

Kidney transplantation: current landscape and future directions

Siân Griffin

Consultant Nephrologist, Cardiff



Declaration for Siân Griffin

I have the following financial interest or relationships to disclose with regard to the subject matter of this presentation:

- Consulting fees
 - Alexion, AstraZeneca, Bayer, CSL Vifor, Hansa, Novartis, Traverso
- Clinical trial steering committees:
 - TSC Chair, GAMECHANgER-1 (Regulatory T cells in sensitised patients to improve outcomes after HLA-Ab incompatible renal transplantation). HRA funded
 - DMC Chair, A phase 2, multi-centre, open label study to evaluate the safety and efficacy of AT-1501 in patients undergoing kidney transplantation. Elodon Pharma

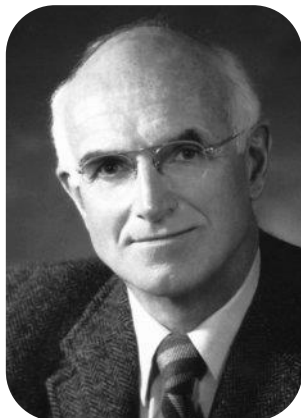
Myths and Miracles



Kidney Transplantation



- Boston, 1954
- Ronald and Richard Herrick
- Over 100 000 transplants carried out each year
- Preferred treatment for end stage kidney disease



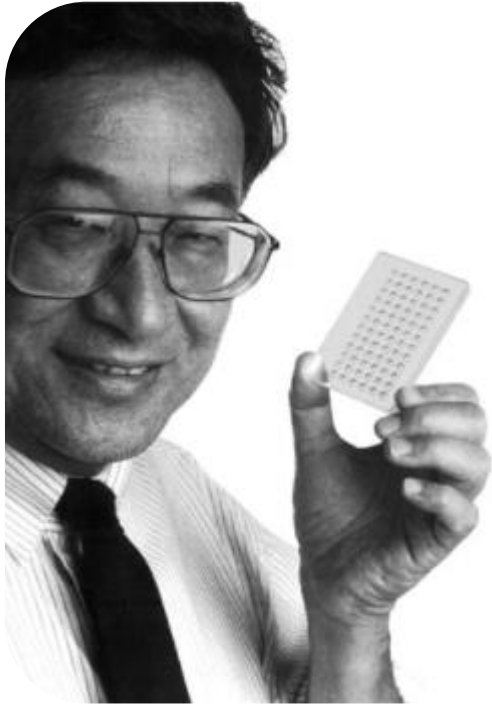
The Nobel Prize in Physiology or Medicine 1990

[Joseph E. Murray](#) and [E. Donnall Thomas](#)

“for their discoveries concerning organ and cell transplantation in the treatment of human disease”

THE
NOBEL
PRIZE





Paul Terasaki, 1929 - 2016

The New England Journal of Medicine

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Volume 280

APRIL 3, 1969

Number 14

SIGNIFICANCE OF THE POSITIVE CROSSMATCH TEST IN KIDNEY TRANSPLANTATION*

RAMON PATEL, M.R.C.P., AND PAUL I. TERASAKI, PH.D.



Gila River Relocation Centre, Arizona



The New England Journal of Medicine

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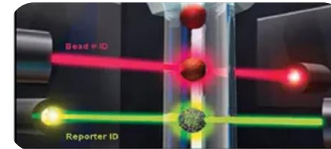
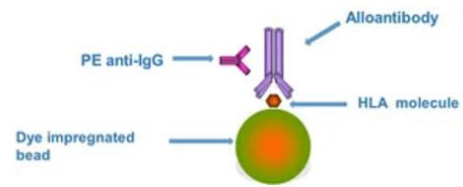
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Paul Terasaki, 1929 - 2016



Gila River Relocation Centre, Arizona



Uned Ymchwil Arennol Cymru
Wales Kidney Research Unit





Professor Sir Roy Calne, 1930 - 2024

CASTAWAY'S FAVOURITE



Antonín Dvořák

Symphony No. 9 in E minor 'From the New World'
Orchestra: Philadelphia Orchestra Conductor: Carlo Maria Giulini
DVOŘAK SYMPHONY NO 9. EMI.

Preliminary Communications

Combined Immunosuppressive Action of Phytohaemagglutinin and Azathioprine (Imuran) on Dogs with Renal Homotransplants

Brit. med. J., 1965, 2, 154-155

THE LANCET

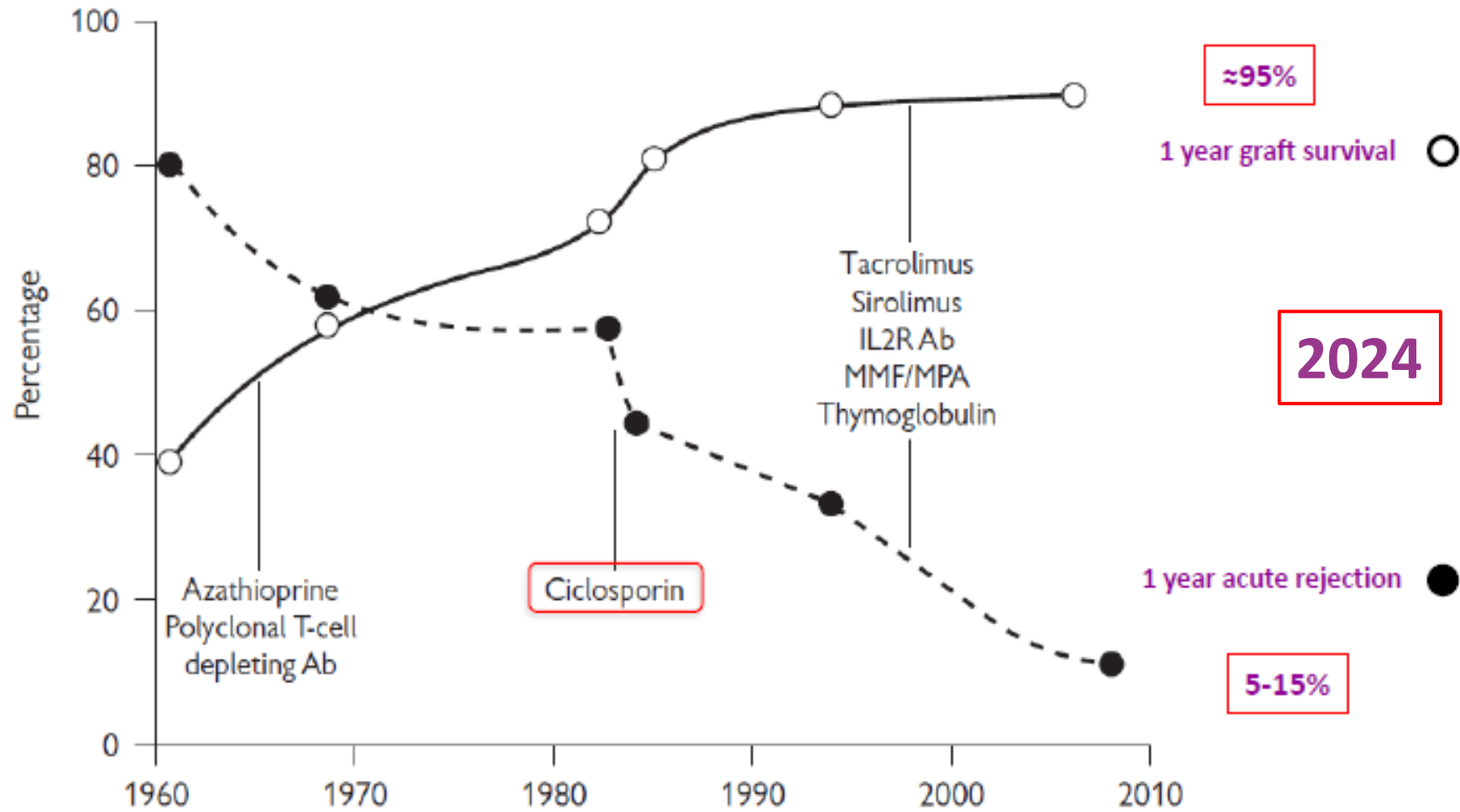
VOLUME 312, ISSUE 8104, P1323-1327, DECEMBER 30, 1978

