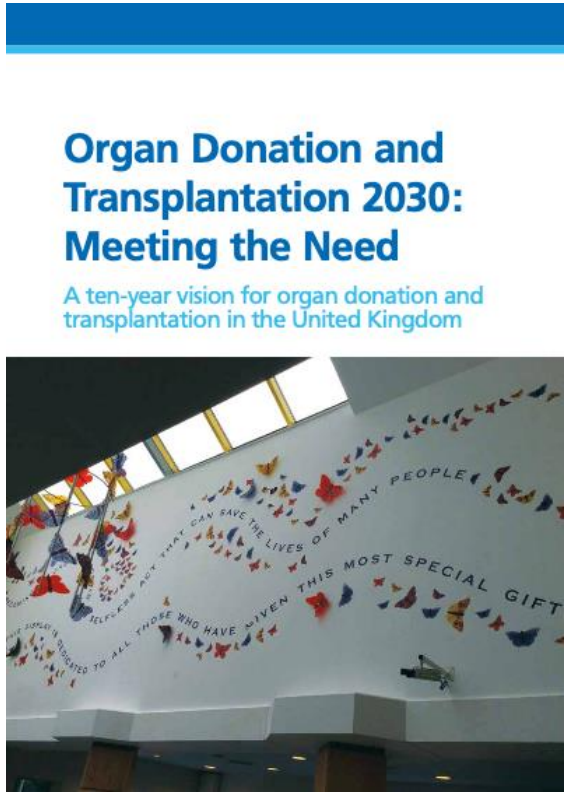


Our new Strategy

- *A world leading*
- *organ donation and transplantation system*

Living donor liver transplantation (LDLT) for both adults and children is now included in the UK wide strategy for organ donation and transplantation 2030: Meeting the need
The rationale for LDLT is to:
Ensure equity of access to all options for LT- including current and new technologies (e.g. normothermic regional perfusion (NRP); machine perfusion) and maximising utilisation of DCD organs
Opportunity for planned LT (especially related to new indications)
Improve timeliness of LT
Allowing all patients to consider LDLT as an option

5 Outcomes

1. Commissioners and all UK health departments will work together to ensure that there is **appropriate funding** to support a fully integrated **UK-wide LDLT programme**
2. Commissioners, clinicians and NHSBT will ensure that **appropriate infrastructure, systems and processes** are in place to **embed the culture of LDLT widely** within transplant and referring centres and **maximise the benefit of LDLT for suitable recipients**
3. NHSBT, clinicians, commissioners and other authorities will ensure that **LDLT outcomes are monitored** and **that information is accurately interpreted** and utilised **to support state of the art donor and recipient care**
4. Clinicians and NHSBT will ensure that **all potential recipients and their donors are informed about the options for LDLT** to minimise waiting times and improve outcomes, **regardless of where they live in the UK**
5. NHSBT, clinicians, society and individuals will ensure that **awareness of LDLT is enhanced and 'fit for purpose' across all sectors of society** in **all four UK countries**

Figure 4.2 Donation and transplantation rates of organs from DCD organ donors in the UK, 1 April 2021 – 31 March 2022

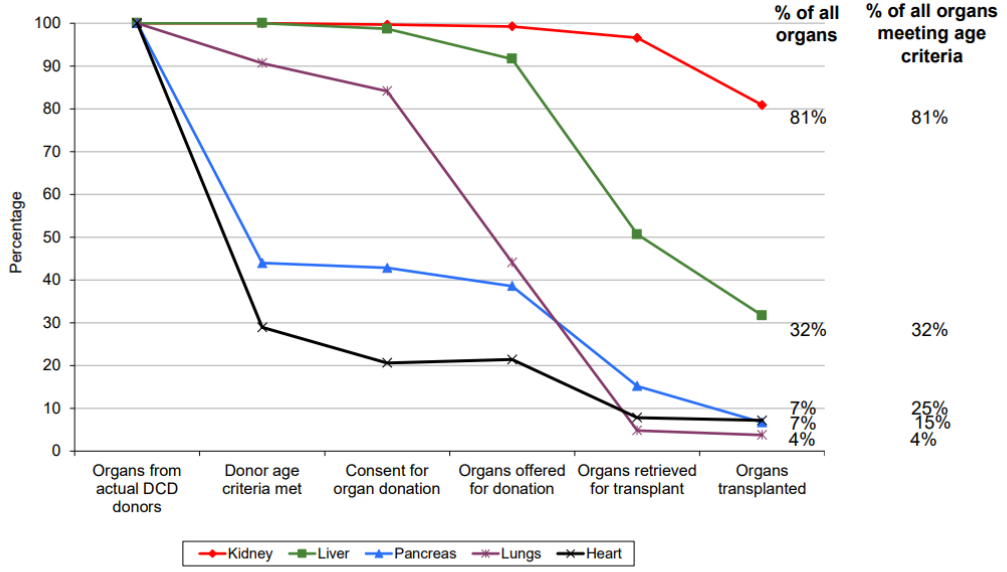
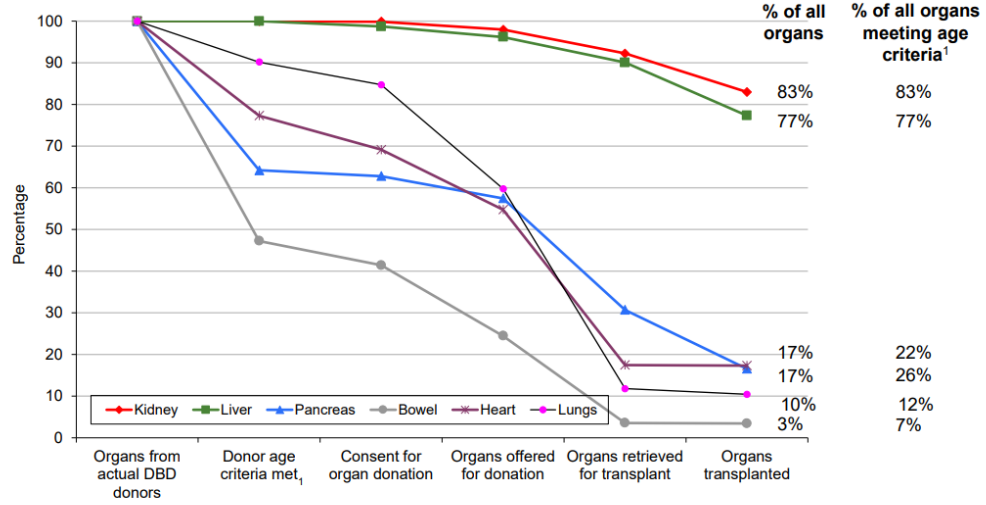


