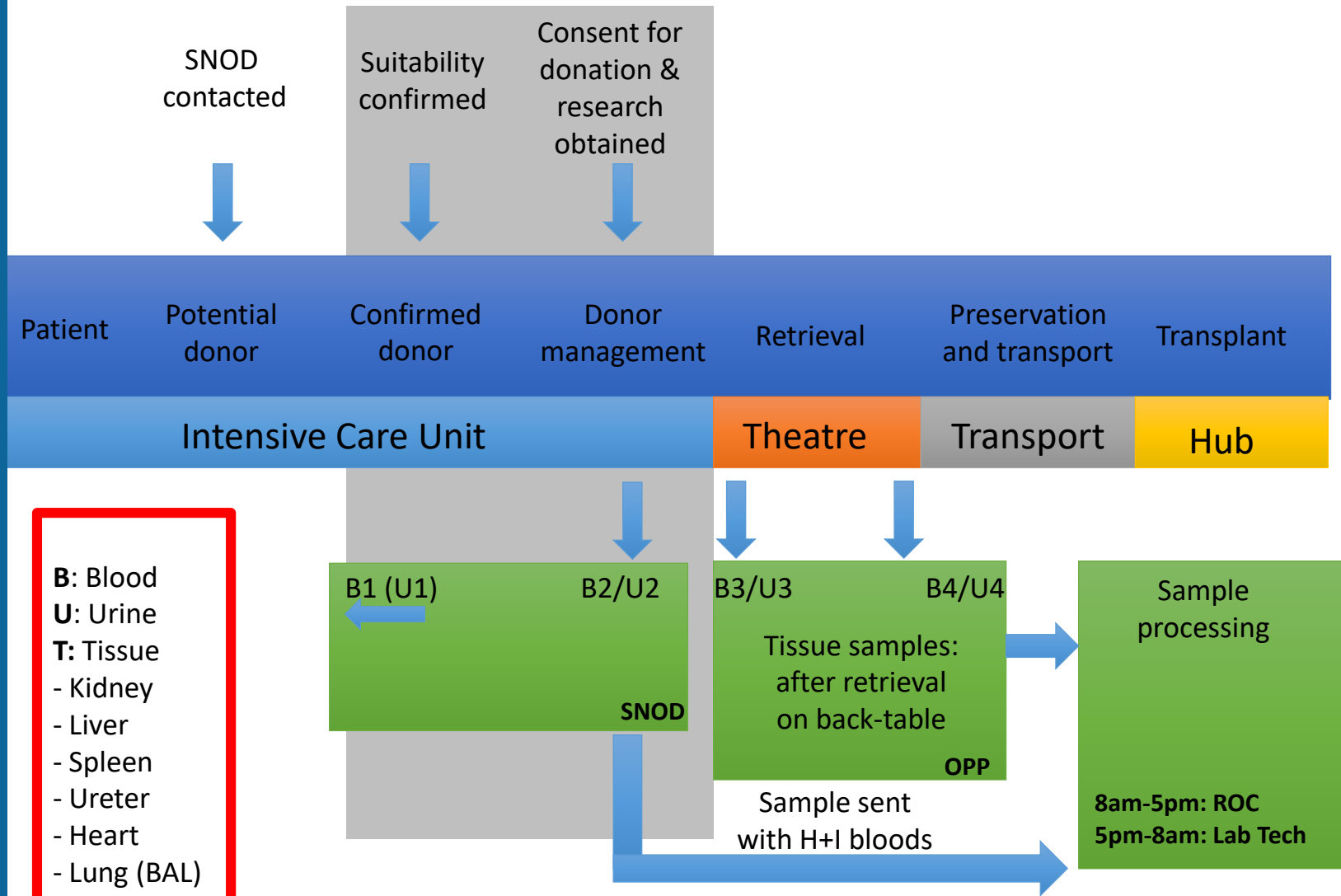
- Establish a robust biobank infrastructure
- Integrate clinical donor data & recipient outcomes
- Develop a national consortium & scientific platform
- Support mechanistic research with focus on injury and repair
- Facilitate identification of profiles & biomarkers predicting transplantability & outcomes
- Streamline research collaboration & facilitate service development & clinical studies

Concept

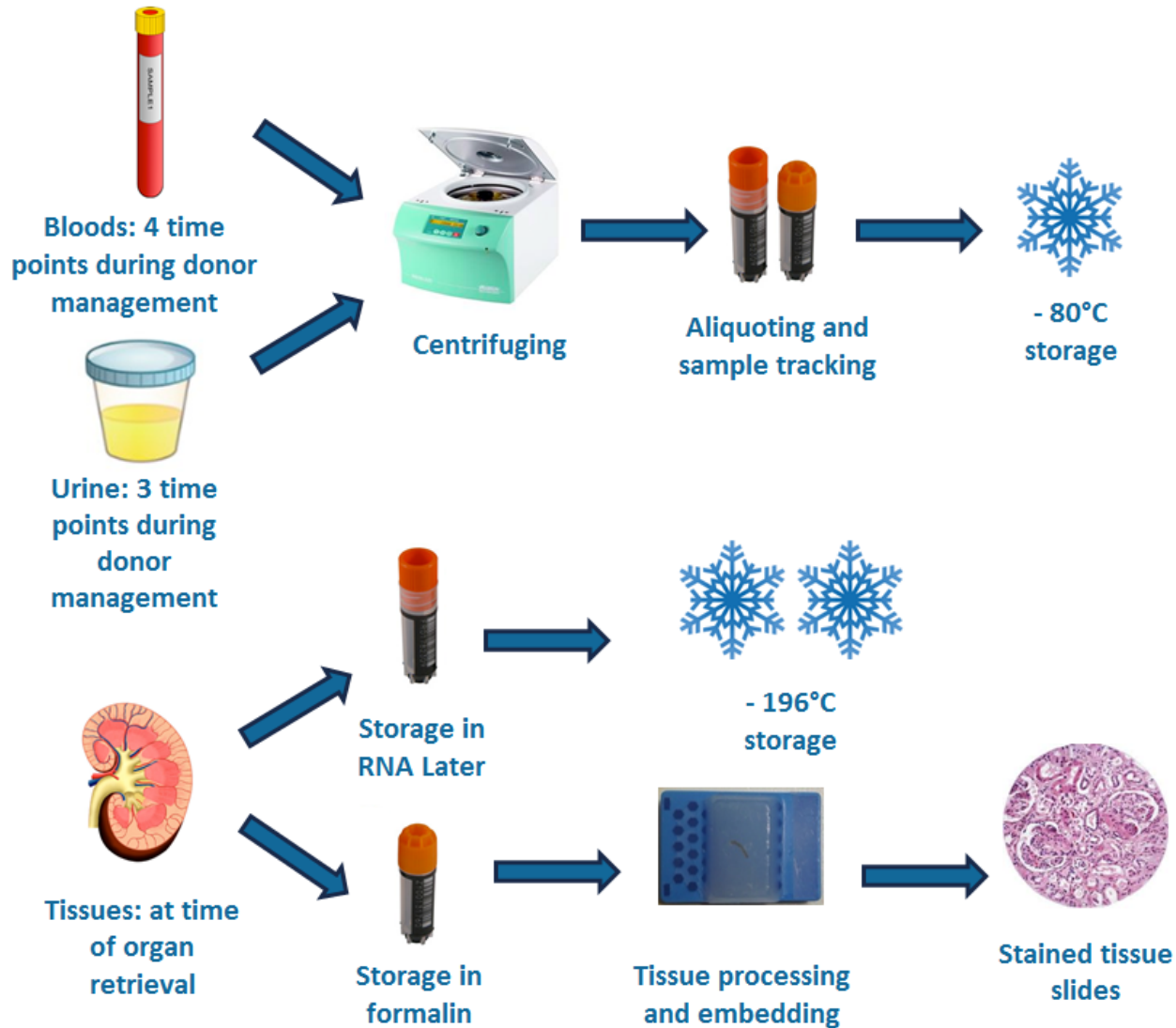


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Complex logistics in general hospitals and out-of-hours



Collection, processing and storage ...



