2021 Annual Research Report

Central Northern Adelaide Renal and Transplantation Service (CNARTS)

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



Health Central Adelaide Local Health Network

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Welcome message

It is a great pleasure to deliver the 5th Annual Research Report from the Central Northern Adelaide Renal and Transplantation Service (CNARTS) at the Royal Adelaide Hospital, Central Adelaide Local Health Network.

2021 continues to be a challenging year, as we balanced the ongoing enormous needs of patients with kidney disease as they navigated the coronavirus pandemic, with our desire to pursue world class research to achieve better patient care.

CNARTS research activity continues to have a strong patient-centred research agenda. Our multidisciplinary research team continues to grow, bringing in people from many research groups and networks – medical, nursing, scientific, dietetic, exercise physiology, psychology and consumer co-investigators.

In 2021 we saw major initiatives and successes:

- Consumer engagement with our participation in a NHMRC Centre of research excellence (CRE) for consumer partnership in Kidney research.
- 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
- CNARTS researchers were awarded \$9,962,913 in category 1 funding and \$1,186,272 in other funding
- 74 publications from CNARTS researchers
- 49 accepted abstracts at various conferences
- 17 higher degree students were supervised (including 13 PhD, 1 Masters and 3 Honours).

We continue to receive fantastic support from our research funding partners - The Hospital Research Foundation, Kidney Transplant Diabetes Research Australia and the RAH Hospital Research Fund. This ongoing support has been absolutely critical in progressing research ideas in a highly competitive grant environment.

We would like to thank all the patients who partner with us throughout the stages of research design, execution and implementation. Your stories remain our inspiration and motivation to advance care for people living with kidney disease.



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, with over 1700 kidney failure patients. 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. The different types of transplants performed include kidney transplants, simultaneous kidney-pancreas transplant 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, hereditary pancreatitis, transplantation and diabetes.

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.



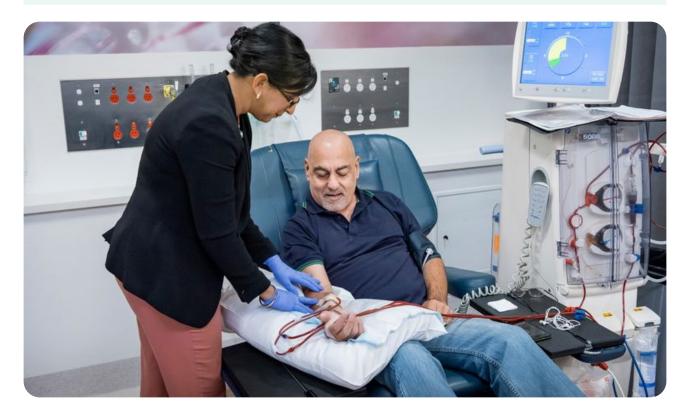
Since 1981, the Royal Adelaide Hospital (RAH) Research Fund has been raising funds for life-saving medical research at the RAH.

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**
- Gastrointestinal symptoms, dietary intake and changes in gut microbiome pre and post kidney transplant. \$30,000
- Phenotypic and Genotypic Analysis of Hereditary Pancreatitis in South Australia.
 \$38,830

The INJECT fundraising campaign by the RAH Research Fund has raised over \$55,000



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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 Centralised Research & Clinical Data Warehouse with up-to-date dashboards in real time for the Central and Northern Adelaide Renal and Transplantation Service (CNARTS). \$200,000



a charity of The Hospital Research Foundation Group

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.



\$56,107 raised at Gala Ball!

In 2021, KTDRA's valued supporter and fundraising champion Helena Kollias raised an outstanding \$56,107 for hereditary pancreatitis research at a Gala Ball on 3 September 2021!

More than 250 people filled the Adelaide Town Hall for the event, with the night's MC being Kerry Harrigan, whose wife Margaret was the first person in SA to receive an islet cell transplant which cured her of Type 1 diabetes.



Guests were also treated to a talk from Prof Toby Coates, who spoke about the life-changing work his team is undertaking in the fight against pancreatitis.





Local Lions Clubs Raise \$30,000 for Medical Equipment

In 2021, the Lions Club of Yankalilla and District raised an incredible \$30,000 to purchase two muchneeded Chiller Units to help facilitate a life-changing procedure that cures people of debilitating pancreatitis. The Chiller Units are part of the state-of-the-art Biospherix Chamber that was established in Adelaide in 2021, to enable faster and safer Total Pancreatectomy with Islet Auto Transplantation (TP-IAT) procedures.



The purchase of the Chiller Units was proudly facilitated through Kidney Transplant Diabetes Research Australia which also funded the new Adelaide-based Biospherix Chamber. The Lions Club of Yankalilla and District along with others raised an incredible \$15,000 for the Units, with the Australian Lions Foundation matching their efforts by providing a further \$15,000 grant.

Awards and Fellowships



Prof Patrick Toby Coates

was awarded the Officer of the Order of Australia (AO) for distinguished service to renal medicine, to professional medical organisations, and to tertiary education.



Dr Erandi Hewawasam

received the inaugural Women's Health Research Translation Network Early and Mid-Career Researcher Fund (\$15,000) from the Australian Health Research Alliance (AHRA).



Cheng Sheng "Nick" Chai

graduating with first class honour's degree for his project "The immunogenicity of COVID vaccine in South Australian kidney transplant recipients".



The Dialysis Start Program

at Central Northern Renal and Transplantation Service (CNARTS) was awarded the best program in the category of 'Improving Safety and Quality' at the 2021 SA Health Awards.



Dr Belinda Stallard

was awarded the SOMANZ President's Award for the Best Clinical Oral Presentation for her presentation - "What do you want to know and how do you want to know about it?" Consumer perspectives of pregnancy counselling and education in women with kidney disease: a national survey"



Prof Stephen McDonald

was the winner of the Advancing equity for Aboriginal and Torres Strait Islander Peoples and Māori category at the Australian and New Zealand Society of Nephrology (ANZSN) conference for his presentation "Kidney transplant outcomes among Aboriginal and Torres Strait Islander people - the gap is closing"

McDonald S, Owen K, Hughes J, Khanal N, Bateman S

Background: Aboriginal and Torres Strait Islander people constituted 15% of those who commenced dialysis 2001-2019 aged <65 years but received 5 % of deceased donor (DD) kidney transplants. Previous work showed this discrepancy is in waitlisting not allocation. Poorer outcomes among Indigenous recipients have been cited as a reason in qualitative studies.

Aim: Examine graft and patient survival among Indigenous compared with nonindigenous people

Methods: ANZDATA Australian DD1 recipients 2001-19; shared frailty Cox models adjusted for age and comorbidities

Results: Of 9244 transplant recipients, 442 were Indigenous. Median time (dialysis start to transplantation) was 3.5 years among Indigenous and 2.8 years among non-indigenous people. Indigenous recipients were on average 6 years younger, more likely to be female, smokers, and have diabetes or coronary artery disease. All significantly affected outcomes and were included in multivariate analyses.

Graft survival for all groups has improved over time. The adjusted hazard ratio (HR) for graft failure for Indigenous vs non-indigenous people transplanted 2001-2003 was 2.04 [95% Cl 1.13-2.00]. This progressively fell to 0.90 [0.50-1.63] for those transplanted 2016-2019. The interaction was significant (p=0.03); HR reducing 0.98 [0.96-0.99] per year. No interaction was seen for diabetes or age. For death-censored graft survival, the initial adjusted HR of 2.1 [1.4-2.9] fell by 0.96 [0.96-1.01] per year (p=0.05). For patient survival, the adjusted HR did not significantly change (HR 1.8 [1.3-2.5] in 2001-03; 1.5 [0.8-2.6] in 2016-19. However, this interaction was not significant (p=0.2).

Conclusions: There are substantial differences in the profile of Indigenous (vs non-indigenous) transplant recipients. Historically, graft and patient outcomes for Indigenous transplant recipients were poor. Critically, this "gap" in graft (but not patient) survival in transplantation is closing.

