# 2022 Annual Research Report

Central Northern Adelaide Renal and Transplantation Service (CNARTS)



Shaping the future of health with world-class care and world-class research



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This report is produced by Dr Richard Le Leu and A/Prof Shilpa Jesudason on behalf of CNARTS. Any queries about the content please contact Dr Rlchard Le Leu (richard.leleu@sa.gov.au)

# Welcome Message

We are delighted to present the 6th Annual Research Report from the Central Northern Adelaide Renal and Transplantation Service (CNARTS) at the Royal Adelaide Hospital, Central Adelaide Local Health Network.

Over the past year, our dedicated team of multidisciplinary researchers, consumers and scientists have continued to work tirelessly to advance knowledge and care for our patients.

CNARTS had a highly productive year in 2022, with exciting new projects and significant progress of existing studies. With the return of in person conferences and meetings we had opportunity to share our work across Australian and internationally, building strong collaborations and research networks.

In this report, we highlight the significant achievements of our team, through our laboratory studies, clinical trials, cohort studies and quality improvement initiatives.

We are proud to share this progress and our unit's accomplishments with our consumers and community, our research teams, organisation, external collaborators and funding supporters.

We thank every person engaged with CNARTS as we continue to strive towards research and clinical excellence to make positive impacts on the lives of our patients.

Finally – If there is a project of initiative you would like to learn more about, we would be delighted to connect with you and share our work further. Contact details can be found at the end of the report. We hope you enjoy reading this Annual Report.



A/Prof Shilpa Jesudason Chair of CNARTS Clinical Research Group



**Prof Randall Faull** Acting Head of Unit Renal

# **CNARTS - about us**

The Central Northern Adelaide Renal and Transplantation Service (CNARTS) is the largest renal unit in South Australia and the third largest renal unit in Australia, caring for over 1700 patients with kidney failure, and many thousands more at all stages of chronic kidney disease. CNARTS currently provides dialysis services to approximately 740 dialysis patients, including supporting 138 home dialysis patients (107 home peritoneal dialysis and 31 home haemodialysis). In 2020 CNARTS established a shared care program in haemodialysis with all metropolitan units now participating, with 41 patients currently participating in this program. CNARTS also provides supportive care to 170 patients and supports around 1000 existing transplant recipients and performs 65-80 transplants per year, including kidney, kidney-pancreas and islet cell transplants.

### **Mission statement**

CNARTS has a strong culture of research, developing pioneering ideas and advancing knowledge in crucial areas of kidney disease.

We aim to:



Improve the understanding of the science underpinning kidney disease and diabetes



Conduct translational research that is patient-centred and leads to improvements in treatments, outcomes and the patient experience



Advance the use of new technologies, methodologies and treatments for the benefit of kidney patients



Support and mentor staff and students to pursue research at all levels, building a highly skilled research workforce that will lead us into the future

# **Research Sponsors**

We are very grateful for the generous donors and fundraising organisations who support our research efforts. Without this support we would not be able to progress projects to improve the lives of people living with kidney disease.





The Hospital Research Foundation (THRF) Group fights against disease and illnesses by funding vital medical research and patient care services in our community.

https://www.hospitalresearch.com.au/

THRF Group are passionate about supporting world-class medical research to find cures and improve care for families here in Australia and around the world, as well as fighting to eliminate kidney disease and diabetes through world-class translational medical research.

THRF Group and Kidney, Transplant and Diabetes Research Australia (KTDRA, part of THRF Group), have been a long-time supporter of CNARTS and kidney, transplant and diabetes research by funding a number of CNARTS projects, including:

- Supporting the establishment of the state-of-the-art Biospherix Chamber in Adelaide to enable faster and safer Total Pancreatectomy with Islet Auto Transplantation (TP-IAT) procedures to cure people of debilitating pancreatitis. \$1,100,000
- Supporting women with kidney disease to overcome their challenges to become mothers.
   \$150,000
- Funding research investigating various diet recommendations to improve the overall gut health in kidney transplant recipients and prevent diarrhoea immediately after transplant.
   \$70,418
- Funding organ preservation to improve the quality of deceased donor organs. \$58,142
- Supporting research into the epidemiology of hereditary pancreatitis in South Australia.
   \$45,300
- Funding for a Central and Northern Adelaide Renal and Transplantation Service (CNARTS) Clinical database that will help us understand how we care for patients, the quality of care they get and their outcomes - we can then be sure that our care is world class, \$200,000

### Kidney, Transplant and Diabetes Research Australia and The Hospital Research Foundation (THRF) Group

The Kidney, Transplant and Diabetes Research Australia and The Hospital Research Foundation (THRF) Group provided a **\$1.4 million grant** to purchase a *Biospherix* Chamber that will be a game-changer for patients who require a unique medical procedure to alleviate excruciating pain.











### High tea fundraiser a sell out!

Link to News/Stories

Organiser Helena Kollias and her team raised **\$22,305** for KTDRA!

The MC Professor Toby Coates introduced Associate Professor Shilpa Jesudason, who spoke about the work being done in obstetric nephrology and how it helps women with kidney disease to have a family.

The guests heard from Adela, who lives with a chronic kidney disease. Adela gave an insight into her amazing journey and how this new research funded by The Hospital Research Foundation Group benefitted her personally.

A HUGE thank you to Helena Kollias, her magnificent team of volunteers and guests who came along to support KTDRA.





### Pia Lee - fundraising event at family restaurant, Seoul Sisters (total raised \$4,099)

Pia is a student at Concordia College, and part of her studies was to undertake a Personal Project.

Her father had a kidney transplant, and Pia wanted to do her project on KTDRA. She planned and organised the fundraising event which was held at her Dad's restaurant Seoul Sister - Hallifax Street.

The fundraising night included silent auction, music and Korean inspired finger food and drinks.



# Karren & John Hunt – held a Gatsby Dinner with friends (Bordertown SA)

Total amount raised \$4,750



Since 1981, the Royal Adelaide Hospital (RAH) Research Fund has been raising funds for life-saving medical research at the RAH.

https://www.rahresearchfund.com.au/

Current research projects supported by the RAH Research Fund include:

- Improving Management of Needle Distress during the Journey to Dialysis through Psychological EduCation and Training (The INJECT Study). \$50,000 (2020). Further to this grant, The INJECT Fundraising Campaign by the RAH Research Fund has raised over \$55,000.
- Gastrointestinal symptoms, dietary intake and changes in gut microbiome pre and post kidney transplant. \$30,000 (2020-21).
- Phenotypic and Genotypic Analysis of Hereditary Pancreatitis in South Australia. \$38,830 (2021-22).
- Improving the self-management for people with chronic kidney disease through a patient activation approach \$35,000 (2022-23).

# **Awards and Fellowships**



## The Centre for Clinical and Experimental Transplantation (CCET)

was awarded the *Minister's Research and Innovation award* at the 2022 SA Health Awards for their project 'Kidney and Islet Transplantation'. This award recognises those who demonstrate outstanding results in healthcare through research and innovation.

To learn more about Kidney and Islet Transplantation program watch the video - <u>https://youtu.be/511lss480jo</u>



### The INJECT Program

Managing Needle Fear in Haemodialysis Patients was a finalist in the *Minister's Research and Innovation award* at the 2022 SA Health Awards.

To learn more about the program watch the video - <u>https://youtu.be/QC7tWAmQR3A</u>



### **The AKction team**

The AKction team were awarded *The University of Adelaide award for Outstanding Achievement* in the category of Excellence in Research (Team).

The Aboriginal Kidney Care Together, Improving Outcomes Now is an innovative and unique research project that is improving kidney care for and with Aboriginal patients by privileging and acting on the voices of Aboriginal patient experts, their families and community members. Based within the Adelaide Nursing School, co-led by Dr Kim O'Donnell and Associate Professor Janet Kelly, AKction brings together patient experts, academics, healthcare professionals, peak bodies and key stakeholders to collaboratively co-design innovated and responsive models of kidney care within and across health and support services.

AKction set an example and a precedent for exceedingly high quality, culturally safe research.



### **INJECT study investigators**

Helping haemodialysis patients manage their fear of needles - Associate Prof Shilpa Jesudason and Gorjana Radisic on behalf of the INJECT study investigators were a finalist at the *World Class Care Quality & Improvement Showcase CALHN World-class Care Quality and Improvement Showcase 2022.* 

Award Winner! Young Investigator Award CLINICAL SCIENCE Georgina Irish



### **Dr Georgie Irish**

was the winner of the Young Investigator award in Clinical Sciences category at the Australian and New Zealand Society of Nephrology (ANZSN) conference for her presentation "Should I have a transplant? using flexible parametric models to predict survival after kidney transplant waitlisting".

Using the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, this project included Australian adults waitlisted for first kidney-only deceased donor transplants over 2007-2020. This project developed flexible parametric models for waitlist and post-transplant survival. Covariates were decided using backwards elimination and the baseline hazard function was modelled using cubic splines.

Dr Georgie Irish also won the 'Early Career Research Award' at the Transplant Society of Australia and New Zealand Annual Scientific Meeting.



### Mahdi Mohd Nor

won the People Choice award at Renal Society of Australasia conference in Darwin for his presentation 'Dying to talk: a clinical audit on uptake of advanced care directives (ACD) among patients with kidney disease'. This project examined ACD uptake among a high-risk population of renal patients and showed that ACD uptake remains poor.



### Dr Sam Bateman and Kelli Owen

won the People's Choice Award for best presentation at the IRNET National Aboriginal and Torres Strait Islander Health Research Showcase. Their presentation was called "The Survival Benefit of Kidney Transplantation for Aboriginal and Torres Strait Islander People". Sam and Kellie did a combined presentation of epidemiology, storytelling and interpretive dance.

# **Research Funding**

### **Clinical Research Group**

### \$200,000

### 2021-2022 Kidney, Transplant and Diabetes Research Australia (KTDRA) Project Grant

S Jesudason, P Clayton, R Le Leu

Central and Northern Adelaide Renal and Transplantation Service (CNARTS) Clinical Data Base Project.

This database 'future-proofs' CNARTS data management for years to come by greatly improving efficiencies and capabilities in data management for CNARTS busy clinicians and providing the flexibility to expand data collection along with service developments and evolving treatments.

### \$35,000

**2022 RAH Research Committee – Allied Health Clinical Research Grant** L Lunardi, A Britton, M Borlace, R Le Leu, A Xu, P Bennett, S Jesudason Improving self-management for people with chronic kidney disease through a patient activation approach.

### \$50,000

### 2022 Health Services Charitable Gifts Board (HSCGB)

S Jesudason, A Burke, K Collins, R Le Leu, K Hill, A Chur-Hansen, S McDonald

A Novel Program to Reduce Fear and Pain of Dialysis Needles.

### \$16,400

### 2022 Health Services Charitable Gifts Board (HSCGB)

J Zhang, P Bennett, A Xu, R Le Leu The clinical utility of post-haemodialysis blood glucose levels.

\$1,950,172

### 2021-25 NHMRC Ideas Grant

K O'Donnell, J Kelly, K Owen, R Tsetsakos, N Sinclair, S Bateman, J Lavoie Als: S Jesudason, R Le Leu, O Pearson, T Mackean, S McDonald, S Crail, E Garrard, M Arnold-Chamney, L Jamieson

AKction2: Aboriginal Kidney Care Together - Improving Outcomes Now

This project brings together Aboriginal kidney patients and families, health professionals, health services, academics and researchers improve the experiences and outcomes of kidney care for and with Aboriginal\* patients, families and community members and kidney health services in South Australia.

### \$593,970

#### 2021-24 Canadian Institutes of Health Research

C Bohm, P Bennett, G Castillo, B Corradetti, M Di Nella, S Jesudason, J MacRae, C McIntyre, J Penny, J Presseau, K Tennankore, S Thompson, N Verdi, K Wilund, B Waldvogel

Trial of Intradialytic Cycling Kidney Exercise Rehabilitation for Cardiac Stunning in Hemodialysis (TICKERS\_HD).

### **Centre for Clinical and Experimental Transplantation**

\$500,276	}	2020-2022 Commercial in Confidence (International) T Coates and C Drogemuller Intracutaneous Ectopic Pancreas (IEP) creation by seeding Human Stem Cell-derived Islets (HSCI) into integrated BTM.
\$20,000	}	2021-2022 Health Services Charitable Gifts Board (Australia) J Scaffidi, C Drogemuller and T Coates The Development of Chimeric Antigen Receptor(CAR) Regulatory T Cells as a Novel Therapy for Type 1 Diabetes.
\$380,000	}	2021-2023 The Juvenile Diabetes Research Foundation (International) T Coates and C Drogemuller Proof of concept trial of intracutaneous islet transplant. 2-SRA-2022-1086-M-B.
\$370,000	}	2021-2023 The Juvenile Diabetes Research Foundation (Australia) T Coates and C Drogemuller Proof of concept trial of intracutaneous islet transplant 2-SRA-2022-1096-M-B.
\$20,000	}	2022-2023 Research Collaboration Grant University of Wollongong (Australia) T Coates and C Drogemuller Pre-vascularised 3D printed constructs for pancreatic islet transfer and transplantation.
\$750,000	}	2022-2025 Targeted Translation Research Accelerator (TTRA) Program (Australia) S Grey, C Drogemuller and T Coates Restoring glucose control in T1D patients with genetically engineered GARV-AAV2-A20-islet cells – a first in Human safety and efficacy trial. TTRARP2097

### **\$2,014,561**

#### 2022-2027 The Medical Research Future Fund (MRFF)

T Coates, C Drogemuller, H Pleass, R Couper, J Chen, S De Sousa, S Khurana, L Palmer, Professor A Brown, N Rogers, D Torpy HEPATA: Hereditary Pancreatitis and AutoIslet Transplant Trials in Australia.

The aim of this project is to collect the evidence required for TP-IAT to become a reimbursed medical procedure for the treatment of hereditary pancreatitis (HP) (grant term 2022-2027). To achieve this, 24 HP patients will undergo TP-IAT and the impact on disease progression, quality of life, reduction in pain medication, hospitalisations, health costs and economic impacts will be determined. This will allow a formal application to the government for assessment of TP-IAT to become a reimbursed medical procedure.

### **ANZDATA, ANZOD and BEAT-CKD**

\$150,000

#### 2021-2022 The Hospital Research Foundation

S Jesudason, E Hewawasam, C Green, S McDonald The Kidney Mums Project: Advancing pregnancy planning and care for women with kidney disease

The Kidney Mums Project aims to transform the experiences and outcomes of women living with kidney disease who wish to achieve motherhood. The Kidney Mums toolkit will be developed to support women and their clinicians to navigate decisions about pregnancy and deliver best-practice care for positive maternal and foetal outcomes.

\$2,500,000

### 2021-2025 National Health and Medical Research Council – Centre of Research Excellence

A Tong, J Craig, C Hawley, G Wong, D Johnson, N Scholes-Robertson, S McDonald, K Howard, S Jesudason, A Teixera-Pinto

Partnering with patients with chronic kidney disease to transform care and outcomes (CRE-PACT)

The mission of this project is to transform the care and health of people with CKD by answering patient/caregiver-prioritised research questions and addressing outcomes that are critically important to patients.

### **Clinical Trials**

### \$2,904,210

#### 2022-2027 The Medical Research Future Fund (MRFF)

REMIT: An international, multi-centre, randomised clinical trial to compare Obinutuzumab + Calcineurin Inhibitor to Corticosteroid + Cyclophosphamide treatment regimens in Primary Membranous Nephropathy

C Au Peh, B Bose, D Johnson, V Jha, D Jayne, E Milanzi, M Griffith, J Wetzels, A Kronbichler, A Liew

Professor Chen Au and a team of 20 nephrologists from 12 countries, will receive \$2,904,210 (grant term 2022-2027) to fund an international clinical trial to compare treatment regimens in Primary Membranous Nephropathy, a rare kidney disease that causes leakage of protein in the urine and severe swelling of the body.