Figure 4.1 Donation and transplantation rates of organs from DBD organ donors in the UK, 1 April 2021 – 31 March 2022

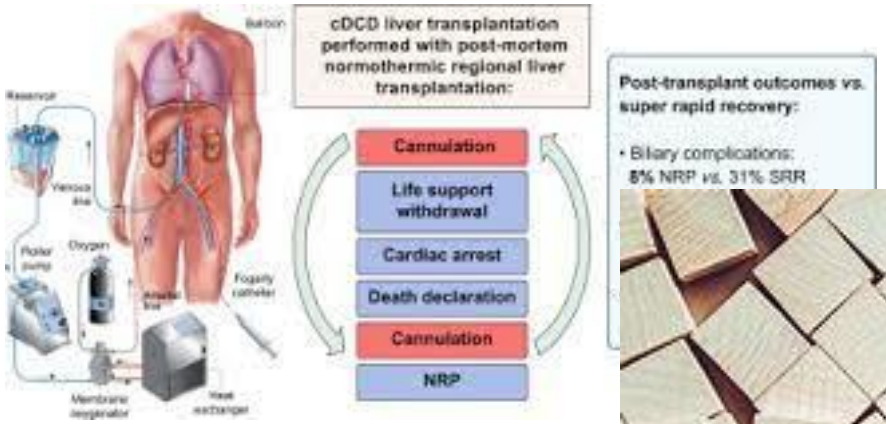


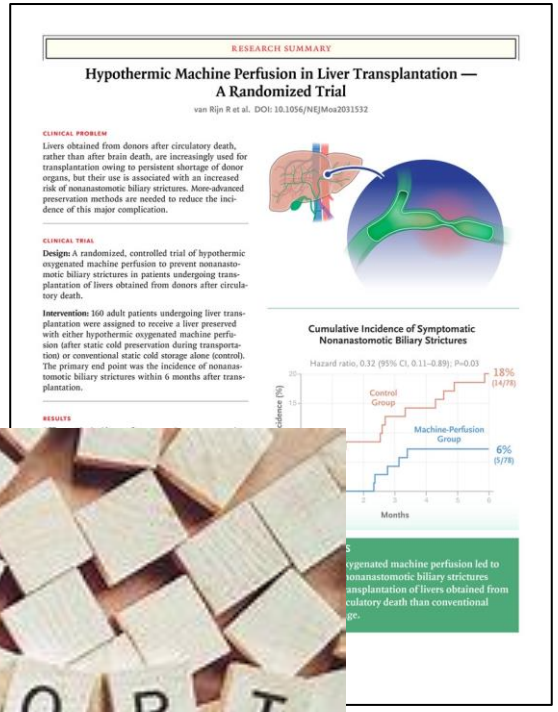
[1] Hearts – in addition to age criteria, donors who died due to myocardial infarction are excluded
Bowels – in addition to age criteria, donors who weigh >=90kg are excluded

Un-met need

DCD and DBD

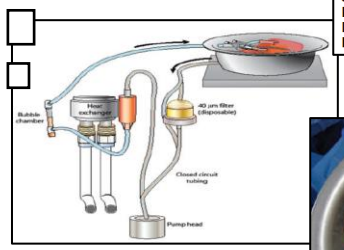
New Technologies'

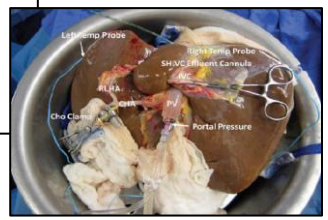


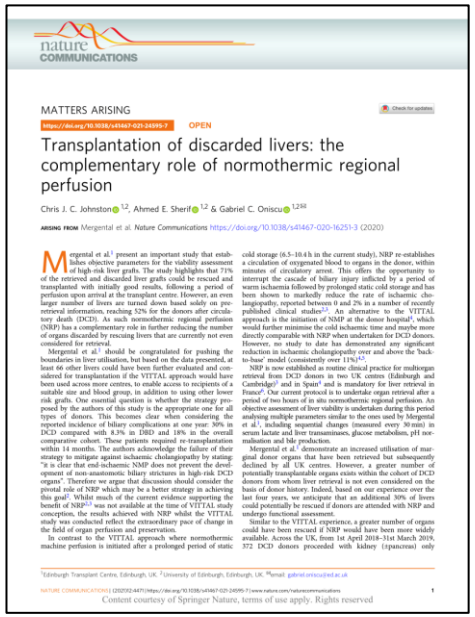


Hypothermic Machine Preservation in Human Liver Transplantation: The First Clinical Series

J. V. Guarrera[a,*], S. D. Henry[a], B. Samstein[a], R. Odeh-Ramadan[a], M. Kinkhabwala[d], M. J. Goldstein[a], L. E. Ratner[a], J. F. Renz[c], H. T. Lee[b], R. S. Brown, Jr.[a] and J. C. Emond[a]



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Transplantation of discarded livers: the complementary role of normothermic regional perfusion

Chris J. C. Johnston[1,2], Ahmed E. Sherif[1,2] & Gabriel C. Oniscu[1,2]✉

ARISING FROM Mergental et al. Nature Communications https://doi.org/10.1038/s41467-020-16251-3 (2020)

Mergental et al.[1] present an important study that establishes objective parameters for the viability assessment of high-risk liver grafts. The study highlights that 71% of the retrieved and discarded liver grafts could be rescued and transplanted with initially good results, following a period of perfusion upon arrival at the transplant centre. However, an even larger number of livers are turned down based solely on pre-retrieval information, reaching 52% for the donors after circulatory death (DCD). As such normothermic regional perfusion (NRP) has a complementary role in further reducing the number of organs discarded by rescuing livers that are currently not even considered for retrieval.