Sustainable userfriendly sample collection ...

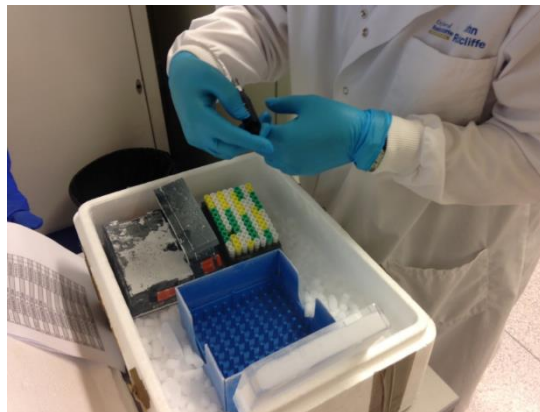


Working in partnership with

MRC Medical
Research
Council

NHS
Blood and Transplant

Lab tissue & aliquot preparation



Working in partnership with

MRC
Medical
Research
Council

NHS
Blood and Transplant

Developing a National Consortium

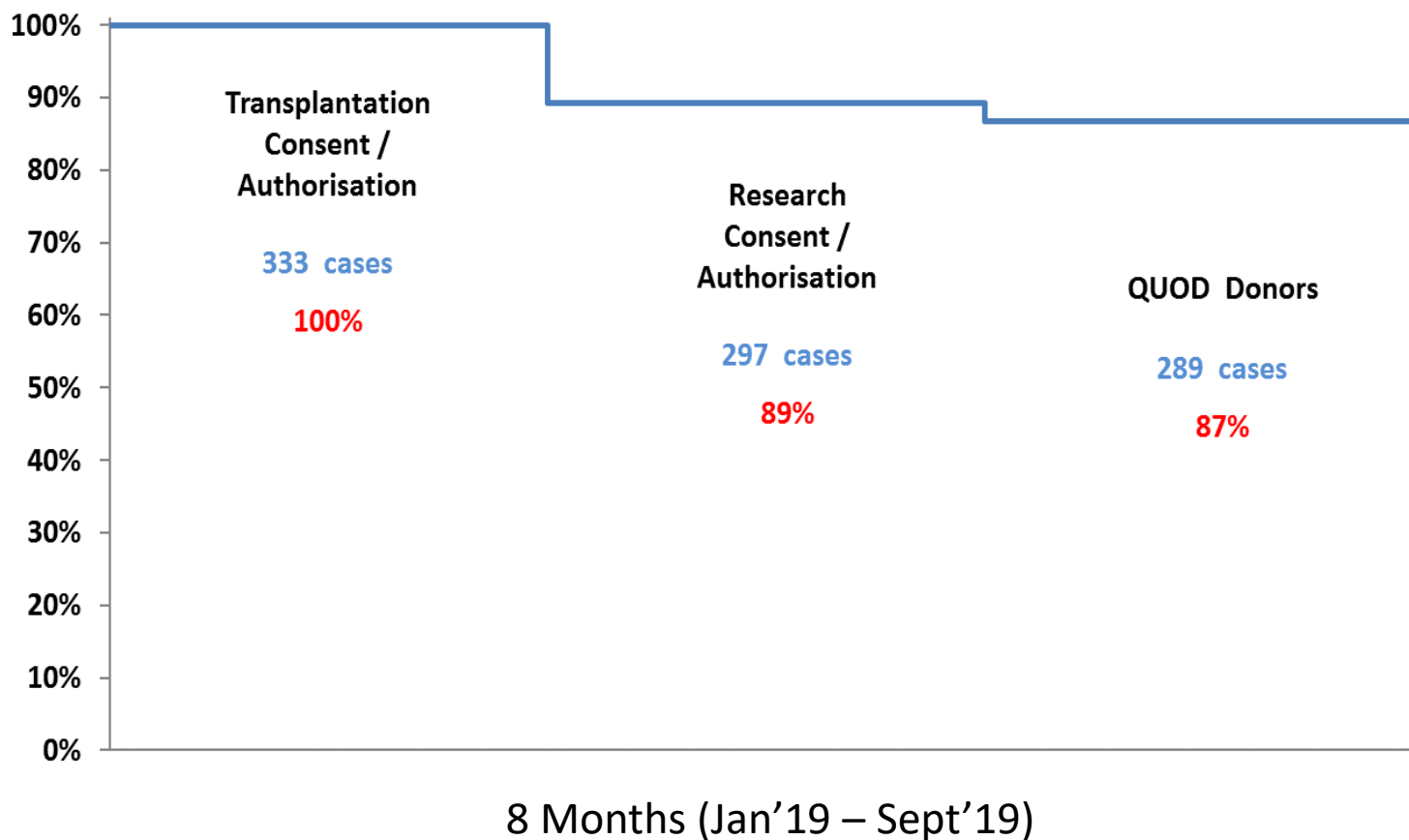
- Collaborative Programme NHSBT & Academic Centres
- Authorised by HTA in permitted hospitals: capture 90% of donors using NHSBT's licence
- Supporting academic research, NHS service evaluation & clinical trials

- More than 250 SNODs taking consent
- ICU teams supporting collection of samples
- 9 abdominal and 6 cardiothoracic NORS teams
- 19 H&I labs processing samples
- 8 QUOD recipient labs with technicians
- Support from NHSBT ODT staff and Stats Unit



Support from families and public

Consent for research and QUOD



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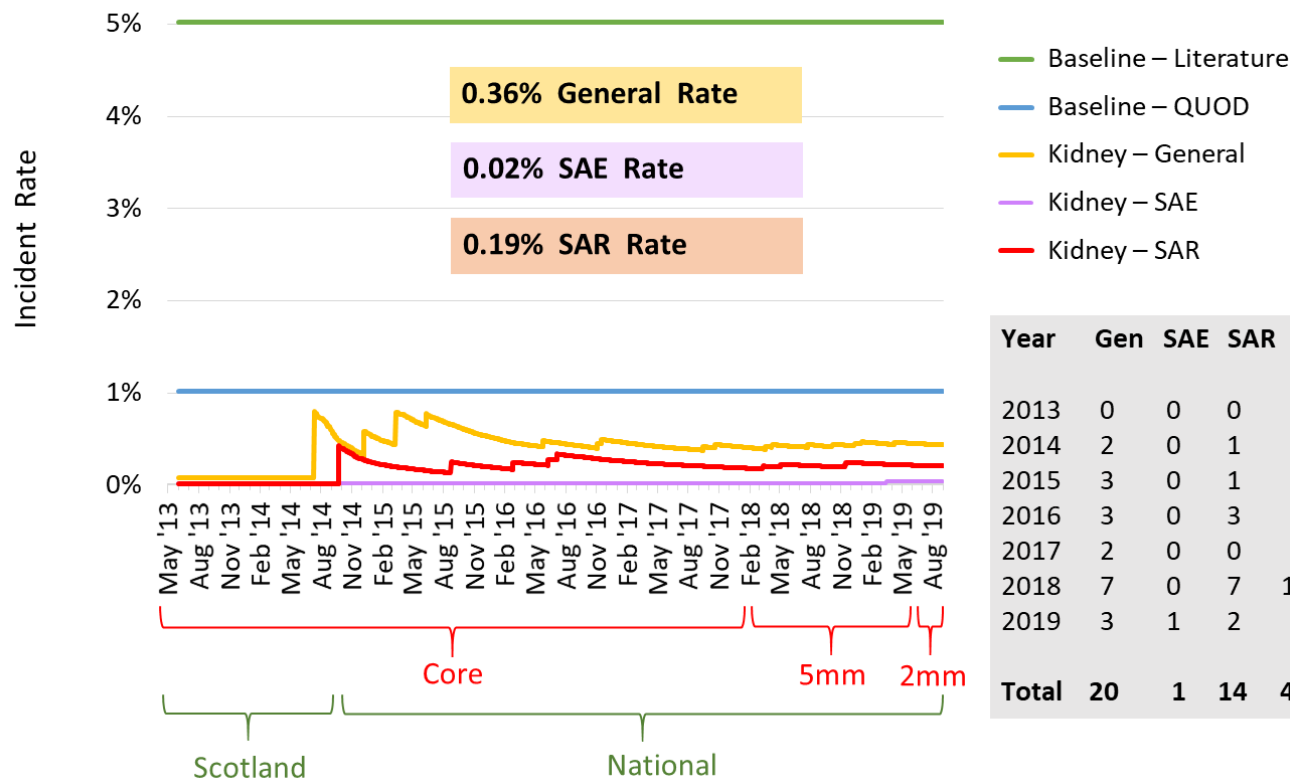
Quality management

- For high quality: standardisation of collection, processing and archiving
- Training of professionals involved: against appropriate procedures, training records kept up to date
- Fully compliant with the legislation involved
 - NHSBT HTA Research licence to collect
 - University HTA Research licence to store
 - National Research Ethics Service registered as Research Tissue Bank: permission to research
- Regulatory HTA inspections/audits



QUOD related incidents (2013 ...)