The REMIT trial will compare Obinutuzumab + Calcineurin Inhibitor to Corticosteroid + Cyclophosphamide treatment regimen in Primary Membranous Nephropathy Primary Membranous Nephropathy. Currently, treatment involves giving corticosteroid and cyclophosphamide. Unfortunately, this treatment has many undesirable side effects. Hence, we need to find better treatment with less side effects. This trial will compare new treatment comprising of obinutuzumab and calcineurin inhibitor to the old treatment.

# **Clinical Research Group**

- The Clinical Research Group (CRG) coordinates, fosters and provides oversight for all clinical research projects (not including clinical trials) within CNARTS.
- The CRG operates under the direction of the Executive Committee and is committed to enhancing research collaborations between various disciplines (medical, nursing and allied health) and facilitating sharing of knowledge and expertise, mentorship and guidance for researchers at all stages of their career.
- The CRG is currently pursuing mixed methodology research across a range of patientcentred themes, with the goal of evidence-based change to clinical practice and improvement of clinical care.
- The CRG Executive provides governance for CNARTS on all research projects using CNARTS patients and/or data.
- Monthly meetings via Zoom alternating Monday and Wednesday (chaired by Dr Richard Le Leu) to discuss and share current clinical research within CNARTS.

### **Vision Statement**

To embed a culture of research into daily clinical practice within CNARTS

### **Executive Committee**

A/Prof Shilpa Jesudason (Chair of CRG),Dr Richard Le Leu (CRG Research Co-ordinator),Prof Randall Faull, Tiffany Whittington,A/Prof Phil Clayton, Dr Michael Collins andAnthony Meade

### Project Staff in 2022:

Dr Richard Le Leu (Clinical Research Co-ordinator) Ms Gorjana Radisic (Research Officer) Ms Samantha Welke (Project Officer)



### **CRG Projects For 2022**

# Improving Management of Needle Distress during the Journey to Dialysis through Psychological EduCation and Training (The INJECT Study)



Lead - A/Prof Shilpa Jesudason

**Team** - G Radisic, R Le Leu, F Donnelly, K Hill, A Burke, K Collins, A Chur-Hansen, B Tan, S Muthuramalingam, L Macauley, S McDonald

(Collaboration with the School of Psychology, University of Adelaide and Clinical Psychology, CALHN)

The INJECT program, developed by our multidisciplinary group is a multifaceted program that encompasses several studies:

- 1. A novel tool to measure needle fear in patients before and after they start dialysis Measuring Needle Fear (MNF) tool.
- 2. Dialysis Nurse education program best practice for trauma free cannulation and support of patients with needle fear.
- 3. A novel Cognitive Behaviour Therapy modules to empower patients to effectively selfmanage needle fear.
- Developing solutions for pain management inflicted by arteriovenous fistula (AVF) cannulation

   trialling a Buzzy device a non-invasive, non-pharmacologic alternative for pain management
   to injectable local anaesthetic in a small cohort of patients at CNARTS.

These studies have led to a significant knowledge gain regarding needle fear in dialysis and its management. We have devised, codesigned and developed new educational and patient support resources to address this problem within CNARTS and beyond. Our objective now is to translate research findings from the INJECT program into clinical practice within CNARTS and evaluate the use and effectiveness of the program. We plan to embed identification and active self-management of needle fear into routine care for dialysis patients.

The INJECT program was selected as a finalist for the SA Health Awards in 2022 in the category "Minister's Research and Innovation" which recognises the work that demonstrates outstanding results in healthcare through research and innovation.

### Funded by:

- The Health Services Charitable Gifts Board (HSCGB) (\$52,000)
- RAH Research Committee Clinical Project Grant (\$50,000)
- RAH Research Fund The INJECT campaign (\$52,000)

# Gastrointestinal symptoms (GI), dietary intake and changes in gut microbiome pre and post kidney transplant



#### Lead - Anthony Meade

**Team** - N Watson, R Le Leu, G Rogers (SAHMRI), J Choo, S Sims, P Clayton, T Coates, S Jesudason *(Collaboration with the Microbiome and Host Health Programme, SAHMRI)* 

Collaboration with the Microbionie and Host Health Frogramme, SA

This project investigated dietary intake and the frequency of GI symptoms and changes in the gut microbiome pre and post kidney

transplant. The results showed that diet did not alter between pre- and post-transplant. Overall, the diet quality was poor, with low fruit, vegetables, legumes and wholegrains intake at both pre- and post-transplant. Significant gut dysbiosis (a microbial imbalance or dysfunction) was observed post-transplant, with falls in butyrate-producing bacteria (which are friendly gut bacteria that produce a substance called butyrate) which helps maintain a healthy gut.



### Funded by:

- Allied Health, Pharmacy and Nursing RAH Research Committee (\$30,000)
- Kidney, Transplant and Diabetes Research Australia (KTDRA) (\$50,000)

## Fit, strong or active: What should we focus on to improve the lives of peritoneal dialysis (PD) patients?



Lead - Brett Tarca (PhD candidate)

**Team** - T Wycherley, P Bennett, A Meade, R Le Leu, S Jesudason, K Ferrar (*Collaboration with Allied Health and Human Performance, University of South Australia*)

This research study is exploring the modifiable physical factors that predict physical functioning for patients receiving peritoneal dialysis (PD). This 12-month longitudinal cohort study will assess physical activity levels /

sedentary behaviour, muscle strength and cardiorespiratory fitness as predictors of physical function at three time points (baseline, 6 months and 12 months) in PD patients. Data collection concluded in November 2022 with the final number of completed assessments at each timepoint as follows; Baseline (n=83), 6-month follow up (n=39), 12-month follow-up (n=28). A manuscript is currently being prepared with the results highlighting that all modifiable physical factors were related to physical function at baseline, however, cardiorespiratory fitness appears to be the strongest and most consistent factor associated with physical function.

## **Ecological Momentary Assessment to Explore Fatigue, Mood and Physical Activity Levels in People Receiving Peritoneal Dialysis**



Lead - Brett Tarca (PhD candidate)

**Team** - T Wycherley, S Jesudason, T Boyle, P Bennett, A Meade, R Le Leu, M Borlace, M Ovenden, K Ferrar (*Collaboration with Allied Health and Human Performance, University of South Australia*)

This research study is exploring the fluctuations and relationships between fatigue, mood and physical activity for people receiving peritoneal dialysis (PD). This 7-day intensive longitudinal will explore the within day and day to day experience that people experience through the use of mobile technology (ecological momentary assessment). Ecological momentary assessments allow for capturing of data in real-time and real environments with survey questions triggered at 5 times throughout each day. A study protocol has been published in Peritoneal Dialysis International (https://dx.doi.org/10.1177/0896860821992243.) Data collection concluded in November 2022 with 48 participants completing the protocol. A manuscript is currently being prepared with the results showing; 1) within-day fluctuations in fatigue that appear to be at their least severe in the mid-morning to early afternoon before progressively rising, peaking at bed

time, 2) higher fatigue level was associated with decreased energy and poorer mood, 3) higher amount of physical activity completed was associated with lower fatigue levels and improved mood and 4) high feasibility with the majority of participants finding the App and mobile phones easy to use with potential that this type of technology could help manage their condition. Preliminary feasibility and acceptability results were presented at the International Society for Peritoneal Dialysis Congress in Singapore (August 2022).



### Funded by:

• Allied Health Professional Collaborative Grants SA Health, The Hospital Research Foundation-UniSA (\$21,000)

### Aboriginal Kidney Care Together- Improving Outcomes Now - AKction2



**Co Leads** – Dr Kim O'Donnell & A/Prof Janet Kelly **Team** – K Owen, R Lester, N Sinclair, S Bateman, J Lavoie, I Williamson, J Kartinyeri, R Gadd, D Champion, S Champion, O Pearson, T Mackean, S Jesudason, S McDonald, M Arnold Chamney- Ujvari, R Le Leu, L Jamieson, K Herman, K Varcoe-Temple, A Cormick, T Stevenson, L Rix.

(Collaborations are being established with Community members, University of Adelaide, CNARTS services and sites, SAHMRI, ANZDATA, The National Indigenous

Kidney Transplantation Taskforce, Kidney Health Australia, Menzies School of Health Research NT, Beyond Content SA)

AKction2 is now in the third year of the five-year NHMRC funded project. We began 2022 by reviewing progress so far, and planning activities within each of the four sub studies: Indigenous Governance, Peer Support, Kidney Journeys and Cultural Safety. AKction utilises a decolonising participatory action research methodology with repeated cycles of Look and Listen, Think and Discuss, Take Action Together, and Review Effectiveness. Our research focus and activities are co-designed in collaboration with Aboriginal Community members and organisations, health and education services and other projects. This is a deliberate strategy to ensure that the research we undertake is responsive to need, impactful, avoids duplication and that the results, new approaches and processes, improved models of care and changes to 'usual practice' are embedded within services and locations. This helps to establish longevity and sustainability, and to ensure that what is learned will live on and be impactful beyond the five years of the AKction2 project.

In 2022 AKction Reference team members, Chief Investigators, Associate Investigators and research team worked closely with Kidney Health Australia and CARI on the Recommendations for Culturally Safe Kidney Care for First Nations Australians. This included being part of the writing and reference groups, conducting consultations back with community members about the near final draft of the guidelines, co-designing and filming a video and co-facilitating the community focused launch of the recommendations at Kanggawodli. AKction Reference team members / experienced kidney warriors co-presented the launch at the 2022 Australian and New Zealand Society of Nephrology Annual Scientific meeting (ANZSNASM) in Sydney and at Kanggawodli.

#### https://www.croakey.org/holding-that-space-game-changing-kidney-project-has-researchactivism-at-its-core/

AKction Reference Team and research team members also attended a number of national conferences, presenting keynote and oral papers and posters. The teams concluded the year by winning the University of Adelaide Award for outstanding Achievement in the category of Excellence in Research (Team).

#### Funded by:

• AKction 2 is funded by: NHMRC Ideas Grant (\$1,950,172)

# Improving the self-management for people with chronic kidney disease through a patient activation approach



Lead – Laura Lunardi (PhD candidate)

Team – R Le Leu, S Jesudason, A Xu, L Matricciani, P Bennett

This study aims to measure the patients' level of knowledge, skill, and confidence using a patient activation survey in patients with chronic kidney disease (CKD) stage 5 not receiving dialysis and examine the potential association between patient activation level and patient demographic and clinical characteristics, adherence to treatment and health care utilisation in CNARTS. A total of 204

patients were recruited. This study showed that only a small proportion of patients with CKD have the knowledge, skills and confidence (patient activation) to self-manage their chronic condition. This study will serve as a platform for developing further studies to investigate components that work to increase patient engagement in positive health behaviours for an active role to self-manage their CKD.

### Funded by:

• 2022 Allied Health, Pharmacy and Nursing RAH Research Committee (\$35,000)

### Implementing Pathways for Integrated Tertiary and Primary Care of Advanced Chronic Kidney Disease (CKD)



Lead – A/Prof Shilpa Jesudason

**Team** – S Welke, R Faull, R Le Leu, T Whittington, C Bollen, A Kellie, A Britton, F Donnelly, S McDonald, J Yeoh

This CRIPS project undertook extensive qualitative research to: (1) Understand and define the healthcare experience for patients commencing chronic dialysis, particularly regarding the interface between primary-tertiary healthcare. (2) Develop, implement and evaluate strategies to improve primary

care integration and support for patients commencing dialysis treatments.

In co-design with key stakeholders, this project applied the research findings to develop and implement specific system-level initiatives for improved tertiary - primary care integration and individualised patient education and support for consumers approaching end stage kidney failure, including:

- monitored GP email address: health.cnartsadmin@sa.gov.au
- web site redevelopment
- renal specific discharge summary
- new service brochure
- inpatient 'update GP contact details' signage
- Health Pathways SA Nephrology page: online GP resource: <u>https://southaustraliaproject.healthpathwayscommunity.org/</u>
- Preparing for Dialysis Toolkit Patient and GP resources; includes GP escalation of care/ED avoidance plan
- Patient Reported Experience Measure (PREMs) survey: post dialysis commencement

### Funded by:

• CALHN CEO Clinical Rapid Implementation Project Scheme (CRIPS) (\$200,000)

# Improving the therapeutic use of vancomycin in patients undergoing dialysis treatment



Lead - Dr Lachlan McMichael

**Team** - L Paradiso, R Le Leu, M Ward, D Foster, J Latte, H Tran, S Jesudason, S Jahan, R Faull, S Reuter Lange

(Collaboration with School of Pharmacy & Medical Sciences, University of South Australia)

This project will determine the pharmacokinetics of vancomycin in patients receiving maintenance haemodialysis treatment to guide optimal and safe

administration of vancomycin in the treatment of serious gram-positive bacterial infections. Two cohorts will be examined: a prospective sampled cohort and a historical retrospective cohort. Currently the prospective cohort has recruited 8 patients with a target recruitment of 15 patients. The retrospective review of patients that received vancomycin during dialysis (2015-2019) has identified 225 patients, and details of vancomycin dosing, including date/time of administration, dose, infusion duration and indication are being examined.

### Funded by:

• Allied Health Research Collaboration grant (\$22,000).

### Benefits and Burdens of Kidney Transplantation for First Nations Australians



Lead - Dr Sam Bateman (PhD Candidate)

Team - S Jesudason (Principal Supervisor), O Pearson, P Clayton, S McDonald

Sam is progressing well through her PhD investigating models of care for Aboriginal and Torres Strait Islander people living with kidney disease. In 2022, Sam had a focus on research translation with the publication and launch of the CARI Recommendations for Culturally Safe Clinical Kidney Care For First Nations Australians and the publication of "Real Ways of

Working Together: co-creating meaningful Aboriginal community consultations to advance kidney care." Sam is currently working with other CNARTS staff and collaborators from the NT on a co-created and coordinated Peer Navigator program to support First Nations people on their journeys through chronic kidney disease and work towards decolonising mainstream health systems. Sam has taken on roles of convenor of the ANZDATA Aboriginal and Torres Strait Islander Working Group and contributor to the South Australian Chronic Disease Diabetes Leadership Group. She continues to work under the guidance and governance of the AKction research and reference teams and deeply values and respects the impact they have on her work and her professional and personal growth.

### Funded by:

- NHMRC post-graduate scholarship
- RACP Jacquot Award for Excellence Research Entry
- BEAT-CKD post-graduate scholarship

### **Decision Making in Deceased Donor Kidney Transplant Offers**



Lead - Dr Alison Weightman (PhD Candidate)

**Team** - P Clayton (Principal Supervisor), S Coglan, S Moodie, M Ladhani, D Stephenson

This is a qualitative research project investigating the processes and opinions of stakeholders in decision making at the time of deceased donor kidney transplant offers. The project is being led by Dr Alison Weightman and forms part of her PhD. Interviews are being conducted with multiple

different groups including transplant nephrologists, non-transplant nephrologists, new transplant patients and patients on the transplant waiting list. The aim of the project is to gain a greater understanding of the information exchange and decision-making procedures occurring when a deceased donor kidney transplant is offered to a recipient, as well as the priorities of all participants in this process.

#### Funded by:

University of Adelaide Research Training Program Stipend

## Descriptive overview of deaths from withdrawal after renal transplantation progress



Lead – Dr Sadia Jahan

Team - P Clayton

This retrospective audit investigated the causes of withdrawal from kidney transplantation and investigated the patient characteristics within this patient group. Data analysis is currently underway.

