UKKW 2024

UK KIDNEY WEEK 2024

ABSTRACTS
ORAL PRESENTATIONS

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Best clinical abstracts

271: Assessing baseline cardiovascular disease for kids initiating kidney replacement therapy: the ABCD4Kids study

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Biography - Rukshana Shroff

Rukshana Shroff, MD, FRCPCH, PhD, is a Consultant in Paediatric Nephrology at Great Ormond Street Hospital for Children in London UK, and holds an academic position in Nephrology (Associate Professor) at University College London. Her research focuses on cardiovascular disease in childhood chronic kidney disease (CKD), including laboratory work, clinical research studies and clinical trials. She is the PI on a multicentre study comparing long-term outcomes of conventional hemodialysis and hemodiafiltration in children. She currently holds a prestigious senior fellowship from the National Institute for Health Research (NIHR) to continue research into mineral dysregulation in CKD. She has published more than 150 original articles, reviews and book chapters in the fields of nephrology and dialysis. Dr Shroff is on the Executive Committee for KDIGO. She has served on the recent KDIGO CKD-MBD guideline update group and two guideline committees for the National Institute for Health and Care Excellence (NICE). She serves on the editorial board of the Clinical Journal of the American Society of Nephrology, Pediatric Nephrology and Peritoneal Dialysis International. She leads the CKD-Dialysis Working Group of ERKNet and is a board member of the ESPN CKD and Dialysis working groups.

Abstract

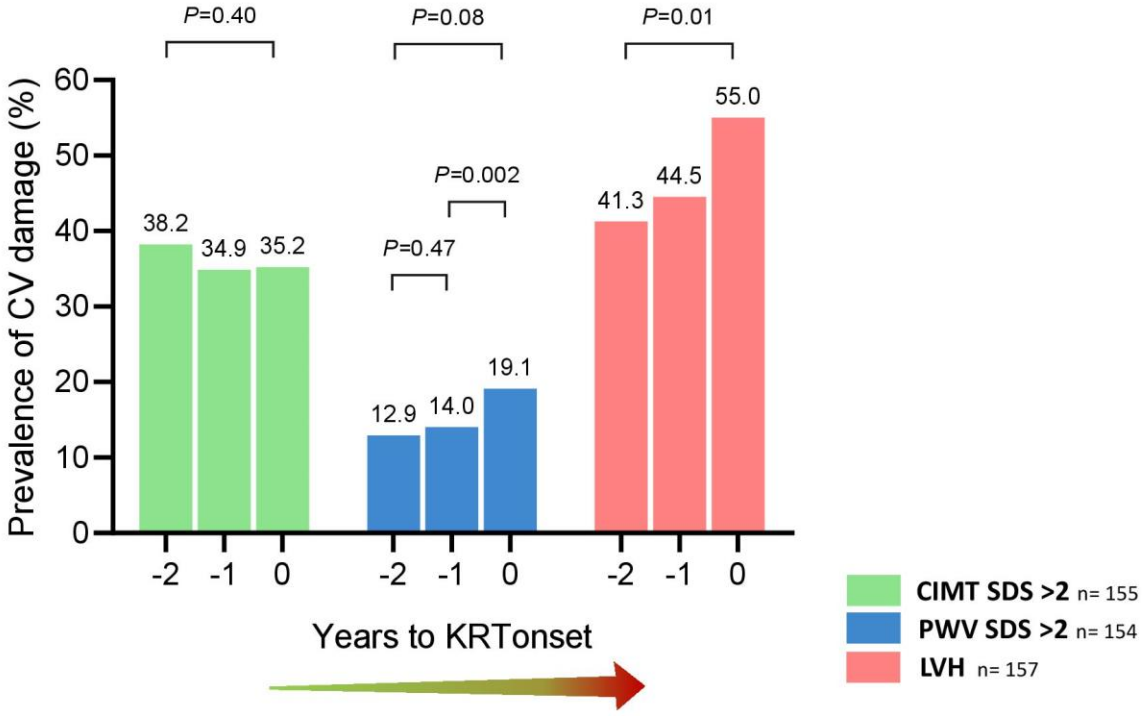
Introduction: Cardiovascular disease (CVD) is a significant cause of morbidity and mortality in children with end-stage kidney disease. Information on progression of CVD preceding kidney replacement therapy (KRT) in children is limited. We explored the CVD burden in pre-KRT patients from two prospective pediatric multicenter cohorts: the Cardiovascular Comorbidity in Childhood CKD (4C) and Haemodiafiltration, Heart and Height (3H) studies.

Methods: Patients with CKD stage 4-5 approaching KRT were evaluated at three time points: median 2-yr, 1-yr and 35 days before KRT start. CV measures (carotid intima-media thickness, cIMT-SDS, pulse wave velocity, PWV-SDS and left ventricular mass index, LVMI) and CV risk-factors (traditional and uremic) were measured at all time points. Trajectories of CV measures during follow-up and their association with CV risk factors were analyzed by longitudinal mixed-method (LMM) regression.

Results: 248 incident KRT patients, median age 14 years, 63% boys and eGFR 12.2ml/min/1.73m^2 at KRT start were included. 82 (33%) were pre-emptively transplanted. At KRT initiation, pre-emptively transplanted patients had higher eGFR and lower diastolic BP and PTH, and higher hemoglobin and albumin, compared to patients starting dialysis (P<0.001). At KRT start, CV risk-factors were prevalent; 91.9% and 78.6% had >2 and >3 risk-factors, respectively. Hypertension was ambulatory (62.9%), masked (29.4%) and uncontrolled (20.1%). Incident KRT patients had high CV burden: elevated cIMT-SDS and PWV-SDS in 43% and 25% respectively and LV hypertrophy in 49% (**Fig**). A longitudinal LMM analysis controlling for age, sex and country showed a significant increase in PWV-SDS and LVMI over the 2-years preceding KRT onset (β=0.18 ± 0.08 SDS per year; P=0.02, and

β=2.04 ± 0.73 g/m$^{2.7}$ per year; P=0.006, respectively); the linear slope of cMIT-SDS remained unchanged. The prevalence of elevated PWV-SDS increased over 1-year and LV hypertrophy increased over 2-years prior to KRT-start (adjusted odds ratio, OR 0.33, P=0.002 and OR 0.54, P=0.01, respectively). The prevalence of structural vascular damage (elevated cIMT-SDS) significantly exceeded functional vascular stiffness (elevated PWV-SDS) at all time points (P<0.001; **Fig**). The linear association of structural and functional vascular measures was limited to patients with elevated cIMT-SDS (β=0.61; P=0.03). Time-varying diastolic blood pressure and body mass index were associated with all CV measures: cIMT SDS (ß=0.15, P=0.013; ß=0.15, P=0.021), LVMI (ß=1.27, P=0.04; ß=1.7, P=0.013) and PWV-SDS (ß=0.14, P=0.044; ß=0.20, P=0.008), respectively. LMM models show attenuation of linear slopes of CVD progression on controlling for modifiable risk-factors.

Conclusion: Patients with advanced CKD exhibited a high CVD burden, characterized by early structural vascular damage and accelerated vascular stiffness in the years preceding KRT-onset. Targeting modifiable risk-factors, such as, hypertension, fluid overload, obesity, dyslipidemia, hyperparathyroidism, hypoalbuminemia, and metabolic acidosis, that contributed significantly to long-term CVD, attenuated CVD progression.



464: Hematuria Resolution with the APRIL-Blocking Monoclonal Antibody, Sibeprenlimab, in Patients with IgA Nephropathy in a Phase 2 Randomized Controlled Trial

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Biography - Jonathan Barratt

Dr. Barratt leads the Renal Research Group within the College of Life Sciences University of Leicester. His research is focused on a bench to bedside approach to improving our understanding of the pathogenesis of IgA nephropathy a common global cause of kidney failure. Dr. Barratt is the IgA nephropathy Rare Disease Group lead for the UK National Registry of Rare Kidney Diseases (RaDaR) and a member of the steering committee for the International IgA Nephropathy Network. He works closely with pharmaceutical companies interested in new treatments for IgA nephropathy and is Chief Investigator for a number of international randomised controlled Phase 2 and 3 clinical trials in IgA nephropathy and was a member of the FDA and American Society of Nephrology Kidney Health Initiative: Identifying Surrogate Endpoints for Clinical Trials in IgA Nephropathy Work group.

Abstract

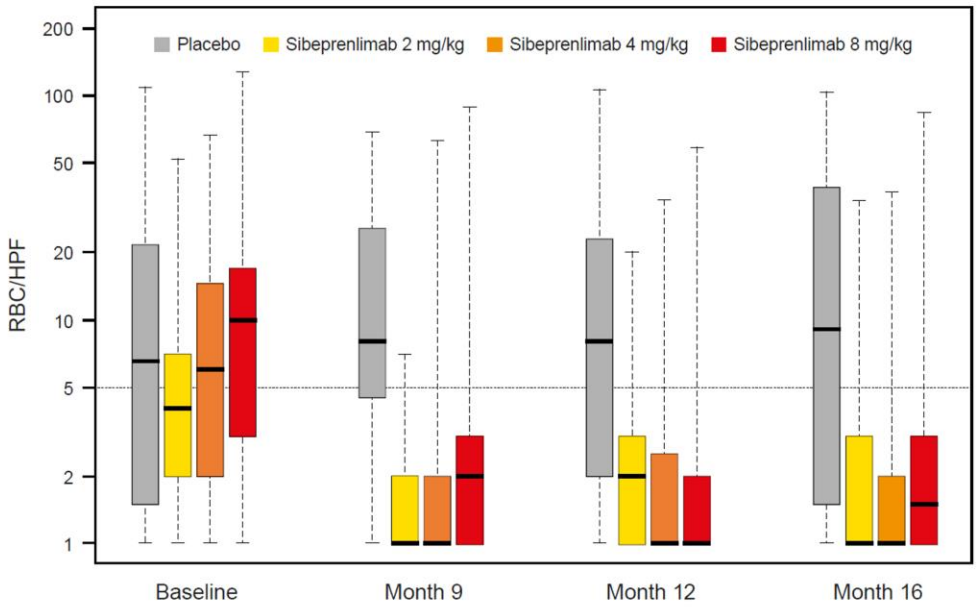
Introduction: A PRoliferation-Inducing Ligand (APRIL) is a key driver in the immune-related pathogenesis of immunoglobulin A nephropathy (IgAN). Sibeprenlimab, a humanized IgG_2 monoclonal antibody that blocks APRIL, demonstrated acceptable safety with robust uPCR reduction and eGFR stability at 12 months in a Phase 2 study of patients with IgAN.[1] Defined criteria for remission in IgAN are varied, and include reduction of proteinuria below certain thresholds (<1.0 g/d, < 500 mg/d and < 300 mg/day) as well as remission in hematuria (reduction in red blood cell [RBC] count to <5 RBC/high power field [HPF]).[2–4] We report the effect of sibeprenlimab on hematuria resolution and remission of proteinuria.