Mergental et al.[1] should be congratulated for pushing the boundaries in liver utilisation, but based on the data presented, at least 66 other livers could have been further evaluated and considered for transplantation if the VITTAL approach would have been used across more centres, to enable access to recipients of a suitable size and blood group, in addition to using other lower risk grafts. One essential question is whether the strategy proposed by the authors of this study is the appropriate one for all types of donors. This becomes clear when considering the reported incidence of biliary complications at one year: 30% in DCD compared with 8.3% in DBD and 18% in the overall comparative cohort. These patients required re-transplantation within 14 months. The authors acknowledge the failure of their strategy to mitigate against ischaemic cholangiopathy by stating "it is clear that end-ischaemic NMP does not prevent the development of non-anastomotic biliary strictures in high-risk DCD organs". Therefore we argue that discussion should consider the pivotal role of NRP which may be a better strategy in achieving this goal[2]. Whilst much of the current evidence supporting the benefit of NRP[2,3] was not available at the time of VITTAL study conception, the results achieved with NRP whilst the VITTAL study was conducted reflect the extraordinary pace of change in the field of organ perfusion and preservation.

In contrast to the VITTAL approach where normothermic machine perfusion is initiated after a prolonged period of static cold storage (6.5–10.4 h in the current study), NRP re-establishes a circulation of oxygenated blood to organs in the donor, within minutes of circulatory arrest. This offers the opportunity to interrupt the cascade of biliary injury inflicted by a period of warm ischaemia followed by prolonged static cold storage and has been shown to markedly reduce the rate of ischaemic cholangiopathy, reported between 0 and 2% in a number of recently published clinical studies[2,3]. An alternative to the VITTAL approach is the initiation of NMP at the donor hospital[4], which would further minimise the cold ischaemic time and maybe more directly comparable with NRP when undertaken for DCD donors. However, no study to date has demonstrated any significant reduction in ischaemic cholangiopathy over and above the 'back-to-base' model (consistently over 11%)[4,5].

NRP is now established as routine clinical practice for multiorgan retrieval from DCD donors in two UK centres (Edinburgh and Cambridge)[3] and in Spain[4] and is mandatory for liver retrieval in France[6]. Our current protocol is to undertake organ retrieval after a period of two hours of in situ normothermic regional perfusion. An objective assessment of liver viability is undertaken during this period analysing multiple parameters similar to the ones used by Mergental et al.[1], including sequential changes (measured every 30 min) in serum lactate and liver transaminases, glucose metabolism, pH normalisation and bile production.

Mergental et al.[1] demonstrate an increased utilisation of marginal donor organs that have been retrieved but subsequently declined by all UK centres. However, a greater number of potentially transplantable organs exists within the cohort of DCD donors from whom liver retrieval is not even considered on the basis of donor history. Indeed, based on our experience over the last four years, we anticipate that an additional 30% of livers could potentially be rescued if donors are attended with NRP and undergo functional assessment.

Similar to the VITTAL experience, a greater number of organs could have been rescued if NRP would have been more widely available. Across the UK, from 1st April 2018–31st March 2019, 372 DCD donors proceeded with kidney (±pancreas) only

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Keywords: Normothermic machine perfusion · Liver transplantation · Ischaemia reperfusion injury · Organ utilisation

Introduction

The maintenance of solid organs ex vivo in a functioning state is a far from novel concept. In 1812, Le Gallois wrote that *"if one could substitute for the heart a kind of injection of arterial blood, either naturally or artificially, one would succeed easily in maintaining alive indefinitely any part of the body whatsoever"* [1]. However, it wasn't until over 100 years later, in 1935 when Alexis Carell and Charles Lindbergh demonstrated the viability of abdominal organs perfused with oxygenated serum at normothermia for several days [2]. Thomas Starzl pursued this work further in the 1960s and indeed the first successful human liver transplants were performed following the pretreatment of livers with machine perfusion of diluted oxygenated blood [3]. In the subsequent years, interest in normothermic machine perfusion (NMP) reduced, largely due to the advent of cold preservation solutions which were less expensive and facilitated the transportation of organs from deceased donors [4]. However, in recent years, there has been a resurgence of interest in NMP. This is largely due to the need to expand the donor pool by successfully transplanting high risk or "marginal organs". In this article, we will focus on NMP's role in liver preservation and transplantation.