## The impact of point of care ultrasound (POCUS) training on dialysis access assessment and cannula placement



Nurses in Country Health undergoing POCUS training

Lead – Prof Stephen McDonald Team - A Biddle, J Childs, K Hill (Collaboration with School of Nursing, University of South Australia)

The project aim was to examine the impact of POCUS provision and education for nursing staff on confidence in cannulation and to understand the patient experience at three regional hospital haemodialysis units in South Australia. Funding received from The Hospital Research Foundation provided a POCUS machine and dedicated nursing education at each of the three sites. A pre-

test post-test model was used to assess the individual nurses perceived competency before and after the delivery of a series of online modules and face to face training. Patient reported outcome measures (PROMs) were also collected to understand the use of POCUS from the client perspective. The online education modules provided the basic principles for the use of POCUS, while the face-to-face training highlighted POCUS's relevance to clinical practice. The nursing surveys showed a statistically significant improvement in staff understanding and confidence in using and interpreting POCUS images to assess a haemodialysis vascular access and attempt cannulation following the training. The PROMs result overall supported the ease and use of POCUS for haemodialysis cannulation. POCUS has the potential to be a valuable tool in regional haemodialysis units to support vascular access canulation and potentially avoid metropolitan transfer due to cannulation difficulties.

### Funded by:

• Health Network - Regional Health Local Network Research Grant (\$43,405)

Open-ended responses of renal nurses in an online survey regarding nurse re-education for managing needle fear and distress during cannulation and dialysis



Lead – Sumaya Abdinoor (Psychology Honours student) Team - A Chur-Hansen (Principal supervisor), G Radisic, S Jesudason (Collaboration with the School of Psychology, University of Adelaide)

This study used qualitative research methods to explore the abilities and strategies implemented by renal nurses when recognising and supporting the fears and distress caused by needling during cannulation as well as

the thinking styles utilised by both nurses and patients. Following an online nurse education program, open-ended survey data was collected from 134 South Australian renal nurses with varying roles and experiences. The data was analysed through the lens of a competency based theoretical framework and prominent codes were identified using qualitative content analysis. Findings provide valuable insight into the ability of nurses in confidently discussing and supporting patients in utilising self-management psychological strategies as well as their own anxiety in relation to cannulation and dialysis. Recommendations for refresher courses are suggested. Findings are transferable in other health settings.

### Audit of fluid and hypotension post transplantation



Lead – Dr Karthik Venkataraman

Team - T Coates

This audit investigated rates of hypotension post transplantation, along with associated fluid therapy administered and rates of complications such as delayed graft function and wound complications within CNARTS kidney transplant patients over 12 months. Key findings showed that 59 of 93

patients with either delayed graft function or slow graft function. Urine output was also lower in hypotensive patients in first 24hr post-op.

## Assessment of the impact of immediate, slow and delayed graft function on graft outcomes

Lead – Dr Karthik Venkataraman

Team - M Collins, G Irish, P Clayton

This study assessed the long-term graft outcomes that are predicted by the state of the graft in the immediate post-transplant period. Using data from the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, we included 17,579 adult kidney-only transplant recipients from 2001 to 2021 (5904 living donor [LD], 9316 donation after brain death (DBD) and 2359 donation after circulatory death). Both slow graft function and delayed graft function were associated with worse graft survival in both LD and DBD recipients, and worse PS in LD recipients. It was concluded that SGF represents a less severe phenotype of poor kidney function post-transplant than DGF, but is independently associated with worse graft outcomes and patient survival in LD and DBD recipients. Interventions aimed at preventing SGF have the potential to improve patient outcomes.

### TREX1 gene mutation and its role in vasculopathy



Lead – Dr Sadia Jahan Team – C Bonner, T Coates

Endothelial progenitor cells are being analyzed from the siblings identified with the TREX-1 mutation. To further investigate vascular dysfunction associated with TREX1 mutations, we performed capillaroscopy (a diagnostic technique which evaluates small vessels of the microcirculation in the nailfold) which showed unusual loop apex, microbleeds, capillary drop

out and dilated capillaries. International collaborations are also underway to investigate potential areas of therapeutic target.

### Use of Local Anaesthetic during Arteriovenous Fistula Cannulation in Patients Attending the Central and Northern Adelaide Transplantation and Renal Services: A Prevalence and Impact Study



Lead – Dr Bee Tan

**Team** – G Radisic, R Le Leu, F Donnelly, L Macauley, K Hill, A Burke, K Collins, A Chur-Hansen, E Duncanson, B Tan, S McDonald, S Jesudason

The project aims to screen for the prevalence and impact of LA use during the AVF cannulation in the patient population dialysed at four CNARTS sites: Royal Adelaide Hospital, Lyell McEwin Hospital, The Queen Elizabeth Hospital and Hampstead Dialysis Unit. A patient self-administered

questionnaire about their local anaesthetic experiences is given to patients to complete. Patients will be surveyed for their age, gender, history of diabetes, location of the dialysis unit, haemodialysis vintage, type of fistula, the length of time since and numbers of fistula creation, and pain intensity due to fistula cannulation. The first question is asking the patients if they use LA. If the answer is Yes to LA, the patients are then to answer additional questions starting with the route of LA administration, the effectiveness of LA, and rate the pain associated with LA administration. The last question is to ascertain their enthusiasm to consider using a noninvasive device than LA and record their name (if agreeable) to be able to follow them up in the future. Currently n=59 surveys have been collected from LMH and a few from Hampstead Dialysis Centre. Next step is to survey RAH and QEH sites.

### The clinical utility of post-haemodialysis blood glucose levels



Lead – Jing Zhang

Team – R Le Leu, A Xu, P Bennett

This study will explore the clinical utility of post-haemodialysis (HD) blood glucose levels (BGL) for people with diabetes receiving maintenance HD. Clinical utility refers to the likelihood that a test will, by prompting an intervention, result in an improved health outcome. The design will be a retrospective chart review from patients receiving HD at Queen Elizabeth

Hospital over a 12-week period. Specific questions to be explored include: What is the rate of post-HD BGLs that are out of normal serum range? What is the rate of post-HD BGLs that are clinically acted upon? What is the type of intervention and outcome of intervention? Is there an association between post-HD BGLS with clinical variables?

### Funded by:

• The Health Services Charitable Gifts Board (HSCGB) (\$16,400)

### What do people with kidney failure approaching dialysis start actually eat?



Lead – Kevin Lau Hei In (Dietetics Masters Student)

Team – R Le Leu, A Meade

This student's Masters project aimed to describe dietary patterns of people at dialysis entry and any change in diet or symptom burden after the initial 3 months of dialysis. This study was a sub-analysis of the Multidisciplinary Assessment at Dialysis Entry (MADE) study conducted with CNARTS patients. Adults with kidney failure were recruited at the

time of commencing dialysis (haemodialysis or peritoneal dialysis) and completed a series of assessments including Integrated Palliative Outcome Score - Renal (IPOS-renal) and a food frequency screener (FFS) at baseline and 3 months after commencing dialysis. At commencement of dialysis there was a significant symptom burden and dietary data showed low intakes of fruit, vegetables, wholegrains and legumes, all markers of overall diet quality. Despite significant improvements in kidney-disease-related symptoms at 3 months after commencement of dialysis there was no change in dietary intakes. Dietitian education at commencement of dialysis should focus on symptom improvement but needs to be followed up once stable on dialysis to improve diet

quality for people.

Kevin presented his findings to the CNARTS CRG and had an oral presentation at the 20th Congress of the International Society of Renal Nutrition and Metabolism, Guangzhou, China.



# Centre for Clinical and Experimental Transplantation (CCET)

The CNARTS laboratory is based at the new biomedical precinct within the University of Adelaide Health and Medical Sciences building. The laboratory has continued its excellence in training the next generation of scientists and clinicians, further enhancing its reputation for producing outstanding independent researchers. The laboratory was founded at the Queen Elizabeth Hospital by Prof Graeme Russ in 1986 and was the first dedicated transplantation immunology laboratory in Australia. Since then, the research interests of the CNARTS laboratory have broadened to include many aspects of kidney disease, diabetes and other diseases of the pancreas.

The laboratory is led by Prof Toby Coates and includes clinician scientists: A/Prof Chen Au Peh and A/Prof Shantanu Bhattacharjya. Chief Scientist A/Prof Chris Drogemuller is Head of the laboratory that includes a team of senior scientists, grant funded scientists, technical officers, PhD and Honours students. Many previous laboratory students have gone onto leadership roles in nephrology and transplantation from the CNARTS laboratory and become independent researchers in leading institutions all around the world. To date, the lab has had 3 prestigious CJ Martin fellowships awarded and a Rhodes Scholar.

### **Vision Statement**

To train the next generation of medical doctors and scientists in basic laboratory science for application to the causes and treatment of renal diseases and organ transplantation.

### Laboratory Staff (featured)

A/Prof Chris Drogemuller (Chief Scientist) Svjetlana Kireta (Senior Medical Scientist) Dr Plinio Hurtado (Senior Grant Funded Scientist) Julie Johnston (Technical Officer) Jodie Nitschke (Senior Grant Funded Scientist) Daniella Penko (Senior Grant funded Scientist) Dr Sebastian Stead (Grant Funded Project) Dr Griffith Perkins (Post-Doctoral Fellow)



### **Students**

Denghao Wu (PhD candidate) Alice Krige (PhD candidate) Brigette Clarke (PhD candidate) Jacqueline Scaffidi (PhD candidate) Bronwyn Dearman (PhD candidate) Nick Chai (PhD candidate) Dylan Barnett (PhD candidate) Jessica Lee (PhD candidate) James Besanko (Masters candidate) James Zuiani (Masters candidate) Annie Lim (Honours candidate)

### **Laboratory Research Projects**

# mTOR inhibitors boost the immune response of kidney transplant recipients to COVID-19 vaccination



**Researchers** – – G Perkins, M Tunbridge, C S Chai, T Salehi, S Kireta, J Johnston, C Drogemuller, P Hurtado, T Coates

Associate Researchers – P Hissaria, B Grubor-Bauk, S Barry, S Chadban

COVID-19 has highlighted the vulnerability of kidney transplant recipients (KTRs) to infectious diseases, and revealed significant impairment in immune response to vaccination associated with immunosuppression use. Novel

vaccination strategies to boost protective immunity, without compromising graft stability, are needed.

In this study, we comprehensively evaluated vaccine-induced T cell immunity in KTRs treated with mTORC1 inhibitors everolimus and rapamycin (sirolimus) during primary vaccination against COVID-19. While KTRs receiving standard immunosuppression responded poorly to vaccination, patients receiving rapamycin produced a T cell response that was greater than that of healthy controls. This response was characterised by high frequencies of highly functional, vaccine-specific T cells, displaying a 'healthy' effector profile and phenotype. In a multicenter, randomised, controlled trial based on these findings, immunosuppression modification with rapamycin prior to booster vaccination of KTRs was found to be safe and feasible, however did not demonstrate efficacy. Accordingly, while rapamycin treatment of mice boosted functional T cell memory to SARS-CoV-2 original-strain and Omicron-specific vaccines, the effect size was significantly greater when rapamycin was administered from the time of primary vaccination, rather than prior to booster dose. Our findings demonstrate, for the first time, a positive effect of rapamycin on vaccine-induced T cell immunity in humans, and provide evidence of the safety and feasibility of immunosuppression modification with rapamycin as an adjuvanting therapy to boost the primary vaccine response in KTRs.

### First in Human INCEPTR trial (INtraCutaneous, Ectopic Pancreas TRial)



**Researchers** – T Coates, C Drogemuller, D Penko, J Johnston, J Nitschke, S Kireta, C Etherton, A Rickard and CNARTS Clinical Trials unit

**Associate Researchers** – J Greenwood, M Wagstaff, D Torpy, B Clarke, T Kay, T Loudovaris, L Mariana

This project is supported by the Juvenile Diabetes Research Foundation International (New York) and

Australia, to develop an alternative extra hepatic site for islet transplantation. It is a collaboration with Prof John Greenwood (the inventor of the material) from the Burns Unit at the Royal Adelaide Hospital and has created a biomedical start-up company – Beta Cell Technology to develop this approach for the clinic.

In 2022, the proof of concept INCEPTR trial (INtraCutaneous, Ectopic Pancreas TRial) was registered and initiated. A first in human trial to investigate islet transplantation into the skin using a novel biodegradable scaffold. Patient 1 had the scaffold implanted into the skin on the inner bicep on the 6th of April followed by the islet transplant into the prepared skin site 29 days later on the 5th of May. In the 9 months following the islet transplant, the patient has experienced significant improvement in blood glucose control, a reduction in daily insulin requirements and remains c-peptide positive (an indication of islet function). This is the first-time islet function in the skin has been achieved and maintained for this length of time. Patient 2 was initiated in late 2022, receiving their scaffold implant, and is currently awaiting an islet transplant.

### Intracutaneous Ectopic Pancreas (IEP) creation by seeding Human Stem Cell-derived Islets (HSCI) into integrated BTM



**Researchers** -T Coates, C Drogemuller, J Nitschke, S Kireta, D Penko, J Johnston

Associated researchers – J Greenwood

This project is a long-standing collaboration between one of the largest international diabetes companies, Novo Nordisk, our islet transplant research team and Beta Cell Technologies. In 2022, we optimised the preclinical

nude rat model to reflect the human clinical intracutaneous transplant protocol. This model will be utilised to provide long-term safety and efficacy data to support a first in human stem cell derived intra-cutaneous (under the skin) islet transplant. The model involves suturing BTM into an elliptical wound created on the back of the rat which promotes tissue integration, for a 3-week period. Following integration, the wound site is folded on itself to create a 'Taco shell" shaped pocket into which stem cell derived islets will be transplanted. We will then determine the transplanted cells ability to rescue diabetes in the rats. The aim of this research is to generate sufficient pre-clinical data to support a first in human trial in the next 2 years.

### The Development of Chimeric Antigen Receptor (CAR) Regulatory T Cells as a Novel Therapy for Type 1 Diabetes



Researchers – J Scaffidi, T Sadlon, V Bandara, S Barry and T Coates

This project is investigating the ability to render regulatory T cells (Tregs) specific for a known autoantigen of type 1 diabetes (T1D) via chimeric antigen receptor (CAR) expression. We propose that these cells will be better able to suppress the autoimmune response that occurs in T1D.

During 2022, we screened our GAD65-specific CAR Tregs generated from

healthy donors for their function in vitro. This year, we aim to manufacture CAR T regs from T1D patient T regs as a proof of concept.

In 2022, Jacqui gave an oral presentation of this work at both the Australasian Diabetes Congress in Brisbane in addition to the Annual Scientific Meeting of the Australian and New Zealand Society for Immunology in Melbourne. She was also awarded a travel grant by JDRF for her conference travel.

### Development of new approaches to measure proteolysis and glycosylation profiling of high and low affinity corticosteroid-binding globulin (CBG) in septic shock using mass spectrometry



**Researchers** – J Lee, T Coates, E Meyer, D Torpy **Associated Researchers** - M Anderson, P Hoffman, P Mittal, C Young, P Hurtado, W Rankin

This project aims to measure different affinity forms and glycoforms of corticosteroid-binding globulin (CBG) in the setting of sepsis. CBG binds cortisol at a high affinity, and the CBG:cortisol binding affinity is reduced

reversibly by pyrexia and acidosis, and reduced irreversibly by neutrophil elastase cleavage at the reactive centre loop (RCL) of CBG, converting high affinity CBG to a low affinity form. These characteristics allow for optimisation of spatiotemporal distribution of free cortisol in the setting of sepsis. Previous research by E Meyer, D Torpy et al, has shown that reduced CBG is an independent predictor of ICU mortality in septic shock patients, highlighting the importance of CBG in septic shock survival.