Research funding

| Clinical | Research Grou | ID |
|----------|----------------------|----|
| Children | | |

| \$200,000 | } | 2021 Kidney, Transplant and Diabetes Research Australia (KTDRA) Project Grant S Jesudason, P Clayton, R Le Leu Centralised Research & Clinical Data Warehouse with up-to-date dashboards in real time for the Central and Northern Adelaide Renal and Transplantation Service (CNARTS) |
|-------------|---|---|
| \$35,000 | } | 2021 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 |
| \$51,272 | } | 2021 Health Services Charitable Gifts Board (HSCGB) S Jesudason, A Burke, K Collins, R Le Leu, K Hill, A Chur-Hansen, S McDonald Improving Management of Needle Distress during the Journey through Psychological Education and Training (INJECT) |
| \$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. 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)

\$593,970

Centre for Clinical and Experimental Transplantation

| \$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. |
| \$500,276 | } | 2020-2022 Commercial in Confidence T Coates and C Drogemuller. Intracutaneous Ectopic Pancreas (IEP) creation by seeding Human Stem Cell-derived Islets (HSCI) into integrated BTM |
| \$1,969,259 | } | 2019-2021 Juvenile Diabetes Research Foundation International 3-SRA-2019-777-M-B T Coates. Proof of Concept Clinical Trial of Intracutaneous Islet Transplantation |
| \$460,000 | } | 2017-2021 The Hospital Research Foundation T Coates. Total Pancreatectomy and Islet Auto Transplantation. |
| \$3,200,000 | } | 2016-2021 Juvenile Diabetes Research Foundation T Coates. Expanding the criteria for human islet transplantation by the development of a drug-free immunosuppressive protocol. |
| \$2,014,561 | } | 2021 The Medical Research Future Fund (MRFF) PT Coates, 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 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

2021-25 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)

Clinical Trials



2021 The Medical Research Future Fund (MRFF) grant term 2022-2027

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 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.
- In 2021, the CRG Executive also became the Advisory Committee for philanthropic entity, Kidney Transplant diabetes Research Australia, a subsidiary of the Hospital Research Foundation Charity.

Vision statement

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



Executive Committee (L-R)

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

Project Staff in 2021:

Dr Richard Le Leu (Clinical Research Coordinator) Ms Gorjana Radisic (Research Officer) Ms Samantha Welke (Project Officer) Emily Duncanson (Research Officer)

CNARTS Consumer Engagement Working Group

- The CNARTS Consumer Engagement Working Group (chaired by A/Prof Shilpa Jesudason) was established in 2021 by the CRG.
- Working group members and their representation include:

Shyam Muthuramalingam (The Australia and New Zealand Dialysis and Transplant Registry, ANZDATA), Janet Kelly (Aboriginal Kidney Care Together- Improving Outcomes Now, AKction), Kellie Owen (National Indigenous Kidney Transplantation Taskforce, NIKTT), Stephen McDonald (ANZDATA and Renal Community of Practice), Jayne Wilkie (Renal Community of Practice), Gorjana Radisic (Improving Management of Needle Distress during the Journey to Dialysis through Psychological EduCation and Training, INJECT), Sam Welke (CNARTS Integrated Care project), Anne Britton (CNARTS Clinical Practice), Dana Cotton (CNARTS Quality and Safety), Richard Le Leu (CNARTS Clinical Research Group).

• This consumer engagement group brings together a broad group of CNARTS stakeholders that involve consumer engagement and allows collaboration, sharing of knowledge and growth of consumer partners.

CRG projects for 2021

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, E Duncanson, R Le Leu, F Donnelly, L Macauley, K Hill, A Burke, K Collins, A Chur-Hansen, B Tan, S McDonald

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

Our multidisciplinary team including consumer partners has developed "INJECT" – a novel intervention that aims to better identify needle

distress among dialysis patients as part of routine care and empower patients to self-manage needle distress with the support from nurses. We have involved patients and gained patient feedback at every stage of the project. The intervention has been informed by qualitative interviews with dialysis patients and nurses. In this study we are testing feasibility and acceptability of multicomponent intervention which encompasses patient self-management program and nurse education program. The nurse education program is designed to promote best practice cannulation techniques, and to improve nurses' ability to recognise needle fear in dialysis patients and provide information and strategies to support patients who experience needle fear. Patient self-management program is a Cognitive Behaviour Therapy based intervention which aims to empower patients to self-manage their fear of needles. The program is underpinned by psychologist input, research team and dialysis nurses' support. We will also identify barriers and facilitators to implementing a pragmatic trial to improve needle fear in patients.

Thus far, Nurse education program has been completed and the findings indicate that the program can improve nurses' ability to recognise needle fear in dialysis patients and provide information and strategies to support patients who experience needle fear. The protocol manuscript has been published in Journal of Pilot and Feasibility studies. The recruitment of patients into the study is still underway with 10 patients being recruited into the study. We have also formed a dedicated consumer advisory panel for needle fear related projects.

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), P Clayton, T Coates, S Jesudason

(Collaboration with the Microbiome and Host Health Programme, SAHMRI)

This project investigated dietary intake and the frequency of GI symptoms, including diarrhoea, over three time-points: pre-transplant, 2-weeks and

26-weeks post-transplant. This project also examined the gut microbiome for changes between pre-transplant and 2-weeks post-transplant and to determine its capacity to ferment non-digestible carbohydrates and to generate short chain fatty acids. Preliminary results have shown a significant gut dysbiosis post-transplant.

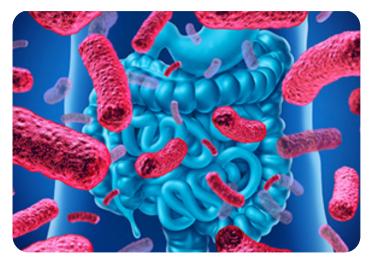
A manuscript was published on the work that examined the GI burden and dietary intake in patients with CKD with or without dialysis.

Meade A, Le Leu R, Watson N, Jesudason S, Clayton P, Faull R, McDonald S, Trimingham C. Gastrointestinal symptom burden and dietary intake in patients with chronic kidney disease.

J Ren Care. 2021 Dec;47(4):234-241.

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. To date, 107 patients have been recruited, 83 have completed baseline assessment, 39 have had 6-month follow ups with 27 completing the 12-month assessment. Recruitment is on-going.

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). 40 participants completed the protocol in 2021 with preliminary results showing high feasibility for ease of mobile phone use and the majority to date agreed that mobile apps could help them manage their condition. Recruitment is on-going.

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 Katinyeri, R Gadd, Kuranye Owen, D Champion, S Champion, O Pearson, T Mackean, S Jesudason, S McDonald, S Crail, M Arnold Chamney, R Le Leu, L Jamieson, K Herman, K Varcoe-Temple, A Cormick, T Stevenson, L Rix.

(Collaboration with Community members, University of Adelaide, SAHMRI, ANZDATA, The National Indigenous Kidney Transplantation Taskforce, Kidney Health Australia)

AKction2 builds on and extends AKction1, with a stronger emphasis on Indigenous Governance. Three of the AKction1 Reference Group members with lived experience of kidney disease are now Chief Investigators, working alongside researchers and nephrologists to lead the project. AKction Reference Group members are repositioned as AKction Reference Team members in recognition of their central role directing how we bring communities together, vision making, decision making and knowledge sharing in AKction 2 and other kidney care projects. Akction2 is framed around four interconnected sub studies; Indigenous Governance, Kidney Journeys, Aboriginal Peer Support and Cultural Safety. The first year is focused on Indigenous Governance and ensuring that Aboriginal preferred ways of knowing, being and doing are deeply embedded into the project processes and desired outcomes. We are co-designing new ways of working together in Brave Spaces, bringing together Aboriginal community members, health professionals, concurrent projects and researchers. We are actively decolonising research and organisational processes and interactions, identifying strength and gaps, and building in processes for critical reflection and shared decision making. Establishing and embedding Indigenous Governance, while comprehensively planning the implementation of each sub study, has been crucial to ensure that Aboriginal community members are meaningfully involved in all aspects of this kidney health research project.

Funded by:

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

Reducing Unplanned Chronic Dialysis Start – 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, K Richards, J Yeoh

The CRIPs project is developing sustainable models of care for integrating primary care services with and throughout CNARTS and reducing unplanned dialysis starts through the development, implementation and evaluation of a range of evolving studies.

This project will empower clinical leadership in ongoing research by providing staff with holistic qualitative data about CNARTS strengths and improvement opportunities, and engaging staff in practical research translation and ongoing practice evaluation.

Seventy-six one-to-one interviews were conducted with key internal and external stakeholders to collect comprehensive qualitative data about CNARTS service delivery across all key service points.