Donor kidney biopsies of transplanted kidneys



2018 Kidney incidents

General:

1 x Core Biopsy
6 x 5mm Punch Biopsy

SAR:

2 x Core Biopsy
5 x 5mm Punch Biopsy

2019 Kidney incidents

General:

2 x 5mm Punch Biopsy
1 x 2mm Punch Biopsy

SAE:

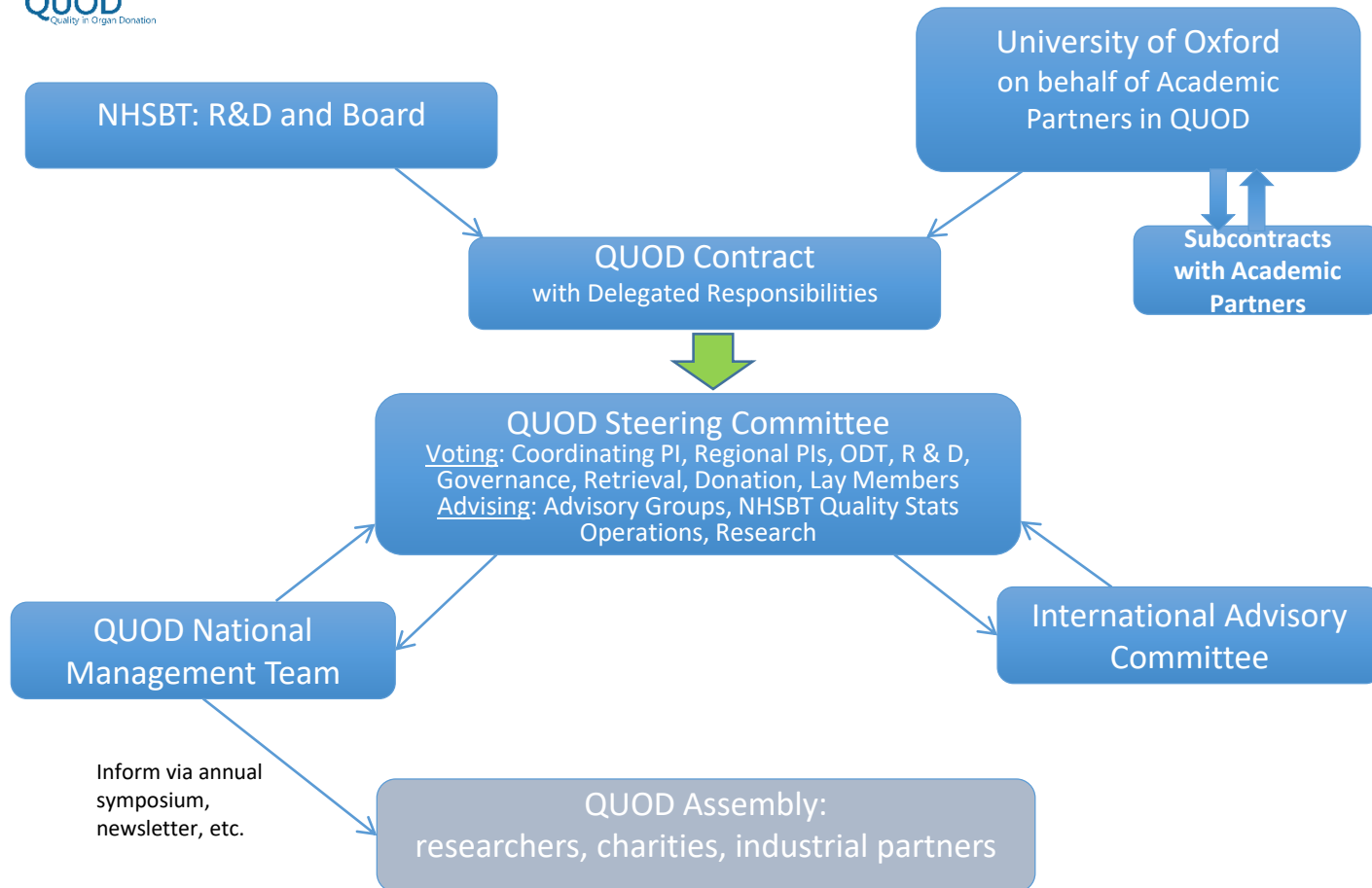
1 x 5mm Punch Biopsy

SAR:

2 x 5mm Punch Biopsy

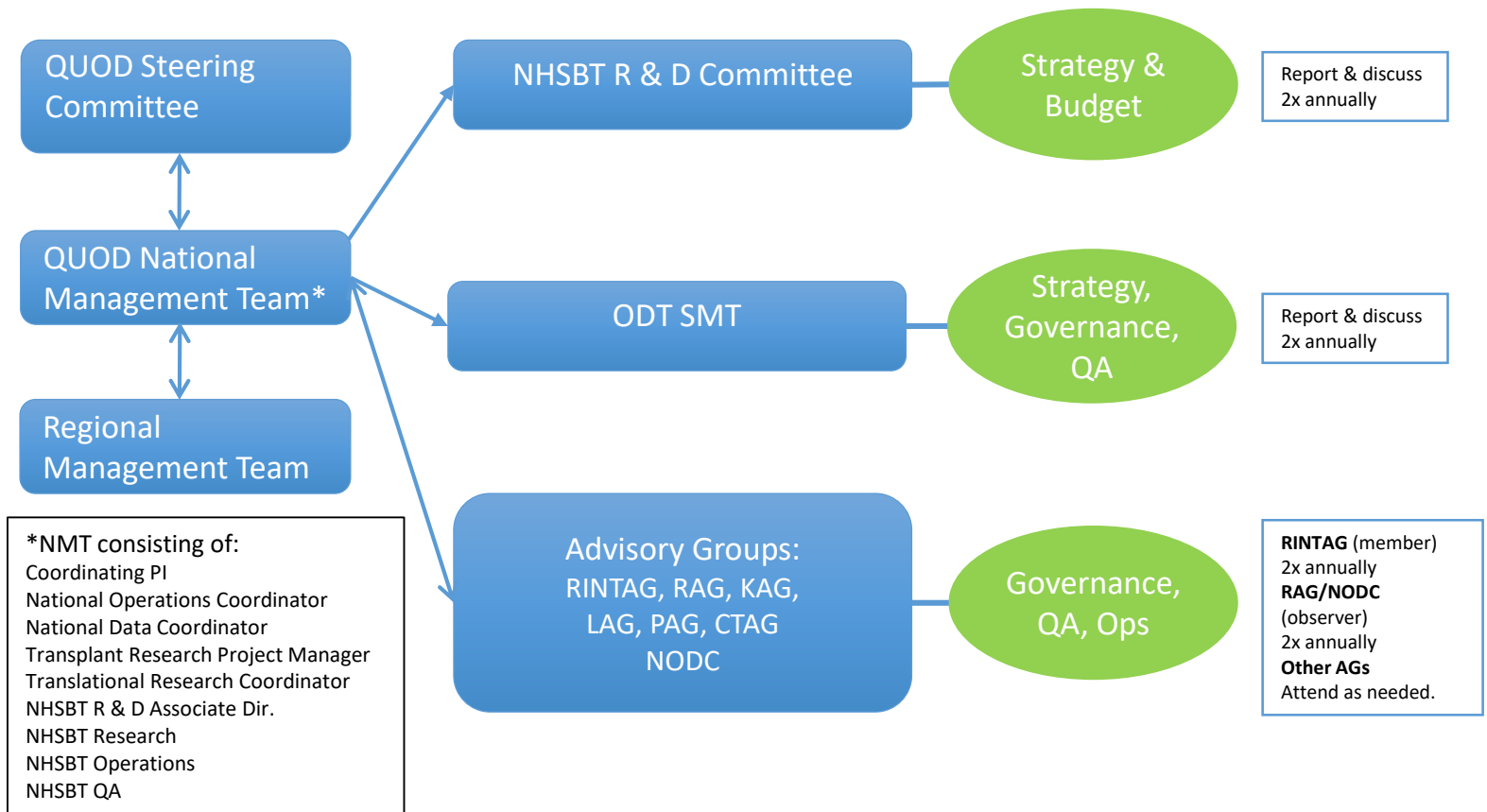


QUOD Governance: Legal & Financial



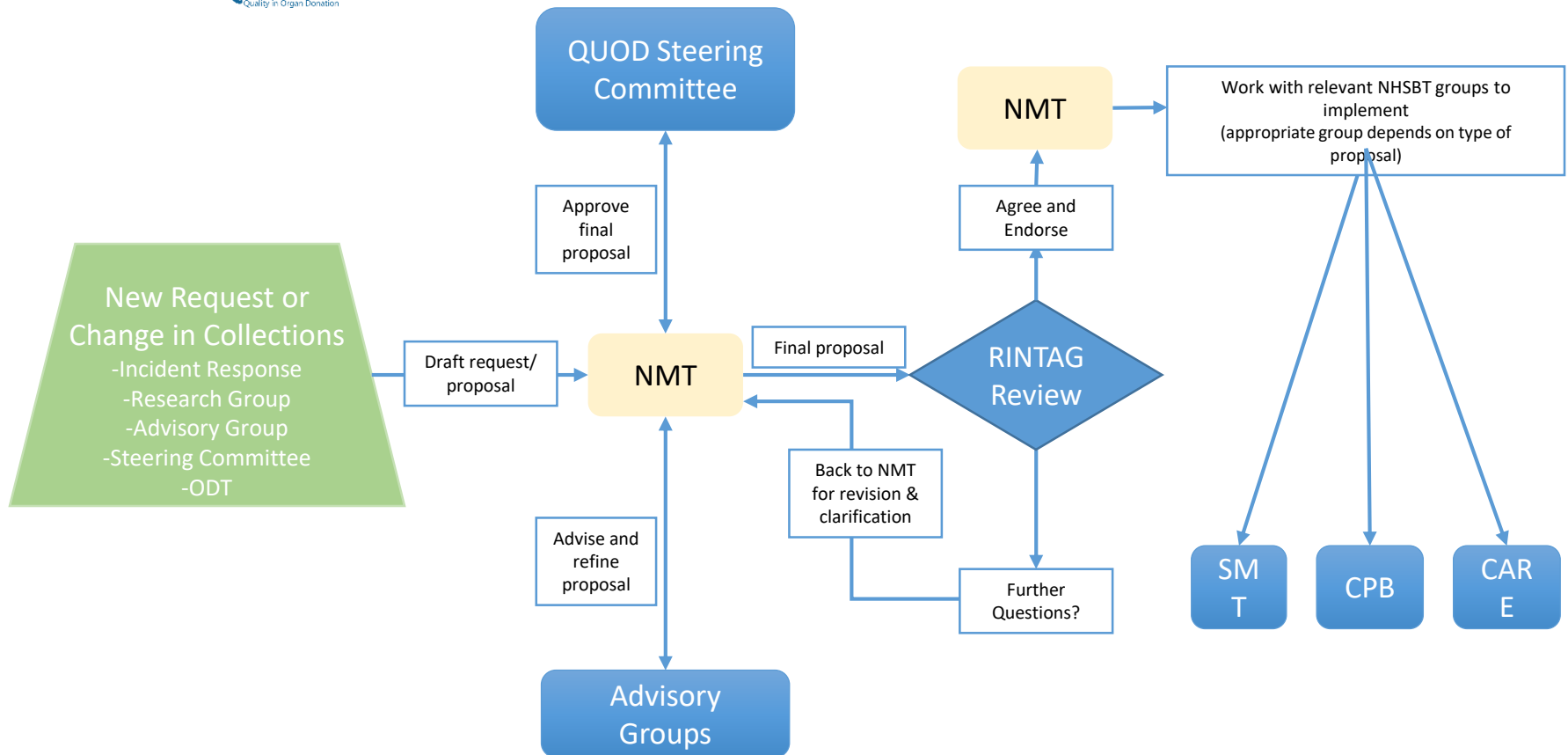


QUOD Governance: Ops & Reporting





QUOD Governance: Change Process



Transparency: financial plan for QUOD

- Financial support for QUOD = costs for infrastructure
- 450K per year: sampling & data of 90% of UK donors
- No overhead charge by Academic Partners

However:

- Requirement by NHSBT Board to reduce financial burden on NHSBT
- Agreed plan for QUOD to recoup some costs through low threshold sample fee (Tier 1, 2, 3)
- Increase cost recoupment of 10% in 17/18; 15% in 18/19; 20% in 19/20 ...
- While budget absorbs new cost for additional sample collection
- Agreed proposal to reduce burden for NHSBT with 50% by 2023

Working in partnership with

Bioresource key figures

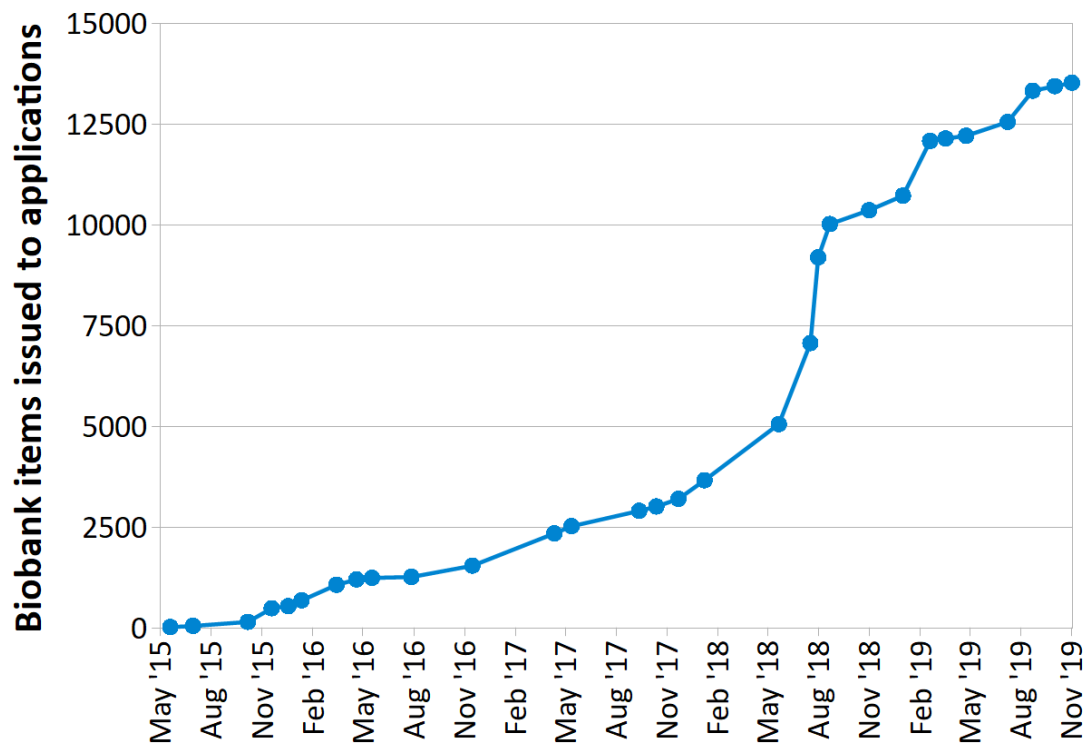
- **Date** **1 November 2019**
- **Donors** **4,537**
- **Samples** **81,392 in total, including:**
 - **Blood** **42,754 samples**
 - **Urine** **9,938 samples**
 - **Kidney** **11,429 samples (5,780 biopsies)**
 - **Liver** **6,018 samples (3,023 biopsies)**
 - **Ureter** **6,595 samples (3,327 biopsies)**
 - **Spleen** **3,366 samples (3,366 biopsies)**
- **BAL** **93 samples**
- **Heart** **1199 samples (600 biopsies)**