Methods: VIS649-201 (NCT04287985; ENVISION) is a global multicenter, randomized (1:1:1:1) study evaluating monthly intravenous (IV) sibeprenlimab (2, 4, or 8 mg/kg) vs placebo for 12 months (with 4 months of follow-up) in adults with IgAN on optimized supportive treatment, who have eGFR ≥30 mL/min/1.73m^2, and proteinuria ≥1.0 g/d or urine protein creatinine ratio (uPCR) ≥0.75 g/g. Efficacy endpoints include change from baseline in 24-hour uPCR at Month 12 (primary) and eGFR at Months 12 and 16, change in 24-hour proteinuria over time (key secondary) and change in microscopic hematuria (RBC/HPF) over time (exploratory). Hematuria was assessed by automated urine microscopy in a central laboratory.

Results: A total of 155 patients were randomized and treated (sibeprenlimab 2 mg/kg n=38; 4 mg/kg n=41; 8 mg/kg n=38; placebo n=38); 146/155 (94.2%) received all 12 treatment doses. Baseline characteristics were generally balanced between groups. Median follow up was 16.0 months. Key results including impact of sibeprenimab on proteinuria and eGFR were recently published.[1] Sibeprenlimab recipients showed marked reduction in microscopic hematuria at Months 9, 12 and 16 vs placebo (Figure 1). At month 12, 21 patients had proteinuria ≤300 mg/day, and 10 (47.6%) of these patients also had ≤5 RBC/HPF (1, 2, 6 and 1 in the 2, 4, 8mg/kg cohorts and placebo, respectively). Hematuria response corresponded to proteinuria response, with proteinuria reductions showing dose-dependent sibeprenlimab activity.[1]

Discussion: This Phase 2 study of patients with IgAN demonstrated robust hematuria resolution by sibeprenlimab at all study doses from Months 9 through 16, while in the placebo group hematuria persisted throughout the study. Observed resolution in hematuria, proteinuria and eGFR profiles over time indicate that APRIL blockade with sibeprenlimab may stabilize kidney function, likely through reduction of glomerular inflammation. These results suggest a favorable efficacy and safety profile of sibeprenlimab as a disease-modifying agent in IgAN and support its further evaluation in an ongoing global Phase 3 trial (NCT05248646).

Figure 1: *Change from Baseline in Hematuria (RBC/HPF) Over Time.*



Box plots show median, 25%–75%, and minimum and maximum values. RBC/HBF, red blood cells per high power field

References

[1]Mathur M, et al. *NEJM* in press; [2]Suzuki Y, et al. *Clin Exp Nephrol* 18, 481–486 (2014); [3]Reich HN, et al. *J Am Soc Nephro* 18, 3177–3183 (2007); [4]Canney M, et al. *J Am Soc Nephro* 32, 436–447 (2021)

Study Registration Number (e.g. ClinicalTrials.gov, EudraCT, PROSPERO)

NCT05248646

444: The clinical value and cost effectiveness of a 6-month digital health intervention to improve physical activity and health-related quality of life in CKD (Kidney BEAM)

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Biography - Dr Sharlene Greenwood

Dr Sharlene Greenwood is a Consultant Renal Physiotherapist at King's College Hospital, Honorary Reader at King's College London University, Past President of the UK Kidney Association and co-founder and Chief Medical Officer of Kidney Beam. Sharlene has more than15 years of experience as a specialist renal physiotherapist. She leads a clinical and research team of 16 therapists, leading on various research and clinical innovation projects in renal, cardiac and physical activity. Sharlene is passionate about supporting and encouraging exercise services for patients with Chronic Kidney Disease.

Abstract

Introduction: The utilisation of digital health interventions to enhance physical activity and improve health-related quality of life (HRQoL) in people with chronic kidney disease (CKD) may be a clinically meaningful and cost-effective intervention to redress an inequity in provision of in-person physical rehabilitation services for people living with this chronic condition. The Kidney BEAM trial evaluated the clinical value and cost effectiveness of a physical activity digital health intervention (DHI) for people living with CKD.

Methods: A single-blind randomised controlled trial recruited 340 adult participants and randomly assigned (1:1) them to either the Kidney BEAM physical activity DHI or a waitlist control. The primary outcome was the Kidney Disease Quality of Life Short Form 1.3 Mental Component Summary (KDQoL-SF1.3 MCS) between baseline and 24 weeks. Secondary outcomes included the KDQoL-SF1.3 Physical Component Summary and other KDQoL-SF1.3 sub-scales; and the European Quality of Life 5 dimension, 5 level (EQ5D-5L) questionnaire. Outcomes were analysed by an *intention-to-treat* approach utilising an analysis of covariance model, with

baseline measures and age as covariates. A prospective formal cost-effectiveness analysis was also performed. Data on hospital utilisation, primary care consultations, and prescribed medications were collected for the 12 weeks before, during, and after a 6-month physical activity DHI.

Results: Two hundred and twenty-nine participants completed the trial at 24 weeks (Kidney BEAM: n=93; waitlist control: n=136). All 340 randomised participants were included in the *intention-to treat* analyses. At 24 weeks there was a significant difference in mean adjusted change in KDQoL MCS score between Kidney BEAM and waitlist control of 5.9 {95% confidence interval: 4.4 to 7.5} arbitrary units (p<0.0001). KDQoL burden of kidney disease (p=0.0017), quality of social interaction (p<0.0001), sleep (p<0.0001), physical functioning (p=0.0003), role physical (p=0.014), pain (p=0.0002), general health (p=0.0018), emotional wellbeing (p<0.0001), role emotional (p=0.0058), social function (p<0.0001) and energy/fatigue (p<0.0001) all improved in favour of the intervention. There was a significant mean adjusted change in the EQ5D-3L utility score of 1.0 {95% confidence interval: 0.007 to 0.13} unit (p<0.0001) in favour of the intervention. Data from the base-case within trial analysis showed a 93% and 98% chance of KB being cost-effective compared with control participants at a willingness to pay of £20,000 and £30,000 per quality-adjusted life year (QALY) gained.

Discussion: These results demonstrate that the Kidney BEAM physical activity DHI is a clinically effective and cost-effective means to improve HRQOL in patients with CKD. This is the first large randomised controlled trial of a clinically effective, cost-effective, and practically deliverable physical activity intervention for people living with CKD; the findings should be implemented nationally and further research conducted to scale in other countries.

Study Registration Number (e.g. ClinicalTrials.gov, EudraCT, PROSPERO)
ClinicalTrials.gov number, NCT04872933.

482: Sickle cell trait and APOL1 high risk genotype increase the risk of ESKD similar to that of having diabetes in British Africans

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Biography - Dr Mark Gilchrist
Mark Gilchrist is a Senior Clinical Lecturer in the Diabetes and Vascular Centre at the NIHR Exeter CRF and Honorary Consultant Nephrologist at Torbay Hospital. Mark's research interests include genetics of kidney disease and diabetic kidney disease. Mark is part of the Exeter team on BEAT-DKD, an EU funded study examining potential biomarkers for progression of diabetic kidney disease.

Abstract
Introduction: Little is known of the risk of end-stage kidney disease (ESKD) in British Africans with Sickle Cell Trait or *APOL1* High-risk genotypes. We aim to determine the prevalence of the *APOL1* high-risk genotype and genetically defined Sickle Cell Trait in British Africans and their association with ESKD.

Methods: We analysed 7380 British Africans from a UK population cohort, UK Biobank. It contains deep phenotypes, biomarkers, and DNA sequence data. We used whole exome sequencing data to identify carriers of known *APOL1* high risk genotypes (G1G1, G1G2, G2G2) and SCT (heterozygous carriers of p.Glu7Lys in *HBB)*. We identified individuals with ESKD (in receipt of renal replacement therapy including kidney transplant) using self-report, hospital admissions records, and general practice records. We used a cox proportional hazard model to determine the risk of ESKD with these genotypes adjusted for age, sex, hypertension, smoking and diabetes.

Results: 1131/7380 (17.9%) British Africans carry the APOL1 High risk genotype whereas 860/7380 (14.3%) had genetically defined SCT. Both risk states were found in 216/7380 individuals. Together, 32.2% carry one or both of these variants and 36/2207 (1.6%) developed ESKD. Of those with neither SCT nor APOL1 HR genotype 32/5173(0.67%) developed ESKD.

The multivariable cox-proportional hazard model showed that *APOL1* high risk genotype increased the risk of ESKD by two-fold (HR 2.12-95% CI 1.19-3.79), p=0.011. Surprisingly, the risk of ESKD was also two-fold higher in SCT carriers (HR 2.59 95% CI 1.44-4.68), p=0.002 independent of APOL1 genotype. This risk was of ESKD for people with either SCT or the APOL1 high risk genotype was similar to that associated with diabetes (HR 2.75 95% 1.58-4.80), p<0.001.

The polygenic score for eGFR did not change the risk of ESKD in these carriers.

Conclusions: We show for the first time that 1 in 3 British Africans carry either two APOL1 high-risk variants or sickle cell trait, both of which double the risk of ESKD. These genetic risk factors increase the risk of developing ESKD to a level similar to that resulting from diabetes. A sensible starting point would be a trial of screening and aggressive management of conventional risk factors for ESKD.