The rich qualitative data collected has directly informed the development of a number of substudies and projects to address the identified opportunities and challenges to integrated care. These include:

- A suite of dedicated tertiary-primary communication pathways: direct GP enquiries email address; co-designed service web page and service brochure
- An audit of renal patient discharge summaries including assessment of content and timely receipt by the correct GP; co-design of a new discharge summary template with education for medical and administration staff
- Development and implementation of a multidisciplinary Dialysis Start Program model of care, inclusive of internal clinical coordination processes and communication materials for GPs, providing additional support for patients commencing chronic dialysis (*winner of a 2021 SA Health Award*)
- Development of CNARTS service and referral information in Health Pathways SA (on-line GP and primary health professionals' clinical information and service and referral data base)
- Co-design of a new supportive and integrated service model for patients as they approach the requirement for chronic dialysis treatment 'Preparing for Dialysis Toolkit'
- Planning for the development of GP Kidney Champions across SA, in conjunction with KHA
- Preparation of manuscript presenting the unique insights gained thorough one aspect of the analysed qualitative data collected "The Patient Perspective of the Tertiary-Primary Interface in Renal Care"
- Commencement of an outcomes report for future use in evidence-based service model planning and development.

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)

Two cohorts of patients will be included for assessment within this study. A historical cohort and prospective cohort. The prospective part we 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. Currently the prospective component has recruited 8 patients with a target recruitment of 15 patients. The historical therapeutic drug monitoring (TDM) cohort will comprise patients previously receiving vancomycin treatment, from which routine vancomycin TDM data and will be sourced from patient medical records. This research will help establish optimal dosing and monitoring strategies that maximise therapeutic success and minimise adverse effects in haemodialysis patients receiving vancomycin.

Funded by:

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



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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 now halfway through her PhD investigating models of care for Aboriginal and Torres Strait Islander people living with kidney disease. She works under the guidance and governance of the AKction research group and is honoured to be a chief investigator on the AKction2 project (NHMRC Ideas Grant). She has formed strong relationships with the AKction

reference team including deeply respectful patient-expert partnerships with key members which are increasing research capacity and providing authentic two-way learning opportunities for all.

Through this first part of her PhD Sam and the AKction team have:

- described and published a process of co-creating meaningful and respectful community engagement workshops for Aboriginal and Torres Strait Islander people living with kidney disease
- reviewed the current models of care for First Nations people of Australia, New Zealand, Canada and the USA living with kidney failure
- informed and authored the models of care section of the KHA-CARI guideline for The Management of CKD for Aboriginal and Torres Strait Islander Australians
- -established and presented the survival benefit of kidney transplantation for Aboriginal and Torres Strait Islander people eligible for transplant

Over the next 18 months Sam will be working to establish the benefits of peer support models for Aboriginal people living with kidney failure through a qualitative analysis of the Keeping on Track to Transplant program in Port Augusta. She will be investigating issues of equity in predialysis care through an ANZDATA analysis of dialysis access key performance indicators for Aboriginal and Torres Strait Islander Peoples. Most importantly, she will continue to listen, learn and reflect - continuing her own journey of decolonisation.

Funded by:

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



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Decision Making in Deceased Donor Kidney Transplant Offers



Lead - Dr Alison Weightman (PhD Candidate) **Team** - P Clayton (Principle Supervisor), M Ladhani, S Moodie, D Stephenson, S Coglan

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 will be conducted with multiple

different groups including transplant nephrologists, non-transplant nephrologists, new transplant patients, patients on the waiting list and family members of deceased donors. 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 will investigate the causes of withdrawal from kidney transplantation and investigate the patient characteristics within this patient group. The study is due for completion in 2022.

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



Lead – Prof Stephen McDonald,

Team - A Biddle, J Childs, K Hill

(Collaboration with School of Nursing, University of South Australia)

This project surveyed the nursing staff at several rural health dialysis units to understand their perceived competence in assessing vascular access with the use of duplex ultrasonography. In tandem, we collected cannulation data from these sites to assess the incidence of miss-cannulation and retrieval

to the Royal Adelaide Hospital for vascular access issues. Subsequently portable ultrasound machines were sited at these units and UniSA developed a renal nurse specific 'point of care ultrasound surveillance' online training module which site staff are now undertaking. In April the UniSA team will travel to these sites to provide hands-on training to supplement the online modules. We will evaluate the training through repeated surveys of nursing staff and repeated cannulation data collection with a final report expected later in 2022.

Funded by:

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

Knowledge, skills, and attitudes of renal nurses working with patients undergoing haemodialysis who fear needles



Lead – Tahlia Masotti (Psychology Honours student)

Team - A Chur-Hansen (Principal supervisor), E Duncanson, R Le Leu, S Jesudason

(Collaboration with the School of Psychology, University of Adelaide)

This study aimed to identify the core knowledge, skills, and attitudes of renal nurses, and how they approach working with dialysis patients experiencing fear of needles. Seventeen pre-existing interviews with South Australian

renal nurses were analysed via thematic analysis to explore the experiences of working with patients undergoing haemodialysis. Information was coded according to a competency framework, detailing thirty-six features of knowledge, skills, and attitudes (KSAs) of nurses regarding the management of patients' needle fear. KSAs were then categorised to describe seven competencies pertinent to renal nursing and working with patients with fear of needles. Two main themes: Flexibility, and Responsibility, overarched all KSAs and competencies. The challenging and multi-faceted nature of needle fear was detailed by participants as a hindrance to effective care. Recommendations for continued professional development for renal nurses are suggested, highlighting the need for the education and resources specific to working with patients with needle fear.

How does the experience of haemodialysis impact a patient's ability to cope with a fear of needles and the needling procedure?



Lead – Bronwyn Harris (Psychology Honours student)

Team - A Chur-Hansen (Principal supervisor), E Duncanson, R Le Leu, S Jesudason

(Collaboration with the School of Psychology, University of Adelaide)

The aim of this project was to explore patient fear around needles and identify processes to better manage the fear of needles. Interview data from fifteen haemodialysis patients was provided by the Central

Northern Adelaide Renal and Transplantation Service (CNARTS). The interviews went through a thematic analysis coding process and were ultimately grouped into five overarching themes. These interviews were analysed under the theoretical lens of the transactional model of stress and coping, with three coping methods, emotional-, task- and avoidance oriented, to explore the coping of haemodialysis patients. The central themes were, Challenges with the physical procedure, Emotional responses to sources of pain, Regaining control through selfreliance, Improved outcomes through patient-centred care and Influence of nursing skills on psychological outcomes.

This study provided valuable insight into the mechanisms that affect patent coping during dialysis, and the data was used in the development of a patient-led and nurse-supported intervention to be delivered by a health psychologist to address needle fear in dialysis patients.

Medication safety in dialysis patients: The implementation of a patientfocused strategy to minimise medication errors



Lead – Dr Karthik Venkataraman

Team – H Tran, F Donnelly, M Sharma, S Jesudason

The aims of this project were to evaluate the prescribing patterns in our dialysis patients and evaluate patients' attitudes to medication prescribing. Participants included CNARTS dialysis patient (in centre + home). Paper questionnaire was delivered by dialysis nurses, pharmacy intern or via telephone by investigators or home therapy nurses. 187 responses were

received from a total number of patients that were able to respond to the survey of 383 (48.8% response rate). Conclusions from the project included:

- Our dialysis patients have a variety of prescribers, this is important to be mindful of
- Webster pack use is quite common in our dialysis cohort
- Our patients will generally question new medications

Audit of fluid and hypotension post transplantation

Lead – Dr Karthik Venkataraman Team – S Jahan, Z Kuah, T Coates

Case note review to audit rates of hypotension post transplantation, along with associated fluid therapy administered and rates of complications such as delayed graft function and wound complications will be undertaken.

Karthik intends to develop this study as part of a Masters project in 2022 whereby a Pilot randomised controlled trial of an Advanced Recovery Protocol on Post Operative Hypotension in Living Donor Kidney Transplantation will be conducted.

Factors associated with dialysis withdrawal following modality change from peritoneal dialysis to haemodialysis



Lead – Dr Sarah Tan

Team – G Lincoln, C Yeap, P Clayton

Utilising the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA), we performed a retrospective observational cohort study to identify the risk factors for dialysis withdrawal following a switch from peritoneal dialysis (PD) to haemodialysis (HD). Dialysis withdrawal is a common cause of mortality among this cohort, comprising 19.6%. Risk

factors for withdrawal following modality change include older age at PD initiation, having a comorbidity, and living remotely.

Dying to talk: A clinical audit on uptake of Advanced Care Directives among patients with kidney disease.

Lead – Dr Sarah Tan

Team – L Lunardi, M Nor, A Flabouris, S Crail

The aim of this audit was to examine advanced care directive (ACD) uptake among a high-risk population of renal patients. We performed a medical audit utilising electronic medical records of renal patients who died in a large tertiary centre between 2019-2021. Data was collected data regarding demographics, comorbidities, dialysis, ACD completion, and events occurring during the terminal admission. 90 patients were identified. Only 10% (n = 9) of patients had completed an ACD prior to admission. ACD uptake remains poor among renal patients. ACD uptake should be encouraged among this high-risk cohort, particularly for those with ESKD on dialysis.