The Dilemma Facing Liver Transplantation

The potential of liver transplantation to save the lives of patients with end-stage liver disease is limited by a shortage of donor organs. There are insufficient numbers of deceased donor livers available to meet waiting list demands and as a result, many patients die before they could benefit from a life-saving transplant. In the UK, the number of patients listed for a liver transplant has almost doubled in the last 10 years and as a result of the donor organ shortage, 15–20% of patients die whilst awaiting transplantation [5]. This concerning waiting list mortality rate is comparable to other regions [6, 7]. Although living donation can help to increase the donor pool, this is not available in every country and does not help the

This article is part of the Topical Collection on *Machine Preservation of the Liver*

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Unmet need: patients

- In 21/22
  - 10,259 patients on the list
  - 6269 patients on the active waiting list
  - 429 patients died on the list
  - 770 such patients died or were de-listed for deterioration

  - 1763 consented donors
  - 1397 actual donors who donated 1 or more organs which were transplanted
  - 3415 patients received a deceased donor transplant

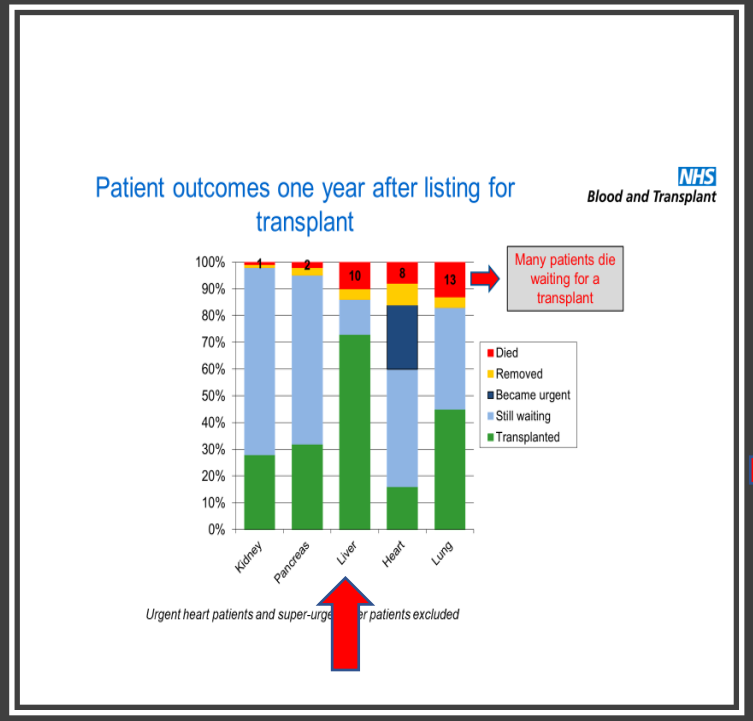
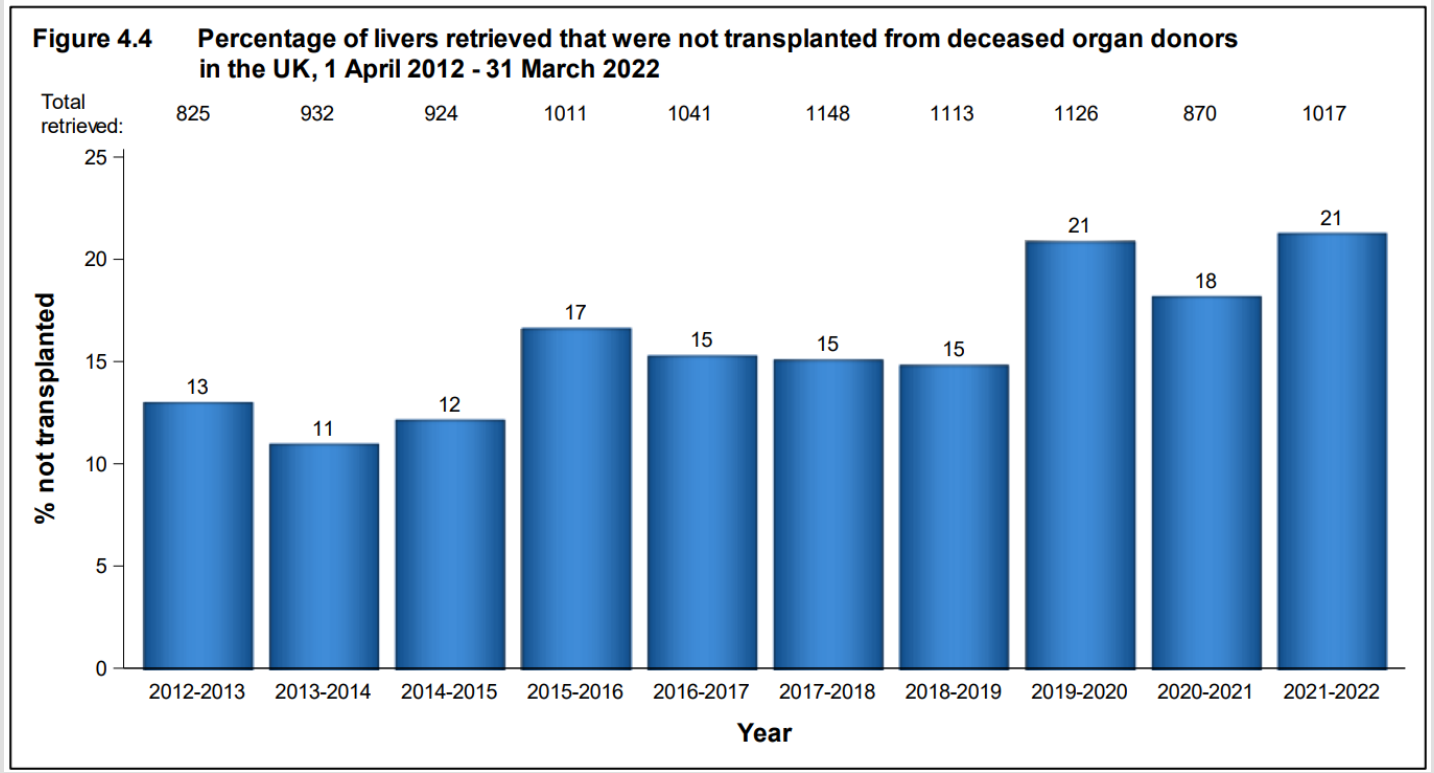


Table 2.3 Number of patient deaths on transplant lists in the UK, 1 April 2020 and 31 March 2022