357: Ethnic differences in long-term kidney failure after COVID-19 infection: an observational matched cohort study of adults in England using the OpenSAFELY platform

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Biography - Dr Viyaasan Mahalingasivam

I am an NIHR Research Fellow in the Department of Non-Communicable Disease Epidemiology at London School of Hygiene & Tropical Medicine as well as an Honorary Consultant Nephrologist at Barts Health NHS Trust and Homerton University Hospital NHS Foundation Trust. My research interests are in the prevention and management of chronic kidney disease in areas of socioeconomic deprivation. My current Fellowship is focused on long-term kidney outcomes after COVID-19 and the economic effects of the pandemic on kidney care. I work on electronic health records using the OpenSAFELY platform and the Stockholm CREAtinine Measurements (SCREAM) project based at Karolinska Institutet in Sweden as an affiliated researcher.

Abstract

Introduction: In the UK, ethnic differences in outcomes after COVID-19 have been well-documented since the beginning of the pandemic, while inequalities in kidney disease have been a concern for many decades. We sought to investigate ethnic differences in long-term kidney failure after COVID-19 and interrogate potential causal mechanisms.

Methods: We undertook a cohort study using electronic health record data on the OpenSAFELY platform. We identified adult COVID-19 survivors between February 2020 and December 2022, and matched them on age, sex and location with up to three people from the general population. We categorized each individual's ethnicity as white, South Asian, black, mixed or other and excluded those with missing data. Our outcome of interest was kidney failure, defined as incident dialysis, kidney transplantation or estimated glomerular filtration rate <15 ml/min/1.73m^2.

We used Cox models to obtain ethnicity-specific hazard ratios (HR) for kidney failure: i) adjusted only for matching factors (minimally-adjusted), ii) with additional adjustment for several other covariates (fully-adjusted). We performed likelihood ratio tests for interaction by ethnicity.

We investigated the effect of adjustment by each covariate alone to determine confounding patterns by ethnicity. We then stratified COVID-19 by hospitalization, to assess whether ethnic differences were due to differential ascertainment of COVID-19 (as biased ascertainment is less likely with hospitalised COVID-19).

Results: We analysed 2,516,030 individuals with COVID-19 and 5,649,105 matched comparators **(Table 1)**. The distribution of ethnicities was similar in both groups. There was slightly higher prevalence of some comorbidities in the COVID-19 cohort and they were more likely to have been vaccinated.

For black ethnicities, we found the HR increased from 3.81 (95%CI 2.78-5.24) with the minimally-adjusted model, to 4.50 (95%CI 2.92-6.92) with the fully-adjusted model, while it decreased for white, South Asian and other ethnicities **(Figure 1)**. *P*-values for interaction were <0.0001.

Adjusting for CKD stage alone increased the HR in black ethnicities further to 5.32 (95% CI 3.55-7.96) with similar direction of effect in South Asian, mixed and other ethnicities. Ethnic differences persisted with COVID-19 hospitalisation: HR 10.12 (95%CI 6.72-15.26) for South Asian, and 16.34 (95%CI 8.54-31.27) for black ethnicities, compared to 7.20 (95%CI 6.38-8.12) for white ethnicities.

Discussion: We found strong evidence of ethnic differences in long-term kidney failure, with the greatest impact on black ethnicities. CKD stage was a negative confounder, suggesting heightened risk in people without pre-existing advanced CKD. Disproportionate effects in black ethnicities are consistent with reports of increased acute kidney injury (AKI) during COVID-19 hospitalisation in the UK.

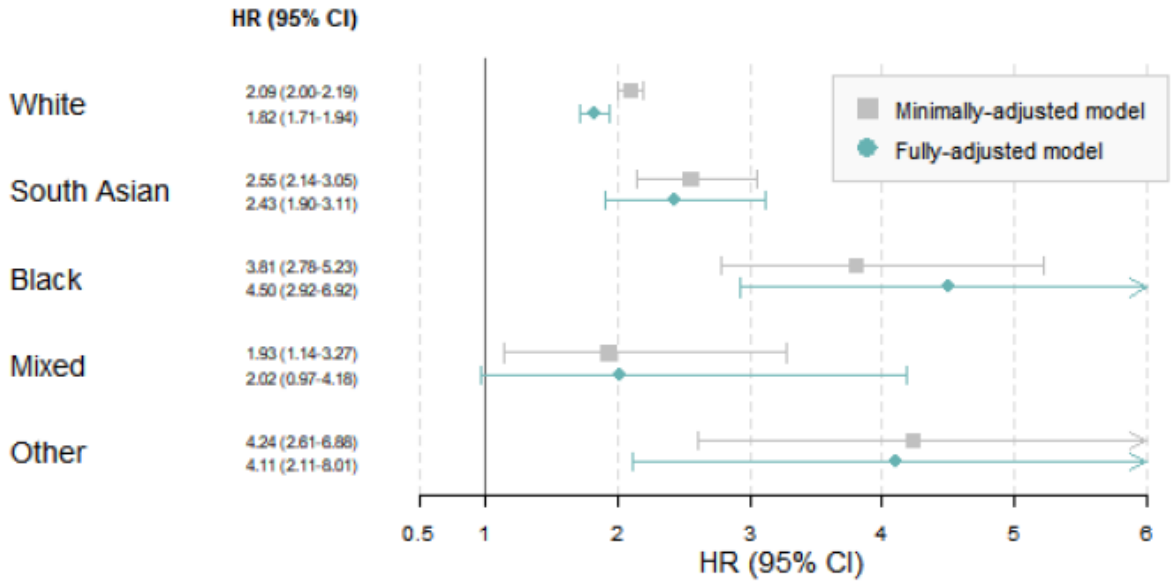
Explanations for ethnic inequalities include longstanding inadequate provision of healthcare and public health, as well as unmeasured social determinants (such as income and occupation). Furthermore, in individuals of African ancestry, apolipoprotein L1 (APOL1) genetic risk variants have been found to be associated with AKI during COVID-19 hospitalisation and may be contributing to longer-term kidney outcomes. Access to APOL1 genotyping remains underdeveloped in the UK.

Existing disparities in kidney outcomes have been widened by the COVID-19 pandemic. Community-led infrastructures need to be built to mitigate ongoing impacts and prevent future harms.

Table 1 Descriptive characteristics for the COVID-19 cohort and the matched cohort drawn from the general population.

	COVID-19 cohort	Matched cohort
Total	2,516,030	5,649,105
Ethnicity, n (%)		
White	2,183,415 (86.8)	4,847,455 (85.8)
South Asian	198,570 (7.9)	439,465 (7.8)
Black	60,525 (2.4)	149,565 (2.6)
Mixed	32,330 (1.3)	72,910 (1.3)
Other	41,185 (1.6)	139,715 (2.5)
Median age (IQR)	48 (37-59)	49 (38-60)
Female sex, n (%)	1,464,385 (58.2)	3,381,335 (59.9)
Median baseline eGFR (IQR)	89.4 (75.4-101.8)	88.5 (74.6-100.8)
Previous acute kidney injury, n (%)	54,340 (2.2)	75,165 (1.3)
Cardiovascular diseases, n (%)	243,305 (9.7)	506,305 (9.0)
Diabetes, n (%)	321,315 (12.8)	688,585 (12.2)
Hypertension, n (%)	544,935 (21.7)	1,222,810 (21.6)
Immunosuppressive diseases, n (%)	62,090 (2.5)	123,550 (2.2)
Non-haematological cancer, n (%)	162,555 (6.5)	357,485 (6.3)
Median GP consultations prior year (IQR)	4.0 (1.0-10.0)	4.0 (1.0-9.0)
Median hospital admissions 5 years (IQR)	0.0 (0.0-2.0)	0.0 (0.0-1.0)
COVID-19 vaccination status, n (%)		
Pre-vaccination	954,230 (37.9)	2,289,055 (40.5)
1 vaccine dose	140,725 (5.6)	278,620 (4.9)
2 vaccine doses	881,245 (35.0)	1,771,835 (31.4)
3 vaccine doses	507,460 (20.2)	1,230,265 (21.8)
4 vaccine doses	32,365 (1.3)	79,335 (1.4)

Figure 1 Ethnicity-specific hazard ratios for kidney failure after COVID-19. The minimally-adjusted Cox model was adjusted only for matching factors (age, sex and location), stratified by matched set. The fully-adjusted Cox model was adjusted additionally for index of multiple deprivation, rural/urban, smoking, body mass index, previous acute kidney injury, chronic kidney disease stage, cardiovascular diseases, diabetes, hypertension, immunosuppressive diseases, cancer, previous GP visits, previous hospitalisations and COVID-19 vaccination, stratified by matched set. *P*-values for interaction were obtained by likelihood ratio tests. HR = hazard ratio, CI = confidence interval



260: Using a digital health intervention ('My Kidneys & Me') to improve dietary choices in people living with non-dialysis CKD

Dr Courtney Lightfoot[1,2], Ms Gurneet Sohansoha[1,2], Ms Ella Ford[1,2], Dr Noemi Vadaszy[1,2], Dr Thomas Wilkinson[1,2,3], Dr Matthew Graham-Brown[4,5], Prof Alice Smith[1,2]

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Biography - Dr Courtney Lightfoot

Courtney is a mixed methods researcher working with the Leicester Kidney Lifestyle Team. Her role involves the development, evaluation, and implementation of complex (digital) health interventions to support people with kidney disease to better (self-)manage their health and lifestyle behaviours. Her work focuses on helping people with kidney disease to live well by empowering them to take a more active role in their health and healthcare.

Abstract

Introduction: Effective self-management of chronic kidney disease (CKD) has the potential to reduce adverse health risks. We co-developed a digital health intervention (DHI), 'My Kidneys & Me' (MK&M), to support people with non-dialysis CKD to better self-manage their health and lifestyle. MK&M included theory-based educational and action sessions about a healthy balanced diet, underpinned by behaviour change techniques plus trackers for dietary goals. Here we report findings on dietary behaviours from a multicentre randomised control trial of MK&M.