Statin prescribing in the peri-transplant period- A clinical audit



Lead – Prof Toby Coates **Team** – F Kette

Renal transplantation is associated with a significant increased burden of cardiovascular disease, the result of which markedly increases morbidity and mortality for this patient cohort. The underlying causes of the elevated cardiovascular risk include transplant specific insults such as poor graft function and immunosuppressive medications, as well as traditional risk-

factors associated with baseline end-stage renal disease that persist despite transplantation, including hypertension, dyslipidaemia, diabetes and obesity. Strategies for minimising concomitant disease burden in transplant recipients aim to improve long term transplant outcomes, given death with a functioning graft is the most common cause of graft loss. Among this patient cohort, under the KDIGO guidelines treatment with statins has been suggested for all adult patients (2B) to modulate cardiovascular risk. Given this, we conducted an audit of the last 100 transplant recipients to evaluate both the continuation, and new prescribing practices of statins in the peri-(renal) transplant period within CNARTs. It was found that of the 100 patients receiving a kidney transplant, only 47 of these patients were on statin therapy at the time of transplantation. However, following transplantation, through the variable follow up duration over the last 100 patients, only 23 patients were on statin therapy at the time of the audit being performed, with only 1 patient being newly commenced, and 22/47 continued, on a statin. Based on the KDIGO guidelines and given the elevated cardiovascular risk profile, there is a significant under prescribing of statins among the renal transplant patient cohort.

'Back to the machine' Transition from transplant to dialysis



Lead – Dr Sadia Jahan **Team** – S Crail, F Donnelly, J Hopkins

The aims of this retrospective single centre cohort study are to review the characteristics of this subset of patients and outline the trend of renal function in the months leading up to the transition to dialysis as well as the cause of their failing graft. Sixty-seven patients were identified to have commenced dialysis from transplant in the study period between 2015 and

mid-2020. Out of those who commenced dialysis as outpatients, the cause of graft failure was progressive renal dysfunction, uraemia and fluid overload. Those who commenced dialysis as an inpatient were due to sepsis, GI bleed, gastroenteritis, or AKI during pregnancy. Acute graft dysfunction requiring commencement of dialysis has a steeper deterioration of renal function in comparison to those who commenced dialysis as an outpatient.

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 Dr Rob Carroll. Principal Medical Scientist A/Prof Chris Drogemuller manages 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 (Principal Medical 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 Ernesto Hurtado (Grant Funded Scientist) Denghao Wu (Grant Funded Scientist /PhD candidate) Dr Sebastian Stead (Grant Funded Project)

Students

Griffith Perkins (PhD candidate) Alice Krige (PhD candidate) Brigette Clarke (PhD candidate) Jacqueline Scaffidi (PhD candidate) Bronwyn Dearman (PhD candidate) Nick Chai (Honours Student)



We aim to:

Enhance the treatment of Type 1 Diabetics (T1D) with poorly controlled disease through our allo-islet transplant program and associated research projects.

Deliver better clinical outcomes to T1D patients with renal failure through the establishment of the simultaneous kidney-whole pancreas transplant program.

Advance the understanding of hereditary pancreatitis in the Australian population and provide a curative treatment through the Total Pancreatectomy and Islet-Auto Transplant (TPIAT) program.

CCET projects for 2021

Concurrent Vaccination of Kidney Transplant Recipients and Close Household Cohabitants against COVID-19



Researcher Griffith Perkins with kidney-transplant patient Mike Thompson (picture Keryn Stevens)

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

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

When COVID-19 vaccines became available in Australia last year, immunocompromised individuals, including transplant recipients, were given priority status to receive their vaccination. However, transplant recipients receive medications that suppress the immune system in order to protect the transplanted organ, and may therefore not be afforded the same level of protection from vaccination as the general

population. Based on this hypothesis we initiated the REVAX Trial with the objective of giving concurrent vaccine doses to the close household cohabitants of kidney transplant recipients. This allowed us to compare vaccine responses between kidney transplant recipients and healthy individuals, and to evaluate 'ring vaccination' as a strategy to limit exposure of vulnerable transplant recipients to SARS-CoV-2.

A strong neutralising antibody response to vaccination is the best protection against infection and disease. Kidney transplant recipients in our study had an average antibody response after two vaccine doses that was >1,000-fold lower than the average for healthy individuals. By contrast, 100% of cohabitants demonstrated a neutralising antibody response indicative of protection from infection, suggesting that priority vaccination of cohabitants is a necessary and useful strategy for the ongoing roll-out of COVID-19 vaccines.

Immune Checkpoint Inhibitors in Renal Transplant Patients with Incurable Cancer - multi centre study



Researchers – R Carroll, B Hockley, J Johnston and S Kireta **Associate Researchers** – H Tan, A Taylor, Prof M Boyer, J Zalcberg and K Wyburn

Using immune profiling including urinary CXCL-10 to define risk of rejection in those treated with immune checkpoint inhibitors. Completed mulitcentre study - article in submission.

The Biodegradable Temporizing Matrix as an Alternative Site for Human Islet Transplantation



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

Associated researchers – J Greenwood, S Grey, B Dearman, S Walters, T Kay, T Loudovaris, L Mariana

This project is supported by the Juvenile Diabetes Research Foundation International (New York), where an alternative extra hepatic site for islet transplantation is being developed. 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.

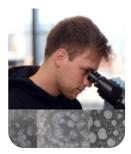
Notwithstanding the ongoing challenges COVID-19 presented in 2021 we were able to perform seven large animal experiments to examine the suitability of intracutaneous islet transplant to treat type 1 diabetes. These experiments confirmed the ability of the site to support islet survival and function. Based on the data obtained from the completed JDRF studies, a first in human "Proof of Concept" clinical trial of intra-cutaneous islet transplantation will be trialled in 2022. The trial is funded through JDRF with 3 patients to undergo the procedure initially and if successful will be followed up with an additional 5-10 patients.

Intracutaneous Ectopic Pancreas (IEP) creation by seeding Human Stem Cellderived 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 commercial in confidence and comprises a collaboration between one of the largest international diabetes companies, our islet transplant research team and Beta Cell Technologies. In 2021 we completed a pilot nude rat study to establish a model that reflects the human clinical intracutaneous transplant protocol. Briefly, BTM is sutured into an elliptical wound created on the back of the rat and allowed to integrate for 3 weeks. Following integration, the wound site will be folded on itself to create a pocket into which stem cell derived islets will be transplanted to rescue chemical induced diabetes. Following on from this pilot study to define the model we will initiate a larger project to measure the safety and success of HSCI to rescue diabetes in the nude rat. The aim of this research is to generate sufficient pre-clinical data to support a first in human trial in the next 2 years.

Regulation of IL-10 secretion by human B cells



Researchers – G Perkins, P Hurtado, T Coates Associated Researchers - J Kim, S Stead, C Hope

We are working with blood samples from transplant recipients, allergic individuals, and patients with systemic lupus erythematosus to explore dysregulation of an immunosuppressive immune cell subset called regulatory B cells in these disorders. We have identified a cytokine network that underpins this dysregulation, and have developed several novel

laboratory assays to investigate how impaired regulatory B cell function might contribute to disease.

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 2021, we successfully optimised CAR binding to the antigen of interest in T cells. We also optimised the manufacturing process of CAR

Tregs and began to screen their function in vitro by testing their suppressive function and expression of typical Treg markers. Screening will continue this year, with the aim to manufacture CAR T regs from T1D patient T regs as a proof of concept.

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

Researchers – B Clarke, S Kireta, J Johnston, D Penko, J Nitschke, C. Drogemuller, T Coates, D Torpy

Associated Researchers – C Christou, J Greenwood, J Kollias, 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 intracutaneous site for cell transplantation in a large animal model. 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.

In 2019 and 2020, we developed a protocol for the isolation and primary culture of porcine adrenocortical cells and were able to demonstrate cell survival and preservation of dynamic endocrine function in short-term culture. In late 2020, we started our first in vivo experiments, performing autologous intra-cutaneous adrenocortical cell transplantation in a bilaterally adrenalectomised porcine model. This experiment is designed as a proof of concept study to demonstrate survival and endocrine function in vivo of cultured adrenocortical cells. This experiment remains in progress at the time of report. Demonstration of success in these autograft studies will lead to further experiments evaluating porcine adrenocortical allografts using the same model. This project is supported by a Royal Adelaide Hospital Clinical Project Grant and is being undertaken in collaboration with Beta-Cell Technology. Ligasure Exact devices to assist with surgical adrenalectomy have been donated by Medtronic.