Integrated access of clinical donor & recipient data to facilitate selection of relevant variables

Variables in the UK Transplant Registry

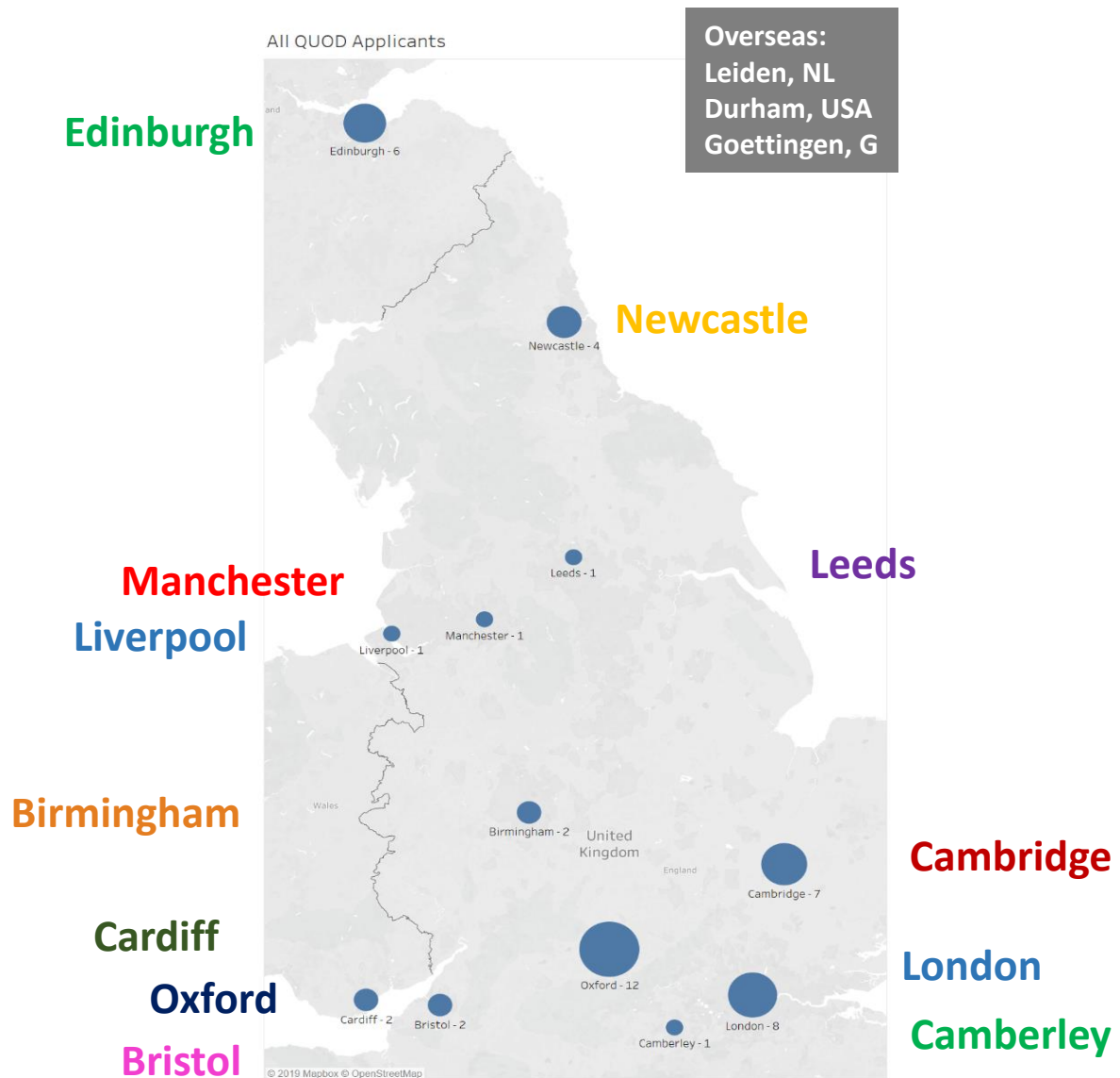
<input type="checkbox"/>	1138	Recipient age	Format: number
<input type="checkbox"/>	1139	Recipient sex	Categories: 1 - Male 2 - Female
<input type="checkbox"/>	1140	Recipient height (units: cm)	Format: number
<input type="checkbox"/>	1141	Recipient weight (units: kg)	Format: number
<input type="checkbox"/>	1142	Recipient ABO blood group (including, where known, sub-types of A)	Format: string up to 3 characters
<input type="checkbox"/>	1143	Recipient Rh blood group	Categories: N - Neg P - Pos
<input type="checkbox"/>	1144	Recipient ethnic origin	Categories: 1 - White 2 - Asian or Asian British 3 - Black or Black British 4 - Chinese/Oriental 6 - Mixed, please specify 7 - Other, please specify 9 - Unknown If code 6 (Mixed) or 7 (Other), then can be additionally specified in a separate field
<input type="checkbox"/>	1145	Recipient ethnic origin - further details	Text
<input type="checkbox"/>	1146	Diabetic complications - Myocardial infarction	Categories: 1 - No 2 - Yes
<input type="checkbox"/>	1147	Diabetic complications - CVA	Categories:

Research support and impact



- Biobank items issued to applications: 13,530
- Total number of research project applications: 57
- New applications at preliminary stage: 13
- Applications approved by the Steering Committee: 44
- Applications 16 completed by QUOD and 28 in progress

Research support: geographic reach




Research capacity building & impact


- 27 known publications and presentations (excluding theses)
- 2/8 presentations in the Medawar Award session of the BTS
- Samples provided for 8 DPhil/PhD projects
- Samples provided for 9 Fellows (clinical, academic clinical, and clinical research)

12.05 pm Establishing a whole pancreas biopsy collection protocol for the Quality in Organ Donation (QUOD) Biobank
M. Honkanen-Scott¹, M. Bourne¹, J. Doyle¹, N. Dyson¹, Y. Bury², D. Tiniakos², R. Ploeg³, W. Scott¹, J. Shaw^{1,1}*Institute of Cellu
Tyne* **Mitochondrial Dysfunction Is a Common Feature of** *pon*
Kaisar et al. *Clin Proteom* (2016) 13:26
DOI 10.1186/s12014-016-9126-9 Clinical Proteomics

HEPATOLOGY 

P | Original Article |  Full Access

st Normothermic Machine Perfusion (NMP) Inhibits
Proinflammatory Responses in the Liver and Promotes
Regeneration

Wayel Jassem , Emmanuel Xystrakis, Yasmeen G. Ghnewa, Muhammed Yuksel, Oltin Pop, Marc Martinez-Llordella, Yamen Jabri, Xiaohong Huang, Juan J. Lozano, Alberto Quaglia ... [See all authors](#) ✓

First published: 18 December 2018 | <https://doi.org/10.1002/hep.30475> | Citations: 4

Research impact: results

Highlighted findings from publications and presentations:

- Proteomic profiles of deceased donor kidney biopsies obtained prior to transplantation correlate with allograft function at one year
- Identification of clinically relevant exosome proteins associated with transplant outcome from donor plasma
- 240 candidate genes that are significantly associated with DGF and a smaller number with long term GFR
- Donor/recipient serotype mismatch may be a useful tool for stratifying the risk of BK virus disease.
- Validated pathology scoring system for EM microscopy of pancreas tissue and endocrine cells.