	2020-2021 Total	2021-2022 Total	2021-2022 Adult	2021-2022 Paediatric
Kidney & pancreas patients	**363**	**287**	**286**	**1**
Kidney	337	268	267	1
Kidney & pancreas	24	16	16	0
Kidney & pancreas islets	0	0	0	0
Pancreas	2	1	1	0
Pancreas islets	0	2	2	0
Cardiothoracic patients	**79**	**67**	**61**	**6**
Heart	28	22	17	5
Heart-lung	2	1	0	1
Lung(s)	49	44	44	0
Liver patients	**70**	**67**	**65**	**2**
Intestinal patients	**3**	**2**	**2**	**0**
Other multi-organ patients[1]	**10**	**6**	**5**	**1**
ALL PATIENTS	**525**	**429**	**419**	**10**

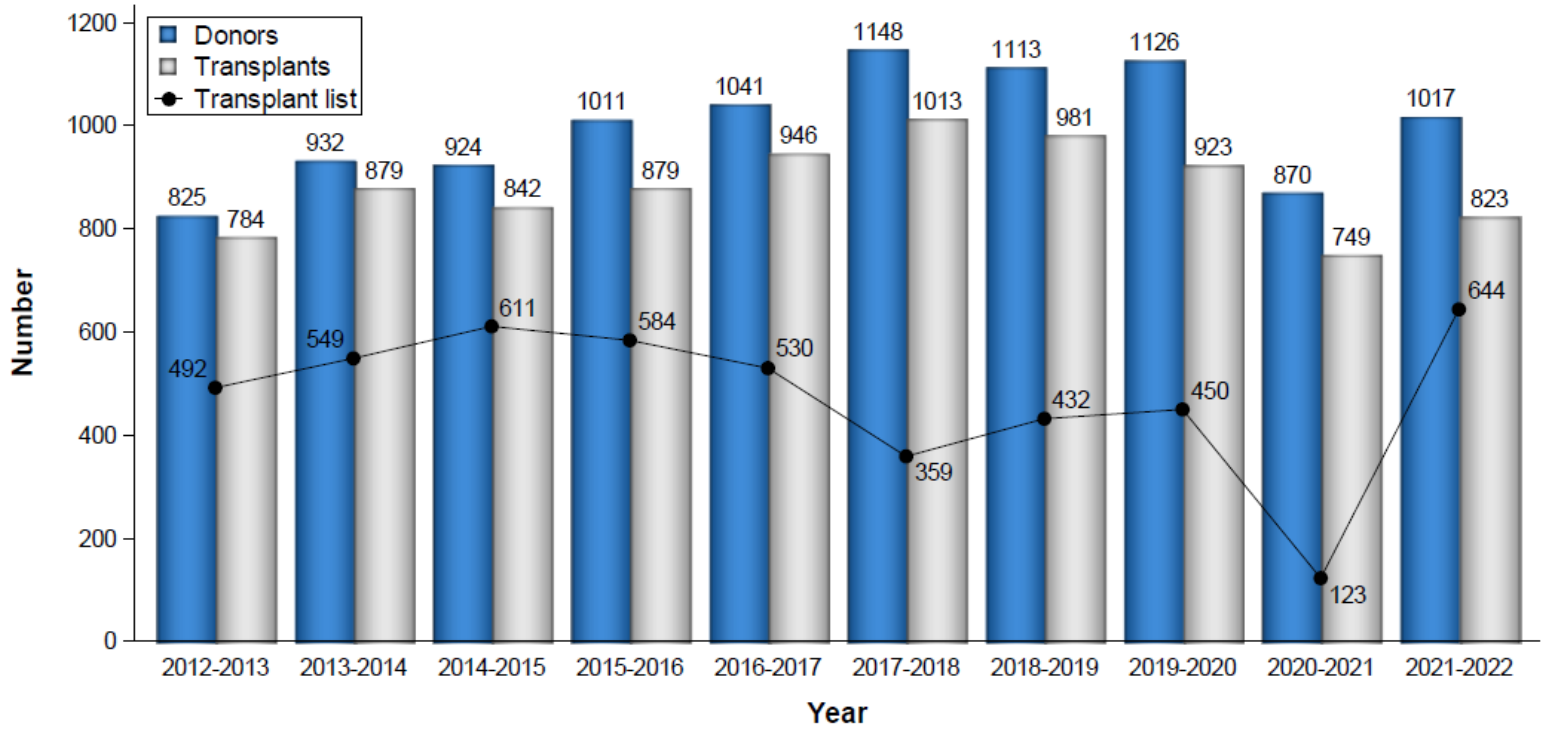
[1] Includes patients waiting for kidney and heart transplants (1 in 2020/21), kidney and liver transplants (1 in 2020/21, 2 adult in 2021/22), liver and heart transplants (1 in 2020/21, 1 paediatric in 2021/22) and liver and lung transplant (7 in 2020/21, 3 adult in 2021/22)

Livers not utilized



Liver waiting list

Figure 8.1 **Deceased donor liver programme in the UK, 1 April 2012 - 31 March 2022, Number of donors, transplants and patients on the active transplant list at 31 March**