CYCLOSPORIN A IN PATIENTS RECEIVING RENAL ALLOGRAFTS FROM CADAVER DONORS

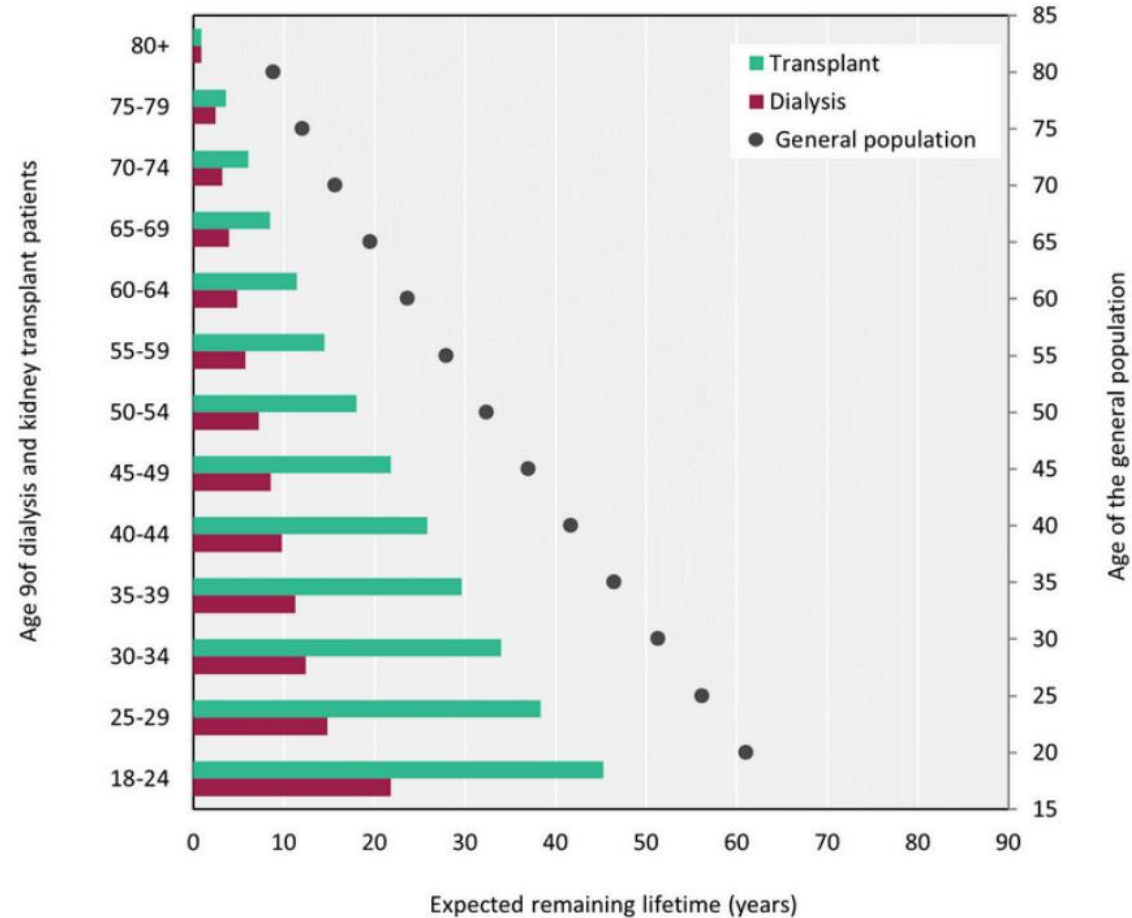
R.Y. Calne · S.Thiru · P.McMaster · G.N.Craddock · D.J.G.White · D.B.Evans · et al. [Show all authors](#)



Evolution of Immunosuppression

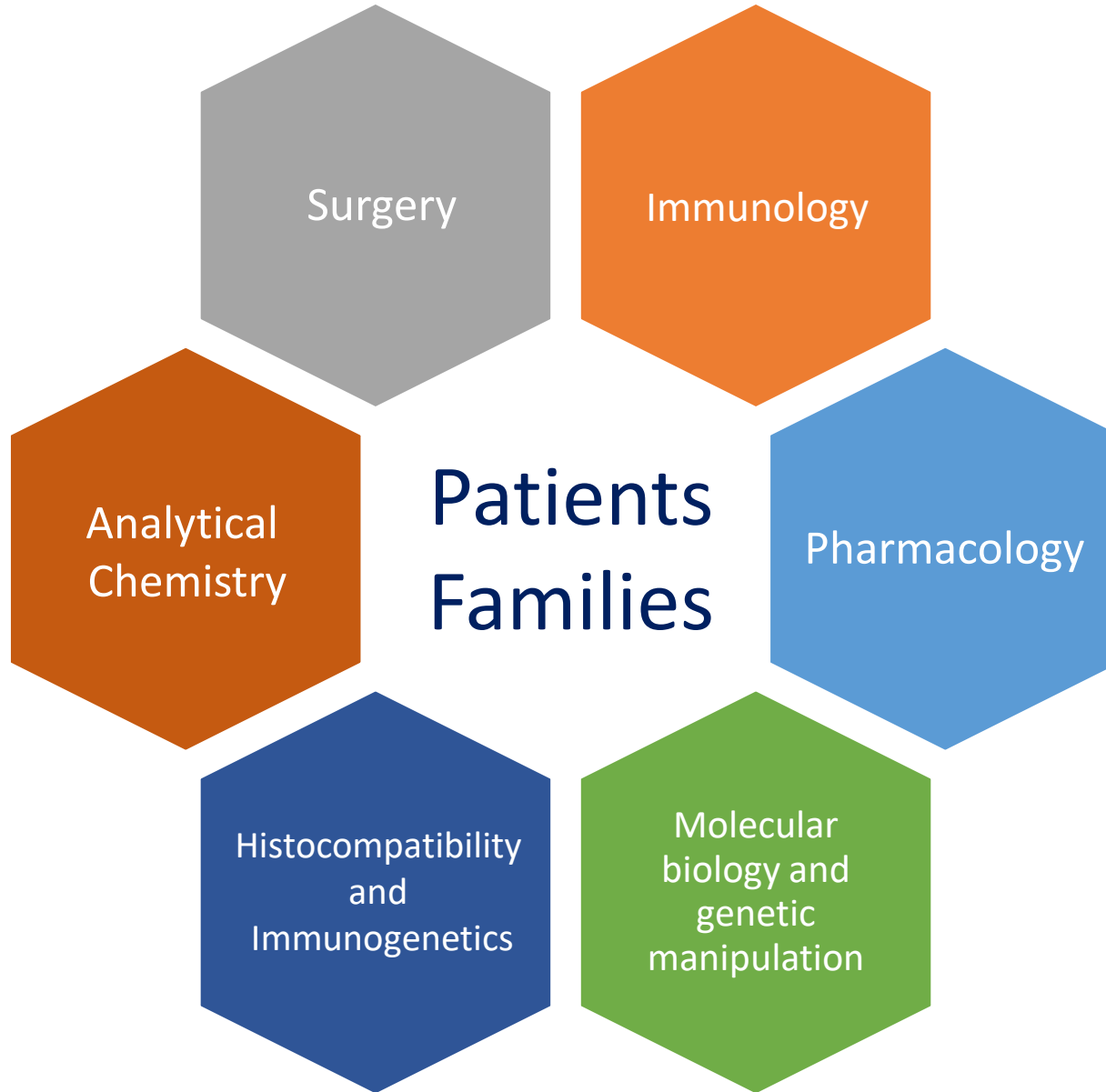


Life expectancy with End Stage Kidney Disease





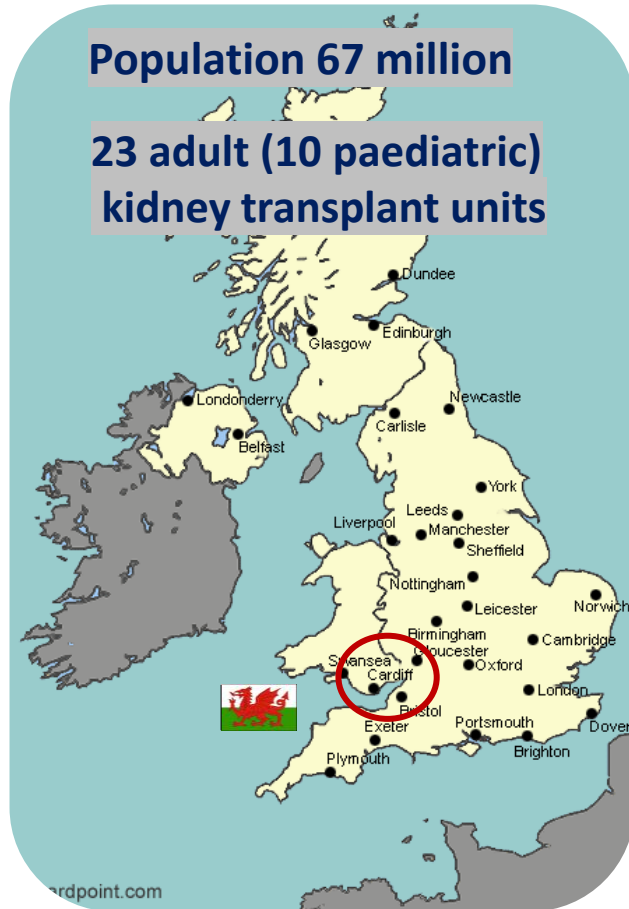
Legality
Regulation
Infrastructure
Ethics