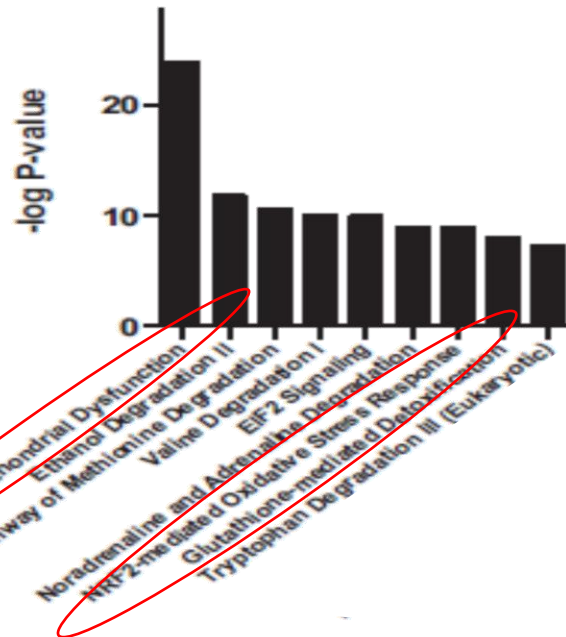


Donor characterisation: Insight into mechanisms of injury

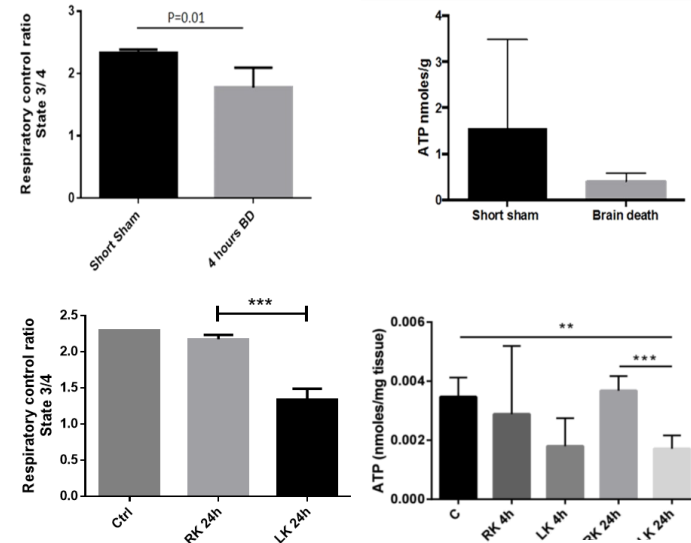
Letizia Lo Faro

Question: which molecular pathways of injury render organs susceptible to further damage upon transplant? Can we profile the injury of different donor types?

Mitochondrial dysfunction, oxidative stress and energy depletion are key features after brain death identified by proteomics



Mitochondrial function and tissue ATP levels are significantly decreased in BD and IRI





Kasia Bera

Rush to retrieve or wait to repair?

Understanding systemic sequelae of brain death

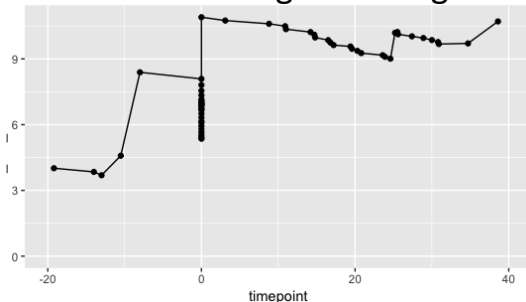
Aim: improve survival & quality of organs by understanding serum changes during donor management

How hostile is brain death as an progressively pro-inflammatory environment?

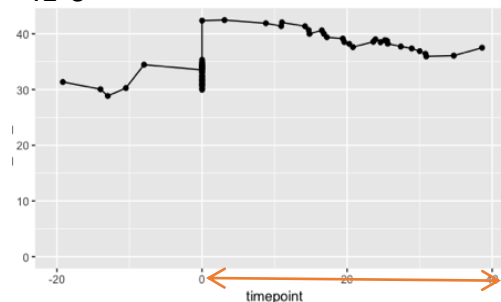
Methods: QUOD *serum* samples ICH donors with duration of brain death 3-38h, ELISA, cumulative average analysis

Future questions: organ-specific outcome, treatment targets, contribution of brain injury in DCD

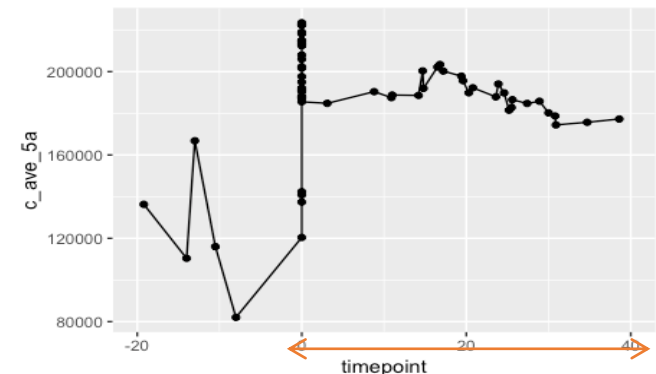
GFAP: marker of glial damage



IL-6



C5a – complement



**... with longer duration of brain death:
shift from pro- to anti-inflammatory environment**

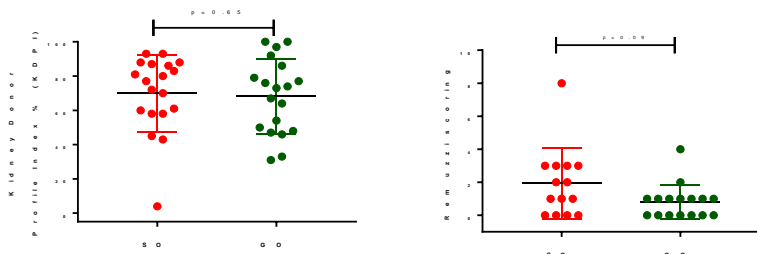


Can we identify biomarkers of donor organ quality predictive of kidney transplantation outcomes ?

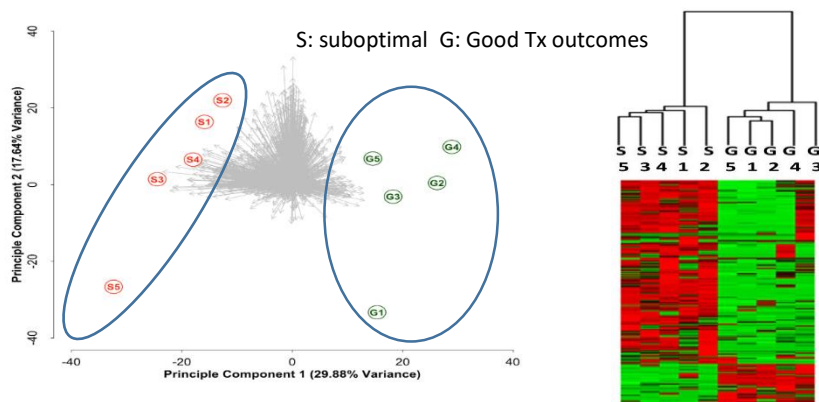
Subclinical proteomic changes in donor kidneys correlate with transplantation outcomes