The epidemiology and costs of chronic pancreatitis in South Australia



Researchers – T Bampton, C Drogemuller, T Coates

The management of chronic pancreatitis (CP) results in a significant burden to healthcare. It is characterised by episodes of severe pain, often necessitating hospitalisation and high doses of opioid medication to achieve analgesia. There are no comprehensive data examining the epidemiology or costs of CP in Australia. Data linkage is a rapidly growing field of study, allowing researchers a high level of statistical power to find modest effect sizes with large volumes of unbiased data.

This project therefore involved close collaboration with SA NT Datalink, an organisation that allows research access to administrative data generated by both State and Commonwealth Governments on the population of SA. A total of 2,576 index cases with CP were identified over a 20-year period within South Australia. This allowed for estimations of the prevalence and incidence of a condition previously undescribed epidemiologically within Australia. Additionally, captured within the dataset were numerous data points relating to health-care utilisation, including days in hospital, emergency department visits, time in ICU and procedures undergone in hospital, for example. The CP cohort were identified as having significantly higher health-care utilisation than all comparator groups using the same health-care metrics. Such data are vital to inform health service decision-making regarding the future of CP management.

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 SLE-derived 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, T Radford, C Etherton, 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 we have been able to establish 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. Once the islets have been isolated they are then transplanted back into the patient's liver where they will remain and following a short period of engraftment will 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 December we officially opened our Biospherix System, housed in SA Pathology Frome Road. Currently, the islet isolation process is performed in Melbourne requiring the pancreas to be flown by commercial airline to Melbourne and then a return flight to Adelaide with the islets to infuse back into the patient. During the ongoing COVID-19 pandemic this became impossible due to border closures and lack of flight availability. Therefore, the establishment of our own isolation capability in Adelaide became even more crucial, above the needs to reduce the inherent risks in such transport of the organ and tissue and to reduce the operative time for the recipient.

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 (ovine) 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.

Initial large animal experiments were conducted in 2019, completing "living donor" and "donation after brain death" static cold storage models for use as controls (neither with any warm ischaemic damage to speak of). 12 months delay with formal interruption to PhD occurred in 2020 due to COVID-19 pandemic. Large animal work recommenced and completed in 2021, consisting of 3 further groups of animals ("donation after cardiac death/DCD" static cold storage controls, DCD anterograde persufflation treatment group and DCD retrograde persufflation treatment group) together with all laboratory work. Initial results suggest improved early kidney function in persufflation groups. Remaining data analysis and thesis write-up to occur in 2022.

The Genetic Epidemiology of Hereditary Pancreatitis in South Australia



Researchers – T Coates, D Wu, C Drogemuller, S De Sousa, D Adelson **Associated Researchers** – L Palmer, K Kassahn

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 5 pedigrees and 4 individual probands comprising 47 individuals were recruited for the project. 4 families possess the mutation PRSS1(3 family with R122H, 1 family with A86T). In total, 23 PRSS1 and 9 SPINK1 variant carriers across multiple generations were identified, 13 of which self-identified as Indigenous Australian. Our estimated prevalence of HP in South Australia is much higher than the value of 0.1-0.3/100,000 previously described in European populations. 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

During the end of 2020 and 2021, alternative methods for skin substitute fabrication were explored with an international expert of engineered skin to evaluate a hybrid biopolymer scaffold. This multi-component, hybrid scaffold combined with autologous skin cells to fabricate a novel skin substitute was tested to definitively close full-thickness wounds in a porcine model. These results show the novel skin substitute prevents the inherent contraction of collagen materials and optimises the porosity of the polyurethane scaffold. We propose that with refinement, this skin substitute could readily be scalable to address several medical indications. This material would significantly impact extensive burns and other acute and chronic wounds that would benefit therapeutically to reduce donor site harvesting, numbers of skin autografting procedures, and long-term morbidity from scars. To the best of our knowledge, this is the first documentation on using polyurethane and collagen as a novel scaffold to fabricate skin substitutes for extensive, full-thickness wounds.

The immunogenicity of COVID vaccine in South Australian kidney transplant recipients



Researchers – N Chai (Honours Student, Adelaide University), G Perkins, C Drogemuller, T Coates

Kidney transplant recipients (KTRs) are particularly vulnerable to severe disease from SARS-CoV-2 infection. For this reason, transplant recipients were given a priority status for COVID-19 vaccination in Australia, however, the efficacy of vaccines to elicit a protective immune response in this group of patients is questioned due to long-term treatment with immunosuppressants. This project investigated the vaccine-induced

immunological response in our South Australian kidney transplant cohort.

We assessed vaccine responses in 46 KTRs compared with 46 of their close household contacts. Following 2 vaccine doses, only 32% of KTRs produced anti-SARS-CoV-2 spike-specific IgG compared with 100% of healthy cohabitants. The median of antibody titre for KTRs was 1000-fold lower than cohabitants. The capacity of antibody to neutralise live virus was heavily impaired in transplant recipients. With respect to cellular immunity, on average, the frequency of spike-reactive IFN-gamma T cells were 10-fold lower in KTRs after 2 doses of vaccine compared to their cohabitants. Interestingly, we found that patients who receiving rapamycin as part of their immunosuppressant have exhibited higher spike-reactive IFN-gamma secreting T cell responses than healthy cohabitants and those patients on standard care of therapy (tacrolimus, mycophenolate, and prednisolone), suggesting that rapamycin has an immunostimulatory effect on T cell immunity during vaccination. The mechanism by which rapamycin enhances anti-viral T cell function is the subject of my ongoing PhD research in the CNARTS Renal Lab.

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 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.

The Better Evidence And Translation – Chronic Kidney Disease (BEAT-CKD) is a collaborative research program that aims to improve the lives of people living with chronic kidney disease in Australia and globally by generating high-quality research evidence to inform healthcare decisions made by patients, health professionals, and policy makers. BEAT-CKD addresses the entire spectrum of CKD, from early-stage chronic kidney disease, through to dialysis, and kidney transplantation.

BEAT-CKD is funded by a NHMRC Program Grant (1092957) and include the Chief Investigators: Prof Jonathan Craig, Prof David Johnson, Prof Jeremy Chapman, A/Prof Carmel Hawley and Prof Stephen McDonald and Associated Investigators: A/Prof Shilpa Jesudason and Dr Phil Clayton. This grant awarded in 2016-2021 (\$10,141,300) supports national research and translation platforms including ANZDATA.

(http://beatckd.org/)

ANZDATA Research staff:

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Current Projects

https://www.anzdata.org.au/anzdata/research/registry-projects/

Exploring patient travel to in-centre haemodialysis



Lead - Prof Stephen McDonald

Team - C Davies, K Dansie, E Duncanson, S Jesudason, S Ullah, A Gulyani, D Keuskamp, P Clayton

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 – Prof Stephen McDonald

Team - S Muthuramalingam, K Hurst, S Jesudason

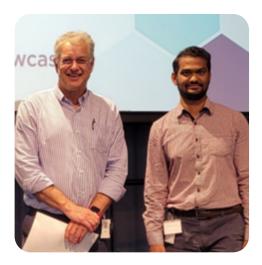
Apart from our business-as-usual publication of the Consumer infographic summary for the year 2020 and Catching Some AIR Project infographic specific to Aboriginal and Torres Strait Islander Peoples of Australia, we covered lots of areas in terms of development of framework and guidelines for nephrological societies and other pillar members within BEAT-CKD program. One of the significant milestones was the consultation with the consumer groups and the implementation of the Australian and New Zealand Society of Nephrology (ANZSN) consumer engagement framework. This framework will aid the appointment of consumers to the Society's key advisory committees and welcome consumers to the Society's scientific and policy meetings. As a part of the ANZDATA governance structure, a Consumer and Community engagement working group was established along with the development of terms of reference documents for the ANZDATA Consumer Advisory Panel. The next step involves recruiting

consumers to the panel and organising the working group meeting.

As a part of the Kidney Health Australia's National Strategic Action Plan's Kidney Consumer Research Network project, we conducted a Rural and Remote Kidney Patients Yarning Session to hear consumer stories from rural/remote and regional Australians to address the inequity in Kidney care. This one-day event was attended by more than 50 indigenous consumers from Pt Augusta, Broome, Cairns, Armidale, Adelaide, Geraldton, and Darwin.