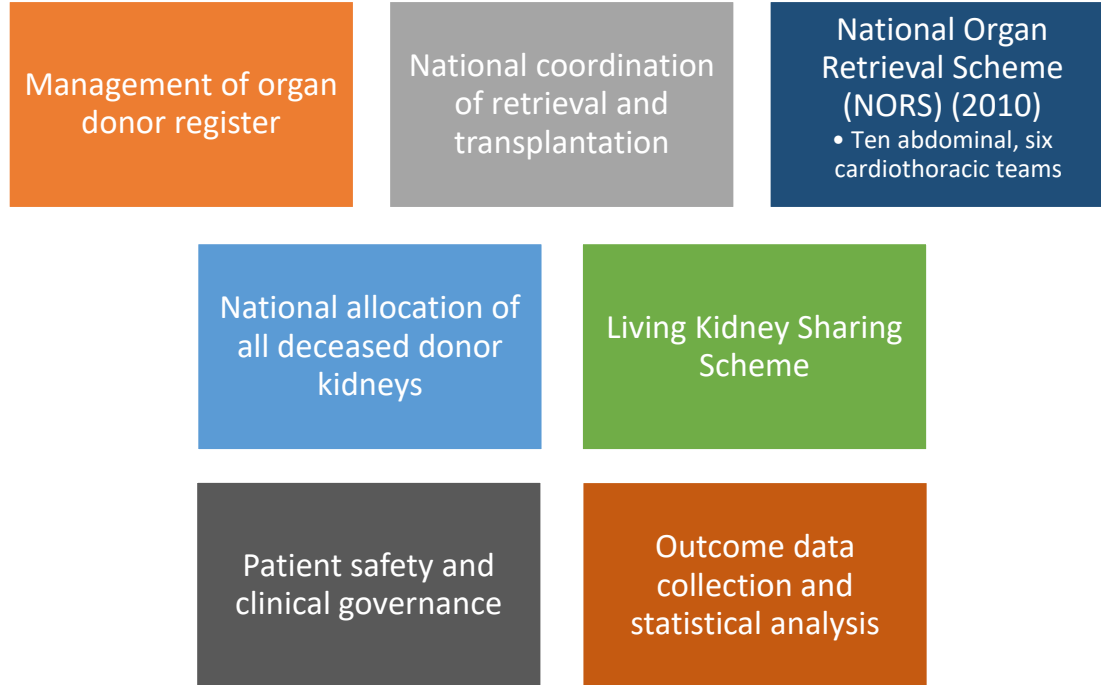
Doctors
Nurses
Clinical scientists
Technicians
Coordinators
Pharmacists
Psychologists
Dieticians



Organisation of transplantation in the UK



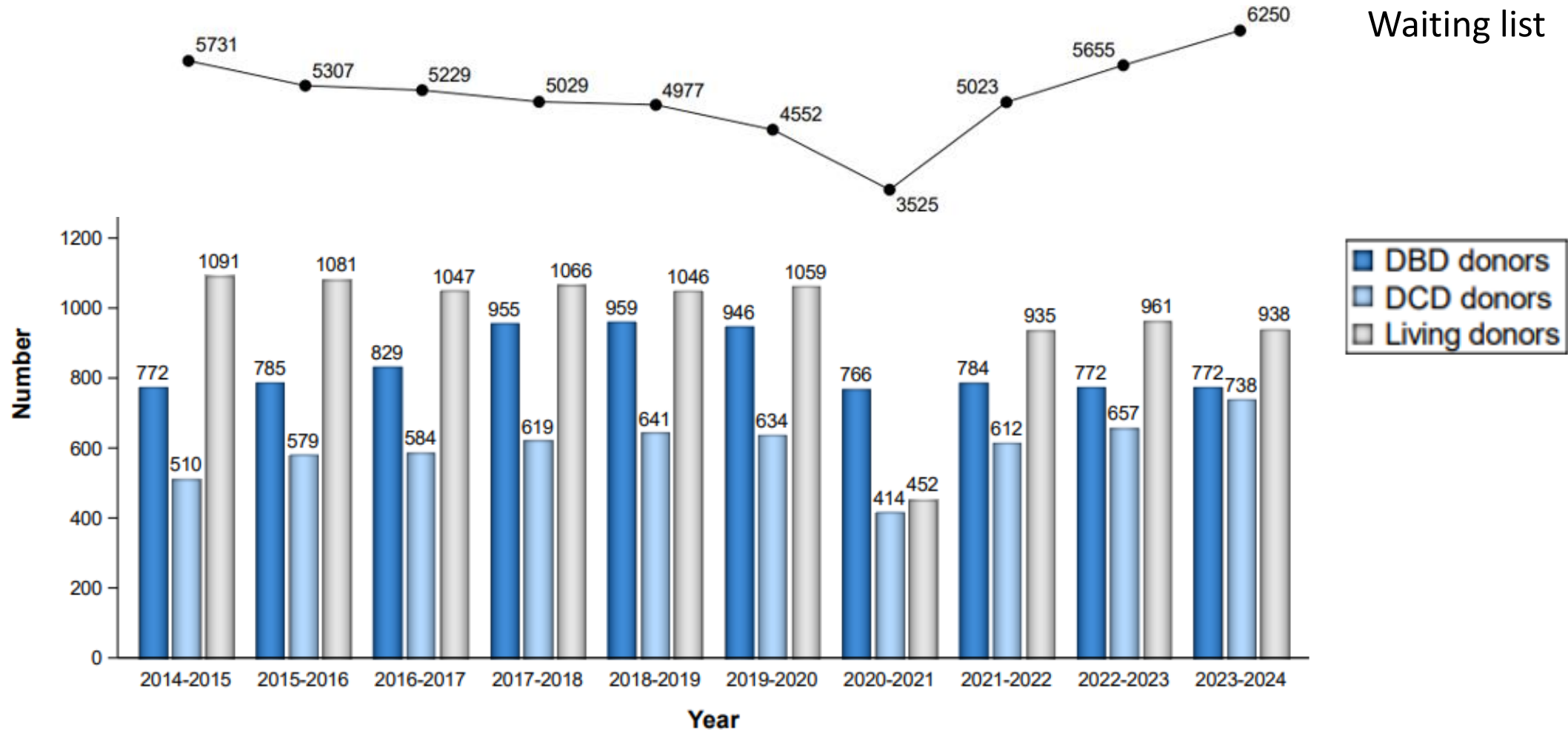
Blood and Transplant



<https://www.odt.nhs.uk/>

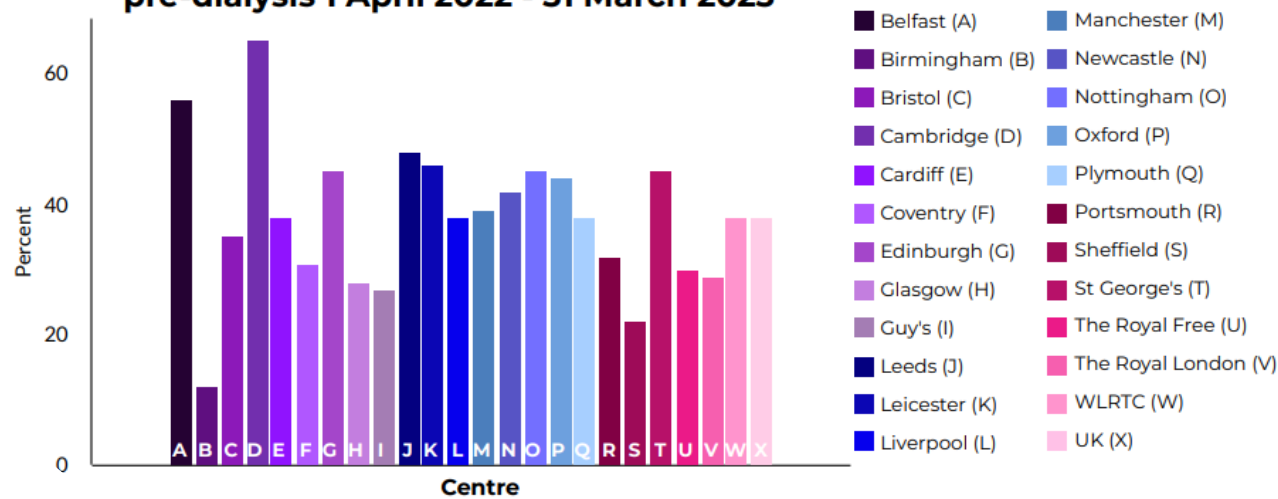
Kidney donation and transplantation in the UK