Maria Kaisar

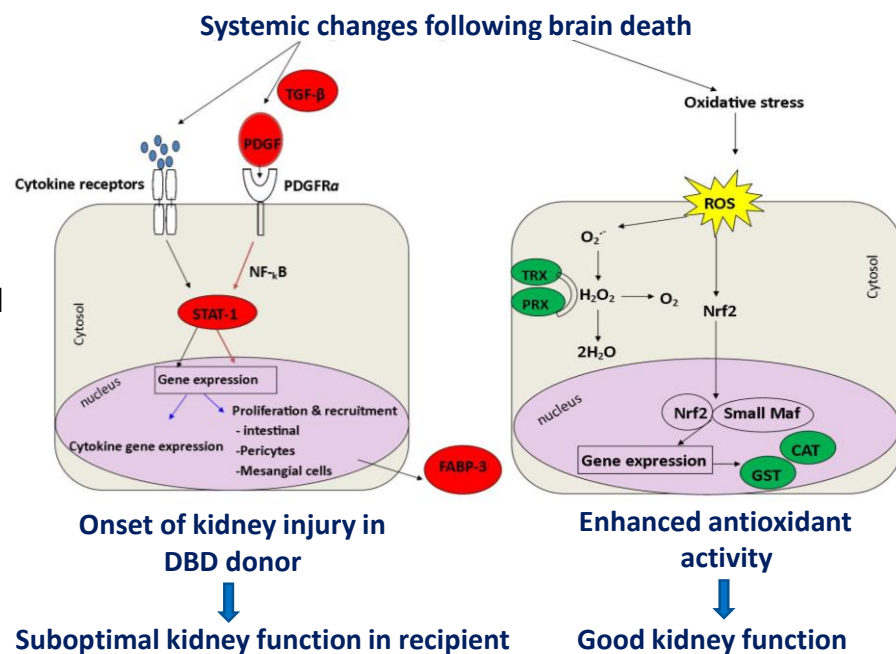
Current clinical tools could not discriminate between donor kidneys with opposing extremes in post-transplantation outcomes



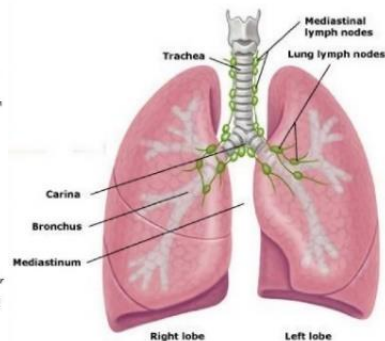
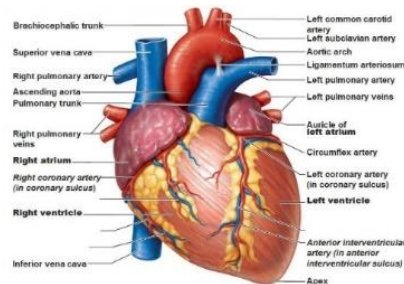
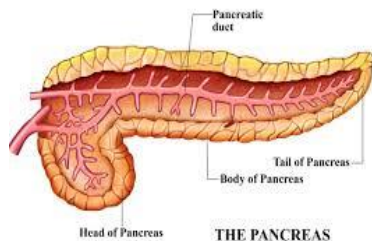
Proteomic profiling could distinguish the donor kidneys with good from those with suboptimal post-transplantation outcomes



Donor organ quality depends on the balance of parallel activation of pathways of injury and repair



QUOD MRC Expand Grant

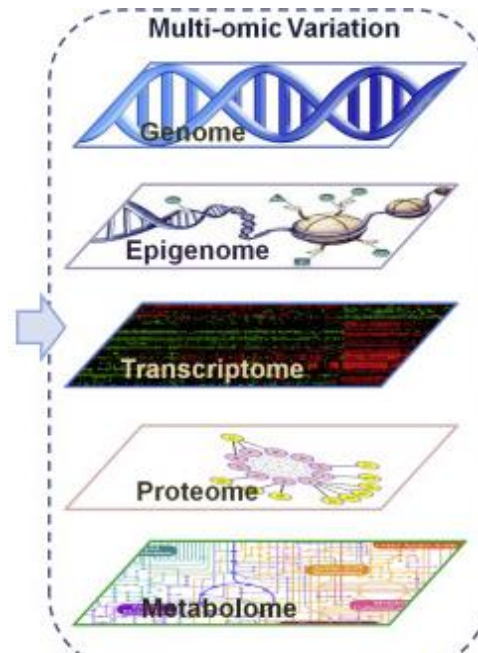


- Collection of **whole organs** in addition to samples
 - To determine **transcriptome and proteome** of donor organs
 - Creating **organ atlas** with state-of-the art pathology & imaging
 - Delivering a **searchable data library**
-
- Better understanding of normal vs diseased & causes of stress
 - Optimise transplant success, but also help prevent or reverse chronic diseases

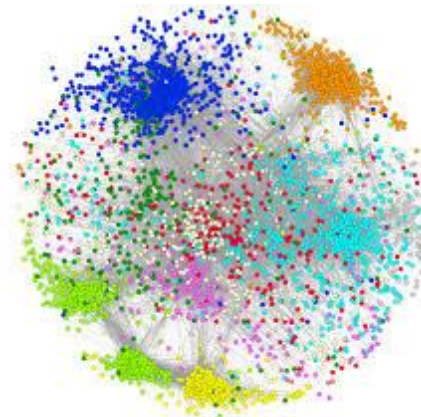
Insight in biology of acute & chronic organ injury