Methods: 420 participants aged ≥18 years with CKD stages 3-4 were recruited from 26 hospitals and randomised 2:1 to intervention (MK&M) (n=280) or control (n=140) groups. The UK Diabetes Diet Questionnaire (UKDDQ) was collected at baseline and 20-weeks via an online survey. The UKDDQ asks respondents how often they consumed certain foods and drinks (e.g., vegetables, fruits, sugary drinks, processed meat) over the last month on a 6-point Likert scale. Items are scored on the frequency of consumption ranging from 5 (healthiest) to 0 (least healthy) and classified into "healthy" (4&5), "less healthy" (2&3) and "unhealthy" (0&1) choices. The mean UKDDQ score was calculated from the 20 items, giving a final score ranging from 0-5. Access to and usage data of MK&M were collected, alongside a rating of usefulness (0 (not useful at all) to 10 (very useful)). Linear regression models tested between-group differences, adjusted for baseline values. Within-group changes were estimated using paired t-tests.

Results: Of the 280 participants assigned to the intervention group, 225 (80%) activated their MK&M accounts and used MK&M at least once. Over 20-weeks, the 'Eating a healthy balanced diet' educational session was accessed by 107 (48%) participants, who viewed the session an average of 10.5 (±5.4) times and spent an average of 11.0 (±15.0) minutes on it. Over 20-weeks, the 'How to eat a healthy balanced diet' action session was accessed by 77 (35%) participants, who viewed the session an average of 12.1 (±5.7) times and spent an average of 7.5 (±6.7) minutes on it. Participants rated 'Eating a healthy balanced diet' 8.0/10, and 'How to eat a healthy balanced diet' 7.6/10. The health eating tracker was used by 32 (14%) participants and rated 7.3/10. 30 (13%) participants set healthy eating goals (mean:1.6 (±1.2)), including making healthier food choices.

44% MK&M (n=122) and 40% control (n=55) participants had a median UKDDQ score in the healthy range (≥4) (mean:3.3±0.4) at baseline. This increased by 45% to 64% in MK&M participants (3.4±0.4) and by 28% to 51% in

control participants (3.4±0.5). Significant differences between the MK&M and control groups were observed for changes in the number of healthy (±0.8, P=0.024) and less healthy dietary choices (±0.5, P=0.027). The MK&M group had significant increases in the number of healthy food choices (+0.7, P=0.005) and significant decreases in the number of less healthy food choices (-0.6, P=0.009), whilst the control group had a significant increase in the number of unhealthy food choices (+0.3, P=0.048).

Conclusion: The use of MK&M DHI improved dietary food choices, with increases in the number of healthy food choices. People with CKD are interested in and actively engaged with DHIs to support healthy dietary habits. MK&M can be used to support individuals living with non-dialysis CKD to improve their dietary behaviours.

Study Registration Number
ISRCTN18314195

404: Assessing kidney function in pregnancy: gestation specific centile reference ranges for serum creatinine, urea, cystatin c and beta-2-microglobulin

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Biography - Katherine Clark
Katherine Clark is a specialist clinical midwife researcher with interests in renal and hypertension disorders in pregnancy, particularly acute kidney injury. She is Research and Innovation Lead for Women's Health at King's College Hospital. Katherine has been awarded numerous research grants, particularly in kidney disease in pregnancy and her main work is currently funded by a Kidney Research UK Stoneygate Allied Health Professionals Fellowship. She is in the final stages of a PhD at King's College London and works with an international network to enhance nurse and midwife led research and clinical development projects. Katherine is a member of a number of national and international networks including the Rare Renal Disease Registry (RaDaR) Pregnancy and CKD Study Group and she was on the Renal Association guidelines committee for the Renal Disease in Pregnancy guidelines. Katherine is active on twitter as @renalmidwife.

Abstract
Introduction: Deterioration in maternal kidney function is associated with adverse pregnancy outcomes and long-term morbidity and mortality for mother and baby. Lack of accurate assessment of kidney function, with well described thresholds for normality accounting for physiological adaptation across gestations, makes personalised care in pregnancy challenging. Serum creatinine is recommended to assess kidney function in pregnancy. Urea guides commencement of dialysis. Cystatin C provides an estimate glomerular filtration rate (GFR) and beta-2-microglobulin is a marker of tubular injury. The usefulness of cystatin c and beta 2 microglobulin in pregnancy are yet to be determined. This study aims to define normal centile ranges in pregnancy for serum creatinine, urea, cystatin c and beta-2-microglobulin.

Methods: Prospective cohort study of women receiving antenatal care at two UK tertiary hospitals (2018-2021) recruited to Pregnancy Adaptations in Renal disease study (REC15/WA/0009) and Prediction of pregnancy complications study (REC02-03-033).

Inclusion criteria: 6 weeks gestation to postpartum discharge, singleton pregnancy.

Exclusion criteria: pre-pregnancy eGFR<90mls/min/1.73m^2, haematuria, proteinuria, or structural abnormalities; previous acute kidney injury (AKI); chronic hypertension; diabetes; connective tissues disease; thrombophilia; cardiovascular disease.

Venous serum samples were taken at recruitment and routine ultrasound appointments and stored at -80'C prior to analysis. Serum creatinine (enzymatic), cystatin C, beta-2-microglobulin (Siemens ADVIA 1800) and urea (Clinical Chemistry Analyser) were quantified according to manufacturer's instructions.

Participants who later developed a risk factor for AKI (hypertensive disorder of pregnancy, gestational diabetes, preterm birth (before 37 weeks gestation) or evidence of placental insufficiency) were excluded from the main analysis and presented as a separate cohort.

Xrigls command was used in Stata 18.0 to allow reference interval estimation using generalized least squares.

Results: 539 participants were included. 444(82.4%) had an uncomplicated pregnancy and delivery and 95(17.6%) developed a risk factor for AKI (Table 1). Table 2 describes means for all biomarkers at each gestational window by sub-group.

Table 1 Demographics by group according to CKD risk stratification. Continuous variables presented as mean (standard deviation) and categorical variables presented as number (percent) unless stated otherwise.

Characteristics	**No Risk Factors** N=444	**New AKI Risk Factor** N=95
Maternal age (years)	33.0 (4.8)	32.4 (5.4)
Body Mass Index	24.7 (5.2)	25.9 (5.4)
Ethnicity, n (%)		
- Black	72 (16.2)	24 (25.2)
- White	323 (72.8)	61 (64.2)
- South Asian	13 (2.9)	4 (4.2)
- East Asian	13 (2.9)	6 (6.3)
- Mixed	23 (5.2)	0 (0.0)
Parity		
- Nulliparous	283 (63.7)	66 (69.5)
- Multiparous	161 (36.3)	29 (30.5)
Smoking	10 (2.3)	3 (3.2)
Index Pregnancy		
Assisted Conception	12 (2.8)	4 (4.2)
First Trimester Blood Pressure (mmHg)		
- SBP	116.7 (9.4)	118.0 (11.0)
- DBP	70.6 (6.8)	72.4 (8.7)
Hypertension		
- Pregnancy Induced Hypertension	0 (0.0)	16 (17.8)
- Pre-eclampsia	0 (0.0)	15 (16.7)
Gestational diabetes	0 (0.0)	31 (34.4)
Pregnancy Outcome		
Livebirth	444 (100.0)	88 (92.6)
Stillbirth	0 (0.0)	1 (1.1)
Neonatal death	0 (0.0)	1 (1.1)
Outcome not available	0 (0.0)	5 (5.3)
Gestational Age (weeks)	40.1 (1.1)	37.8 (2.8)
Neonatal unit admission	14 (3.2)	16 (17.8)
Birth weight (g)	3447.3 (416.9)	2875.7 (814.9)
Apgar score below 7, n (%)		
5 min	3 (0.7)	4 (4.2)
10 min	1 (0.2)	2 (2.1)

Table 2 Mean, standard deviation and 95% confidence intervals for all biomarkers at three gestational time points for participants with no risk factors and new risk factors for AKI. Chi-squared analysis or ANOVA were performed to compare timepoints in each risk group and to compare each risk group at one time point and P-values presented. P-value <0.05 was considered statistically significant and these values are in red.

Biomarker	Group	Gestation	11-14 weeks	19-24 weeks	32-38 weeks	p-value
Creatinine (umol/l)	No Risk	Mean	48.8	48.0	48.4	0.33
		SD	7.7	7.3	8.9	
		95% CI	48.1- 49.6	47.2 – 48.7	47.5 – 49.3	
	New Risk	Mean	48.2	47.2	50.5	0.08
		SD	8.4	7.9	10.4	
		95% CI	46.4 – 50.1	45.4 – 48.9	47.8 – 53.23	
		p-value	0.43	0.13	0.03	
Urea (mmol/l)	No Risk	Mean	3.57	3.11	3.04	<0.001
		SD	1.16	0.80	1.92	
		95% CI	3.46 – 3.68	3.03 – 3.20	2.85 – 3.24	
	New Risk	Mean	3.44	3.04	3.04	<0.001
		SD	0.96	0.98	0.93	
		95% CI	3.23 – 3.65	2.82 – 3.26	2.79 – 3.28	
		p-value	<0.001	<0.001	0.60	
Cystatin C (mg/L)	No Risk	Mean	0.71	0.77	1.09	<0.001
		SD	0.10	0.10	0.21	
		95% CI	0.70 – 0.72	0.76 – 0.78	1.07 – 1.11	
	New Risk	Mean	0.72	0.80	1.24	<0.001
		SD	0.13	0.14	0.36	
		95% CI	0.70 – 1.75	0.77 – 0.83	1.15 – 1.34	
		p-value	0.06	0.01	<0.001	
Beta-2-microglobulin (mg/L)	No Risk	Mean	1.35	1.51	1.72	<0.001
		SD	0.26	0.31	0.37	
		95% CI	1.33 – 1.38	1.48 – 1.54	1.68 – 1.76	
	New Risk	Mean	1.37	1.48	1.91	<0.001
		SD	0.29	0.29	0.55	
		95% CI	1.31 – 1.44	1.42 – 1.55	1.76 – 2.05	
		p-value	0.63	0.46	<0.001	

Cystatin C had greater variability with increasing gestation even in those with no risk factors (Figure 1). Figure 2 shows centile charts for all biomarkers for those with no AKI risk factors.