Waiting list

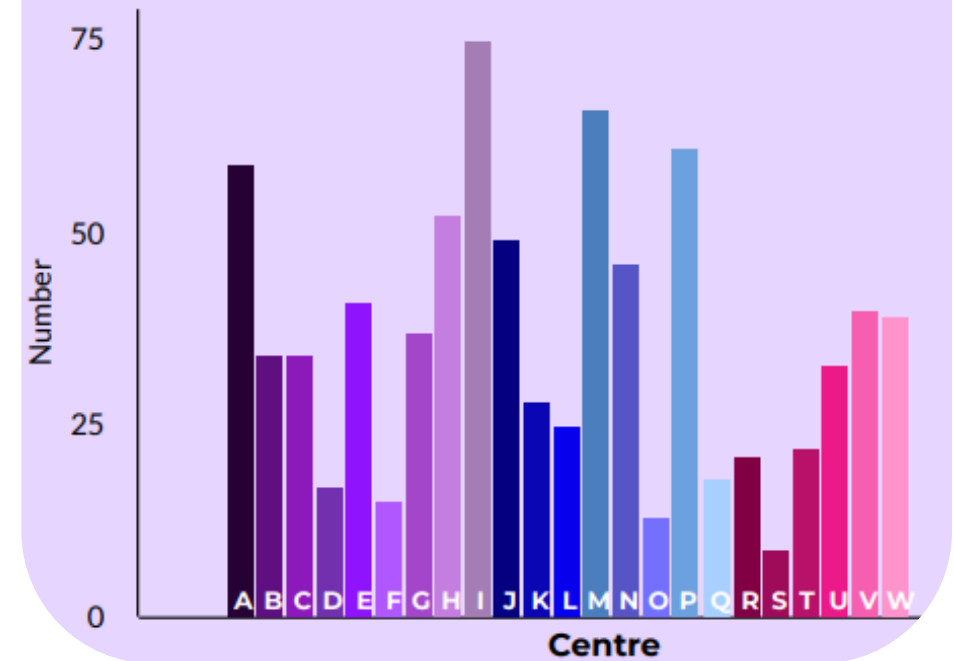


ADULT KIDNEY TRANSPLANTS FROM LIVING DONORS

Percentage of transplants pre-dialysis 1 April 2022 - 31 March 2023



Number of transplants between 1 April 2022 - 31 March 2023



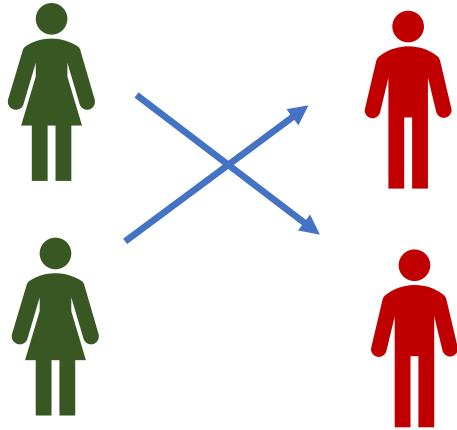
UK Living Kidney Sharing Scheme

- Established 2007
- Donor recipient pairs registered for three monthly matching runs
- Stipulate maximum acceptable donor age and HLA mismatch
- Option to modify blood group and unacceptable antigen profile compared to deceased donor listing
- Declare any special donor circumstances (usually anatomical)