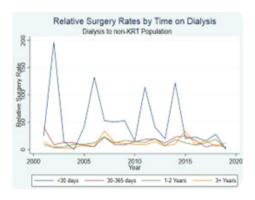


Yarning session with our Indigenous consumers from rural, remote and regional areas of Australia to hear patient stories



Shyam Muthuramalingam with SAHMRI Executive Director Prof. Steve Wesselingh during the award of the Early career Mid-Career Researcher poster prize at the SAHMRI Research Showcase. Consumer shared their stories and identified core themes as consumer champions and patient navigators as enablers and barriers like systemic racism and burden of travel for Kidney patients in rural Australia in terms of access to kidney care. ANZDATA hosted the Consumer and Community Engagement Summit 2021 in partnership with Health Translation SA as a part of SAHMRI Consumer **Engagement Community of Practice and ANZDATA** consumer engagement activities were presented by Shyam and Erandi presented on "Pregnancy with kidney disease: Consumer Engagement. Shyam presented at the Consumers Health Forum of Australia's (CHF) summit Shifting Gears, the inaugural Australia and New Zealand Consumer Experience and Leadership in Healthcare Summit, under the stream: Consumer Leadership about the Coproduction of Consumer-Specific ANZDATA Reports of Registry Data.

Data linkage



Lead – Prof Stephen McDonald

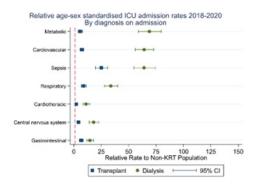
Team - C Davies, K Dansie, D Keuskamp, G Lincoln, P Clayton

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 end-stage kidney disease 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. Further analyses will look at outcomes of joint replacement for KRT patients.

Cardiothoracic Surgery Registry – Early in 2022 a national linked dataset will be 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 for developing end-stage kidney disease (treated with KRT) after cardiac surgery, and (2) the risks of cardiac surgery for KRT patients. **Intensive Care Registry** – Early in 2022 a national linked dataset will be 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.

Intensive Care Units – In 2022 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 end-stage kidney disease (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". In 2021 the Sharesource data was 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.

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



Lead – A/Prof Shilpa Jesudason

Team - E Hewawasam, P Clayton, C Davies, R Danner, B Stallard, J Hopkins, S McDonald

Parenthood Consumer advisory group members: Jane Boag, Charmaine Green, Laura Heffernan, Brooke Huuskes, Carolina Maistry, Kelli Owen, Shyamsundar Muthuramalingam, Adela Tolic, Amber Williamson

This year our group progressed many projects. Some of our activities included:

• We are thankful to The Hospital Research Foundation for awarding us \$150,000 under the 2021 Women's Health Grant Round to the project titled "The Kidney Mums Project: Advancing pregnancy planning and care for women with kidney disease ". This program of work will address Aboriginal and Torres Strait Islander perspectives on pregnancy with CKD, establish a multi-site prospective cohort study of CKD in pregnancy, and develop risk algorithms and decision aids to help women and clinicians navigate difficult decisions about pregnancy with CKD.

- Project Manager and Post-Doctoral Research Fellow Dr Erandi Hewawasam's abstract at the 2021 World Congress of Nephrology was one of the top two abstracts submitted to the congress and presented in the "Late-breaking clinical trials and best of abstracts" session.
- Dr Hewawasam was one of the 36 recipients of the inaugural Women's Health Research Translation Network Early and Mid-Career Researcher Fund (\$15,000) by the Australian Health Research Alliance (AHRA).
- We also presented at conferences organised by The Transplantation Society of Australia and New Zealand, Australia and New Zealand Society of Nephrology, Society of Obstetric Medicine of Australia, Transplant Nurses Association Conference, and Australian and NZ Society for Medical Research-SA annual meeting.
- Members of the parenthood consumer advisory group have been involved in designing research studies, setting research priorities, developing data collection tools and consumerfriendly visual summaries of research outputs. Consumer partner Adela Tolic (pictured) presented at Consumer and Community Engagement Summit (SAHMRI and Health Translation SA) and shared her story with the wider clinical and research community. https:// www.hospitalresearch.org.au/community-story/adela-is-living-well-with-kidney-disease/
- Our work on the factors influencing fertility rates in Australian women receiving kidney replacement therapy was published in the journal of Nephrology Dialysis Transplantation. This study also validated the accuracy of the ANZDATA registry parenthood data for the first time. https://doi.org/10.1093/ndt/gfab157
- With collaborators Prof. Allison Tong and Dr Mel Wyld, we conducted an qualitative interview study with Australian kidney doctors to understand their perspectives on the management of pregnancy in women with chronic kidney disease.
- We conducted a national survey of women with kidney disease, with > 100 participants providing their perspectives of pregnancy education in women with kidney disease. We are hoping to develop educational resources for both patients and clinicians based on the findings of these studies.
- In collaboration with researchers at the Lyell McEwen Hospital led by Prof Margaret Arstall, we established a prospective registry for maternal kidney and cardiac diseases in pregnancy in SA (the CAROSA study).
- Renal Advanced Trainee Dr Rhea Danner undertook evaluation of the completeness of the ANZDATA parenthood data collection over time as the registry has evolved.



Meeting virtually with our consumer advisory group



Our parenthood advisory group member Ms. Adela Tolic presenting at the at Consumer and Community Engagement Summit (SAHMRI and Health Translation SA).

Patient reported outcome measures (PROMS) in Australia & New Zealand Renal units and the ANZDATA Registry – Symptom Monitoring WIth Feedback Trial (SWIFT)

Lead - Prof. Stephen McDonald

Team - L Greenham, K Dansie, S Jesudason, P Bennett, R Morton (CI)

SWIFT (Symptom monitoring WIth Feedback Trial) is a novel two-arm cluster randomised trial testing the hypotheses that symptom monitoring using the IPOS-Renal questionnaire with feedback to clinicians and patients, improves 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 commenced recruitment at the Lismore Base Hospital and Gosford Hospital in NSW in April 2021. These units have just completed their 9-month data collection. In December, John Hunter Hospital completed their baseline data collection. The SWIFT Team would like to acknowledge and thank all those involved in data collection despite the challenges of COVID-19 pandemic. SWIFT has now enrolled 18 units across New South Wales and Queensland. We are currently working with the South Australian and the West Australian dialysis units. We anticipate rolling out to SA and WA in the first half of 2022, as well as continuing to onboard our NSW and QLD units.

Our newly initiated units include:

NSW: Concord Hospital, Royal Prince Alfred Hospital. QLD: Logan Hospital, Princess Alexandra Hospital, Redlands Hospital, Mackay Base Hospital.

Additionally, to enable participation of as many patients as possible, the trial surveys and patient information sheet and consent forms have been translated into 7 languages: (Simplified Chinese, Traditional Chinese, Korean, Vietnamese, Modern Standard Arabic, Italian and Greek). We are confident this will facilitate participation of those from culturally and linguistically diverse backgrounds. Lastly, SWIFT has developed a clinician-focused sub-study. This qualitative interview study aims to understand the usual practices for symptom monitoring and management for adults managed on haemodialysis. The sub-study will be conducted with interested clinicians by the SWIFT team in parallel with the randomised trial.

Improving impact and outcomes of ANZDATA hospital-specific performance reports

Lead – Prof Stephen McDonald

Team - C Davies, E Hewawasam, M Sypek, P 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.

Markov Modelling of prevalent dialysis and kidney transplant patient populations



Lead – Prof Stephen McDonald Team - C Davies, D 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 is developing 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).

Decision making in Kidney Transplantation



Lead – G Irish (PhD Candidate)

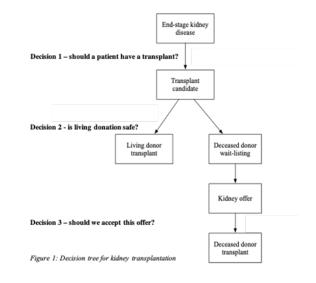
Team - P Clayton (Principle Supervisor), T Coates, J Hersch

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: Australian and New Zealand Living Kidney Donor Profile Index

Risk scores may aid risk quantification and decisionmaking in kidney transplantation. The Living Kidney Donor Profile Index (LKDPI) was developed in the USA to choose between living donors. On previous analyses we found the original LKDPI is moderately discriminatory but poorly calibrated in Australia and New Zealand. We have developed a new risk prediction score for overall graft survival in adult recipients of a living kidney donor transplant in an Australian and New Zealand population based on the ANZDATA registry. This has been validation in a UK population.



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 been submitted to the American Transplant Congress.