We aim to further investigate the impact of relative abundance of different CBG affinity forms and glycoforms on septic shock outcome, and to measure these using mass spectrometry. We are collaborating with the proteomics team at UniSA and Macquarie University on this project. In 2022, we have successfully purified CBG from serum, allowing for adequate detection of CBG by mass spectrometry; we are in the process of further optimising the assay to optimise detection of peptides of interest.

This project is supported by HSCGB grants from the Royal Adelaide Hospital Endocrine Unit, and Margorie Hooper travel grant (RACP foundation) was awarded to J Lee to facilitate collaboration with Sydney.

# Adrenal cell transplantation for Addison's disease using biodegradable temporising matrix technology



**Researchers** – B Clarke (PhD candidate), S Kireta, P Hurtardo, T Coates, D Torpy

**Associated Researchers** – C Christou, J Greenwood, J Kollias, J Johnston, D Penko, J Nitschke, C Drogemuller, E Concannon

The aim of the project is to explore the use of adrenocortical cell transplantation as a novel approach to the treatment of primary adrenal insufficiency, specifically evaluating an intra-cutaneous site for cell

transplantation. There is a need to improve the outcomes for individuals with Addison's disease, as morbidity and mortality remain significantly increased compared to the general population, even with current gold standard medical therapy.

A pilot study of autologous adrenocortical cell transplantation into a cutaneous site using integrated biodegradable temporising matrix in a large animal model was completed during the course of 2021 and completed early 2022. Adrenocortical cell survival and proliferation at the transplant site was inconsistently demonstrated. Though these results hold some promise,

further development of this approach is necessary. Currently the project is focused on evaluating laboratory techniques to optimise primary cell culture yields of adrenocortical cells and development of a strategy to better characterise the cell isolate prior to transplantation.

This project has been undertaken in collaboration with Beta-Cell Technology and is supported by a Royal Adelaide Hospital Clinical Project Grant and HSCGB grants from the Royal Adelaide Hospital Endocrine Unit. Surgical equipment used in the large animal model was donated by Medtronic.

### Studying the role of cell-free DNA (cfDNA) in SLE pathogenesis



Researchers – P Hurtado, E Hurtado and C Peh

Lupus nephritis is a kidney disease caused by systemic lupus erythematosus (SLE). The presence of circulating antibody to self-DNA and an increased expression of type I interferon-regulated genes, termed IFN signature, play a central role in disease pathogenesis. The possible contribution of circulating small fragments of DNA released from dying cells, known as cell-free DNA (cfDNA), to disease pathogenesis is the focus of our

research. Our group has been studying the characteristics of cfDNA in SLE patients, particularly the ability of DNA to induce interferon. In addition, we aim to examine molecular patterns of SLEderived cfDNA in relation to disease activity. These studies will enhance our understanding of the pathogenic mechanism underlying SLE pathogenesis, which could in turn improve the way the disease is diagnosed, treated, and monitored.

### **Total Pancreatectomy and Islet Auto Transplantation (TPIAT)**



**Researchers** – T Coates, C Drogemuller, S Kireta, D Penko, J Johnston, J Nitschke, C Etherton, A Rickard, D Wu, G Perkins, C Russell

Associated researchers – D Torpy, S Khurana, J Chen, J Couper, R Couper, E L Neo

With the generous support of the hospital research foundation and the state government we have established a new clinical program for the

treatment of hereditary pancreatitis. The program involves removing a patient's own pancreas, thus removing the source of chronic pain and also removing the likelihood they will go on to develop pancreatic cancer in their 40-50's. Once the pancreas has been surgically removed it is processed to isolate the islets within, the cells responsible for secreting insulin and controlling our blood sugar levels. The islets are then transplanted back into the patient's liver where they will remain and secrete insulin in response to changing blood glucose levels. This transplant procedure will prevent the patient from becoming overtly diabetic and in some cases not requiring any exogenous insulin at all to control their blood sugar levels.





Excitingly, in 2022 we had a visit from the Governor, Her Excellency the Honourable Frances Adamson AC, to view the new facility and hear about the exciting work of CCET. In addition, we hosted several Lions Club Presidents to show them through the facility and thank them for the fund-raising support provided to purchase critical equipment housed within the Biospherix system.

In 2022, CCET was successful in applying for a Medical Research Future Fund (MRRF) grant to support ongoing clinical activity within the TPIAT program (Approx. \$2million over 5 years). The major goal of this project is to capture the data required in support of the TPIAT procedure becoming a government funded medical procedure available to all Australians living with this disease.

# Persufflation in an ovine model of kidney transplantation as a means of organ preservation



**Researchers** – T Coates, A Krige, C Russell, C Drogemuller, J Johnston **Associated Researchers** – L Palmer, K Pappas

This PhD project is investigating prolonged (24 hour) persufflation preservation (gaseous perfusion preservation) in a large animal model of kidney auto-transplantation as an alternative to static cold storage, in order to ameliorate ischaemia reperfusion injury. In addition, two forms of prolonged persufflation (anterograde and retrograde) will be assessed ex

vivo to investigate the most effective method of organ preservation prior to transplantation.

26 sheep kidney auto-transplants were performed between 2019 and 2021 of which the donor models included living donor (n=8), donation after brain death with static cold storage (n=6), donation after cardiac death (DCD) with static cold storage (n=4), DCD with anterograde persufflation (n=4) and DCD with retrograde persufflation (n=4). The transplanted kidneys were assessed for ischaemic damage and function with a urinary assay for Kidney Injury Molecule-1 (KIM-1), histology, inulin clearance testing and a novel imaging method of assessing glomerular filtration rate using MRI. Additionally, the potential deleterious effects of gaseous perfusion were assessed by way of myography on the intra-renal vessels, as well as immunohistochemistry.

Though sample numbers are small, the assessments of the intrarenal vessels are promising and suggest that the use of persufflation does not result in endothelial damage. Additionally, the function of the persufflated DCD kidneys was not inferior to those preserved with static cold storage (current standard of care). Larger numbers are likely needed to confirm the effects of persufflation on transplanted kidneys. Data analysis is ongoing.

### The Genetic Epidemiology of Hereditary Pancreatitis in South Australia



**Researchers** – D Wu, C Drogemuller, T Coates **Associated Researchers** – S De Sousa, D Adelson

Hereditary Pancreatitis (HP) is a debilitating condition caused by inheritance of a variety of genetic mutations. HP results in inflammation of the pancreas from a young age, chronic abdominal pain, and dependency upon pain management opioids. Severe cases of HP are candidates for total pancreatectomy and islet auto transplant (TP-IAT) surgical treatment. This

project is the first to identify Australian families suffering from HP and assess correlation between phenotypic disease outcome and genotypic variant. Patients with HP were identified from existing hospital records and interviewed for phenotype. Salivary biosamples were obtained from patients and family members to be whole-exome-sequenced (WES) and analysed in silico using bioinformatics toolkits (GATK).

A total of 21 pedigrees comprising 155 individuals were recruited for the project. Overall, 76% of HP presented with clinical onset before the age of 10. Ongoing opioid usage for pain management in the HP cohort was 55% and 64% of patients reported ongoing moderate to severe pain.

Strikingly, HP was 67 times more prevalent in Indigenous populations than non-Indigenous. Our estimated prevalence of HP is higher than previously described and disproportionately affect Indigenous populations. The percentage of HP patients requiring lifelong analgesics is alarming and genetic factors are an important cause of pancreatitis in Australian children. Bioinformatics analyses of WES genotypic data yielded three potentially pathogenic variants identified outside of known HP-associated gene: ECE1, GJA5, and SPTBN5. The study described the prevalence of HP in an Australian population for the first time, highlighted the importance of utilising genetic studies to guide medical decision-making in HP, and successfully established a patient database for candidates of TP-IAT treatment.

### The Development of a Tissue-Engineered Skin Substitute utilising a Biodegradable Polyurethane Scaffold in a Novel Bioreactor for the Treatment of Extensive, Full-Thickness Burns



Researchers – B Dearman, T Coates

Associated Researchers – J Greenwood, S Boyce

Conferring my degree in October 2022, the PhD project has advanced into a leading role as Principal Scientist for the Skin Engineering Laboratory, Royal Adelaide Hospital, with the vision to produce engineered skin for clinical use. During this candidature, five peer-reviewed papers were published. The final manuscript reported the long-term follow-up of the first-in-human use of the

two-stage strategy for large burns. This patient suffered 95% burns to his body. The NovoSorb biodegradable temporising matrix (BTM) was applied to 85% as the first stage, followed by his own laboratory-grown skin (Composite Cultured Skin-CCS). Translating this research from bench to bedside has been a highlight of my candidature and career thus far. Inset image of Dr Bronwyn Dearman with a burns survivor who is now four years post-burn, lives independently, drives a modified motor vehicle and enjoys gardening.

### Exploring the adjuvant effect of mTOR inhibitor on boosting vaccineinduced T cell responses in immunocompromised transplant patients



**Researchers** – N Chai (PhD candidate, Adelaide University), G Perkins, C Drogemuller, T Coates

The mammalian target of rapamycin (mTOR) is a metabolic integrator that regulates cell growth, proliferation, and autophagy/apoptosis. It plays an essential role in modulating immune cell activation, differentiation, and function. Previous preclinical studies have demonstrated that suppressing mTOR activity by its inhibitor, rapamycin, paradoxically

promotes the formation of antigen-specific memory T cells in the context of vaccination or viral infection in mouse models. However, recent human clinical trials have revealed that replacing immunosuppressive medication with rapamycin does not further improve both cellular and antibody responses to COVID-19 booster vaccination. Therefore, optimizing the use of rapamycin to maximize the immunostimulatory effect on T cell response without compromising other immune cell function needs to be addressed before applying it to humans.

In 2022, we investigated the effect of rapamycin on primary and booster vaccine responses. Peri-vaccination of rapamycin has shown an increase in the average magnitude and quality of vaccine-specific T cells in mice. The greater stimulatory effect was observed in mice commencing rapamycin prior to primary vaccination rather than during the booster phase. Interestingly, rapamycin was also associated with the induction of an antigen-responsive naïve cell population but highly expressed the SCA-1 marker, indicative of the stem-like memory T cell (Tscm) phenotype. This suggests that the inhibition of mTOR by rapamycin promotes the formation of Tscm.

Regarding to humoral response, mice administered with rapamycin indicated significantly higher titres of anti-SARS-CoV-2 spike RBD IgM but lower titres of RBD IgG following the first dose of vaccination. However, after repeat vaccination, no significant differences were observed in antibody titres between rapamycin-treated and untreated mice.

Our experiment results suggest that rapamycin has the potential to boost the immunological response to vaccination. The underlying mechanism by which rapamycin regulates B and T cell function will be further investigated in my ongoing PhD research in the CNARTS Renal Lab.

### The Molecular Analysis of Persufflated Ovine Kidneys – A Novel Means To Improve Kidney Transplant Function



**Researchers** – A Lim (MBBS/Honours Student, University of Adelaide), T Coates, C Drogemuller, A Krige, J Johnston

Kidney transplantation is the mainstay treatment for ESRD. With the current shortage in kidney organ availability, research has investigated the use of ECD and DCD kidneys. These suboptimal grafts are associated with poorer graft function. Given their susceptibility to warm-ischaemic, cold-ischaemic and ischaemic-reperfusion injuries, we explore other techniques of

preservation with the potential to protect, repair, regenerate and immunomodulate these kidney grafts. This study investigates oxygen persufflation as a preservation technique as compared to gold standard static cold storage using molecular analysis methods. Three experimental groups underwent 24 hours of kidney organ preservation in a warm-ischaemia-induced sheep animal model. Urine and biopsy samples from the transplanted kidneys were analysed in the various timepoints and analysis was run on urine samples to determine NGAL concentrations using ELISA. Biopsy samples were assayed using RT-PCR of 7 key injury molecular biomarkers: TIMP1, TLR2, TLR4, EGR1, TGFB1, EDN1 and HSPA2. TUNEL staining was performed using post-transplant biopsy samples to determine cellular apoptosis levels. We found that in general, PSF preservation technique is non-inferior as compared to gold standard SCS technique and has the potential to protect and repair ECD and DCD kidney grafts.

## **Characterisation of Pancreatic Organoids in hereditary pancreatitis and normal individuals**



**Researchers** – J Zuiani (Masters candidate, University of Adelaide), G Perkins, S Grey, C Drogemuller, T Coates

Hereditary pancreatitis (HP) is a chronic disease caused by a series of HP associated genetic mutations. This condition manifests in adolescence, leading to inflammation, severe abdominal pain, and the eventual development of pancreatic fibrosis, endocrine and exocrine insufficiency and a substantially increased risk of pancreatic cancer. There is currently a

lack of models to effectively study the disease, as the gene mutations involved lack sufficiently homologous animal counterparts. As such, this project aims to develop an organoid model to study hereditary pancreatitis.

This model will allow for investigation into the phenotypic differences and mechanisms of patient specific gene mutations through the use of both healthy control and patient derived organoids. This model will also aim to provide a platform for the development and testing of new potential HP treatments.



# Organ preservation and resuscitation by isothermic oxygenated machine perfusion in an ex-vivo porcine model



**Researchers** – D Barnett, J, Bastian, A, Kanhere, D Daniel, R Bhattacharjya, T Coates, S Bhattacharjya

There is a constant supply and demand mismatch in organ transplantation which prevents the ever-increasing number of Australians who would benefit from this life-saving treatment from receiving it in a timely fashion. As a result, clinicians are relying on more and more marginal organs that previously would

have been discarded without the ability to assess organ quality or predict likelihood of function following transplant.

Machine perfusion technologies offer the potential to both evaluate the quality of organs ex-vivo and potentially even resuscitate damaged organs prior to transplantation. Because of this there has been a significant interest in the investigation of normothermic machine preservation for this purpose. This technology however remains expensive and complicated resulting in limited uptake in clinical practice. In an effort to simply the process of machine perfusion we are investigating whether it is possible to remove temperature manipulation completely from the machine perfusion.

In the last 12 months our group has successfully trialled a proprietary machine perfusion rig using a porcine organ block and demonstrated organs continue to consume oxygen and demonstrate function over a preservation period of 5 hours at isothermia. We have also been able to modify a commercial dialysis machine using an oxygenated balanced electrolyte solution and blood to function as a surrogate to transplantation and investigate the impact of isothermic machine perfusion on subsequent ischaemia reperfusion injury. In order to run these experiments we have also perfected a method of en-bloc organ retrieval in a porcine model that explants the liver, small bowel, kidney and pancreas for ex-vivo testing. Each organ can subsequently be split so that each can be examined individually.

In the subsequent 12 months we will be assessing how well cells are able to maintain ATP currency during preservation at isothermia as well as examining their structural changes with light microscopy and comparing to similar preservation times with normothermic machine perfusion and static cold storage.

This project is gratefully supported financially by Kidney, Transplant & Diabetes Research Australia and could not be completed without the assistance from the staff at SAHMRI PIRL.

### **Evaluation of heart transplant transportation device in a pig model**



**Researchers** – J Besanki (Masters candidate, University of Adelaide), J Betrame, J Edwards, T Coates

Distances between heart transplant donor and recipients are limited by the ability to store and transport a heart out of the body effectively for an extended period of time. This project aims to evaluate a novel organ transplant device which is expected to be able to provide and maintain adequate oxygen concentration,

nutrients and effectively remove metabolic waste. The method of perfusion of this device is slow flow hypothermic celsior which is re circulated for 6 hours. Cold storage can only safely preserve DCD hearts for 4 hours. Currently we have completed five out of six recirculation studies, pilot transplant and 1st transplant with device which have been of modest success.