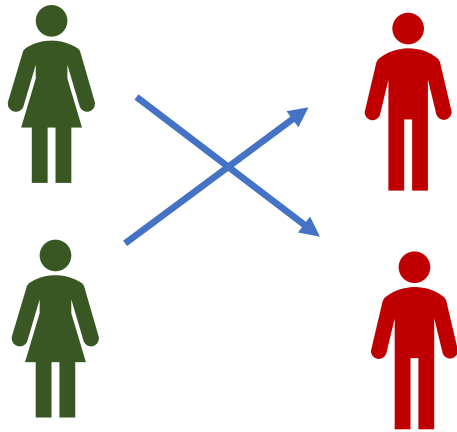
UK Living Kidney Sharing Scheme

2007 Two-way paired exchange

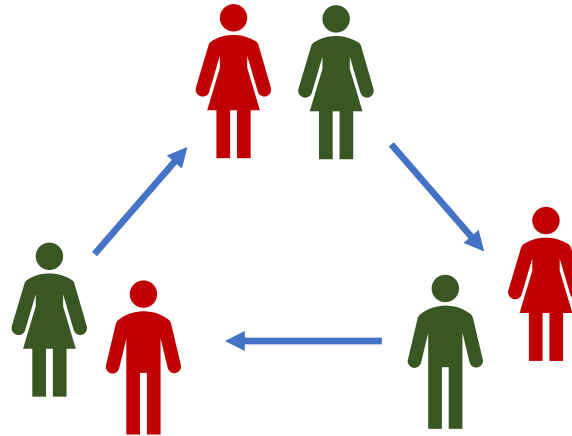


UK Living Kidney Sharing Scheme

2007 Two-way paired exchange

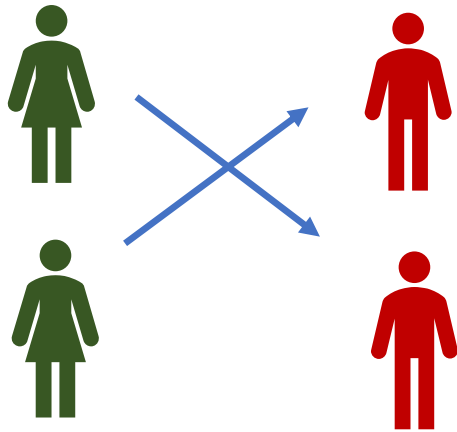


2008 Three-way pooled exchange

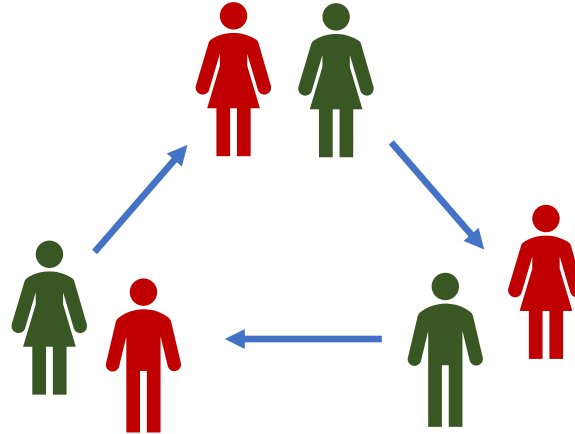


UK Living Kidney Sharing Scheme

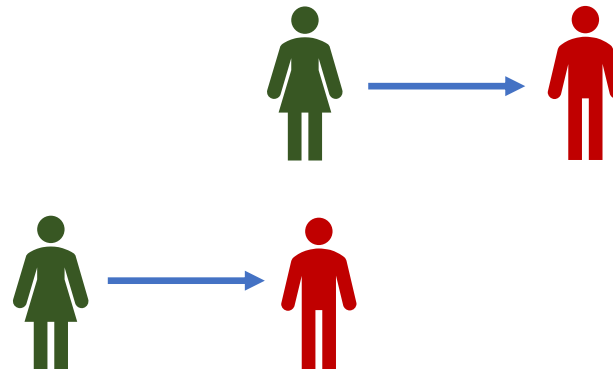
2007 Two-way paired exchange



2008 Three-way pooled exchange

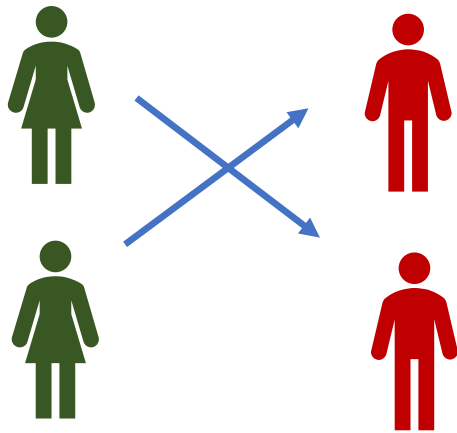


2012 Short altruistic donor chain

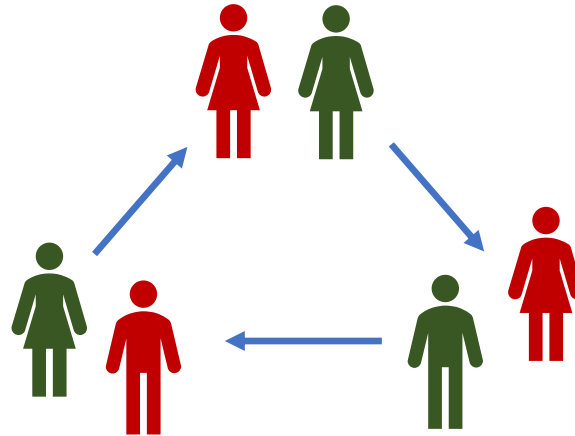


UK Living Kidney Sharing Scheme

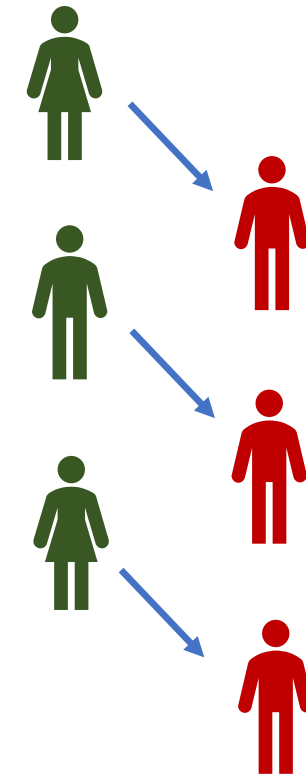
2007 Two-way paired exchange



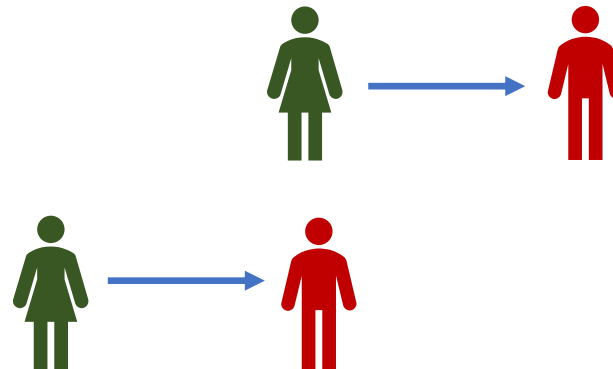
2008 Three-way pooled exchange



2015 Long altruistic donor chain



2012 Short altruistic donor chain



One day. Six operations. Three kidneys. The story of an organ donor chain

📷 From top: Ryan donated a kidney to Ben, whose dad Steve donated a kidney to David, whose wife Martha donated a kidney to Lee, who is Ryan's best friend
Photograph: David Yeo and Robert Seale/The Guardian



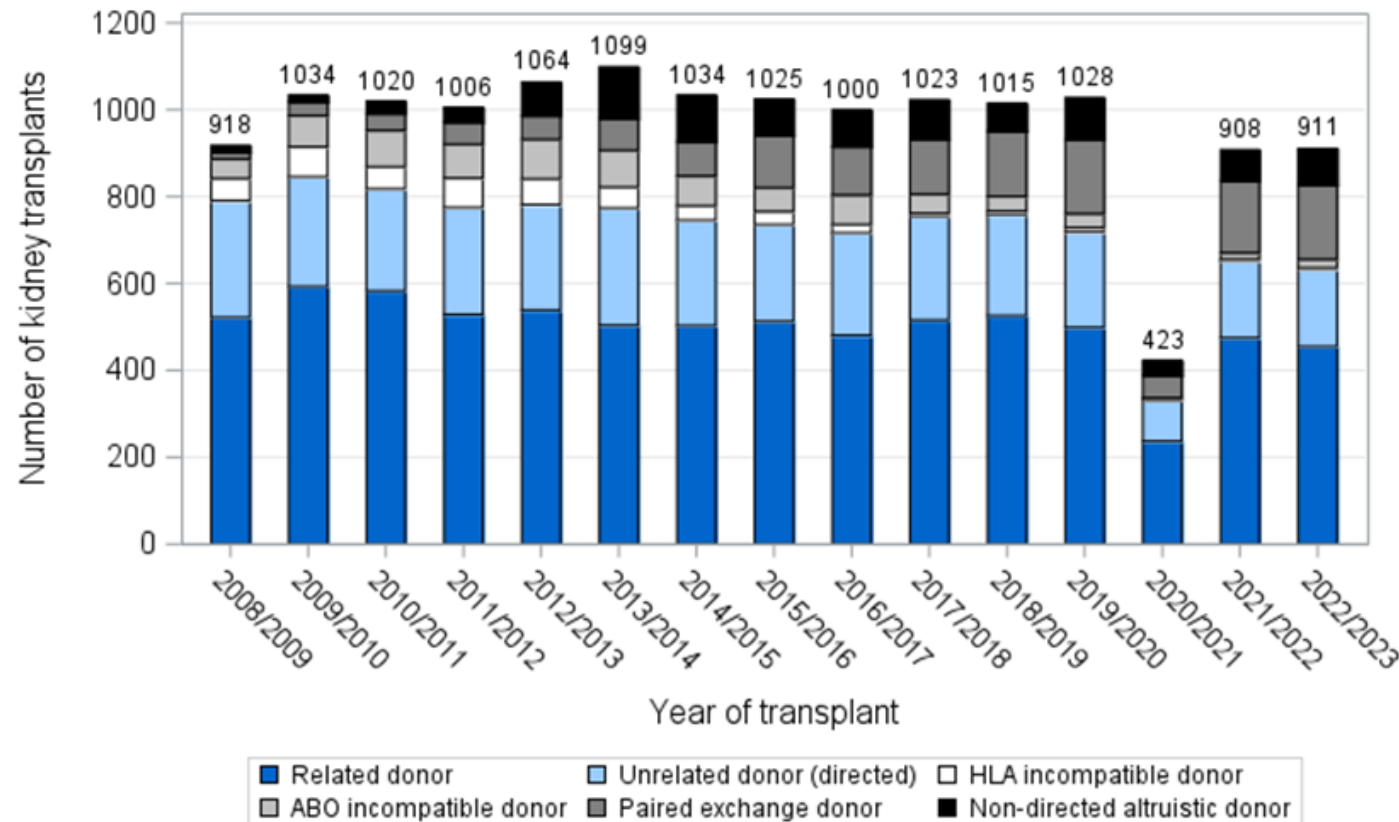
UK Living Kidney Sharing Scheme

Optimising opportunities

- Registration of compatible pairs for a better match (HLA, age)
- Antibody incompatible transplants possible
- Non-simultaneous surgery allowed
- Non-directed altruistic donors included as default choice
- Long non-directed altruistic chains
- Potential for international collaboration

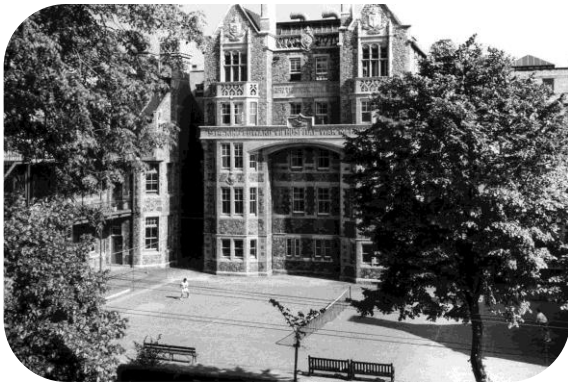
2000th recipient transplanted in Cardiff

UK Living Donor Transplants by type



- Rise in transplants via LKSS has coincided with fall in antibody incompatible transplants
- Transplants via LKSS account for 21% of all living donor kidney transplants in the last 5 years (6% of all kidney transplants)

Transplantation in Cardiff



HOSPITAL TOPICS

Integrated Regional Haemodialysis and Renal Transplantation Centre

R. A. BRANCH,* M.B., M.R.C.P. ; G. A. COLES,† M.B., M.R.C.P. ; D. L. CROSBY,‡ M.B., F.R.C.S. ;
J. HENRY JONES,§ M.D., M.R.C.P. ; M. SUSSMAN,|| B.S.C., PH.D., M.I.BIOL. ; W. J. C. THOMAS,¶ M.B., F.R.C.S.

British Medical Journal, 1970, 1, 291-294



Summary: During the first year of an integrated hospital haemodialysis/home dialysis/renal transplantation service 56 patients with chronic renal failure were accepted for treatment. Twenty-five of these have had a cadaveric renal transplant, seven are established on home dialysis, and 18 are still receiving maintenance dialysis in the 10-bedded hospital unit. The overall survival rate is 66%. The rate of referral from the immediate vicinity of the unit of patients suitable for treatment by these methods was about 25-30 per million per year.

Welsh innovation

Welsh Health Minister celebrates that 'Opt-out organ donation scheme has transformed lives'

Five years ago Wales led the way in the UK by introducing a soft opt-out system of organ donation.