Figure 1 Box Plots of all biomarkers for those with no risk factors for AKI at three gestational time points

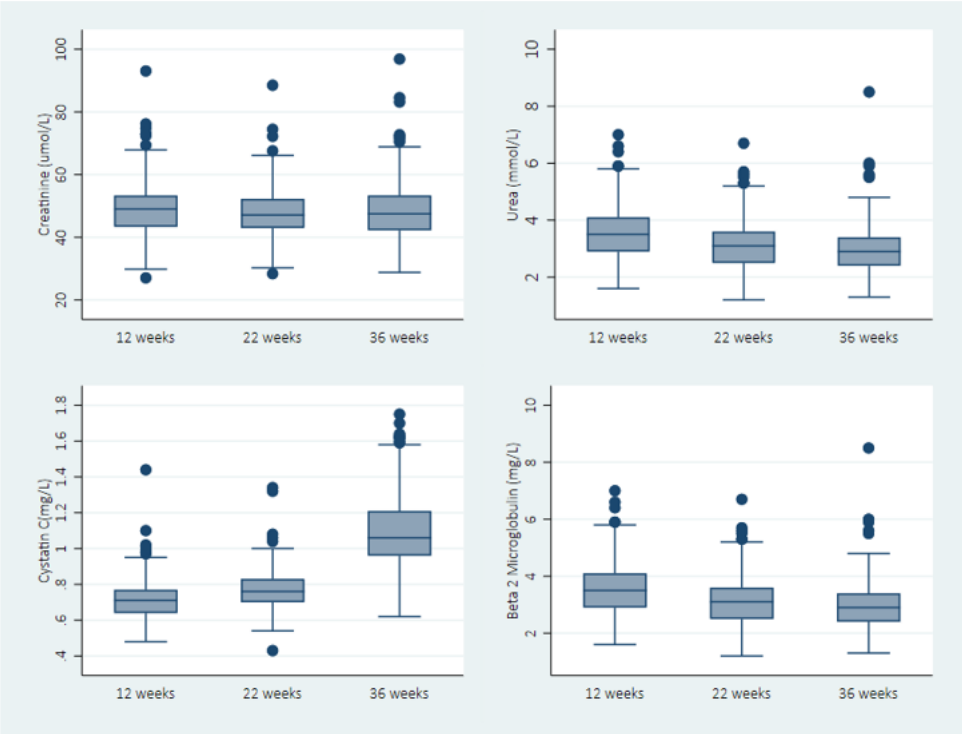
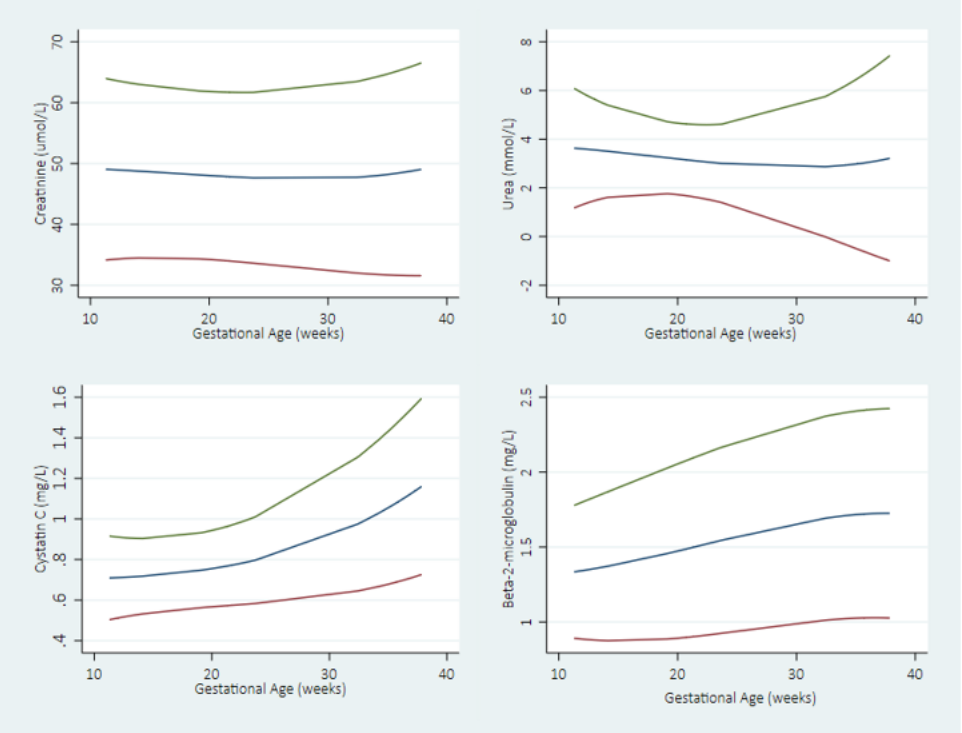


Figure 2 Centile charts generated from the 444 participants with no risk factors for AKI for all biomarkers with the 3rd centile represented by a red line, 50th centile by a blue line and the 97th by a green line



Discussion: In this ethnically diverse population, mean and median serum creatinine values were lower than previous reports in population cohorts. Serum creatinine above 63umol/l at any gestation of pregnancy was above the 97th centile and may represent pathology. Urea values above 5.5umol/l in the first and third trimester, and 4.6mmol/l in the second warrant further assessment. Cystatin C and beta-2-microglobulin vary increasingly towards term, even in women with no AKI risk factors, thus are unlikely to be useful markers of kidney impairment in pregnancy.

570: Does chronic kidney disease affect the female hormonal profile? A multi-centre UK observational cohort study

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Biography - Dr Mahua Bhaduri

Mahua is an obstetric and gynaecology senior specialist registrar in South London. Mahua graduated from Imperial College in 2013. She became a member of the Royal College of Obstetricians and Gynaecologist in 2019 and joined King's Fertility as a clinical research fellow in reproductive medicine. Mahua's research interests include investigating how chronic kidney disease affect female fertility. Her current research is being competitively funded by the Fetal Medicine Foundation. She is currently undertaking a PhD titled: FERN- Fertility Evaluation in ReNal disease. Mahua has authored several original manuscripts on renal disease, pregnancy and fertility. Mahua is passionate about improving fertility and obstetric care and management for those women with chronic kidney disease who have a desire for pregnancy.

Abstract

Introduction: Chronic Kidney Disease (CKD) is associated with reduced fertility but underlying mechanisms are unclear. It is proposed that CKD leads to dysregulation of the hypothalamus-pituitary-ovarian (HPO) axis, but studies are small, use outdated assays at varied times in the menstrual cycle. We aimed to investigate the relationship between female hormone concentrations assessed with contemporaneous methods in a large cohort of women with CKD and healthy controls.

Methods: Women with CKD (KDIGO definition) were identified from four hospitals sites to attend a study visit at a tertiary fertility unit (Fertility Evaluation in ReNal disease (FERN); IRAS 285546). Healthy controls were recruited via social media or exploring fertility treatment for male factor infertility. Demographic data including age, self-reported ethnicity and body mass index (BMI) were recorded. Medical history including detailed gynaecological and renal data were taken and estimated glomerular filtration rate (eGFR; CKD-EPI 2009 without ethnicity correction) was recorded.

Samples were taken between the first and fifth day of each participant's menstrual cycle or when convenient for women with amenorrhoea. Serum follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, testosterone, oestradiol, progesterone, Anti-Mullerian Hormone (AMH)and b-HCG concentrations were measured according to manufacturers instructions. Data were compared between control and CKD Stage using t-test and Mann Whitney U tests according to distribution.

Results: 164 women were recruited (101 with CKD and 63 healthy controls). Mean age was 34.5 ± 6.1 years, median BMI was 24.8 kg/m2 (IQR 22.2, 28.0 kg/m^2) and 75 (42.1%) were of non-White ethnicity. In the CKD cohort median eGFR was 69.0 mL/min/1.73m^2 (IQR 34.07, 96.5 mL/min/1.73m^2) and 21 (20.8%) women had renal transplants. Demographic, fertility and renal characteristics are summarised in Table 1.

AMH (13.6 vs 18.4 pmol/L; p=0.03) and testosterone concentrations (0.6 vs 0.5 nmol/L; p=0.01) were significantly lower and LH (4.4 vs 5.9 IU/L; p<0.01) concentrations were significantly higher overall in women with CKD compared to controls but there were no differences in FSH, oestradiol, prolactin, progesterone and B-HCG concentrations. LH increased and testosterone and AMH concentrations reduced with CKD severity.

Hormone profiles for control and CKD participants are illustrated in Figure 1. Stratification by CKD stage is summarised in Table 2. b-HCG was positive for three women (3.0%) with CKD with pregnancy excluded by scan.

Discussion: To our knowledge is this the largest prospective study comparing fertility hormonal profiles in women with CKD and healthy controls. Ovarian reserve (assessed by AMH) may be reduced with CKD although at later stages than previously published data, and centile adjustment is needed. We found the HPO axis is also affected in women with CKD but only LH and not FSH is elevated despite both hormones being renally excreted. It is possible that elevated basal LH may prevent the LH surge which triggers ovulation. Lower testosterone concentrations were evident even in stage 1 CKD which could lead to reduced libido reported by women with CKD.

Future work includes exploring longitudinal changes in women with CKD including after transplantation which allow women with CKD and their partners to make informed and timely fertility-related decisions.

Table 1. Baseline characteristics for all patients recruited in the FERN study, stratified for the control group and CKD groups. The CKD group is sub-stratified by stages (1, 2, 3 and 4-5).