# ANZDATA, ANZOD and BEAT-CKD



The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) collects and reports the incidence, prevalence and outcome of dialysis treatment and kidney transplantation for patients with end stage kidney disease across Australia and New Zealand.

The mission of the registry is to improve the quality of care and outcomes for people with end stage kidney disease in Australia and New Zealand by:

- Collecting and analysing accurate and comprehensive data from all patients receiving long term dialysis or kidney transplantation in Australia and New Zealand,
- Producing and disseminating reports,
- Informing the development of practice, policy and health services,
- Working with stakeholders to improve the understanding of kidney disease and outcomes of treatment.

The ANZDATA Registry encourages and enables the highest quality of care for people in Australia and New Zealand with end stage kidney disease by providing information that is complete, accurate, clear, relevant, readily available and timely.

The Australia and New Zealand Organ Donation Registry (ANZOD), records and reports on organ donation within Australia and New Zealand. Donation following death results in transplantation which is an effective and well-established treatment that can restore health and quality of life to those patients suffering end stage organ failure, thereby saving lives. Data related to organ donation and transplantation activity is essential in identifying opportunities for improving care of donors, informing on quality of transplant organs and transplant recipient outcomes. The Registry reports monthly on this web site, the numbers of deceased organ donors and the number of recipients benefiting from donation. An annual report is also produced for download on health outcomes of donation and transplantation.

### **ANZDATA Research staff:**

Prof Stephen McDonald (Executive Officer): stephen@anzdata.org.au A/Prof Dr Phil Clayton (Deputy Executive Officer): phil@anzdata.org.au A/Prof Shilpa Jesudason (Investigator): shilpa.jesudason@sa.gov.au Ms Kylie Hurst (Registry Manager): kylie@anzdata.org.au Ms Kelly Marshall (Project Manager) : kelly@anzdata.org.au Dr Chris Davies (Lead Biostatistician): chris2@anzdata.org.au Ms Kathryn Dansie (Biostatistician): kathryn@anzdata.org.au Ms Feruza Kholmurodova (Biostatistician): feruza@anzdata.org.au Dr Erandi Hewawasam (Post-Doctoral Research Fellow): erandi@anzdata.org.au Dr Dominic Keuskamp (Post-Doctoral Research Fellow): dominic@anzdata.org.au Dr Shyam Muthuramalingam (Consumer Engagement Coordinator): shyam@anzdata.org.au Ms Jasmin Mazis (Patient Engagement Project Officer): jasmin@anzdata.org.au Ms Lavern Greenham (Clinical Research Coordinator: lavern@anzdata.org.au Ms Emily Duncanson (Research Officer & Registered Psychologist): emily@anzdata.org.au Ms Katie Cundale (NIKTT- Senior Project Officer) : katie@anzdata.org.au Ms Kelli Owen (NIKTT- Consumer Engagement Coordinator): kelli@anzdata.org.au Mr Isaac Brown (NIKTT- Junior Research Officer): Isaac@anzdata.org.au Dr Samantha Bateman (PhD candidate): Samantha.bateman@sa.gov.au Dr Georgina Irish (Epidemiology Fellow and PhD candidate): georgina@anzdata.org.au Dr Alison Weightman (PhD candidate): alison@anzdata.org.au

### **Current Projects**

# Pregnancy and parenthood in chronic kidney disease and dialysis and transplant patients

Lead – A/Prof Shilpa Jesudason

**Team** - Erandi Hewawasam, Nishanta Tangirala, Phil Clayton, Chris Davies, Stephen McDonald



**Parenthood advisory group members -** Jane Boag, Charmaine Green, Laura Heffernan, Brooke Huuskes, Carolina Maistry, Kelli Owen, Shyamsundar Muthuramalingam, Adela Tolic, Amber Williamson, Amanda Sluiter

The ANZDATA Parenthood research group (recently rebranded as Pregnancy Kidney Research Australia (PKRA)) led by A/Prof Shilpa Jesudason and Dr Erandi Hewawasam, conducts mixedmethods research into pregnancy with kidney disease.

### **Ongoing projects:**

- 1. Perinatal, ANZDATA, hospital data linkage study
  - Labour and delivery outcomes- Dr Nishanta Tangirala
  - Pregnancies women had before they subsequently started KRT- Dr Sadia Jahan
- 2. Chronic kidney disease and cardiac disease in pregnancy registry with Dr Jarrad Hopkins, Dr Prabha Andraweera, Dr Nishanta Tangirala, Dr Alessandra Orsillo, and Prof Margaret Arstall
- 3. Consumer perspectives of pregnancy education in women with kidney disease: a national survey with Dr Belinda Stallard and Dr Alessandra Orsillo
- 4. Kidney doctors' perspectives on the management of pregnancy in women with chronic kidney disease: an interview study with Dr Mel Wyld and Prof Allison Tong
- 5. Parenthood in people with kidney failure: evolution and evaluation of the parenthood data collection of the ANZDATA Registry with Dr Rhea Danner
- 6. Preeclampsia in pregnancies after kidney transplantation: determinants and impact on pregnancy and graft outcomes with Dr Joe Lu
- 7. Tasmanian CKD Linkage dataset study with access to information about kidney disease, perinatal outcomes, hospital admissions and pathology data- a collaboration with Prof Matthew Jose, Dr Laura Cuthbertson, Alex Kitsos and, Timothy Saunder
- 8. Parenthood experiences and perspectives of Indigenous women with CKD- a collaboration with "Aboriginal Kidney Care Together, Improving Outcomes Now" (AKCTION) Reference Team in SA

### Grant successes:

**The Women's & Children's Hospital Foundation Higher Degree by Research Medical Scholarship** was awarded to the project titled: "Can I have a baby? Complexities in decision making around pregnancy in Australian women with kidney disease" – Dr Nishanta Tangirala. Supervisors: A/Prof Shilpa Jesudason, Dr Erandi Hewawasam

**The Royal Hobart Hospital Research Foundation** grant was awarded to the project titled: "Motherhood with kidney disease: what's going to happen to me (and my baby)?"- Prof Matthew Jose (CI), A/Prof Shilpa Jesudason (AI).

### Consumer engagement activities:

We are very grateful for the contributions of members of the Parenthood Advisory Group to pregnancy in kidney disease research. In 2022, our consumers have been involved in

- Designing research studies
- Setting research priorities
- Developing data collection tools and consumer friendly visual summaries of research outputs

We have held three consumer advisory group meetings in 2022.

### **Fundraisers:**

- Fundraising campaign organised by Kidney, Transplant and Diabetes Research Australia (KTDRA) (raising ~\$25,000 for pregnancy and kidney disease research)- Mrs. Adela Tolic shared her lived experience and perspectives of being part of our consumer advisory group
- International Society of Nephrology Twitter live space activity click here and click here to watch the recording "Pregnancy Matters"



Zoom meeting between members of the parenthood advisory group

### Exploring patient travel to in-centre haemodialysis

### Lead – Prof Stephen McDonald

**Team** - Chris Davies, Kathryn Dansie, Emily Duncanson, Phil Clayton, Shilpa Jesudason, Shahid Ullah, Aarti Gulyani, Dominic Keuskamp

Using ANZDATA data and sophisticated geospatial models, we have performed analyses of travel time and distance between patients residential postcodes and dialysis units, to characterise the burden of travel for patients and identify where patients are treated geographically in Australia. Geospatial analysis is also being used to describe variation in KRT patient incidence across Australia and over the last two decades, with the aim of determining the emergence of hotspots of incidence.

### **Consumer involvement in research**

Lead – A/Prof Shilpa Jesudason and Prof Stephen McDonald

Team - Shyam Muthuramalingam, Jasmin Mazis, Emily Duncanson

**Better Evidence and Translation – Chronic Kidney Disease (BEAT-CKD)** which began as a collaborative research network aiming to improve the lives of people living with chronic kidney disease. The aim is to generate high-quality research evidence to help patients, health professionals, and policy makers make informed decisions about healthcare.

BEAT-CKD was initially established with funding from an NHMRC Program Grant (APP1092957) and supports four research and translation organisations across Australia: the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA), the Australasian Kidney Trials Network (AKTN), Caring for Australasians with Renal Impairment (CARI) guidelines group and Cochrane Kidney and Transplant (CKT). The objectives of BEAT-CKD are to:

- identify promising interventions which address health outcomes of high priority to patients, caregivers, health professionals and policy makers
- provide robust evidence about these interventions
- identify and evaluate strategies to deliver these interventions in diverse clinical settings

In 2021, BEAT-CKD researchers were awarded an NHMRC Centres of Research Excellence: Partnering with Patients with Chronic Kidney Disease to Transform Care and Outcomes (CRE-PACT; APP2007026). CRE-PACT will build upon the work of BEAT-CKD by working collaboratively with patients and caregivers across all stages of research in kidney disease. We will do this by focusing on three broad areas:

**Training** – for patients and researchers, to equip them with the knowledge, resources and skills required to work together effectively.

**Research** – to address the patient-prioritised evidence gaps and apply best-practice patientpartnership in all stages of research from conception, development and design of interventions through to dissemination and implementation.

**Partnership** – to communicate research findings and build national and international relationships that support the implementation of our project findings.(<u>http://beatckd.org/</u>)



Consumers and clinicians come together for the BEAT-CKD, CRE-PACT Launch event at SAHMRI (Kaurna Country)

### Consumer Views of Quality Indicator Reporting in Kidney Care – Qualitative Study

#### Lead – Prof Stephen McDonald

**Researchers** - Emily Duncanson, Nicholas Gray, Chris Davies, Shyamsundar Muthuramalingam, Effie Johns, Zoran Tasevski, Kate McColm, Matty Hempstalk

In 2022, researchers at ANZDATA conducted a qualitative study to explore the views and opinions of people with kidney disease, about quality indicator data of dialysis and transplant centres and ANZDATA's reporting of this information. These outcomes include centres' graft survival and dialysis patient survival rates, transplantation rates, and peritonitis infection rates. In this study, we wanted to find out if this information is important to patients to know, how it may impact their decision-making between kidney services or their experience of care and how we can improve reporting of ANZDATA data for consumers and the public. We also discussed with participants the benefits, potential risks and unintended impacts of public reporting of centre outcomes on patients.

Twenty-seven people with experience of kidney disease from all Australian states and territories participated in an online focus group between August and December. Analysis of focus group transcripts is currently underway, and the next step will be to share a summary of the findings with the participants to get their feedback. The results will then be prepared in a manuscript for publication to a scientific journal and shared with the kidney community.

The investigator team on this study includes consumers, kidney doctors and researchers – consumer partners have so far reviewed the study protocol, the focus group question guide, participated in a pilot focus group and reviewed the study findings and will help to inform the next steps for this work.

### **Data linkage**

### Lead – Prof Stephen McDonald

Researchers - Chris Davies, Kathryn Dansie, Dominic Keuskamp, Phil Clayton

- National Joint Replacement Registry Analysis has started on a large national linked data set between the Australian Orthopaedic Association National Joint Replacement Registry (AOA NJRR) and ANZDATA, examining joint replacements in the treated kidney failure cohort for the period 2003-2016. Early analyses have determined that Australian KRT patients experience higher rates of hip replacement than the non-KRT population, particularly for the diagnosis of osteonecrosis. There is however no difference in the rate of revision surgery between dialysis, transplant and the non KRT population.
- **Cardiothoracic Surgery Registry** –In 2022, a national linked dataset was created between ANZDATA and the Australian and New Zealand Society of Cardiac & Thoracic Surgeons Database (ANZSCTS), which collects data on the majority of cardiothoracic surgical procedures. Key research aims include quantifying (1) the risk of developing end-stage kidney disease (treated with KRT) after cardiac surgery, and (2) the risks of cardiac surgery for KRT patients. Early analyses have determined that Australian KRT patients experienced higher rates of cardiothoracic surgery and worse post-surgical outcomes than the non-KRT population, consistent across most surgical indications. Further analyses will look at the risk of developing treated kidney failure after cardiac surgery.

- Intensive Care Registry In 2022 a national linked dataset was created between ANZDATA and the Australian & New Zealand Intensive Care Society Adult Patient Database, which collects data from over 90% of ICUs. Key research aims include quantifying the incidence, cause and duration of ICU admission for KRT patients. Early analyses have determined that Australian KRT patients experienced higher rates of ICU admission than the non-KRT population, particularly for non-surgical diagnoses. Further analyses will look at quantifying the duration and outcome of ICU admission for KRT patients.
- Intensive Care Units Early in 2023 a linked dataset will be created between ANZDATA, South Australian and Northern Territory Intensive Care Units, inpatient hospitalisation and deaths data. This dataset will look at longer term outcomes of ICU admission and enable quantification of the risk for any critical care patient of developing kidney failure (treated with KRT)
- Sharesource (Baxter) APD The Baxter "Claria" APD device (introduced from late 2018) collects individual treatment characteristics for each session into a database "Sharesource". The Sharesource data has been linked to ANZDATA, negotiating international regulatory and legal hurdles. This enabled for the first time, real-world data about actual events during APD to be examined. Initial analyses showed that patient practices differ on weekends vs weekdays; presumably driven by social factors. Ultrafiltration varies with age, diabetes and time on dialysis among other factors. Understanding these factors and linking them to outcomes will help to provide accurate advice to patients and improve PD experience.

### Symptom Monitoring WIth Feedback Trial (SWIFT) -Patient reported outcome measures (PROMS) in Australia & New Zealand kidney dialysis units and the ANZDATA Registry

Lead – Prof Rachael Morton (Chief Investigator-University of Sydney)

**Researchers** - Lavern Greenham, Paul Bennett, Shilpa Jesudason, Stephen McDonald (Clinical Lead

The Symptom monitoring WIth Feedback Trial (SWIFT) is a novel two-arm cluster randomised trial testing the hypothesis that symptom monitoring using the IPOS-Renal questionnaire with feedback to clinicians and patients, improves the quality of life and overall survival for patients receiving haemodialysis. This trial is conducted in collaboration with the ANZDATA registry in Adelaide and the NHMRC Clinical Trials Centre, University of Sydney.

SWIFT has recruited over 850 participants in 31 units across New South Wales, Queensland and South Australia. 11 units have now completed the trial (Lismore Base Hospital, Gosford Hospital and Hunter New England Health Service).

### Our new units include:

- NSW: Sydney Adventist Hospital
- QLD: Cairns Hospital Satellites (Innisfail Hospital and Smithfield Dialysis unit), Bundaberg Hospital, Sunshine Coast University Hospital, Caloundra Public Hospital, Nambour Hospital and Gympie Satellite
- SA: Royal Adelaide Hospital, Queen Elizabeth Hospital, Hampstead Dialysis Unit

We are currently working through feasibility in Victoria and hoping to commence start-up in the coming weeks. We will continue to work through the start-up of the remaining units in NSW, QLD and SA. The clinician-focused sub-study has commenced with Dr Matthew Anderson and Mr Sam Herzog (SWIFT research assistant) having conducted 12 qualitative interviews with clinicians at a number of participating SWIFT units. This qualitative interview study aims to understand the usual practices for symptom monitoring and management for adults managed on haemodialysis and will be conducted in parallel with the randomised trial. The SWIFT Team would like to acknowledge and thank all those involved in the trial thus far including participants, clinical staff, and research support.



Some members of SWIFT SA and Royal Adelaide Hospital teams at the on-site initiation meeting



SWIFT Investigator meeting held at the ANZSN ASM on 18th October 2022, at Sydney.