NEWS

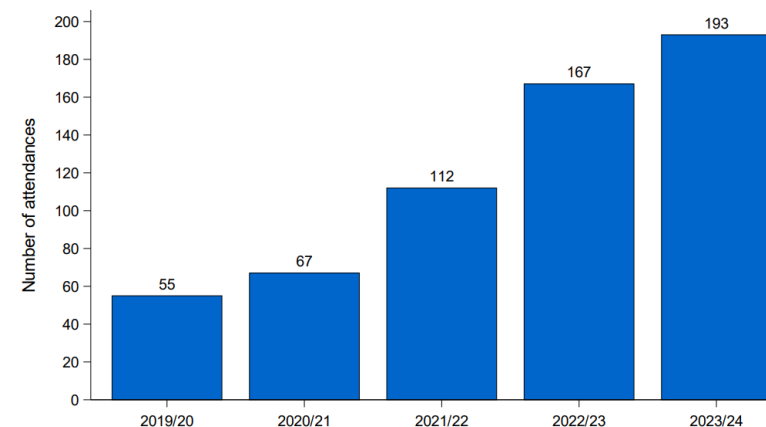
Home | Coronavirus | Brexit | UK | World | Business | Politics | Tech | Science | Health

Wales | Wales Politics | Wales Business | North West | North East | Mid | South West | S

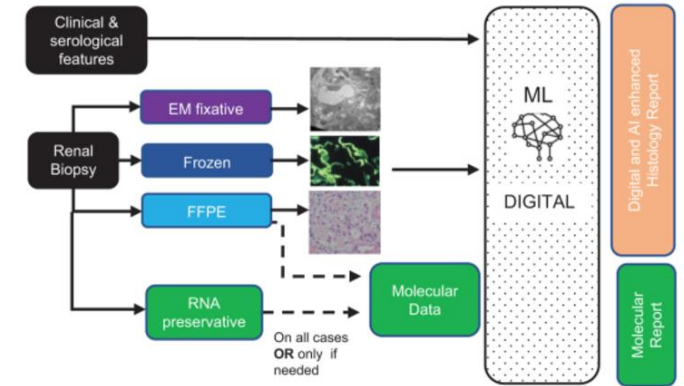
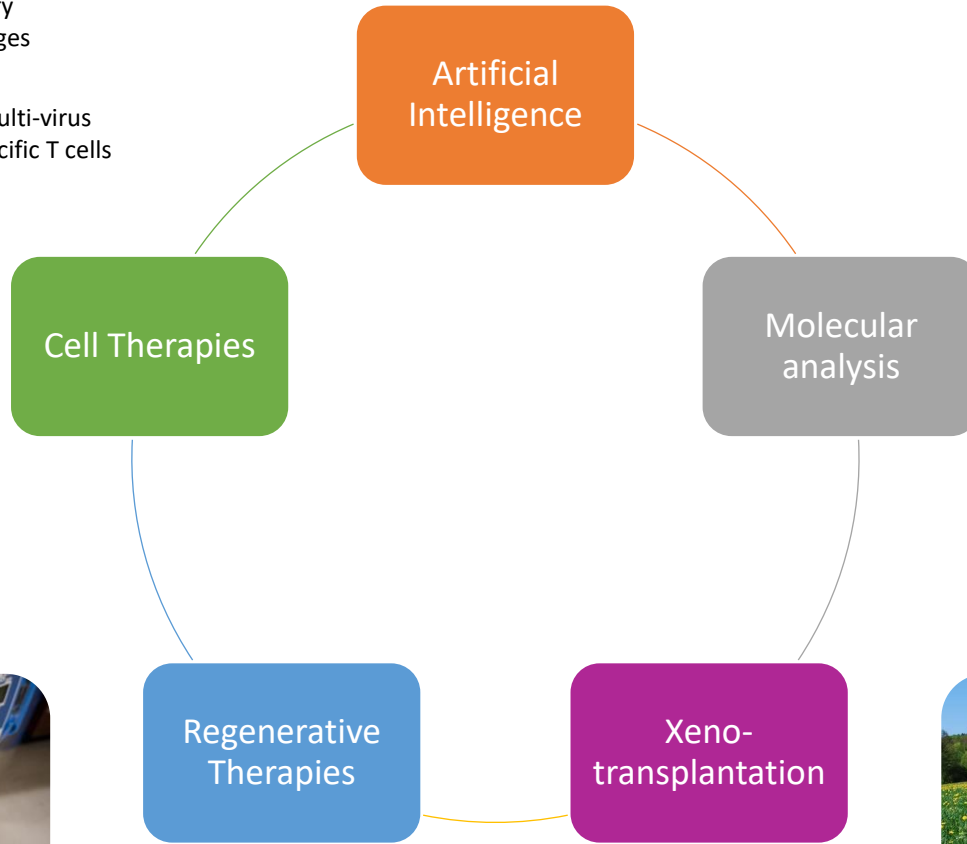
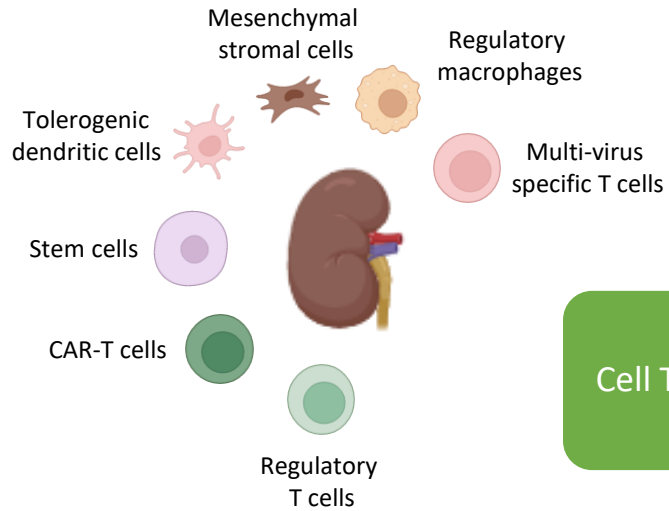
Hepatitis C-infected kidneys used in organ transplants

🕒 6 September 2019

Abdominal Normothermic Regional Perfusion attendances between 1 April 2019 – 31 March 2024



What's coming next?



Organ Utilisation Group (OUG)

Established by the Secretary of State to make recommendations on how to maximise the potential for organ transplantation from living and deceased donors by:

- Making the best use of available resources
- Driving infrastructure improvements
- Supporting innovation

Independent report

Honouring the gift of donation: utilising organs for transplant - summary report of the Organ Utilisation Group

Published 21 February 2023

<https://www.gov.uk/government/publications/honouring-the-gift-of-donation-utilising-organs-for-transplant/>

Excellence in Organ Utilisation—A Quantitative and Qualitative Evidence Base for a New Approach in the UK

Claire Williment^{1*}, Jessica Jones¹, John Forsythe¹, Lisa Mumford¹ and Stephen Powis²

¹NHS Blood and Transplant, Filton, United Kingdom, ²NHS England, London, United Kingdom



ORIGINAL RESEARCH
published: 04 September 2023
doi: 10.3389/ti.2023.11641



Department
of Health &
Social Care

Uned Ymchwil Arennol Cymru
Wales Kidney Research Unit



OUG Recommendations

Theme 1: placing the patient at the heart of the service

Recommendation 8

National multi-organ centres for organ assessment and repair prior to transplantation must be established to provide the optimum practical steps to:

- bring new techniques into everyday clinical therapy as rapidly as possible
- maximise the number and quality of organs available for transplant
- support logistics at transplant units

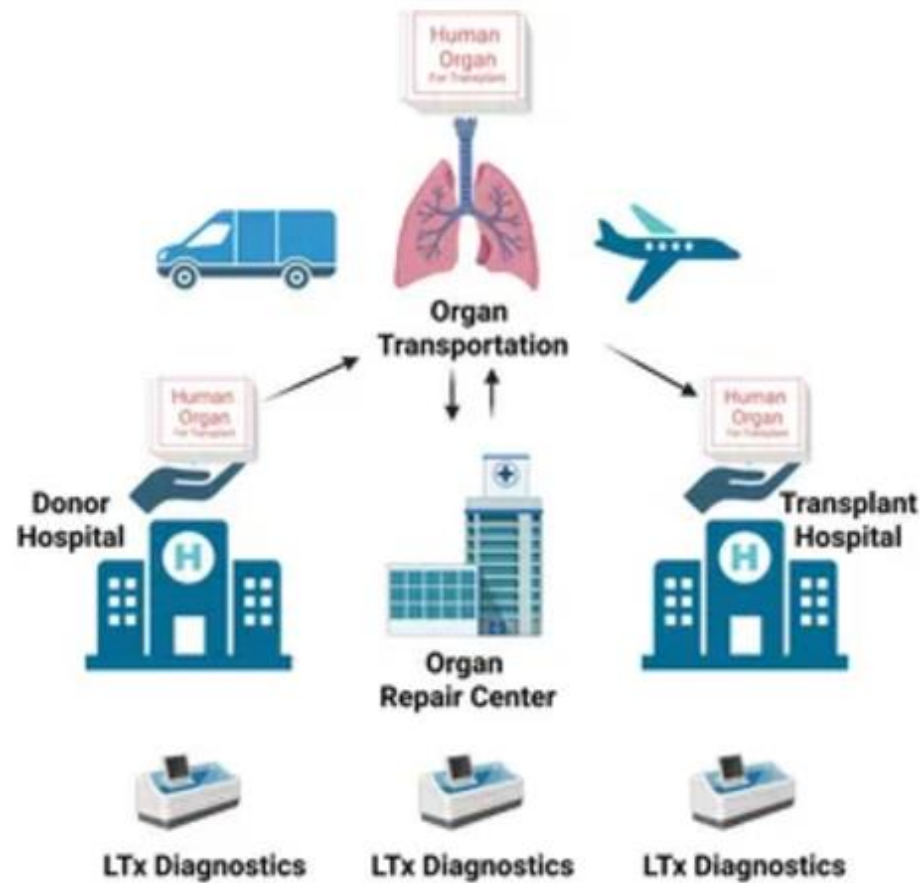
Recommendation 9

A national oversight system must be established that makes the best use of the UK's world-leading innovation in assessment, perfusion and preservation of donated organs.