Baseline characteristics	**All Patients (N= 164)**	**Control (N=63)**	**CKD (N= 101)**	**CKD Stage 1 (N=31)**	**CKD Stage 2 (N=25)**	**CKD Stage 3 (N= 19)**	**CKD Stage 4-5 (N=21)**
Mean Age ± SD, years	34.5 ± 6.1	33.4 ± 4.8	35.1 ± 6.7	33.6 ± 6.8	35.7 ± 5.3	38.4 ± 5.4	33.4 ± 8.6
Median BMI, kg/m² (IQR)	24.8 (22.2, 28.0)	24.5 (22, 26.7)	25.3 (22.7, 29.3)	23.8 (22.9, 26.9)	26.5 (23.0, 31.5)	28.0 (25.2, 31.7)	22.5 (20.6, 25.6)
eGFR, mL/min/1.73m² (IQR)	-	-	69.0 (34.7, 96.5)	114.0 (98.2, 127.0)	77.3 (67.0, 81.9)	39.8 (35.3, 52.6)	8.8 (4.1, 19.4)
Ethnicity Groups, N (%)							
White	95 (57.9%)	43 (68.2%)	52 (51.5%)				
Black	42 (25.6%)	10 (15.9%)	32 (31.7%)				
South Asian	12 (7.3%)	2 (3.2%)	10 (9.9%)				
East Asian	5 (3.1%)	2 (3.2%)	3 (3.0%)				
Mixed	4 (2.4%)	3 (4.8%)	1 (1.0%)				
Other	6 (3.6%)	3 (4.8%)	3 (3.0%)				
Gravida							
0	89 (53.9%)	42 (66.7%)	47 (46.5%)				
≥1	75 (46.1%)	21 (33.3%)	54 (53.5%)				
Parity							
0	117(71.4%)	56(88.9%)	61 (60.4%)				
≥1	47 (28.6%)	7 (11.1%)	40 (39.6%)				

Figure 1. Female hormone profiles stratified by CKD stages. Significant difference between groups is demonstrated with p-value <0.05.

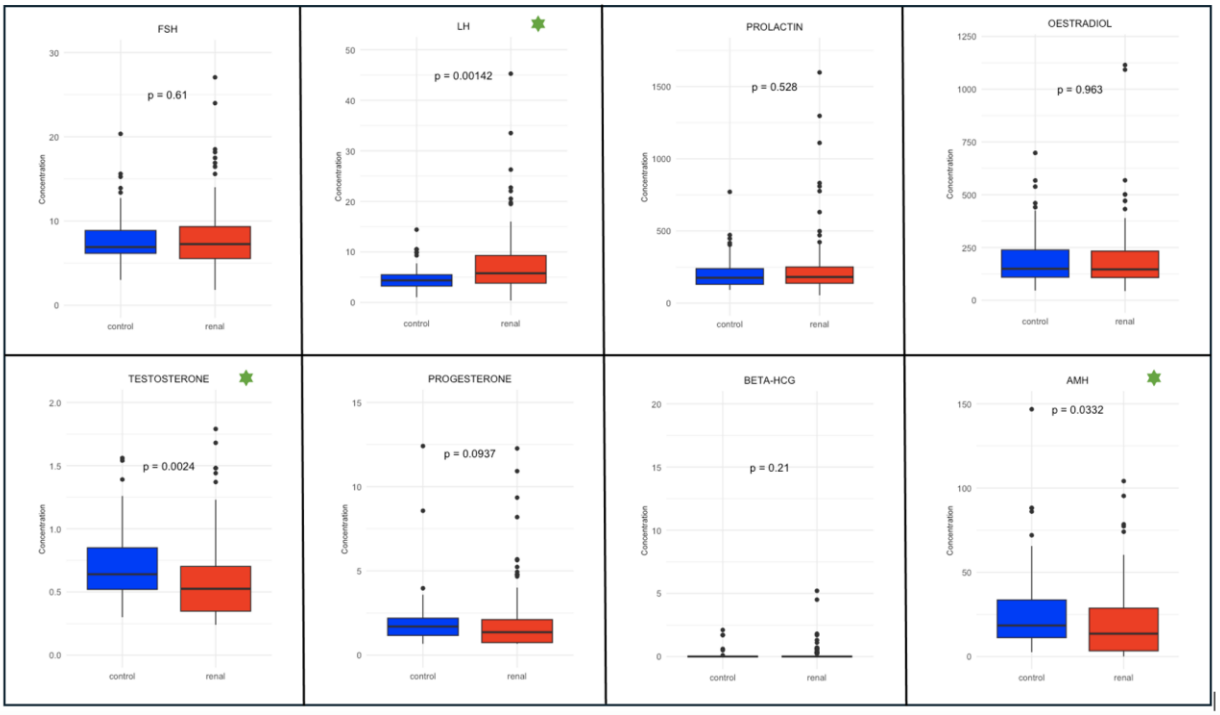

Table 2. Female hormone profiles stratified by CKD stages. Significant difference between groups is demonstrated with p-value <0.05.

Female hormones	CKD Stage 1 (N=31)	CKD Stage 2 (N=25)	CKD Stage 3 (N=19)	CKD Stage 4-5 (N=21)	p-value
FSH, IU/L (IQR)	7.6 (5.3, 9.6)	7.2 (5.8, 9.2)	8.3(7.4, 13.0)	6.2 (4.7, 7.9)	>0.05
LH, IU/L (IQR)	5.2 (3.2, 6.8)	5.5 (4.0, 9.0)	8.8 (4.2, 13.6)	7.1 (3.8, 13.6)	**0.03**
Prolactin, mIU/L (IQR)	173.4 (137.1, 213.8)	158.8 (114.0, 200.0)	168.0 (143.5, 319.1)	240.1 (173.6, 321.7)	>0.05
Oestradiol, pmol/L (IQR)	167.4 (119.1, 257.2)	136.6 (102.4, 184.4)	145.1 (124.6, 253.2)	161.2 (87.3, 235.4)	>0.05
Testosterone, nmol/L (IQR)	0.5 (0.4, 0.7)	0.5 (0.4, 0.7)	0.6 (0.3, 0.7)	0.4 (0.3, 0.8)	**0.01**
Progesterone, nmol/L (IQR)	1.5 (0.7, 3.8)	1.4 (0.8, 1.8)	1.4 (1.1, 2.3)	1.3(0.7, 2.0)	>0.05
hCG, IU/L (IQR)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	**0.01**
AMH, pmol (IQR)	21.5 (6.6, 31.1)	24.0 (12.3, 41.7)	6.5 (2.8, 11.0)	6.8 (2.2, 22.3)	**0.002**

FSH: Follicle Stimulating Hormone; LH: Luteinizing hormone; hCG: human chorionic gonadotrophin; AMH: Antimullerian hormone

Cardiovascular disease in CKD: novel mechanisms, new targets and improved risk prediction

212: Cardiovascular phenotype and prescription of medications for patients on haemodialysis and kidney transplant recipients: Insight from a multi-centre cardiac MRI study

Dr Chandhini Suresh[1], Dr Jennifer Lees[2], Dr Alastair Rankin[3], Professor James Burton[1], Professor Patrick Mark[4], Dr Matthew Graham-Brown[1]

[1]Department of Cardiovascular Sciences, University of Leicester. [2]Senior Clinical Research Fellow/ Honorary Consultant, University of Glasgow. [3]School of Cardiovascular & Metabolic Health, University of Glasgow. [4]Cardiovascular & Metabolic Health, University of Glasgow

Biography - Dr Chandhini Suresh

Foundation Year 1 Doctor graduated from Leicester Medical School currently on the SFP Research track under Dr Matthew Graham-Brown. Has a Masters in Public Health and a BSc Hons in Cellular and Molecular Medicine.

Abstract

Introduction: For patients on haemodialysis or with a kidney transplant, cardiovascular morbidity and mortality associates with pathological changes in cardiovascular structure and function (uraemic cardiomyopathy). Uraemic cardiomyopathy is a common cause for heart failure (HF) in these populations, including HF with reduced, moderately reduced and preserved ejection fractions (HFrEF, HFmrEF and HFpEF). Outcomes for patients with HF and ESKD are poor and medication optimisation is essential. In this multi-centre cardiac MRI study, we describe the cardiovascular phenotypes of patients on heamodialysis and with a kidney transplant and review prescription of cardiovascular medications.

Methods: Patients underwent multi-parametric cardiac MRI scans (3T platform) with full cardiovascular structural and functional assessment. Patients were classified as having HFrEF, HFmrEF and HFpEF or no evidence of HF defined by international criteria. The prescription of HF 'foundation therapies' (beta-blockers, ACE/ARB, MRAs, Neprilysin inhibitors and SGLT2 inhibitors) were reviewed for different patient groups.

Results: 296 patients were included in this study: 156 patients on haemodialysis and 140 kidney transplant recipients. Of the patients, 66% were male, 68% were of white ethnicity, 25% were Asian/Asian British/South Asian, 4% were Black/Black British, 1% were of mixed ethnicity and 2% were of another ethnic background. For patients on haemodialysis, 12.8% (20/156) had HFrEF, 15.4% (24/156) had HFmrEF, 42.9% (67/156) had HFpEF, and 28.8% (45/156) had normal cardiac structure and function. For kidney transplant patients, 2.1% (3/140) had HFrEF, 1.4% (2/140) had HFmrEF, 75% (105/140) and HFpEF, and 21.4% (30/140) had normal cardiac structure/function. For patients on haemodialysis, beta-blockers were prescribed in 40% (8/20), 42% (11/24) and 55% (37/67) of patients with HFrEF, HFmrEF and HFpEF respectively, compared to 66% (2/3), 0% (0/2) and 47% (49/105) of kidney transplant recipients. ACE/ARB therapies were prescribed for 15% (3/20), 25% (6/24) and 21% (14/67) for patients with HFrEF, HFmrEF and HFpEF on haemodialysis and for 100% (3/3), 50% (1/2) and 47% (49/105) of kidney transplant recipients. There were no prescriptions of MRAs, SGLT2 inhibitors or neprilysin inhibitors for any patients on haemodialysis. There were no prescriptions of MRAs, SGLT2 inhibitors or neprilysin inhibitors for kidney transplant patient with HFrEF/HFmrEF. 1% (1/105) and 3% (3/105) of transplant patients with HFpEF were prescribed an MRA or an SGLT2i.