# Improving impact and outcomes of ANZDATA hospital-specific performance reports

Lead - Prof Stephen McDonald

Researchers - Chris Davies, Erandi Hewawasam, Matthew Sypek, Phil Clayton

This project aims to improve the hospital-specific performance reports ANZDATA produces each year, including the statistical methods used to compare performance of Australian and New Zealand dialysis and kidney transplant centres. Changes have already been made to these methods to provide more accurate estimates of relative performance based on a new definition of the number of expected events, and also to control false discovery rates due to multiple comparisons made between centres. Further research is exploring Bayesian and cumulative sum methods, and a survey is planned to assess stakeholder comprehension of reports.

In 2020, we conducted a Heads of Units survey aimed to identify characteristics at centre level that would help the registry in its roles- in particular safety and quality assurance and health service planning. In 2021, a special report on this survey was released, covering the results on a variety of areas including staffing, resources and clinical practice. As expected, a lot of variation was observed with centre characteristics. The survey has been updated and has been disseminated to parent renal units along with the 2021 end-of-year ANZDATA survey. Data collection is ongoing for the project and the updated report will be published in 2023.

# Markov Modelling of prevalent dialysis and kidney transplant patient populations

Lead - Prof Stephen McDonald

Researchers - Chris Davies, Dominic Keuskamp

Dialysis requires dedicated and costly specialised facilities with a large impact on patients' quality of life. Predicting future prevalence and thus demand for services is essential for estimating patient burden and effective management of health care resources. The Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry has developed Markov models to predict dialysis prevalence for the years 2021-2030, based on the data reported to ANZDATA for 2011-2020. The models are built on probabilities for transition between four mutually exclusive states (HD, PD, Functioning Transplant and Death).

### **National Indigenous Kidney Transplantation Taskforce**

#### Lead - Prof Stephen McDonald

**Researchers** - Kelli Owen, Shilpa Jesudason, Jaqui Hughes, Kim O'Donnell, Janet Kelly, , Rhanee Tsetsakos, Nari Sinclair, Samantha Bateman, J Lavoie, Kate Tyrell, Neil Wilkshire, Cedrina Algy, David Crocker, Lachlan Ross, Amy Graham, Heather Hall, Peter Henwood

The National Indigenous Kidney Transplantation Taskforce (NIKTT), established by the Commonwealth to improve access to, and outcomes of, kidney transplantation for Aboriginal and Torres Strait Islander Australians, has created an extensive national network of consumers, clinicians, researchers, and advocates. Projects funded by the NIKTT have found that: outreach assessment clinics to remote parts of Western Australia are exceptionally helpful in ensuring patients have access to workup and subsequent waitlisting; Aboriginal-led education sessions are useful to help both consumers and clinicians understand the unique complexity of transplantation for Aboriginal and Torres Strait Islander peoples with kidney failure; and Patient Navigator programs – where Aboriginal and Torres Strait Islander peoples with lived experience of kidney disease and transplantation help guide other patients through the complicated pathways to care and transplant – are highly valued and effective for patient groups around the country. An extension of this Patient Navigator work was awarded a \$1 million MRFF grant this year, and is led by the NIKTT's Kelli Owen, alongside an innovative model of Investigators that includes the Patient Navigators themselves working with nephrologists and nurses.



NIKTT Gathering in Adelaide in December 2022



IRNet National Aboriginal and Torres Strait Islander Health Research Showcase - Sam Bateman and Kelli Owen won the People's choice award.



Kelli Owen with Hon Linda Burney MP (Minister for Indigenous Australians) at the Straight Talk conference in Canberra <u>https://www.abc.net.au/</u> <u>news/2022-08-19/aboriginal-womencanberra-oxfam-summit-advocatechange-politics/101350438</u>

### **Decision making in Kidney Transplantation**



**Lead** – Dr Georgina Irish (PhD Candidate) **Researchers** - Phil Clayton (Principal supervisor), Toby Coates, Jolyn Hersch

Kidney transplantation is a life-saving treatment for most people with end-stage kidney disease. For some people, however, it causes more harm than good. This PhD project aims to clarify which individuals will benefit from transplantation by personalising information on predicting potential outcomes after transplantation. We will use this to develop a decision tool to

help doctors and patients make these challenging and irreversible decisions. This will maximise the benefits from this precious resource.



### Project: Living kidney donor scores, paired kidney exchange \* Also with Lachie McMichael

We have explored the impact that donor factors have on recipient outcomes in both the Australian and New Zealand and the United States of America to determine whether transplant clinicians should use donor scores (like the LKDPI) to decide if people should enter the paired kidney exchange program. This work has now been published.

Irish GL, McMichael LC, Kadatz M, Boudville N, Campbell S, Chadban S, et al. The living kidney donor profile index fails to discriminate allograft survival: implications for its use in kidney paired donation programs. American Journal of Transplantation. 2022; https://doi.org/10.1016/j. ajt.2022.10.001.

### Project: Temporal validation of the Australian Estimated Post Transplant Survival Score.

The Australian EPTS (EPTS-AU) was developed by re-fitting the US EPTS, without diabetes, to the Australian/NZ deceased donor transplant population over 2002-2013. Since 2018 this score has been reported with all Australian Allocations. We validated this score on a contemporary population to see how it has performed since it was created. This has been submitted to the Nephrology Journal and is undergoing revisions.

## Project: Do decision aids help people who are facing decisions about solid organ transplantation? A systematic review

A systematic review of patient decision aids in solid organ transplant has been completed and now published.

Irish GL, Weightman A, Hersch J, Coates PT, Clayton PA. Do patient decision aids help people who are facing decisions about solid organ transplantation? A systematic review. Clin Transplant. 2023 Feb 6:e14928. DOI: 10.1111/ctr.14928

### Project: Who should be transplanted? Estimating difference in life expectancy

This study will quantify the change in life expectancy derived from kidney transplantation. Statistical methods will be used to estimate the individual patient benefit, defined as predicted incremental survival post-transplantation compared with remaining on the waiting list. This abstract was submitted to TSANZ ASM 2022.

#### Funded by:

NHMRC Postgraduate Scholarship

### The Kidney Failure Risk Equation (KFRE) predicts Kidney Failure: Validation in an Australian Cohort

Lead – Dr Georgina Irish and Dr Matt Jose

Researchers - L Cuthberton, A Kitsis, T Saunder, P Clayton

This project looks at validating the KFRE in and Australian population using the TAS-LINK study population. The KFRE is a risk prediction score to predict the change of someone requiring kidney replacement therapy in the next 2 and 5 years. It has been used internationally but never validated independently in an Australian cohort. This study shows the score works well in Australia and can safely be used for risk prediction. It is currently submitted for publication and awaiting revisions.

### Survival after COVID Infection – impact of treatment modality

Lead – A/Prof Solomon Menahem

Researchers - Georgina Irish, Feruza Kholmurodova, Chris Davies, Stephen McDonald

This project is exploring the characteristics of kidney replacement therapy patients with a COVID-19 infection and examine whether their survival was impacted by treatment modality.

# **CNARTS Clinical Trials Unit**

The Central Northern Adelaide Renal and Transplantation Service (CNARTS) Clinical Trials Unit recruits for and coordinates clinical trials in patients with chronic kidney disease (CKD), kidney failure and renal transplants across metropolitan and country areas of South Australia, Northern Territory and New South Wales. Medications that are standard of care for kidney patients were trialled for the first time in the CNARTS Clinical Trials Unit, thereby bringing new treatments directly to our patients. These medications include Tacrolimus, Everolimus and Myfortic for kidney transplant patients; Aranesp, Mircera and Ferinject for patients with CKD /kidney failure and Tolvaptan for patients with Polycystic Kidney Disease.

We conduct clinical trials in collaboration with Vascular Surgery, Immunology Clinical Trials, the Islet Transplant team, the CNARTS Clinical Research Group, the School of Pharmacy and Medical Sciences, University of South Australia, Australasian Kidney Trials Network (AKTN) and The George Institute.

During the COVID-19 pandemic, the CNARTS Clinical Trials team continued to develop new strategies to meet study requirements for patient visits, study specific laboratory tests and delivery of study medication. Patient visits which were routinely been conducted at the RAH were conducted either off site at The Queen Elizabeth Hospital, Hampstead Dialysis Centre or by phone. These important strategies were implemented to maintain patient safety and continuity of the studies post COVID-19.

During 2022, CNARTS researchers and patients have been involved in over 30 clinical trials. With encouraging results, patients enrolled in several of our studies were offered the opportunity to receive open label medication in open label extension studies. In 2023 we will be commencing new trials in IgA Nephropathy, Membranous Nephropathy, CKD, and treatments for CMV Viraemia, BK Virus and Antibody Mediated Rejection in Kidney Transplant Patients.



### **CNARTS Clinical Trial staff:**

Jenny Latte (Assoc. Nursing Unit Manager), Bronwyn Hockley (Nursing Unit Manager), Meg Hockley (Assoc. Nursing Unit Manager), Karen Fischer (Clinical Trials Assistant)

### 2022 Clinical Trials:

### **Transplant trials:**

**1. CHORUS:** Global Multicentre Kidney Transplant Advagraf Conversion Registry. A noninterventional post-authorisation study (PAS)

Sponsor: Astellas PI: Dr Chii Yeap

**2. MK-8228-002:** A Phase III, Randomized, Double-Blind, Active Comparator-Controlled Study to Evaluate the Efficacy and Safety of MK-8228 (Letermovir) Versus Valganciclovir for the Prevention of Human Cytomegalovirus (CMV) Disease in Adult Kidney Transplant Recipients

Sponsor: Merck Sharp & Dohme PI: A/Prof Robert Carroll

**3. CA209-993ISR:** PD-1 blockade in renal transplant patients with poor prognosis cancer and minimizing risk of organ rejection using comprehensive immune monitoring and screening techniques – a safety study.

Investigator Led & PI: A/Prof Robert Carroll

**4. TMCT-04:** A Randomized Controlled Trial of Urine CXCL10 Chemokine Monitoring Post- Renal Transplant

Investigator Led & PI: A/Prof Robert Carroll

**5. CARSK study:** Canadian-Australian Randomised Trial of Screening Kidney Transplant Candidates for Coronary Artery Disease (https://www.carsk.org/).

Sponsor: The University of Sydney PI: Dr Philip Clayton

**6. IdeS AMR:** Randomized, Open-Label, Multi-Centre, Active Control Study Investigating the Efficacy and Safety of Imlifidase in Eliminating Donor Specific Anti-HLA Antibodies in the Treatment of Active Antibody-Mediated Rejection in Kidney Transplant Patients.

Sponsor: Hansa PI: Dr Philip Clayton

**7. IM103-392:** A phase II, single arm multicentre trial of thymoglobulin, belatacept and sirolimus in pancreatic islet transplant recipients.

Sponsor: The University of Sydney PI: Prof Toby Coates

8. INCEPTR: Intra-cutaneous ectopic pancreas' - A prospective evaluation of a novel treatment for Type I Diabetes Mellitus employing deceased donor islets implanted into modified, preintegrated Biodegradable Temporising Matrix (BTM) dermal replacement

Sponsor: Beta Cell Technologies Pty. Ltd. PI: Prof Toby Coates

**9. BCV-BN01:** Phase II, Open-label, Randomized, Multiple Ascending Dose Confirmation of the Safety and Tolerability of Brincidofovir in Subjects With BK Virus Infection (Viremia) After Kidney Transplantation (BASTION)

Sponsor: SymBio PI: Prof Toby Coates

**10. AT-1501-K102:** A Phase 1b, Multicenter, Open-Label Study to Evaluate the Safety, Pharmacokinetics and Efficacy of AT-1501 in Patients Undergoing Kidney Transplant

Sponsor: Eledon PI: Prof Toby Coates

### **CKD/Glomerulonephritis trials:**

**11. ZENITH:** A Phase 2b, Multicentre, randomised, Double-Blind, Placebo – Controlled, parallel group Dose-Ranging Study to Assess the Efficacy, Safety and Tolerability of Zibotentan and Dapagliflozin in Patients with Chronic Kidney Disease with Estimated Glomerular Filtration Rate (eGFR)  $\geq$  20 mL/min/1.73 m2 D4325C0001

Sponsor: Astra Zeneca PI: A/Prof Chen Au Peh

**12.CLNP023A2301:** A multi-center, randomised, double-blind, placebo controlled, parallel group, phase III study to evaluate the efficacy and safety of LNP023 in primary IgA nephropathy patients. **Sponsor:** Novartis **PI:** A/Prof Chen Au Peh

**13.GOAL study:** Comprehensive Geriatric Assessment for Frail Older People with Chronic Kidney Disease to Increase Attainment of Patient-Identified Goals - A Cluster Randomised Controlled Trial Investigator Led: AKTN PI: A/Prof Shilpa Jesudason

14. M11-001 aHUS Registry: An Observational, Non-Interventional, Multi-Centre, Multi-National Study of Patients with Atypical Hemolytic-Uremic Syndrome.
 Sponsor: Alexion Pharmaceuticals PI: A/Prof Robert Carroll

**15. 021FSGS16010:** A Randomized, Multicenter, Double-Blind, Parallel, Active Control Study of The Effects of Sparsentan, A Dual Endothelin Receptor and Angiotensin Receptor Blocker, On Renal Outcomes in Patients with Primary Focal Segmental Glomerulosclerosis (FSGS)

Sponsor: Travere PI: A/Prof Chen Au Peh

**16. OMS721-IGA-001:** A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of the Safety and Efficacy of OMS721 in Patients with Immunoglobulin A (IgA) Nephropathy (ARTEMIS-IGAN)

Sponsor: Omeros Corp PI: A/Prof Chen Au Peh

**17. NEF-301:** A randomized, double-blind, placebo-controlled study to evaluate efficacy and safety of Nefecon in patients with primary IgA nephropathy at risk of progressing to end-stage renal disease (NeflgArd).

Sponsor: Calliditas Therapeutics AB PI: A/Prof Chen Au Peh

**18. NEF-301OLE:** An open label extension (OLE) Study to the evaluate efficacy and safety of Nefecon treatment in patients with IgA nephropathy who have completed Study NEF-301

Sponsor: Calliditas Therapeutics PI: A/Prof Chen Au Peh

**19. 021IGAN17001:** A Randomized, Multicenter, Double-blind, Parallel-group, Active-control Study of the Efficacy and Safety of Sparsentan for the Treatment of Immunoglobulin A Nephropathy (PROTECT Study)

Sponsor: Travere PI: A/Prof Chen Au Peh

**20. 402-C-1808:** A Phase 3 Trial Of The Efficacy And Safety Of Bardoxolone Methyl In Patients With Autosomal Dominant Polycystic Kidney Disease (FALCON Study)

Sponsor: REATA Pharmaceuticals PI: Prof Randall Faull

**21. 417-201-00007:** A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Trial to Evaluate the Efficacy and Safety of Sibeprenlimab Administered Subcutaneously in Subjects with Immunoglobulin A Nephropathy (Visionary)

Sponsor: Otsuka Pharmaceuticals PI: Dr Chii Yeap

**22. TESTING ON:** Therapeutic Evaluation of Steroids in IgA Nephropathy Global- Post-Trial ObservatioNal Cohort Study

Sponsor: George Institute PI: A/Prof Chen Au Peh

### **Renal Failure/Dialysis trials**

23. RESOLVE: Randomised Evaluation of SOdium dialysate Levels on Vascular Events, Protocol Number: GI-RM-7338.
 https://aktn.org.au/resolve/
 Investigator Led: AKTN PI: A/Prof Philip Clayton

**24. TEACH-PD:** A pragmatic, registry-based, international, cluster-randomised controlled trial examining the use of TEACH-PD training modules for incident PD patients versus existing practices on the rate of PD-related infections.

https://aktn.org.au/teach-pd/

Sponsor: AKTN PI: Professor Stephen McDonald

**25. PHOSPHATE study:** Pragmatic randomised trial of High or Standard PHosphAte Targets in End-stage kidney disease. https://aktn.org.au/phosphate-trial/

Sponsor: AKTN PI: A/Prof Philip Clayton.