Implementation Steering Groups for Organ Utilisation (ISOU)


- Patient engagement
- Trust engagement
- Histocompatibility and immunogenetics
- Assessment and Recovery Centres
- Xenotransplantation

Assessment and Recovery Centres



Organ Recovery Centres

The 20-year paradigm shift toward organ recovery centers: 2500 donors at Mid-America Transplant and broader adoption across the United States

Gary F. Marklin ^{*} , Diane Brockmeier, Karen Spector

Mid-America Transplant, St Louis, Missouri, USA

American Journal of Transplantation 23 (2023) 891–903

- Intensive Care Unit
- Operating room
- Laboratory
- Investigational capacity
- Donor evaluation and management
- Organ retrieval



Organ Recovery Centres, 2022


STA | SOUTHWEST
TRANSPLANT ALLIANCE

First Major Gifts Announced For
Revolutionary Organ Recovery Center



Above: Rendering of Southwest Transplant Alliance's stand-alone organ and tissue recovery center.

“Remarkably, the donor families consented for transfer more than 90% of the times. Donor families are usually exhausted from living at the hospital for days as their loved one is cared for in the ICU. After they are informed that their loved one is deceased, they are generally relieved that they can go home and make funeral arrangements while the donor is managed in the ORC”.

In a First, Surgeons Attached a Pig Kidney to a Human, and It Worked



By [Roni Caryn Rabin](#)

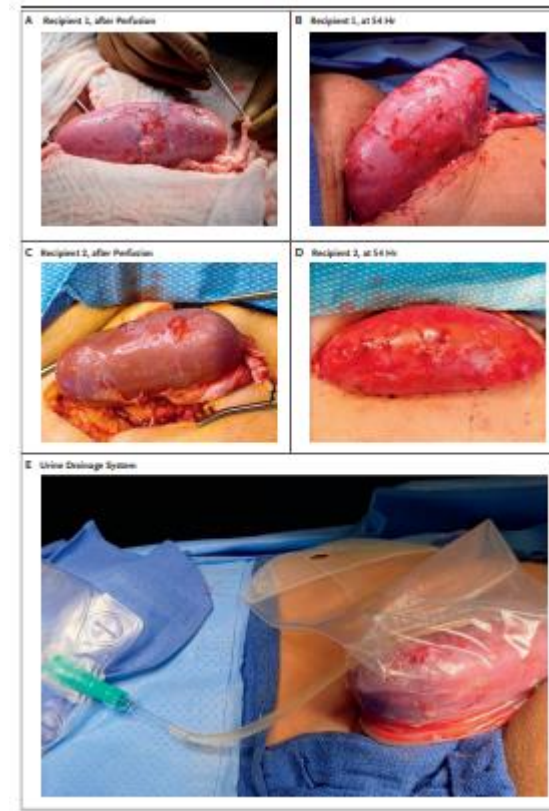
Published Oct. 19, 2021 Updated Oct. 21, 2021



“Medicine is about story-telling, and I have a story to tell”

ORIGINAL ARTICLE

Results of Two Cases of Pig-to-Human Kidney Xenotransplantation



Montgomery RA *et al* NEJM 386:1889, 2022

Organ source

The 10-Gene Edited Pig

The key to xenotransplantation



UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

- Three carbohydrate xenoantigens (GGTA1, β 4GalINT2, CMAH)
- Growth hormone receptor
- Two complement-regulatory (CD55, CD46)
- Two coagulation-regulatory (thrombomodulin, EPCR)
- One anti-inflammatory (HO-1)
- One anti-macrophage (CD47)

<https://www.uab.edu/news/research/item/12567-the-10-gene-pig-and-other-medical-science-advances-enabled-uab-s-transplant-of-a-pig-kidney-into-a-brain-dead-human-recipient>



FIRST PIG KIDNEY TRANSPLANT IN A PERSON: WHAT IT MEANS FOR THE FUTURE

The operation's early success has made researchers hopeful that clinical trials for xenotransplanted organs will start soon.

Nature | Vol 628 | 4 April 2024 | **13**

69 gene edited pig

- 59 to inactivate porcine endogenous retroviruses



Richard Slayman
1962 - 2024

Xenotransplantation - challenges




Immunological

THE LANCET

ARTICLES · Volume 402, Issue 10408, P1158-1169, September 30, 2023 [Download Full Issue](#)

Immune response after pig-to-human kidney xenotransplantation: a multimodal phenotyping study

Prof Alexandre Loupy, MD PhD ^{a,b,1}  Valentin Goutaudier, MD MSc ^{a,b,1} · Alessia Giarraputo, PhD ^{a,c,1} · Fariza Mezzine, MSc ^a · Erwan Morgand, PhD ^a · Blaise Robin, MSc ^a et al. [Show more](#)

nature communications 

Article <https://doi.org/10.1038/s41467-023-47601-7>

Spatiotemporal immune atlas of a clinical-grade gene-edited pig-to-human kidney xenotransplant

Received 12 February 2023
Accepted 1 April 2024
Published online 12 September 2023

[Check for updates](#)

Matthew D. Chung ^{1,2}, Rebecca Adamec ^{1,2}, Elise N. Erman ¹, Christopher F. Field ^{1,2}, Sherrill Liu ^{1,2}, Chao Wang ^{1,2}, Vidya Sagar Hanumanth ¹, Harsh G. Patl ¹, Emma D. Wright ¹, Sabine von Rohden ¹, Stefan Eickhoff ¹, Jakob A. Christ ¹, Vinaya Kumar ¹, Douglas J. Anderson ¹, Morgan E. Crovace ¹, Markela Bell ¹, Stefan Yang ¹, Erin M. Moore ¹, Jennifer L. Freeman ¹, James T. Miller ^{1,2}, Jason Baker ¹, Jackson Perry ¹, David Shaw ¹, William Reed ¹, Shawn C. Little ¹, Alexander F. Rosenberg ^{1,2}, James F. George ^{1,2}, Jeremy E. Lasker ¹, Paola M. Forzan ^{1,2}

Xenotransplantation - challenges



Immunological

THE LANCET

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Prof Alexandre Loupy, MD PhD ^{1,2,3,4,5,6,7}  Valentin Goutaudier, MD MSc ^{8,9,10,11} Alessia Giarraputo, PhD ^{6,7,12} Fariza Mezzine, MSc ⁸ Erwan Morgand, PhD ⁸ Blaise Robin, MSc ⁸ et al. [Show more](#)

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Physiological

nature communications 

Article <https://doi.org/10.1038/s41467-023-38466-x>

Clinical and molecular correlation defines activity of physiological pathways in life-sustaining kidney xenotransplantation

Received: 20 December 2022
Accepted: 4 May 2023
Published online: 13 June 2023

Daniel J. Fel ^{1,2,3}, Grace Lassiter ^{4,5}, Takayuki Hirose ⁶, Robert Policastro ⁷, Ashley D'Amico ⁸, James F. Markmann ⁹, Tatsuo Kawai ^{10,11} & Katherine C. Hall ¹² 

www.kidney-international.org landmark communication

Physiologic homeostasis after pig-to-human kidney xenotransplantation 

see commentary on page 921

Eric Judd¹, Vineeta Kumar², Paige M. Porrett³, Kelly A. Hyndman⁴, Douglas J. Anderson⁵, Maggie E. Jones-Carr⁶, Andrew Shunk⁷, Daniel R. Epstein⁸, Huma Fatima⁹, Akemi Katsurada¹⁰, Ryosuke Satou¹¹, L. Gabriel Navar¹² and Jayme E. Locke¹³ 

Kidney International (2024) **105**, 971–979; <https://doi.org/10.1016/j.kint.2024.01.016>

Xenotransplantation - challenges



Immunological

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nature communications

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Check for updates

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landmark communication

Physiologic homeostasis after pig-to-human kidney xenotransplantation [Check for updates](#)

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Kidney International (2024) 105, 971–979; <https://doi.org/10.1016/j.kint.2024.01.016>

Infectious risk

CDC Centers for Disease Control and Prevention
CDC 24/7 Saving Lives. Protecting People.™

EMERGING INFECTIOUS DISEASES®

EID Journal · Volume 30 · Number 7 · July 2024 · Main Article

Volume 30, Number 7—July 2024
CME ACTIVITY - Perspective

Infectious Diseases and Clinical Xenotransplantation

Jay A. Fishman¹ and Nicolas J. Mueller
Author affiliations: Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA (J.A. Fishman); University Hospital Zurich, University of Zurich, Switzerland (N.J. Mueller)

ESOT Transplant International

published: 07 October 2024
doi: 10.3389/fcim.2024.13491

Monitoring for PERV Following Xenotransplantation

Joachim Denner¹
Institute of Virology, Free University Berlin, Berlin, Germany



Xenotransplantation - challenges



Ethical

Report • 1st March 1996

Animal-to-human transplants: the ethics of xenotransplantation

This report considers the ethical concerns raised by attempts to develop animal organs that can be transplanted into humans.