Conclusion: Heart failure syndromes are highly prevalent in patients on haemodialysis and kidney transplant recipients, but the predominant phenotypes are different. Prescription of prognostically important medications for HF were low in both groups. For some patients there will be clinical reasons why pharmacotherapy is not

optimised, but the reasons for this will be multi-factorial and must be addressed with a standardised approach to practice.

130: Mechanisms of Vascular Pathology Following Peritonitis in Peritoneal Dialysis Patients and Therapeutic Intervention

Dr Esra Cetin[1], Dr Morgane Mazzarino[1], Dr Guadalupe T. Gonzalez-Mateo[2], Dr Valeria Kopytina[2], Dr Maria Bartosova[3], Dr Iva Marinovic[3], Dr Soma Meran[1], Dr Donald Fraser[1], Dr Claus Peter Schmitt[3], Dr Manuel Lopez-Cabrera[2], Dr Mario O. Labeta[1], Dr Anne-Catherine Raby[1]

[1]Cardiff University, Cardiff. [2]Universidad Autonoma de Madrid, Madrid. [3]UniversitatsKlinikum Heidelberg, Heidelberg

Biography - Dr Esra Cetin

Esra Cetin is a research associate at Cardiff University where she completed her PhD degree focusing on the association between infections and increasing cardiovascular risk in peritoneal dialysis patients. She completed her master's degree in biology at Ludwig Maximilian University of Munich and her undergraduate degree in molecular biology at Istanbul Technical University

Abstract

Background: In peritoneal dialysis (PD) patients, cardiovascular (CV) death is 10 times more likely than in the general population and this risk further increases following each peritonitis episode. Damage-Associated Molecular Patterns (DAMPs) play a critical role in inflammatory pathologies, notably via their activation of Toll-like receptors (TLRs), but their specific role in mediating long-term vascular pathology following an infection remains undescribed.

Methods: We investigated a potential role for DAMPs in mediating long-term CV risk following peritonitis by i) characterising the long-term vascular inflammatory changes induced by peritonitis in mice, ii) identifying potential target DAMPs following peritonitis by analysis of *in vivo* and PD patients' plasma samples, iii) mechanistically characterising the potential of our selected DAMP to promote key vascular inflammatory responses by critical cell types *in vitro,* iv) demonstrating, by pharmacologic inhibition, the critical contribution of a DAMP candidate to the maintenance of vascular pro-atherogenic responses following peritonitis in mice.

Results: Bacterial peritonitis in mice was resolved in 24h but led to systemic and vascular inflammatory responses, expected to promote cardiovascular disease, that were maintained up to 28 days. These included higher blood proportions of monocytes and neutrophils, which displayed higher adhesion molecule expression, as well as increased plasma cytokine levels, elevated markers of endothelial activation and increased aortic atherosclerosis-associated gene expression. These findings were maintained in nephropathic animals and exacerbated in animals routinely exposed to PD fluids. In parallel to these changes, a peritonitis episode led to elevated plasma levels of a specific TLR DAMP, Calprotectin, both in animals and PD patients. *In vitro*, Calprotectin could promote typical vascular inflammatory and pro-atherosclerotic responses: monocyte chemotaxis, foam cell formation, via a reduction of cholesterol efflux by macrophages and loss of endothelial resistance. *In vivo,* Calprotectin blockade robustly inhibited the short and long-term vascular inflammatory consequences of peritonitis. Critically, Calprotectin administration during peritonitis did not impair the ability of the mice to clear the infection.

Conclusion: This study reveals the major role that Calprotectin plays in driving long-term vascular pathology following a peritonitis episode and presents the proof of concept that Calprotectin blockade is a viable therapeutic strategy to reduce the detrimental impact of peritonitis on CV risk in PD patients.

Progressing the cardio-renal-metabolic agenda across healthcare settings – now is the time

The association between cardiac structure and function and mortality in patients with end-stage kidney disease on dialysis

Dr Sherna F Adenwalla[1,2], Rachael Stannard[3], Professor Patrick B Mark[4], Dr Jennifer Lees[4], Dr Alastair Rankin[4], Stephanie Burns[2], Dr Daniel S March[1,2], Professor James O Burton[1,2], Professor Gerry P McCann[1], Dr Matthew PM Graham-Brown[1,2]

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Biography - Dr Sherna F Adenwalla

Dr Sherna Adenwalla is an NIHR Academic Clinical Fellow in Renal Medicine at the University of Leicester, and is currently completing Internal Medical Training. During medical school, she undertook an intercalated BSc with the CYCLE-HD team in Leicester (a randomised controlled trial investigating the effect of intra-dialytic cycling on left ventricular mass). After graduating from Leicester, she continued to work within the kidney research team by pursuing work linked to her BSc, around cardiovascular health and physical function in patients with ESKD, but she has also developed an interest in advance care planning (ACP) in patients on dialysis and the challenges around implementation of ACP.

Abstract

Introduction: Patients with end-stage kidney disease (ESKD) are at significantly elevated cardiovascular (CV) risk. The pathophysiological changes observed are collectively termed uraemic cardiomyopathy and include left ventricular (LV) hypertrophy, LV dilatation and myocardial fibrosis. These are driven by a clustering of traditional and non-traditional risk factors. Cardiac MRI is the gold-standard for assessment of cardiac parameters. It is established that patients with ESKD have higher LV mass, aortic stiffness, native T1, and lower strain and LV ejection fraction compared to healthy controls. We hypothesised that in patients with ESKD on haemodialysis, cardiac MRI measures of cardiac and aortic structure and function would associate with all-cause mortality, independent of pre-determined risk factors.

Methods: 130 patients on haemodialysis, recruited to the CYCLE-HD trial between 2015-2018, underwent comprehensive cardiovascular phenotyping with cardiac MRI. Data regarding subsequent transplantation and mortality since enrolment was collected in March-April 2023. The MRI measures used in this analysis were taken from baseline scans and included LV mass index (LVMi), LV ejection fraction (LVEF), aortic pulse wave velocity (aPWV), global native T1, global longitudinal strain and global circumferential strain. Cox-proportional hazard modelling was used to investigate the association between each MRI measure and time to death. Final models included pre-determined covariates known to influence mortality in ESKD; age, sex, diabetes, received transplant since enrolment, dialysis vintage.

Results: Of the 130 patients, median age was 59 years (48, 69), 73% were male and median dialysis vintage was 1.26 years (0.5, 3.4). Up to April 2023, 47 patients had received a transplant since trial enrolment and 73 had died. In multivariate models, global native T1, LVMi and aPWV were significantly associated with mortality, independent of other covariates (Fig 1). For every 1ms increase in T1, the risk of death increased by 0.8%. Therefore, a 30ms increase in native T1 time (suggested clinically important difference) conferred a 27%

increased risk of death. For every 1g/m^2 increase in LVMi, the risk of death increased by 2%; an increase of 6g/m^2 (suggested clinically important difference) conferred a 13% increased risk of death. For every 1m/s increase in aPWV, the risk of death increased by 8%; an increase of 1.5m/s (suggested clinically important difference) conferred an 11% increased the risk of death. A Kaplan-Meier survival curve for global native T1 is shown in Fig 2.

Discussion: In this cohort of patients on haemodialysis, global native T1, aPWV and LVMi measured by cardiac MRI were significantly associated with all-cause mortality. This is the first time that the association between global native T1 and mortality has been explored. These abnormal parameters may be detectable in earlier stages of disease, before fulminant development of cardiomyopathy and heart failure. They may aid cardiovascular risk stratification and are imaging biomarkers suitable for use in clinical and interventional studies. There is potential for a larger prospective validation study and development of risk prediction models that include advanced MRI imaging measures in future.

a)

	Hazard Ratio	95% CI	p-value
Global Native T1 (ms)	1.008	(1.00, 1.02)	0.01
Received Transplant	0.0003	(0.00, 0.17)	0.01
Age (years)	1.033	(1.01, 1.06)	0.01
Received Transplant*Age	1.126	(1.02, 1.25)	0.03
Female	0.877	(0.46, 1.67)	0.69
Diabetes	1.619	(0.99, 2.65)	0.06
Time on Dialysis (years)	0.963	(0.88, 1.05)	0.41

b)

	Hazard Ratio	95% CI	p-value
LV mass index (g/m^2)	1.020	(1.01, 1.03)	<0.01
Received Transplant	0.009	(0.00, 1.10)	0.05
Age (years)	1.048	(1.02, 1.07)	<0.01
Received Transplant*Age	1.062	(0.98, 1.15)	0.16
Female	1.108	(0.61, 2.02)	0.74
Diabetes	1.722	(1.07, 2.77)	0.03
Time on Dialysis (years)	0.954	(0.87, 1.05)	0.34

c)

	Hazard Ratio	95% CI	p-value
PWV (m/s)	1.079	(1.02, 1.14)	0.01
Received Transplant	0.009	(0.00, 0.66)	0.03
Age (years)	1.014	(0.99, 1.04)	0.32
Received Transplant*Age	1.053	(0.98, 1.13)	0.17
Female	1.031	(0.55, 1.92)	0.92
Diabetes	1.650	(0.99, 2.74)	0.05
Time on Dialysis (years)	0.971	(0.88, 1.07)	0.55

Figure 1: Multivariate cox models showing the relationship between a) global native T1, b) LVMi and c) PWV and time to death, adjusted for the covariates listed.

Global Native T1

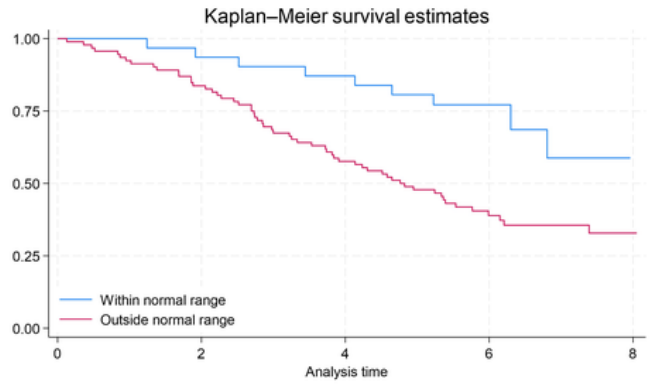


Figure 2: Kaplan Meier survival curve, grouped as within normal range and outside of normal range for Global Native T1 (normal range 1185-1245ms)

Study Registration Number

ISRCTN11299707

125: Is kidney disease predictive of the probability of receipt of invasive coronary angiography or revascularisation after acute coronary syndrome? A systematic review and meta-analysis.