26. TRACK study: Treatment of CVD with low dose Rivaroxaban in Advanced CKD. https://www.tracktrial.org/Sponsor: George Institute PI: A/Prof Shilpa Jesudason.

**27. Patient Activation:** Improving self-management for people with chronic kidney disease through a patient activation approach

Investigator Led & PI: Laura Lunardi RN, NP

28. Improving the therapeutic use of vancomycin in patients undergoing dialysis treatment **Investigator Led & PI:** Dr Lachlan McMichael

**29. ACTIVATE AVF:** A study of the safety and feasibility of the Vessel Restoration System for AVF to promote the physiologic and functional maturation of upper-extremity autologous End-to-Side Arteriovenous Fistulas (AVF) in Patients with Chronic Kidney Disease:

Sponsor: Alucent PI: Dr Ewan Macaulay.

**30. Symptom monitoring WIth Feedback Trial (SWIFT):** A Registry-Based Cluster Randomised Controlled Trial to determine the clinical effectiveness and cost-effectiveness of symptom monitoring with feedback to clinicians and patients compared with standard care in improving quality of life outcomes at 12 months for adults on haemodialysis.

Sponsor: NHMRC Clinical Trials Centre The University of Sydney PI: Prof Stephen McDonald

# **Student Supervision in 2022**

**Ms Sumaya Abdinoor** (Psychology Honours student, University of Adelaide) "Open-ended responses of renal nurses in an online survey regarding nurse re-education for managing needle fear and distress during cannulation and dialysis" thesis accepted 2022.

Supervisors: A Chur-Hansen, G Radisic, S Jesudason

**Mirabel Alonge** (PhD candidate, University of Adelaide) "Using Pharmacokinetic Principles to Improve the Safety of Tacrolimus in Renal Transplant Patients"

Supervisors: B Sallustio, S Jesudason, S Reuter Lange

**Dylan Barnett** (PhD candidate, University of Adelaide) "Organ preservation and resuscitation by isothermic oxygenated machine perfusion in an ex-vivo porcine model"

Supervisors: T Coates, S Bhattacharjya

**Dr James Besanko** (Masters candidate, University of Adelaide) "Evaluation of heart transplant transportation device in a pig model"

Supervisors: T Coates, J Betrame, J Edwards

**Dr Samantha Bateman** (PhD candidate, University of Adelaide) "Benefits and Burdens of Kidney Transplantation for First Nations Australians"

Supervisors: S Jesudason, O Pearson, P Clayton, S McDonald

**Nick Chai** (PhD candidate, University of Adelaide) "Exploring the adjuvant effect of mTOR inhibitor on boosting vaccine-induced T cell responses in immunocompromised transplant patients."

Supervisors: T Coates, G Perkins, C Drogemuller

Maria Chilvers (PhD candidate, University of South Australia) "The experience of dyspnoea (breathlessness) for people living with kidney failure"

Supervisors: K Ferrar, P Bennett, S Jesudason

**Dr Brigette Clarke** (PhD candidate, University of Adelaide) "Adrenal cell transplantation for Addison's disease using Biodegradable Temporising Matrix technology"

Supervisors: T Coates, P Hurtado, D Torpy

**Dr Bronwyn Dearman** (PhD candidate, University of Adelaide) "The Development of a Tissue-Engineered Skin Substitute utilising a Biodegradable Polyurethane Scaffold in a Novel Bioreactor for the Treatment of Extensive, Full Thickness Burns" PhD conferred Dec. 2022.

Supervisors: T Coates, J Greenwood, S Boyce

Kevin Lau Hei In (Dietetics Masters Student, Flinders University) "What do people with kidney failure approaching dialysis start actually eat?" Masters accepted 2022.

Supervisors: A Meade, R Le Leu

**Dr Georgie Irish** (PhD candidate, University of Adelaide) "Decision Making in Kidney Transplantation"

Supervisors: P Clayton, T Coates

**Dr Alice Krige** (PhD candidate, University of South Australia) "Normothermic extra-corporeal perfusion in an ovine model of kidney transplantation as a means of organ preservation."

Supervisors: T Coates, L Palmer

Annie Lim (Honours candidate, University of Adelaide) "The Molecular Analysis of Persufflated Ovine Kidneys – A Novel Means To Improve Kidney Transplant Function"

Supervisors: T Coates, C Drogemuller

Laura Lunardi (PhD candidate, University of Adelaide) "Patient activation in Chronic Kidney Disease"

Supervisors: P Bennett, L Matricciani, R Le Leu

**Griffiths Perkins** (PhD candidate, University of Adelaide) "Regulation of IL-10 secretion by human B cells" PhD conferred Dec. 2022.

Supervisors: T Coates, P Hurtado, C Hope

Jackie Scaffidi (PhD candidate, University of Adelaide) "Chimeric Antigen Receptor T regulatory cells (CAR-Tregs) as a therapy for autoimmune-driven Type 1 Diabetes."

Supervisors: T Coates, S Barry

**Brett Tarca** (PhD candidate, University of South Australia) "Exploring Relationships Between Fatigue, Mood, Physical Function and Physical Activity in People Receiving Peritoneal Dialysis" **Supervisors:** K Ferrar, T Wycherley, S Jesudason, P Bennett

**Dr Alison Weightman** (PhD candidate, University of Adelaide) "Decision Making in Deceased Donor Kidney Transplant Offers"

Supervisors: P Clayton, S Coghlan

**Denghao Wu** (PhD candidate, University of Adelaide) "The genetic epidemiology of hereditary pancreatitis in South Australia"

Supervisors: T Coates, L Palmer, K Kassahn, C Drogemuller

James Zuiani (Masters candidate, University of Adelaide) "Characterisation of Pancreatic Organoids in hereditary pancreatitis and normal individuals"

Supervisors: S Grey, C Drogemuller, T Coates

# **Conference Presentations** 2022

### 2022 Transplantation Society of Australia and New Zealand Annual Scientific Meeting, Adelaide

"Should I have a transplant? using flexible parametric models to predict survival after kidney transplant waitlisting"

### Irish G, Mulley W, Clayton P



"Living donor factors do not discriminate outcomes and should not be used to promote compatible pairs for paired kidney exchange"

Irish G, Chang D, McMichael L, Chadban S, Boudville N, Campbell S, Kanellis J, Sharples E, Kadatz M, Gill J, Clayton P

"The genetic epidemiology of hereditary pancreatitis in Australia and its effect on patients of total pancreatectomy and islet auto translation (TP-IAT)"

### Wu D, Bampton T, Palmer L, Coates PT

"The management of borderline t cell mediated rejection in kidney transplantation" Wyld M, Hughes P, Lim W, Collins M, Pilmore H, **Clayton P**, Van Der Jeud J, Nankivell B, Mulley W

"Defining causes of allograft loss attributed to chronic allograft nephropathy. A 5-year multicentre audit"

Mulley W, Hughes P, Collins M, Wyld M, **Clayton P**, Lee D, Vab Der Jeud J, **Tan S**, Fernando S, Kuo S, **Jahan S**, Pilmore H, Lim W

"Temporal validation of the Australian estimated post transplantation survival score" Irish G, Kanellis J, Wyburn K, Clayton P

"Trajectories of systolic blood pressure decline in kidney transplant donors prior to circulatory death and delayed graft function"

Wong G, Lin Y, Lim W, Teixeira-Pinto A, Yang J, Craig J, **McDonald S**, Chapman J, **Davies C**, Rogers N, Opdam H, Pleass H

"mTOR inhibition is associated with an improved immune response to covid-19 vaccination in kidney transplant recipients"

**Perkins G, Tunbridge M, Salehi T**, Chai C, Hope C, Singer J, **Hurtado P,** Hissaria P, Grubor-Bauk B, Barry S, Chadban S, **Coates T** 

"Outcomes for live kidney donors following nephrectomy in Aotearoa New Zealand: the live donate NZ study"

Chan L, Irish G, Goh T, Alnasrallah B, Davies C, Sypek M, Clayton P, Collins M

Impact of new Victorian key performance indicator (KPI) on renal transplant waitlists for indigenous & non-indigenous patients

Ling R, Mark T, Davies C, McDonald S, Goodman D

"Recipient AT1R antibody status and risk of kidney rejection in simultaneous pancreas and kidney transplantation"

#### Jahan S, Barnett D, Coates T, Bhattacharjya S

"Can early sf36 assessment of QOL in SPK transplants identify patients who may benefit with intensive psychology support?"

#### Jahan S, Barnett D, Bampton T, Coates T, Bhattacharjya S

"Interim safety analysis of switching mycophenolate to sirolimus enhancing covid vaccine response in kidney transplant recipients"

Tunbridge M, Perkins G, Salehi T, Singer J, Ying T, Sim B, Grubor-Bauk B, Hissaria P, Chadban S, Coates T

"A randomized, controlled, blinded trial of inulin vs placebo to boost COVID-19 vaccine response in kidney transplant recipients"

Singer J, Tunbridge M, Perkins G, Salehi T, Ying T, Sim B, Grubor-Bauk B, Coates T, Chadban S

"Gut dysbiosis may contribute to the suboptimal immune response to COVID-19 vaccination in kidney transplant recipients"

Singer J, Tunbridge M, Perkins G, Salehi T, Chai C, Grubor-Bauk B, Coates T, Chadban S

"Non-utilization of kidneys from donors after circulatory determinant of death"

Wong G, Lin Y, Lim W, Teixeira-Pinto A, Yang J, Craig J, **McDonald S**, Pleass H, Rogers N, Opdam H, **Davies C**, Chapman J

"Trends in labour and delivery outcomes among transplanted mothers"

Tangirala N, Hewawasam E, Davies C, Li Z, Sullivan E, McDonald S, Jesudason S

"Parenthood post transplantation: evolution and evaluation of the parenthood data collection of the ANZDATA registry"

#### Danner R, Hewawasam E, McDonald S, Jesudason S

"Do decision aids help people who are facing decisions about solid organ transplantation? a systematic review"

Irish G, Weightman A, Hersch J, Coates P, Clayton P

"Testicular granulomatous vasculitis in a pre-transplant patient"

#### O'Connor S, Coates T

"The impact of banff borderline acute t-cell mediated rejection on transplant outcomes: An ANZDATA analysis"

Wyld M, Hughes P, Lim W, Collins M, Pilmore H, Clayton P, Van Der Jeugd J, Nankivell B, Mulley, W

"Recent trouble with venous thrombo-embolism post transplantation"

#### Thyagarajan N, Jahan S, Venkataraman K, Kuah Z, Coates T

"Retrospective, single-centre cohort study of fluid therapy and hypotension post kidney transplantation"

Venkataraman K, Jahan S, Kuah Z, Coates T

"Back to the machine: transition from transplant to dialysis"

### Hopkins J, Jahan S, Donnelly F, Crail S

"Potassium clearance post kidney transplantation: A single centre audit"

#### Tan S, Jahan S, Coates T

"Transplant renal artery stenosis - an imaging challenge"

#### Tan S, Byrapu P, McDonald S, Coates T

"The development of GAD65-CAR Tregs as a method of immunosuppression for islet transplant recipients"

Scaffidi J, Coates T, Barry S, Sadlon T, Bandara V

## International Society for Quality in Health Care (ISQua), Brisbane



"Improving end of life planning through existing relationships between patients and their specialist nurses in the community"

Stead K, Drummond C, Lunardi L

### American Society of Nephrology (ASN), Orlando, USA

"Concordance Between Site Reporting and Clinical Adjudication of Catheter-Related Infectious Events in Australian and New Zealand Kidney Services"



Catiwa J, Coggan S, Cass A, Gray N, Jan S, **McDonald S**, Polkinghorne K, Talaulikar G, Gallagher M, Kotwal S

"Addressing Disparities in Kidney Health Outcomes for First Nations Peoples of the United States, Canada, Australia, and New Zealand: A Systematic Review"

Riceman M, **Bateman S**, Tunnicliffe D, Lester R, Sinclair N, **Owen K**, Howell M, Pearson O, **McDonald S, Jesudason S** 

"A Phase 1b, Multicenter, Open-Label Study to Evaluate the Safety, Pharmacokinetics, and Efficacy of Tegoprubart (AT-1501) in Patients Undergoing Kidney Transplant"

Tchervenkov J, Coates PT, Kadatz M, Bornstein J, Gill J

"Baseline Characteristics and Representativeness of the BEST-Fluids Trial Participants: A Randomized Trial of Balanced Crystalloid Solution vs. Saline in Deceased Donor Kidney Transplantation"

**Collins M**, Fahim M, Pascoe E, **Clayton P**, **Dansie K**, Varghese J, McConnochie R, Robison L, Reidlinger D, Kiriwandeniya C, Chadman S

## Australian and New Zealand Society of Nephrology (ANZSN), Sydney

AUSTRALIAN AND NEW ZEALAND SOCIETY OF NEWHOLOGY ACCOR STALINA, SYNCHOLOGY 37-19 OCTOBER 2022

"Should I have a transplant? Using flexible parametric models to predict survival after kidney transplant waitlisting" (Winner for Young investigator Award – Basic Science)

#### Irish G, Mulley W, Clayton S

"Models of care to address disparities in kidney health outcomes for First Nations Peoples: A systematic review"

Bateman S, Riceman M, Owen K, Lester R, Sinclair N, Pearson O, McDonald S, Howell M, Tuncliffe D, Jesudason S

"Factors associated with dialysis withdrawal following modality change from peritoneal dialysis to haemodialysis: An Australia and New Zealand Dialysis and Transplant Registry Analysis, 2004-2019"

### Tan S, Lincoln G, Yeap C, Clayton P

"Intensive care admissions for dialysis and transplant patients 2018-2020: An Australian data linkage study"

Keuskamp D, Davies C, Clayton P, Pilcher D, Chavan S, Secombe P, Jones S, Reddi B, McDonald S

"Acute interstitial nephritis with inflammatory bowel disease"

### Jahan S, Xu A, Danner R, Sellars I, Coates PT

"Amyloid post covid-19 vaccine – Any relation?

### Jahan S, Rajandran A, Baharuddin N, Rao N, Tan B

"Treatment intensity of renal inpatients during their terminal admission, a clinical audit"

### Tan S, Lunardi L, Mohd Nor M, Flabouris A, Crail S

"Treatment intensity of renal inpatients during their terminal admission, a clinical audit" **Tan S, Lunardi L, Mohd Nor M**, Flabouris A, **Crail S**  "Parenthood in people with kidney failure: Evolution and evaluation of the parenthood data collection of the ANZDATA registry"

#### Danner R, Hewawasam E, Jesudason S

"Patient and unit factors associated with inpatient dialysis initiation – A single unit retrospective cohort study"

O Connor S, Richards K

### **Renal Society Australasia, Darwin**

"ANZDATA" - Plenary abstract

**McDonald S** 



"Statewide approach to management of COVID-19 positive patients"

#### **Donnelly F**

"The effectiveness of patient activation interventions in adults with chronic kidney disease: a systematic review and meta-analysis of randomized controlled trials"

#### Lunardi L, Hill K, Le Leu R, Bennett P

"Improving self-management for people with chronic kidney disease through a patient activation approach: a cross-sectional survey protocol"

Lunardi L, Le Leu R, Britton A, Xu A, Borlace M, Jesudason S, Bennett P

"Dying to talk: a clinical audit on uptake of advanced care directives among patients with kidney disease"

Mohd Nor M, Lunardi L, Tan S, Crail S

"Journey back to dialysis from transplant"

Donnelly F, Jahan S, Crail S, Hopkins J

"Nurse perspective on education program on needle fear in haemodialysis patient"

Donnelly F, Radisic G, Le Leu R, Hill K, Chu-Hansen A, Collins K, Burke A, Macauley L, Mc Donald S, Jesudason S

"Dialysis start program - a multi-disciplinary approach"

#### **Donnelly F**

"Once we knew it, we couldn't unknow it, nor would we want to – realisations of renal nurses working in indigenous kidney care"

Arnold-Chamney M, Rix L, Tyrell K, Kelly J

## 20th Congress of The International Society of Renal Nutrition and Metabolism (ISRN 2022)

"Applying the principles of sports nutrition and exercise performance to CKD"

### Meade A.

"Symptom burden improves but dietary intake doesn't change when dialysis commences – analysis of the MADE study cohort"

Lau K, Le Leu R, Jesudason S, Bennett P, Shanahan L, Donnelly F, Chur-Hansen A, Collins K, McDonald S, Clayton P, Meade A.