Immunological

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Kidney International (2024) **105**, 971–979; <https://doi.org/10.1016/j.kint.2024.01.016>

Infectious risk



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Monitoring for PERV Following Xenotransplantation

Joachim Denner¹
Institute of Virology, Free University Berlin, Berlin, Germany



Xenotransplantation - challenges



Ethical

Report • 1st March 1996

Animal-to-human transplants: the ethics of xenotransplantation

This report considers the ethical concerns raised by attempts to develop animal organs that can be transplanted into humans.



Infectious risk



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Joachim Denner^{*}
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Phase 1 trials likely to begin in the USA in 2025

Immunological

THE LANCET

ARTICLES • Volume 402, Issue 10408, P1158-1169, September 30, 2023 [Download Full Issue](#)

Immune response after pig-to-human kidney xenotransplantation: a multimodal phenotyping study

Prof Alexandre Loupy, MD PhD ^{1,2,3,4,5,6,7}✉ · Valentin Goutaudier, MD MSc ^{8,9,10,11} · Alessia Giarraputo, PhD ^{8,12} · Fariza Mezzine, MSc ⁸ · Erwan Morgand, PhD ⁸ · Blaise Robin, MSc ⁸ · et al. Show more



Physiological



Eric Judd¹, Vineeta Kumar¹, Paige M. Porrett², Kelly A. Hyndman¹, Douglas J. Anderson³, Maggie E. Jones-Carr¹, Andrew Shunk¹, Daniel R. Epstein¹, Huma Fatima⁴, Akemi Katsurada⁵, Ryousuke Satou¹, L. Gabriel Navar⁶ and Jayme E. Locke⁷

Kidney International (2024) 105, 971–979; <https://doi.org/10.1016/j.kint.2024.01.016>



COMMENT



<https://doi.org/10.1057/s41599-024-04126-7>

OPEN

Is Europe ready for xenotransplantation?

Matthias Kaiser^{1,2}, Penilla Gunther³, Ellen-Marie Forsberg², Vasiliki Mollaki^{4,5}, Espen Rimstad⁶ & Ana Marusic⁷

ISOU group will report at the end of January 2025

Themes:

- Legislation
- Regulatory
- Ethics
- Animal welfare
- Zoonoses – potential testing framework
- Research – qualitative, basic science



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Enable Inspiration
Transform the Treatment of Rare Disease
Expand the Availability of Transplantable Organs



- Potential location of designated pathogen free facility outside the US?
- Healthcare needs, cost

<https://www.unither.com/home>

<https://egenesisbio.com/>

[https://www.cimm.gen.vetmed.uni-](https://www.cimm.gen.vetmed.uni-muenchen.de/research/xenotransplantation/index.html)

[muenchen.de/research/xenotransplantation/index.html](https://www.cimm.gen.vetmed.uni-muenchen.de/research/xenotransplantation/index.html)



Consent/authorisation rates by Organ Donation Services Team

1 April 2019 – 31 March 2024

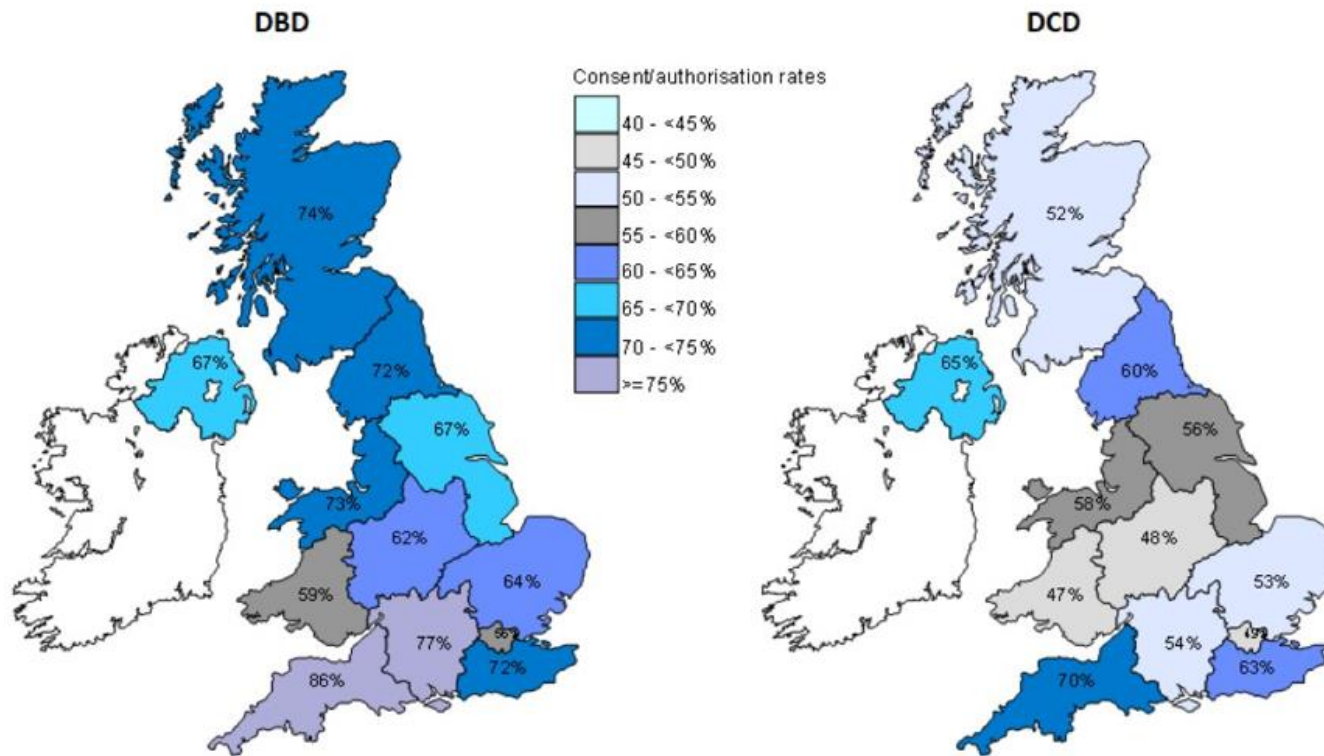
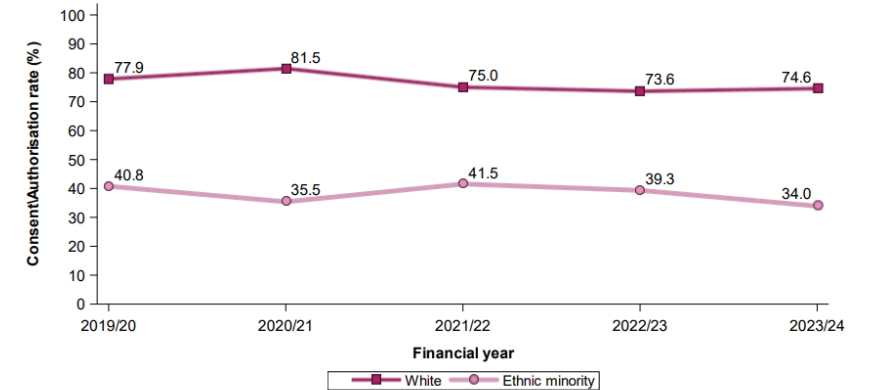
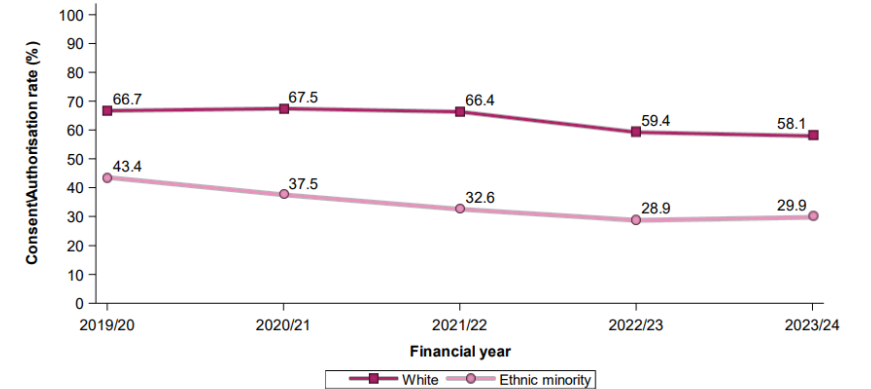


Figure 3.3 DBD consent/authorisation rates by ethnicity, 1 April 2019 - 31 March 2024



Rates should be interpreted with caution due to small numbers of ethnic minority patients' families approached

Figure 3.5 DCD consent/authorisation rates by ethnicity, 1 April 2019 - 31 March 2024



Rates should be interpreted with caution due to small numbers of ethnic minority patients' families approached

Diolch yn fawr