Histology Atlas / Laser capture
microdissection/ Electron
microscopy

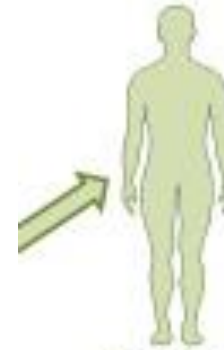


-Omics library

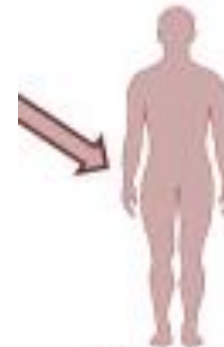


Biological pathways

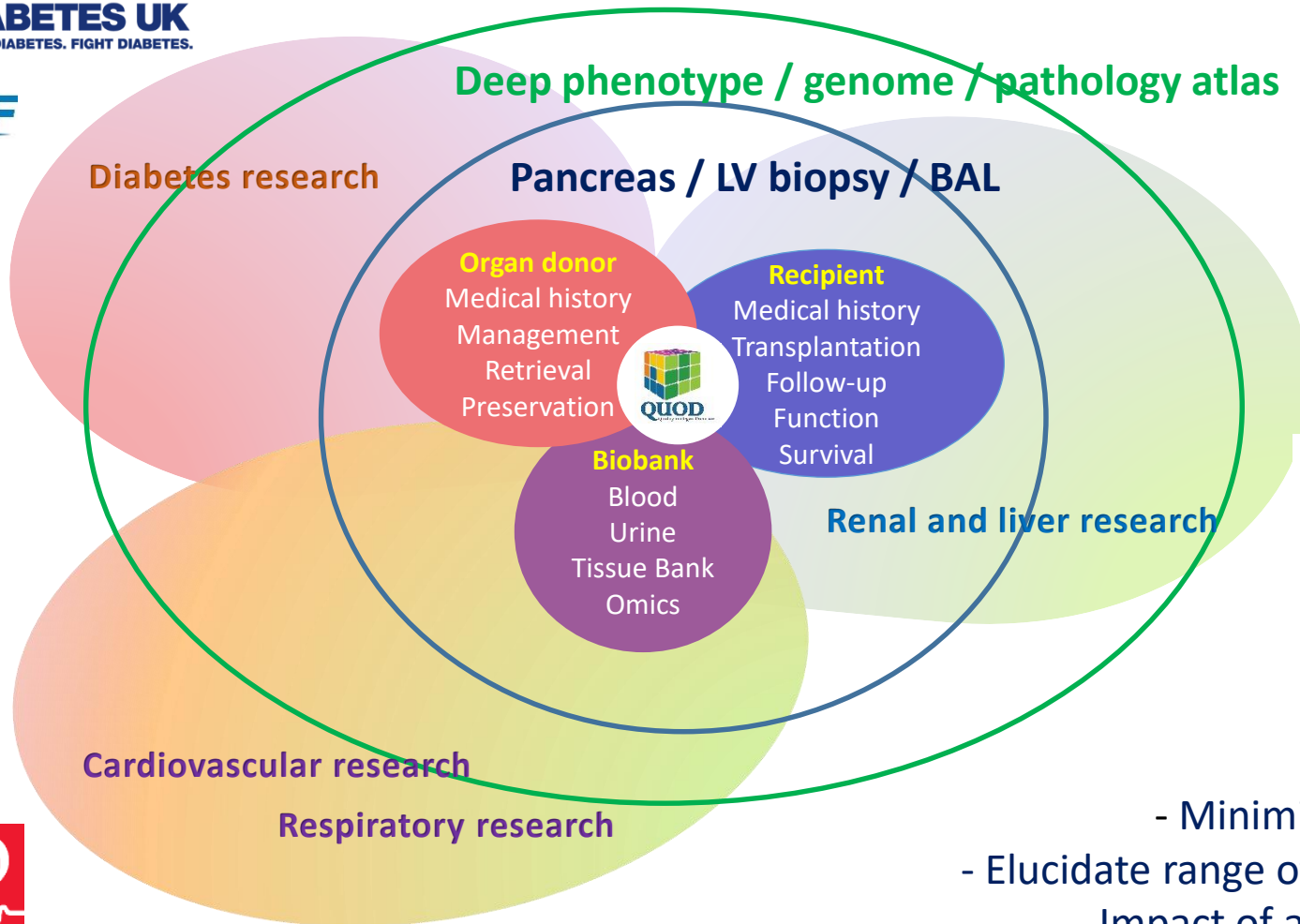
Stratification of risk



Organs transplanted with
good outcomes








Organs transplanted with
suboptimal outcomes



- Minimise artefact
- Elucidate range of normality
- Impact of acute stress
- Chronic disease
- Linked to clinical data
- Circulating biomarkers

Creation scientific platforms & cross-cutting teams



	Platform 1: Heart <i>J. Dark & G. Richardson</i>		Platform 2: Lungs <i>A. Fisher</i>		Platform 3: Pancreas <i>J. Shaw</i>		Platform 4: Islet <i>P. Johnson</i>		Platform 5: Kidney <i>C. Sharpe & M. Clatworthy</i>		Platform 6: Liver <i>G. Oniscu</i>		
Cross-Cutting Technique 1: Genomics <i>TC: A. Gloyn</i>													
Cross-Cutting Technique 2: Proteomics* <i>TC: B. Kessler</i>	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	
Cross-Cutting Technique 3: Pathology <i>TC: D. Tiniakos</i>	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	
Cross-Cutting Human Cell Atlas Single cells <i>TC: S. Teichmann & W. Scott</i>	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	
Other CCT's and TCs as project develops	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	Work Package	
<div> <div>PM (OX): <i>Tim Boland</i></div> <div>PM (NC): <i>Marta Bourne</i></div> </div> <div>PROJECT COORDINATION</div> <div> <div>Op. Lead (OX): <i>Sandrine Rendel</i></div> <div>Op. Lead (NC): <i>Minna Honkanen-Scott</i></div> </div>													
Coordinating PI : <i>Rutger J Ploeg (Oxford & NHSBT)</i> ; R&D Advisor: <i>Nick Watkins (NHSBT)</i>													

Research support: collaboration initiatives

- Support of **NRP** and **PITHIA** as a service development in ODT
- Supporting **BTS** for set-up of UK recipient biobanks system and its scientific network
- Collaboration with **UK Renal Imaging Network** to develop of whole organ imaging assessing donor kidneys and complement the 'organ atlas'
- Support **Human Cell Atlas** project by providing whole organs and hyper-sampled tissues (e.g. heart)
- Support a bid for the **IMI2 Digital Pathology repository** using slides from QUOD samples

14 recent funding applications including QUOD

	Lead Investigator	Institution	Organ	Title	Funder	Amount	Date Submitted	Status
1	Ploeg, R.	Oxford	Heart, Lung, Pancreas	Quality and Safety in Organ Donation Tissue Bank - Expansion to include Pancreas/Islets, Heart, and Lungs	Medical Research Council	£1,688,843.57	2017	Awarded
2	Fisher, A.	Newcastle	Lung	TBD - <i>Evaluation of untransplantable donor lungs for acute lung injury or chronic lung disease</i>	CF Trust	£750,000.00	2020?	Pre-discussion
3	Richardson, G.	Newcastle	Heart	Identifying older donor hearts suitable for transplantation: the use of senescence as a marker of biological age.	Heart Research UK	£200,000.00	Oct-19	2nd Round
4	Bamforth, S	Newcastle	Heart	Single cell atlas of the outflow tract of the heart	Medical Research Council	£450,000.00	Oct-18	Awarded
5	Ho, Ling-Pei	Oxford	Lung	Defining the role of tissue-resident immune cells in alveolar epithelial cell regeneration	Medical Research Council	£855,872.13		Awarded
6	Shaw, J.	Newcastle	Pancreas	Identification, characterisation and spatial distribution of transitional phenotypes in human adult pancreas informed by fetal organogenesis	Medical Research Council	£444,669.28	Oct-18	Declined
7	?	Newcastle	Heart	Mapping fetal conduction and valve development onto the normal adult heart for the Human Cell Atlas	Medical Research Council	£450,000.00	Oct-18	Declined
8	?	Newcastle	Heart	Vascular cell-specific molecular mapping in three human organs	Medical Research Council	£450,000.00	Oct-18	Declined
9	Grunberg, K.	Radboud UMC	all	TBD - <i>Provision of slides for digital pathology library & AI training</i>	IMI2 Call 18	£32,320,000.00	Mar-20	1st Round
10	Ploeg, R.	Oxford	Kidney	Understanding mechanisms of injury and repair and identify clinically relevant targets of intervention during deceased donor management period to improve organ utilisation and transplantation outcomes.	NHSBT	£250,000.00	Jul-19	Declined
11	Richardson, G.	Newcastle	Heart	Senescence as a potential therapeutic target for ischaemia reperfusion injury following acute myocardial infarction.	BHF	£180,000.00	Jul-05	Awarded
12	Sharpe, C.	KCL	Kidney	<i>Fibrosis Project</i>	Medical Research Council	£1,000,000.00	Jan-20	In process
13	Lythgoe, M.	UCL	Kidney	Imaging Kidney Viability Before Transplantation	UCL	£72,292.00	Oct-19	Awaiting

Total value of £9.3m of which £4.7m currently awarded



**Thank you for your ongoing support
and
QUOD is there for you !**

Research support: collaboration with industry

- Contract with **Evotec** for 2 years: £100,000 in core support & request of at least 1,000 samples per year
- Contract with **Novo Nordisk** for 3 years: £150,000 in core support & request of at least 1,000 samples per year , plus medium-term interest in whole organs
- Interest expressed by **Novartis** and **GSK** for collaborative research joining QUOD platform
- Advanced discussions with UK Government initiative: **Medicines Discovery Catapult** for inclusion as official supplier for interested SMEs

Collaboration in research projects involving industry:

- Essential support for infrastructure & science while keeping sample fee low for individual researcher

Research impact: funding

Local to Applicants

Oxford Translational Transplant Research Nucleus	University of Manchester	Oxford Transplant Foundation	Duke Medical Center	Royal Free Charity PhD Fellowship
University of Oxford	Royal College of Surgeons (Edinburgh)	Leeds Ray of Hope Fund	Transplant Dept Papworth	Transplantatie Centrum Leiden
King's College London	Cardiff Transplant Unit - Nephrology and Transplant Research Fund	Kings Liver Research Fund	Renal Allograft Fund (QEH Charity)	Wales Kidney Research Unit
	OUCAGS	Wellington Hospital Fellowship	Oxford NIHR BRC	

External Bodies

NIHR BTRU - Biomarkers & Genomics	MRC-CiC	Diabetes UK	MRC PhD
NIHR BTRU - Organ Donation & Transplantation	Kidneys for Life	European Innovation and Technology Fellowship	Horizon 2020
NIHR ACF	Central Manchester Foundation Trust	British Heart Foundation	Kidney Research UK
Kidney Wales	Wellcome Trust	Institute of Physics and Engineering in Medicine	Kidney Patient Association

Funds from 34 different non-commercial bodies have been used in support of QUOD projects so far