Organ Utilisation Group

Department of Health & Social Care

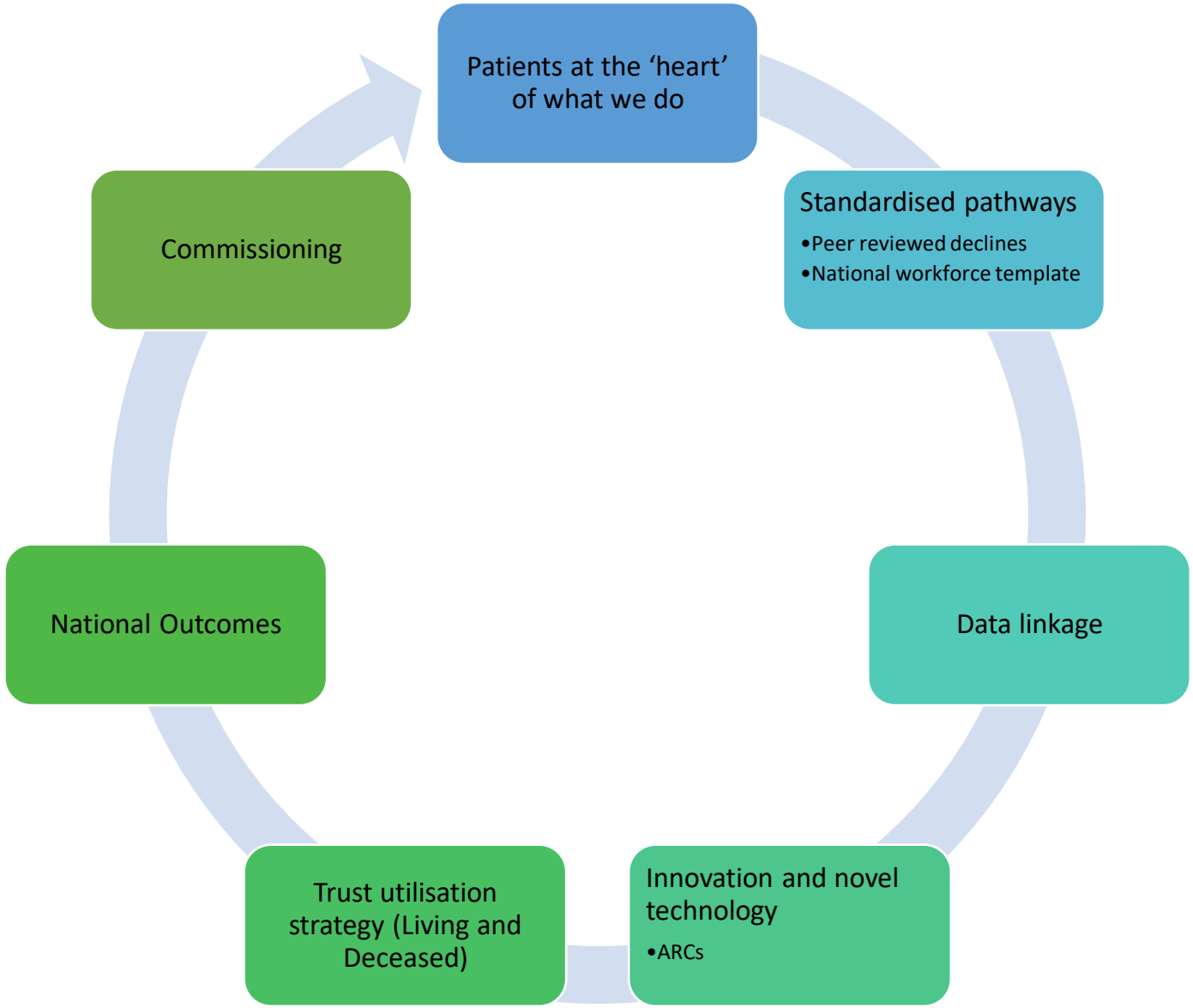
- Multi-disciplinary representation on the Organ Utilisation Group
- Comprehensive stakeholder engagement
- National and international evidence base review
- Subgroups to bring in additional expertise and insight (membership not limited to England)
- Stakeholder Forum to share information, seek views/ comments on direction of travel and drafts. Co-Chairs to represent patients and transplant community
- Website page to provide updates, summaries of meetings etc

OUG Remit

OUG Subgroups	
Standards	Commissioning
Workforce	Systems Architecture & Data Handling

- Established by Secretary of State for Health and Social Care to make recommendations on how to:
  - Deliver improvements in the number of organs that are accepted and successfully transplanted for adult and paediatric patients
  - Optimise the use of the existing skilled workforce, investment and infrastructure
  - **Provide equity of access and patient outcomes**
  - Reduce unwarranted variations in practice
  - **Support innovation**
- Remit in England only, but acknowledge patients cross UK borders and any recommendations for change may impact on other UK countries. Recommendations shared with UK Ministers
- **Transplantation of organs from living and deceased donors**
- Paediatric and adult services
- Task-and-finish group – will be disbanded after recommendations are provided

What we may expect (OUG)



Organ Utilisation Programme Workstream Structure & Projects

NHSBT Organ Utilisation Programme

1 Novel Technology & Innovation

- ARCs
- Imaging
- New digital Tx mgmt. tools
- Donor optimisation

2 Education and Culture

- Utilisation Training
- Criteria & Standards
- OD & Tx Collaboratives

3 Clinical Leadership & Engagement

- OUG
- CLUs
- IOUC initiation
- '22 NOU Conference
- Excellence in OU

4 Data & Insight

- ODTC ToR
- Higher quality donor organ definition
- Aide Memoire
- TRAC Tools
- Lack of Resources Declines Extensions
- Decline reviews

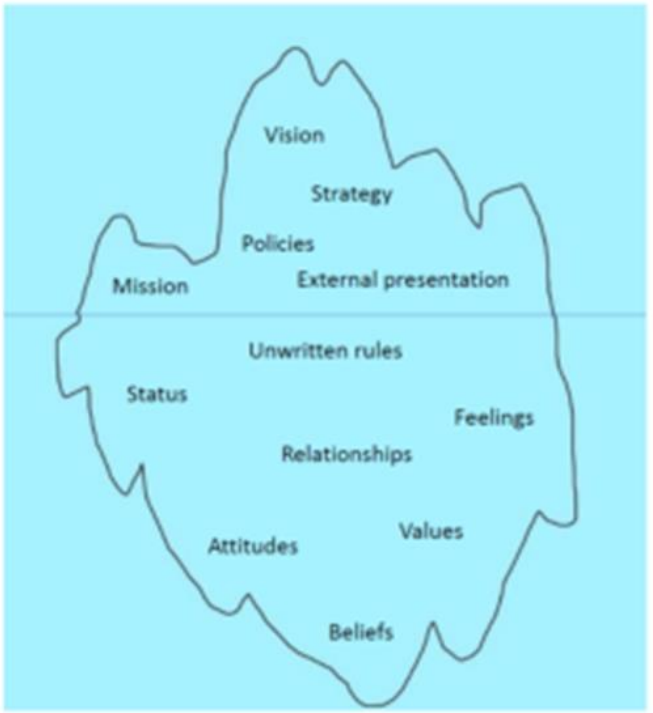
5 Digital Infrastructure for Utilisation