IpProject: 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 abstract will be submitted to TSANZ ASM.

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 submitted for publication. This work was presented at ANZSN ASM.

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 has been submitted TSANZ ASM 2022.

Funded by:

NHMRC Postgraduate Scholarship

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, Royal Adelaide Hospital (RAH) Medical Oncology department and the School of Pharmacy and Medical Sciences, University of South Australia, Australasian Kidney Trials Network (AKTN) and The George Institute.

Due to the ongoing 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 continue to be 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 2021, CNARTS researchers and patients have been involved in over 25 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 2022 we will be commencing new trials in IgA Nephropathy, Membranous Nephropathy, CKD and treatments for BK Virus and Antibody Mediated Rejection in Kidney Transplant Patients.



CNARTS Clinical Trial staff:

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

2021 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. CIRRUS I: A partially-blinded, active-controlled, multicenter, randomized study evaluating efficacy, safety, tolerability, pharmacokinetic (PK) and pharmacodynamics (PD) of an anti-CD40 monoclonal antibody, CFZ533, in de novo and maintenance kidney transplant recipients

Sponsor: Novartis PI: Prof Toby Coates

4. 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

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

Investigator Led & PI: A/Prof Robert Carroll

6. BEST FLUIDS: An investigator-initiated, pragmatic, registry-based, multi-centre, doubleblind, randomised controlled trial evaluating the effect of Plasmalyte versus 0.9% saline on early kidney transplant function in deceased donor kidney transplantation (https://aktn.org.au/ best-fluids/).

Sponsor: AKTN PI: Prof Toby Coates

7. 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

8. 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: Prof Toby Coates

9. 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

CKD/Glomerulonephritis trials:

10. 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

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

11. 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

12. 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

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

14. 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: Retrophin Inc PI : A/Prof Chen Au Peh

15. 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

16. 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

17. 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

18. 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: Retrophin Inc PI: A/Prof Chen Au Peh

19. 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 PI: Prof Randall Faull

ESRD/Dialysis trials

20.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

21. 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

22. 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.

23. TRACK study: Treatment of CVD with low dose Rivaroxaban in Advanced CKD.

https://www.tracktrial.org/

Sponsor: George Institute PI: A/Prof Shilpa Jesudason.

24. ASCEND-D: A phase 3 randomized, open-label (sponsor-blind), active controlled, parallelgroup, multi-center, event driven study in dialysis subjects with anemia associated with chronic kidney disease to evaluate the safety and efficacy of daprodustat compared to recombinant human erythropoietin, following a switch from erythropoietin-stimulating agents, Protocol 200807.

Sponsor: GlaxoSmithKline PI: A/Prof Shilpa Jesudason

25. ASCEND-ID: A 52-week open-label (sponsor-blind), randomized, active-controlled, parallelgroup, multi-center study to evaluate the efficacy and safety of daprodustat compared to recombinant human erythropoietin in subjects with anemia associated with chronic kidney disease who are initiating dialysis, Protocol 201410.

Sponsor: GlaxoSmithKline PI: A/Prof Shilpa Jesudason

Student supervision in 2021

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, A Somogyi

Patrick Asare (PhD Candidate, University of Adelaide) "Role of LC3 associated phagocytosis in COPD and lung cancer"

Supervisors: E Roscioli, P Hurtado, S Hodge

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

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

Supervisors: T Coates, 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"

Supervisors: T Coates, J Greenwood, S Boyce

Talia Gutman (PhD candidate, University of Sydney) "Strengthening Patient Involvement in Research about Chronic Kidney Disease"

Supervisors: A Tong, J Craig, S Jesudason

Ms Bronwyn Harris (Psychology Honours student, University of Adelaide) "How does the experience of haemodialysis impact a patient's ability to cope with a fear of needles and the needling procedure?" thesis accepted 2021, first class honours.

Supervisors: A Chur-Hansen, E Duncanson, S Jesudason

Ms Tahlia Masotti (Psychology Honours student, University of Adelaide) "Knowledge, skills, and attitudes of renal nurses working with patients undergoing haemodialysis who fear needles" thesis accepted 2021, first class honours.

Supervisors: A Chur-Hansen, E Duncanson, S Jesudason

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

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

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 and its effects on patients of TP-IAT."

Supervisors: T Coates, S De Sousa, D Adelson, L Palmer, K Kassahn, C Drogemuller

Nick Chai (Honours candidate, University of Adelaide) "The immunogenicity of COVID vaccine in South Australian kidney transplant recipients"

Supervisors: T Coates, G Perkins, C Drogemuller

Dr Asmaa Zidam (Master Degree Candidate, University of South Australia) "Study of the immunological interaction between the urine derived stem cells with the peripheral blood lymphocytes."

Supervisors: Xin-Fu Xu, P Hurtado

Conference Presentations 2021

2021 Transplantation Society of Australia and New Zealand Annual Scientific Meeting

Online (28 August-1 September 2021)

National Indigenous Kidney Transplantation Taskforce progress (*Plenary session*) McDonald S

Consumer engagement in Indigenous transplantation research (*Plenary session*) **Owen K**

TH1 and TH2 cytokines reciprocally modulate b cell regulatory functions

Perkins G, Kim J, Hope C, Coates T, Hurtado P

Tacrolimus inhibits mitogen and mixed lymphocyte reaction induced pig T-cell proliferation in vitro

Kireta S, Penko D, Nitschke J, Johnston J, Coates T, Greenwood J, Drogemuller C

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

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

Innate immune sensing and tissue remodelling of a biodegradable tempering matrix supported islet graft

Walters S, Bailey J, Cultrone D, **Rojas-Canales D, Drogemuller C, Penko D**, Loudovaris T, Kay T, Korbutt G, Chtanova T, Greenwood J, **Coates T**, Grey S

Intracutaneous biodegradeable temporizing matrix (BTM) as an alternative site for islet transplantation

Penko D, Nitschke J, Johnston J, Kireta S, Drogemuller C, Greenwood J, Coates P

Australian experience with total pancreatectomy with auto islet cell transplant (TP-IAT) to treat chronic pancreatitis

Bampton T, Drogemuller C, Jane H, Lyle P, Kay T, Pleass H, Chen J, Coates T

Maternal characteristics and birth outcomes for mothers after kidney transplantation: An analysis of linked ANZDATA registry and perinatal datasets over 22 years

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

Predicting kidney transplantation outcomes; is donor terminal, admission or highest estimated glomerular filtration rate best?

Irish G, Coates P, Clayton P

Outcomes of steroid-free immunosuppression and therapeutic anti-coagulation in pancreas transplantation - the Adelaide experience of an initial 10 patient cohort

Barnett D, Olakkengil S, Coates T, Bhattacharjya S

Health service utilisation after organ donation among living donors in NSW, Australia: The safebod data linkage study

De La Mata N, Chalasani V, Pleass H, Rosales B, Clayton P, Kelly P, Wyburn K, Webster A

The impact of Victorian key performance indicators (KPIS) on wait listing for kidney transplantation for indigenous and non-indigenous patients starting dialysis

Goodman D, Mark T, Davies C, McDonald S, Atkinson A

The Australian and New Zealand living kidney donor profile index Irish G, Chadban S, Boudville N, Campbell S, Kanellis J, Clayton P

A review of stakeholder preferences for involvement in transplant offers **Weightman A, Clayton P,** Coghlan S

The epidemiology of hereditary pancreatitis in South Australia

Wu D, Coates PT, Palmer L, Bampton TJ, Couper R, Scott H, Chen J

Paediatric kidney transplants from donors aged 1 year and under: An analysis of the Australian and New Zealand dialysis and transplant registry (ANZDATA) from 1963 to 2018

Yao J, **Clayton P**, Wyburn K, Choksi H, Cavazzoni E, Tovmassian D, Lau H, Allen R, Yuen L, Laurence J, Lam V, Pleass H

Why are we not listing Aboriginal and Torres Strait Islander people for kidney transplants? **McDonald S**, Dole K, Boan P, Lim W, Snellin P, Sajiv C, Abeyaratne A

The impact of chronic pancreatitis on the paediatric population of South Australia" **Bampton T,** Palmer L, **Coates T**

Developing a novel porcine autotransplantation model of robotic-assisted heterotopic kidney transplantation

Barnett D, Bhattacharjya S

American Society of Nephrology (ASN)

online (October/November 2021)

Feasibility and Acceptability of Electronic Patient-Reported Outcome Measures (e-PROMs) Collection and Feedback in Haemodialysis Patients