### ISN World Congress of Nephrology (WCN)

"Trends in labour and delivery outcomes among mothers receiving kidney replacement therapy: analysis of linked ANZDATA Registry and Perinatal datasets over 22 years"

Hewawasam E, Davies C, Li Z, Clayton P, Sullivan E, McDonald S, Jesudason S







# **Publications in 2022**

**CNARTS Publications (last 5 years)** 



### **Clinical Research Group:**

**Bateman, S**., M. Arnold-Chamney, **S. Jesudason**, R. Lester, **S. McDonald**, **K. O'Donnell**, K. Owen, O. Pearson, N. Sinclair, T. Stevenson, I. Williamson, and **J. Kelly.** "Real Ways of Working Together: Co-Creating Meaningful Aboriginal Community Consultations to Advance Kidney Care." *Aust N Z J Public Health* 46, no. 5 (Oct 2022): 614-21. <u>https://doi.org/10.1111/1753-6405.13280</u>

**Bennett, P.**, C. Bohm, O. Harasemiw, L. Brown, I. Gabrys, D. Jegatheesan, D. Johnson, K. Lambert, C. J. Lightfoot, J. MacRae, **A. Meade**, K. Parker, N. Scholes-Robertson, K. Stewart, **B. Tarca**, N. Verdin, A. Y. Wang, M. Warren, M. West, D. Zimmerman, P. K. Li, and S. Thompson. "Physical Activity and Exercise in Peritoneal Dialysis: International Society for Peritoneal Dialysis and the Global Renal Exercise Network Practice Recommendations." *Perit Dial Int* 42, no. 1 (Jan 2022): 8-24. 10.1177/08968608211055290

Bennett, P., M. Kohzuki, C. Bohm, B. Roshanravan, S. J. L. Bakker, J. L. Viana, J. M. MacRae,
T. J. Wilkinson, K. R. Wilund, A. H. Van Craenenbroeck, G. K. Sakkas, S. Mustata, K. Fowler, J.
McDonald, G. M. Aleamañy, K. Anding, K. G. Avin, G. L. Escobar, I. Gabrys, J. Goth, M. Isnard,
M. Jhamb, J. C. Kim, J. W. Li, C. J. Lightfoot, M. McAdams-DeMarco, F. Manfredini, A. Meade,
S. Molsted, K. Parker, E. Seguri-Orti, A. C. Smith, N. Verdin, J. Zheng, D. Zimmerman, and S.
Thompson. "Global Policy Barriers and Enablers to Exercise and Physical Activity in Kidney Care." J Ren Nutr 32, no. 4 (Jul 2022): 441-49. 10.1053/j.jrn.2021.06.007

Dedina, L., M. Hassall, **S. Jesudason**, and S. Simon. "Pallid Disc Oedema in a Young Patient: Clinical and Diagnostic Challenge." *Neuroophthalmology* 46, no. 2 (2022/03/04 2022): 95-98. <u>10.1080/01658107.2020.1867873</u> **Duncanson, E., A. Chur-Hansen, and S. Jesudason**. "Patient Perspectives of Coping with Automated Peritoneal Dialysis." *Perit Dial* Int 42, no. 4 (Jul 2022): 344-52. 10.1177/08968608211043411

Fakhouri, F., N. Schwotzer, G. Cabiddu, J. Barratt, H. Legardeur, V. Garovic, A. Orozco-Guillen, J. Wetzels, E. Daugas, G. Moroni, M. Noris, V. Audard, M. Praga, E. Llurba, G. Wuerzner, R. Attini, D. Desseauve, E. Zakharova, C. Luders, K. Wiles, F. Leone, **S. Jesudason**, N. Costedoat-Chalumeau, A. Kattah, V. Soto-Abraham, A. Karras, J. Prakash, L. Lightstone, P. Ronco, C. Ponticelli, G. Appel, G. Remuzzi, V. Tsatsaris, and G. B. Piccoli. "Glomerular Diseases in Pregnancy: Pragmatic Recommendations for Clinical Management." *Kidney Int* 103, no. 2 (Feb 2023): 264-81. <u>10.1016/j. kint.2022.10.029</u>

Hughes, J., **J. Kelly**, A. Cormick, **P. T. Coates**, and **K. O'Donnell**. "Resetting the Relationship: Decolonizing Peer Review of First Nations' Kidney Health Research." *Kidney Int* 102, no. 4 (Oct 2022): 683-86. Accessed 2022/09/20. <u>10.1016/j.kint.2022.08.011</u>

Jackson, T., A. Chur-Hansen, E. Duncanson, and S. Jesudason. "A Qualitative Content Analysis of an Online Forum for People with Kidney Disease: Exploring the Role of Companion and Non-Companion Animals." *J Ren Care* 48, no. 4 (Dec 2022): 220-29. <u>10.1111/jorc.12406</u>

**Jesudason, S**. "Implementing Referral Systems for Nephrology Services: Real World Practice Versus Guidelines." *J Nephrol* 35, no. 5 (Jun 2022): 1369-70. <u>10.1007/s40620-021-01238-0</u>

**Jesudason, S.**, and G. B. Piccoli. "Pregnancy Outcomes after Kidney Transplantation: The Challenges of Success." *Kidney Int* 102, no. 4 (Oct 2022): 697-99. <u>10.1016/j.kint.2022.08.007</u>

**Kelly, J.**, T. Stevenson, M. Arnold-Chamney, **S. Bateman, S. Jesudason, S. McDonald**, K. O'Donnell, O. Pearson, N. Sinclair, and I. Williamson. "Aboriginal Patients Driving Kidney and Healthcare Improvements: Recommendations from South Australian Community Consultations." *Aust N Z J Public Health* 46, no. 5 (Oct 2022): 622-29. <u>10.1111/1753-6405.13279</u>

Lambert, K., E. Neale, L. Nichols, **D. Brauer,** R Blomfield, L. Caurana, J. Isautier, **S. Jesudason**, and A. Webster. "Interventions for Improving Adherence to Dietary Salt and Fluid Restrictions in People with Chronic Kidney Disease (Stage 4 and 5)." *Cochrane Database of Systematic Reviews* 2022, no. 10 (2022). <u>10.1002/14651858.CD015181</u>

Lee, C. S., **R. Tan**, and **N. N. Rao**. "Gadolinium-Induced Acute Graft Pancreatitis in a Simultaneous Pancreas-Kidney Transplant Recipient." *Case Rep Nephrol* 2022 (2022/08/21 2022): 9533266. 10.1155/2022/9533266

McKenzie, A., J. Bowden, J. R. Zalcberg, K. Conroy, J. Fallon-Ferguson, **S. Jesudason**, J. Ansell, A. Anderst, and N. Straiton. "A Snapshot of Consumer Engagement in Clinical Trials in Australia: Results of a National Survey of Clinical Trial Networks and Research Organisations." *Res Involv Engagem* 8, no. 1 (Feb 5 2022): 3. <u>10.1186/s40900-022-00338-w</u>

**Meade, A.**, C. McLaren, and **P. N. Bennett**. "Combining Exercise and Nutrition in Chronic Kidney Disease and Dialysis: Can We Learn from the Performance Nutrition of Athletes?", *Semin Dial* (Feb 3 2022). <u>10.1111/sdi.13060</u>

**Radisic, G.**, L. de la Perrelle, and K. Laver. "Methods of Capturing Process Outcomes in Quality Improvement Trials: A Systematic Review." *J Healthc Qual* 44, no. 3 (May-Jun 01 2022): 131-51. <u>10.1097/JHQ.00000000000336</u> Radisic, G., E. Duncanson, R. Le Leu, K. L. Collins, A. L. J. Burke, J. K. Turner, A. Chur-Hansen, F. Donnelly, K. Hill, S. McDonald, L. Macauley, and S. Jesudason. "Improving Management of Needle Distress During the Journey to Dialysis through Psychological Education and Training-the Inject Study Feasibility Pilot Protocol." *Pilot Feasibility Stud* 8, no. 1 (Feb 4 2022): 28. <u>10.1186/</u> <u>s40814-022-00989-2</u>

Sethi, S., B. F. Poirier, J. Hedges, Z. Dodd, P. Larkins, C. Zbierski, **S. P. McDonald, S. Jesudason**, L. Jamieson, and Akction Group. "Maximizing Oral Health Outcomes of Aboriginal and Torres Strait Islander People with End-Stage Kidney Disease through Culturally Secure Partnerships: Protocol for a Mixed Methods Study." *JMIR Res Protoc* 11, no. 12 (Dec 16 2022): e39685. <u>10.2196/39685</u>

Symons, T., J. Bowden, A. McKenzie, J. M. Fallon-Ferguson, L. Y. Weekes, J. Ansell, R. Murphy, **S. Jesudason**, M. Saxena, A. Nichol, and N. Straiton. "Development of the Consumer Involvement & Engagement Toolkit: A Digital Resource to Build Capacity for Undertaking Patient-Centred Clinical Trials in Australia." *Public Health Res Pract* (Jun 1 2022). <u>10.17061/phrp32122209</u>

**Tarca, B., S. Jesudason, P. N. Bennett**, D. Kasai, T. P. Wycherley, and **K. E. Ferrar.** "Exercise or Physical Activity-Related Adverse Events in People Receiving Peritoneal Dialysis: A Systematic Review." *Perit Dial Int* 42, no. 5 (Sep 2022): 447-59. <u>10.1177/08968608221094423</u>

**Tuckey, N., E. Duncanson, A. Chur-Hansen,** and **S. Jesudason**. "Using an International Online Forum to Explore Perspectives of Caregivers of Patients with Chronic Kidney Disease." *J Nephrol* 35, no. 1 (Jan 2022): 267-77. <u>10.1007/s40620-021-01216-6</u>

van Zwieten, A., and **S. Jesudason**. "Work Participation in Chronic Kidney Disease: Action Is Needed to Avoid Accumulating Health and Social Disadvantage for Patients." *J Nephrol* (Dec 6 2022). <u>10.1007/s40620-022-01526-3</u>

Zen, M., R. Haider, D. Simmons, M. Peek, C. J. Nolan, S. Padmanabhan, **S. Jesudason**, T. I. Alahakoon, N. W. Cheung, and V. W. Lee. "Aspirin for the Prevention of Pre-Eclampsia in Women with Pre-Existing Diabetes: Systematic Review." *Aust N Z J Obstet Gynaecol* 62, no. 1 (Feb 2022): 12-21. <u>10.1111/ajo.13460</u>

### **Centre for Clinical and Experimental Transplantation (CCET):**

Bampton, T, R. Couper, S. Khurana, D. Moore, A. Brown, **C. Drogemuller, D. Wu,** J. Chen, **P. T. Coates**, and L. J. Palmer. "The Epidemiology and Burden of Childhood Chronic Pancreatitis in South Australia." *J Pediatr* 242 (Mar 2022): 93-98 e1. <u>10.1016/j.jpeds.2021.11.068</u>

**Barnett, D.**, S. Jolly, and **S. Bhattacharjya**. "How to Do a Spleen Preserving Porto-Splenic Pancreas Transplantation." *ANZ J Surg* 92, no. 12 (Dec 2022): 3325-27. 10.1111/ans.18004

Barraclough, K. A., D. Metz, C. E. Staatz, G. Gorham, **R. Carroll,** S. W. Majoni, S. Cherian, R. Swaminathan, and N. Holford. "Important Lack of Difference in Tacrolimus and Mycophenolic Acid Pharmacokinetics between Aboriginal and Caucasian Kidney Transplant Recipients." *Nephrology (Carlton)* 27, no. 9 (Sep 2022): 771-79. <u>10.1111/nep.14080</u>

Bose, B., S. V. Badve, D. W. Johnson, C. Hawley, V. Jha, D. Reidlinger, and **C. A. Peh**. "Treatment Preferences for Primary Membranous Nephropathy: Results of a Multinational Survey among Nephrologists in the South Asia Pacific Region." *Nephrology (Carlton)* 27, no. 1 (Jan 2022): 35-43. <u>10.1111/nep.13953</u>

**Carroll, R**., M. Boyer, V. Gebski, **B. Hockley**, J. K. Johnston, S. Kireta, H. Tan, A. Taylor, K. Wyburn, and J. R. Zalcberg. "Immune Checkpoint Inhibitors in Kidney Transplant Recipients: A Multicentre, Single-Arm, Phase 1 Study." *Lancet Oncol* 23, no. 8 (Aug 2022): 1078-86. <u>10.1016/</u><u>S1470-2045(22)00368-0</u>

Chan, J., Z. Kuah, **S. Bhattacharjya**, and **S. A. Olakkengil**. "Recurrent Thromboses and Major Vessel Compressions in Autosomal Dominant Polycystic Kidney Disease." *J Surg Case Rep* 2022, no. 2 (Feb 2022): rjac012. <u>10.1093/jscr/rjac012</u>

**Coates, P. T.**, G. Wong, B. H. Rovin, P. Ronco, Editorial Entire, and Team Management. "A Challenge to the Kidney Community by a Man-Made Crisis." *Kidney Int* 101, no. 5 (May 2022): 854-55. <u>10.1016/j.kint.2022.03.017</u>

Graves, L. E., D. J. Torpy, **P. T. Coates**, I. E. Alexander, S. R. Bornstein, and **B. Clarke**. "Future Directions for Adrenal Insufficiency: Cellular Transplantation and Genetic Therapies." *J Clin Endocrinol Metab* (Jan 6 2023). <u>10.1210/clinem/dgac751</u>

Hensman, C. J., Gooley, J. L., Januszewski, A. S., Lee, M. H., MacIsaac, R. J., Boston, **Australian Islet Transplant Consortium**, R. C Jenkins, A. J. (2022). "Insulin antibodies are prevalent in adults with type 1 diabetes referred for islet cell transplantation and are modified by islet transplantation and immunosuppression: an Australian experience." *Internal Medicine Journal*, 52(8), 1434-1436. <u>10.1111/imj.15867</u>

Jayne, D., M. Walsh, P. A. Merkel, **C. A. Peh**, W. Szpirt, X. Puechal, S. Fujimoto, C. Hawley, N. Khalidi, R. Jones, O. Flossmann, R. Wald, L. Girard, A. Levin, G. Gregorini, L. Harper, W. Clark, C. Pagnoux, U. Specks, L. Smyth, T. Ito-Ihara, J. de Zoysa, B. Brezina, A. Mazzetti, C. A. McAlear, D. Reidlinger, S. Mehta, N. Ives, E. A. Brettell, H. Jarrett, K. Wheatley, E. Broadhurst, A. Casian, and C. D. Pusey. "Plasma Exchange and Glucocorticoids to Delay Death or End-Stage Renal Disease in Anti-Neutrophil Cytoplasm Antibody-Associated Vasculitis: Pexivas Non-Inferiority Factorial Rct." *Health Technol Assess* 26, no. 38 (Sep 2022): 1-60. <u>10.3310/PNXB5040</u>

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