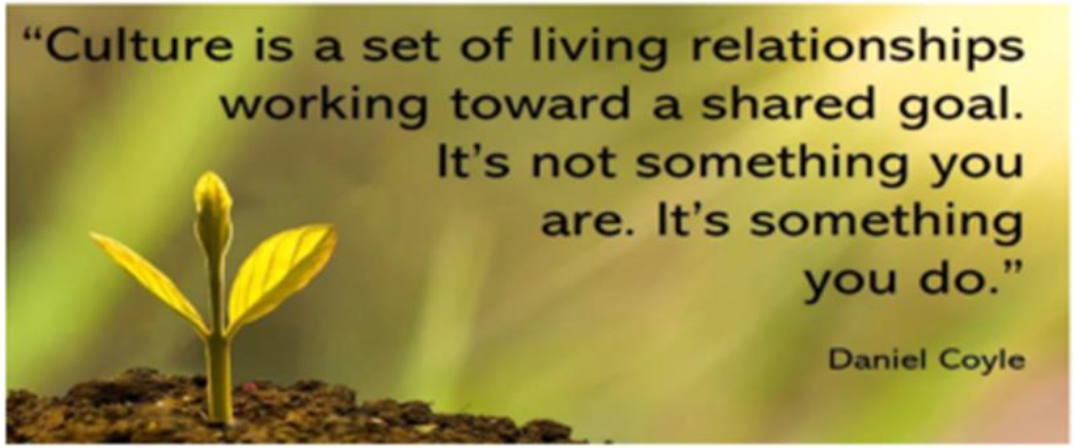
- Secure Image sharing
- Decommissioning and replacement of the Electronic Offering System (EOS)
- One integrated platform across pathway

Key

- Workstream
- Projects (indicative)
- New since 2021
- Business case development required

Changing Culture





Operational Performance

Deceased Donor Transplants

- Q2 saw a downward trend in the number of transplants across all organ types except hearts.
- **Organ utilisation remains above target at 2.50 transplants per donor YTD.**
- The policy enabling donation from selected donors with positive COVID test results has supported more transplants to occur.
- New waiting list registrations continue to increase each month; the transplant waiting list now exceeds 10,500 patients. Around 40% of patients are currently suspended; we will be discussing with centres whether patients who have been suspended for a period of time should be removed.
- Q2 has seen in increase in heart and liver deaths and removals from the waiting list. The OTDT Clinical Team including Advisory Group Chairs are working to understand the reasons for this.
- Mutual aid continues to be promoted by the clinical team..

1,795 [1,934]

Deceased donor transplants YTD

2.50 [2.35]

Transplants per deceased donor YTD

4 areas of change

- **Utilisation**
  - Culture
  - Monitoring
  - Trust responsibility
- **Commissioning**
  - Model change
  - Local vs National
  - Joint ownership
- **Technology and Retrieval**
  - ARCs
  - Shifting to ‘night-time’ model
  - NRP
  - Economy of scale
- **Workforce**
  - Sustainability
  - Renumeration
  - Retention
  - Being valued