Viecelli A, **Duncanson E, Bennett P**, D'Antoine M, **Dansie K**, Tong A, Palmer S, **Jesudason S**, **McDonald S**, Morton R

What Actually Happens at Home? A Data Linkage Study Between ANZDATA Registry and Sharesource

McDonald S, Lincoln G, Kandamby M, Davies C, Duddington M, Hurst K

ISN World Congress of Nephrology (WCN)

April 2021

Maternal characteristics and birth outcomes for mothers receiving kidney replacement therapy: An analysis of linked ANZDATA Registry and Perinatal datasets over 22 years (selected for oral presentation in the Best Abstracts Session – Top 2 Ranked Abstracts of the Meeting)

Hewawasam E, Davies C, Gulyani A, Clayton P, Sullivan E, McDonald S, Jesudason S

The effects of plasma exchange in patients with ANCA-associated vasculitis: an updated systematic review and meta-analysis"

Walsh M, Collister D, Zeng L, Merkel P, Pusey C, Peh CA, Szpirt W, Ito-Hara T, Jayne D

Australian and New Zealand Society of Nephrology (ANZSN)

Online (August/September 2021)

Big data and registries – do they need each other? (*Plenary session*) **McDonald S**

Pregnancy in dialysis (*Plenary session*) **Jesudason S**

Comparison of maternofetal outcomes for births in women before and after commencement of kidney replacement therapy using linked ANZDATA and Perinatal datasets

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

Dialysis incidence and mortality trends for modelling future prevalence

Davies C, Keuskamp D, McDonald S

ICU admissions post kidney transplantation

Kuah Z, Jahan S, Bhattacharjya S, Coates PT

What do you want to know and how do you want to know about it?" Consumer perspectives of pregnancy counselling and education in women with kidney disease: a national survey

Stallard B, Hewawasam E, Jesudason S

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

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

Irish G, Hersh J, Weightman A, Coates T, Clayton P

Kidney transplant outcomes among Aboriginal and Torres Strait Islander people - the gap is closing (*Winner of winner of the Advancing equity for Aboriginal and Torres Strait Islander Peoples and Māori category*)

McDonald S, Owen K, Hughes J, Khanal N, Bateman S

What actually happens at home during peritoneal dialysis? linking ANZDATA and sharesource data

McDonald S, Lincoln G, Kandamby M, Davies C, Duddington M, Hurst K

Survival benefit of deceased donor kidney transplantation for Aboriginal and Torres Strait Islander Australians

Bateman S, Pearson O, Owen K, Tsetsakos R, McDonald S, Jesudason S, Clayton P

Reducing the burden of dialysis catheter complications: a national approach (REDUCCTION)

Kotwal S, Cass A, Coggan S, N Gray N, Polkinghorne K, **McDonald S,** Rogers K, Talaulikar G, Di Tanna D, M Gallagher M

Renal Society of Australasia

Online -June 2021

On the other side of the fence (Plenary session)

Donnelly F

Development and implementation of a nursing education module to address needle fear in patients receiving haemodialysis

Donnelly F, Radisic G, Le Leu R, Chur-Hansen A, Collins K, Burke A, Turner J Hill K, Macauley L, Mc Donald S, Duncanson E, Jesudason S

When the pointy end misses the mark: outcomes of a multi-centre retrospective observational study focussing on the first 6 weeks of haemodialysis access

Jaensch A, Hill K, Xu Q

The exercise perceptions of people treated with peritoneal dialysis

Zeng J, Bennett P, Hill K, Xu A, Borlace M

Working outside the box to enable home haemodialysis patients to train nearer to their own home

Maberley J, Brooks N, Ovenden M

Nurses' role in the recruitment of patients for research in peritoneal dialysis

Ovenden M, Tarca B, Borlace M, Duncanson E, Ferrar K, Southwell P, Le Leu R, Jesudason S, Bennett P

Planning for end-of-life care in dialysis

Hill K, Lunardi L, Bull K

A successful home dialysis program using incremental peritoneal dialysis (IPD)

Borlace M

Urgent start peritoneal dialysis: Our units experience and clinical challenges

Borlace M

Latest Highlights and Developments from the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA)

Hurst K, McDonald S

2021 APS College of Health Psychologists Conference

November 2021 - Virtual

How health and other psychologists are working with a multidisciplinary team to improve patient care for dialysis associated needle distress

Chur-Hansen A, Radisic G, Le Leu R, Duncanson E, Macauley L, Collins K, Burke A, Donnelly F, Turner J, Hill K, McDonald S, Jesudason S

Using an international online forum to explore the experiences of caregivers of patients with chronic kidney disease

Tuckey N, Jesudason S, Duncanson E, Chur-Hansen A

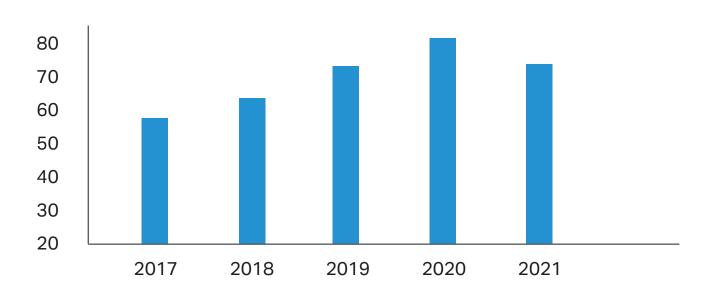
2021 Australian Institute of Aboriginal and Torres Strait Islander Studies (AIATSIS) Summit, Adelaide

May/June 2021

Improving Aboriginal Kidney Care Together O'Donnell K, Owen K, Jesudason S, Kelly J

Publications in 2021

CNARTS Publications 2017 - 2021



Clinical Research Group and Others:

Bennett, PN., Kohzuki, M., Bohm, C., Roshanravan, B., Bakker, S., Viana, J., MacRae, J., **Meade, A**., S. Molsted, K. Parker, E. Seguri-Orti, A. Smith, N. Verdin, J. Zheng, D. Zimmerman, and Thompson, S. "Global Policy Barriers and Enablers to Exercise and Physical Activity in Kidney Care." J Ren Nutr (Aug 12 2021). https://dx.doi.org/10.1053/j.jrn.2021.06.007.

Chen, J., Brown, Jose, M., Brennan, F. Johnson, D., Roberts, M., Wong, G., Hassan, H., Kennard, A., Walker, R. Davies, C., Boudville, N., **Borlace, M**., Hawley, C., and Lim, W. "Temporal Changes and Risk Factors of Death from Early Withdrawal within 12 Months of Dialysis Initiation - a Cohort Study." Nephrol Dial Transplant (Jun 27 2021). https://dx.doi.org/10.1093/ndt/gfab207.

de la Perrelle, L., M. Cations, G. Barbery, **G. Radisic**, B. Kaambwa, M. Crotty, J. A. Fitzgerald, S. Kurrle, I. Cameron, C. Whitehead, J. Thompson, and K. Laver. "How, Why and under What Circumstances Does a Quality Improvement Collaborative Build Knowledge and Skills in Clinicians Working with People with Dementia? A Realist Informed Process Evaluation." BMJ Open Qual 10, no. 2 (May 2021). https://dx.doi.org/10.1136/bmjoq-2020-001147.

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Duncanson, E., Le Leu, R., Shanahan, L., Macauley, L., Bennett, PN., Weichula, R., McDonald, S., Burke, ALJ., Collins, KL., Chur-Hansen, A., and S Jesudason. "The Prevalence and Evidence-Based Management of Needle Fear in Adults with Chronic Disease: A Scoping Review." *PLoS One* 16, no. 6 (2021): e0253048. <u>https://dx.doi.org/10.1371/journal.pone.0253048</u>.

Hill, K., Q. Xu, A. Jaensch, A. Esterman, R. Le Leu, J. Childs, R. Juneja, and S. Jesudason. ""Outcomes of Arteriovenous Fistulae Cannulation in the First 6 Weeks of Use: A Retrospective Multicenter Observational Study"." *J Vasc Access* 22, no. 5 (Sep 2021): 726-32. <u>https://dx.doi.</u> <u>org/10.1177/1129729820954717</u>.

Hill, K, Neylon, K., Gunn, L., **Jesudason, S**., Sharplin, G., **Britton, A., Donnelly, F.**, Atkins, I., and M Eckert. *Sustaining the Renal Nursing Workforce*. Vol. 17, vol. 2: Cambridge Publishing, 2021. <u>https://search.informit.org/doi/10.3316/informit.240844118919811</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* (Nov 19 2021). <u>https://dx.doi.org/10.1111/jorc.12406</u>.

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