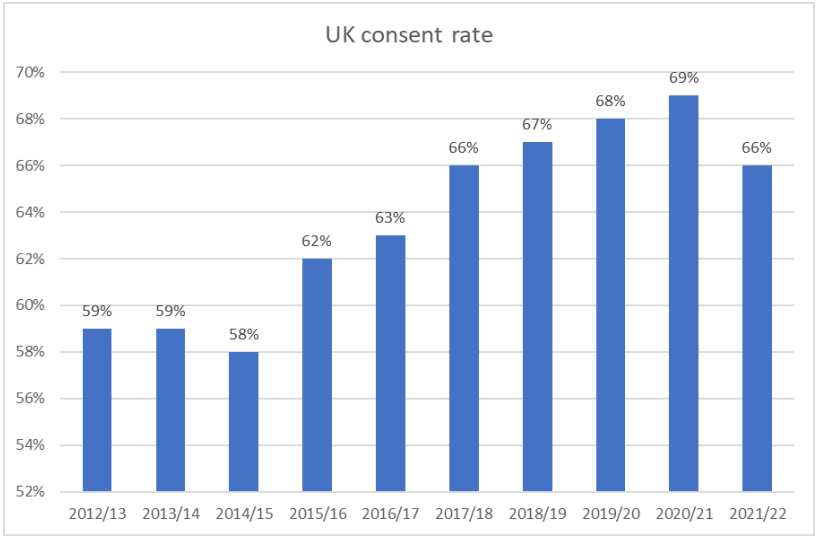
The consent challenge

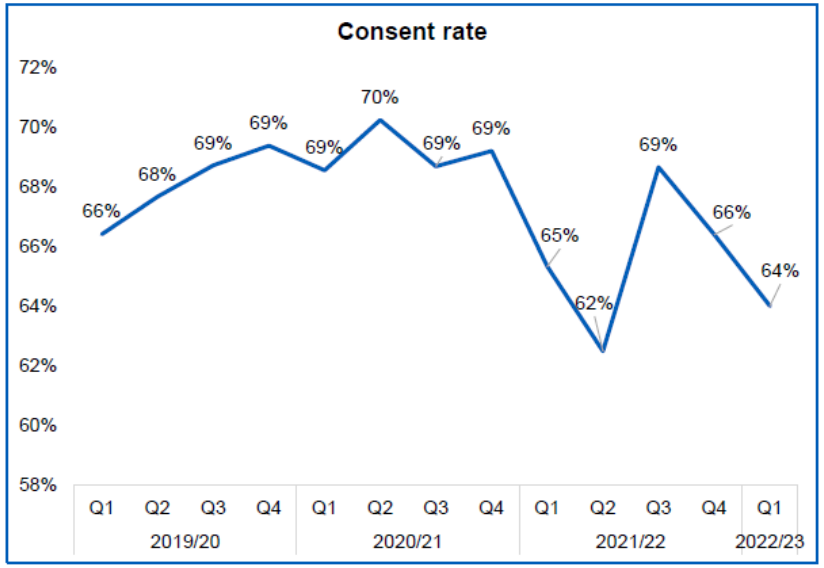
Whilst initially consent rates were positive following the implementation of the opt-out system, consent rates at the end of last financial year are back to 2017/18 levels and YTD (2022/23) the consent rate is at 62% in the UK against a target of 72%

Factors impacting the number of deceased organ donors:

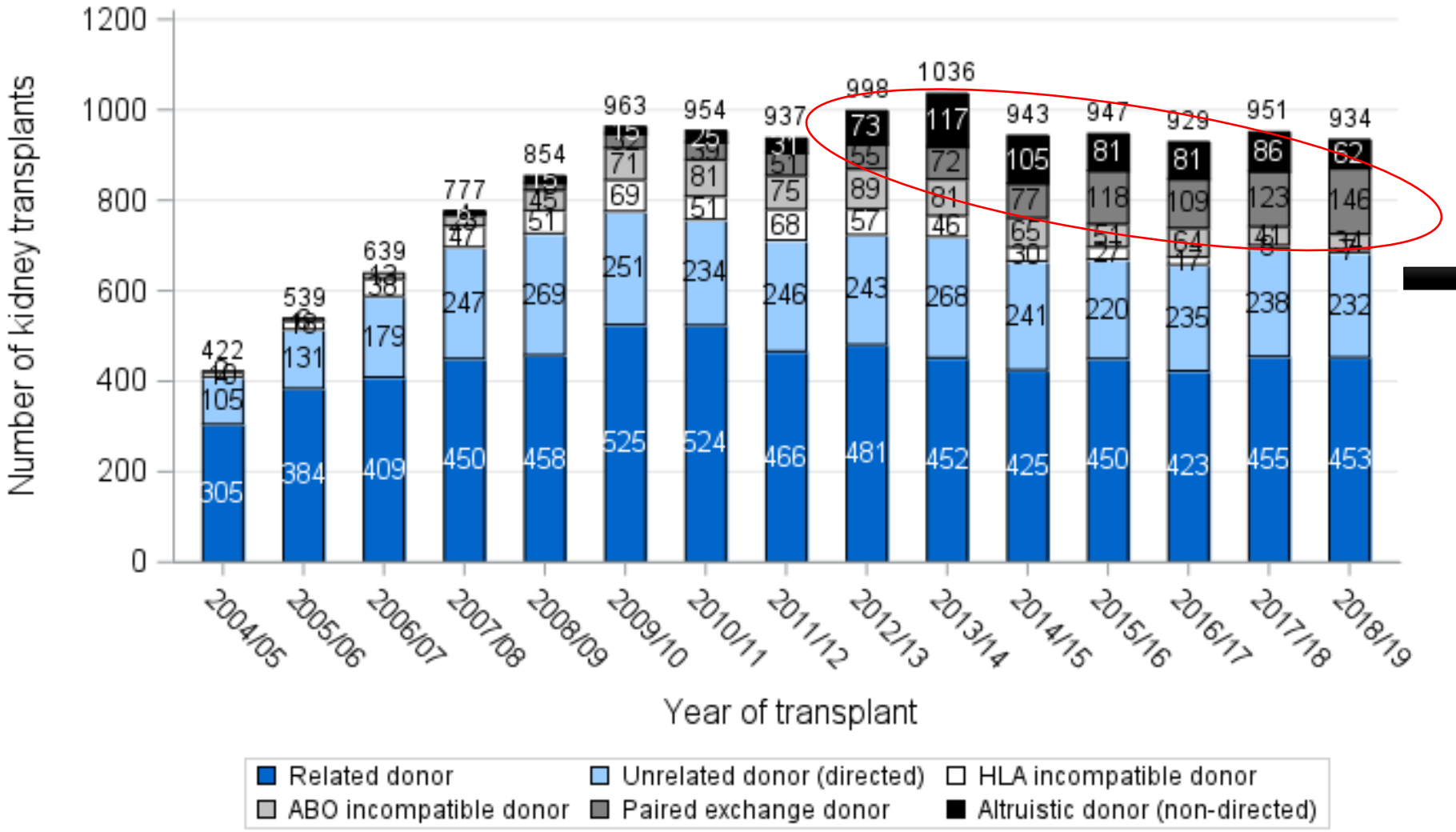
- **Eligible** pool: Down 15% verse pre-pandemic. Hypothesis that people are dying outside of the ICU/ED setting. Acord study in progress to provide insight
- **Neurological death testing:** Testing rates down and actions in place, but those potential donors who aren't tested will progress via DCD donor pathway
- **Consent rate:** Impacted by volume of expressed (verbal) opt-outs and unsupported deemed consent. Hypothesis that family NHS experience prior to donation being discussed could also be an impacting

Consent rate for an expressed decision remains at 90%, whilst consent rate for deemed consent is 59% YTD





Adult living donor transplants



1600 transplants enabled through schemes, to date