Dr Jemima Scott[1,2], Dr Matthew Letts[1,2], Dr Wafaa Hajee-Adam[3], Dr Carol Chau[4], Dr Tom Johnson[1,5], Professor Fergus J. Caskey[1,2], Dr Pippa Bailey[1,2], Dr Lucy E. Selman[1], Professor Yoav Ben-Shlomo[1]

[1]University of Bristol, Bristol. [2]North Bristol NHS Trust, Bristol. [3]Barts Health NHS Trust, London. [4]Royal United Hospitals Bath, Bath. [5]University Hospitals Bristol & Weston NHS Trust, Bristol

Biography - Dr Jemima Scott

Jemima Scott is a trainee in kidney medicine in Bristol. She is currently undertaking an NIHR funded doctoral research fellowship investigating equality and equity in management of myocardial infarction for people with kidney disease.

Abstract

Introduction: Cardiovascular disease is the primary cause of morbidity and mortality amongst people with kidney disease (KD). It is unclear whether KD affects the probability of receipt of invasive coronary management after acute coronary syndrome (ACS), and if any observed variation may be explained by differences in individual patient characteristics or comorbidity.

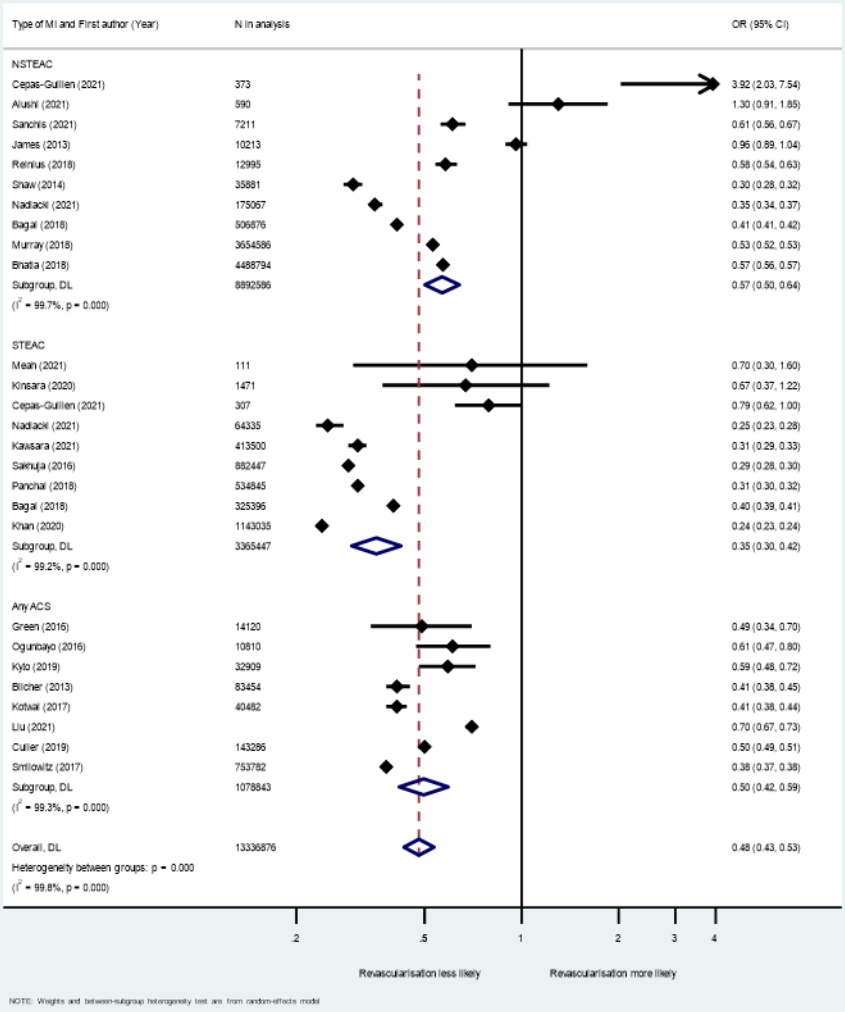
Methods: We searched EMBASE, MEDLINE, SCOPUS, CENTRAL and the NIHR's website of funded studies to identify articles referring to ACS and invasive coronary management in high-income countries over the past 12 years until 29th September 2023. Full text articles were included if data on rates of invasive coronary angiography (ICA) and/or revascularisation were reported in people with KD, defined as estimated glomerular filtration rate (eGFR) <60ml/min/1.73m^2, or some other proxy measure. Risk of bias was assessed via ROBINS-E. Random effect meta-analyses, due to pre-specified heterogeneity, were used to determine the average effect (odds ratios; OR) of KD on: i) ICA and ii) revascularisation, stratified by ACS type and KD severity. Certainty of evidence was assessed using GRADE.

Results: From 15,138 articles, we extracted data from 27 observational study reports including 13,165,810 individuals. Following ACS, people with KD were less likely to receive either ICA (OR=0.36; 95% Confidence Interval (CI) 0.28-0.46) or revascularisation (OR 0.47;95%CI 0.42-0.53). Disparity in receipt of revascularisation was more marked following ST-elevation ACS than non-ST-elevation ACS (OR 0.35 (95% CI 0.30-0.42) versus 0.57 (0.50-0.64) respectively). These associations persisted despite adjustment for demographic characteristics and comorbidities (adjusted ORs 0.48 (95% CI 0.31-0.74) and 0.63 (0.50-0.78) respectively). Certainty of the evidence was moderate or high for 10 of 11 outcomes.

Discussion: In high-income countries, KD is associated with reduced receipt of ICA and revascularisation after ACS. These disparities are not fully explained by differences in patient characteristics or comorbidity and appear counter to current guidelines. It is unclear whether reduced rates of invasive investigation and treatment are appropriate or if they reflect inequity in access to care.

Figure 1. Forest plot showing study estimates for receipt of revascularisation following ACS in people with KD versus those without, stratified by ACS type.

Probability of receipt of revascularisation after ACS in people with versus without KD, by ACS type



NOTE: Weights and between-subgroup heterogeneity test are from random-effects model

Weighing in on kidney health in Scotland

343: To assess the effectiveness of a 12-month remote weight management clinic for patients with chronic kidney disease and diabetes aiming for transplant

Annika Baird, Eimear Hamilton, Bryan Conway, Hannah Herron

Renal Department, Royal Infirmary of Edinburgh

Biography - Annika Baird

I am a Specialist Renal Dietitian at the Royal Infirmary of Edinburgh. Since graduating from King's College London in 2009, I have worked in a wide range of inpatient and outpatient specialties across Kent, New Zealand and Scotland. I have been working in renal medicine since 2016, where as a dietitian I feel I am a valued member of the multidisciplinary team, caring for the nutritional management of these complex patients. I have worked over a range of caseloads within renal including simultaneous pancreas-kidney (SPK) transplant, inpatients, clinics and dialysis patients. I am passionate about service improvement with a particular focus on the prehabilitation of patients aiming for transplant.

Abstract

Introduction: The number of patients with diabetes and chronic kidney disease (CKD) who are obese is increasing and is associated with worse outcomes and reduced access to transplantation. Weight management in this population is complex; commercial programmes and low-calorie meal replacement interventions are often unsuitable due to renal dietary restrictions and there can be delays in accessing NHS weight management services. The aim of this project was to pilot a remote renal dietetic-led clinic providing specialist weight management advice for patients with diabetes and CKD aiming for renal transplantation.

Methods: Recruitment criteria were: patients with diabetes who had BMI >30kg/m^2; CKD 3b-5 (but not on dialysis); and who were aiming for transplant. Recruited patients were sent a clinic letter by post inviting them to opt in within two weeks. Patients who opted in were contacted by phone or video call (depending on their preference) at baseline, then at 3, 6, 9 and 12 months. Topics discussed included weight history, previous weight loss attempts, barriers to change, any renal dietary restrictions, physical activity levels, diabetes management, renal function, blood pressure, medications and whether the patient consented to referral into the local NHS Weight Management Service. Specific, achievable patient led goals were agreed that would facilitate weight loss while also incorporating renal and diabetes dietary management. Following the initial consultation, relevant written resources were posted to the patient including a newly designed 'Working towards a healthy weight with kidney disease' leaflet. On completion of the 12-month telephone clinic, patients were invited to complete an online feedback questionnaire.

Results: 34 patients were invited with 19 (53%) opting to take part. Of the patients who opted in: 63% were male, the mean age was 61 years, mean eGFR was 26 and mean HbA1c was 65. At the baseline assessment, mean BMI was 37.6kg/m^2 and 74% reported doing minimal exercise. 74% of patients opted for a phone call rather than a video consultation. Fifty-three percent of those who opted-in completed the 12-month clinic duration. Of these, mean weight loss was 5.6kg (5.3%, p=0.01) over 12-months. All patients who responded to the feedback questionnaire reported that the initial baseline appointment was 'helpful to very helpful'. 83% reported that there was exactly the right amount of follow up appointments and that their knowledge around nutrition and weight loss had improved a lot. 53% of patients consented to referral to the local NHS Weight Management Service for ongoing support following this remote clinic.

Discussion: This project demonstrated that a remote dietetic-led clinic providing specialist weight management advice for patients with diabetes and CKD was successful in achieving significant weight loss.

Transforming patient pathways and reducing health inequalities through early detection, diagnosis and better treatment

96: Global health inequalities of chronic kidney disease: A systematic review and meta-analysis examining prevalence and disparities in age, sex and socio-economic status

Dr Rachael Duff[1], Dr Omodolapo Awofala[2], Mr Muhammad Tahir Arshad[2], Dr Emilie Lambourg[2], Dr Peter Gallacher[3], Dr Neeraj Dhaun[3,4], Dr Samira Bell[2,5]

[1]Queen Elizabeth University Hospital, Glasgow. [2]Department of Population Health and Genomics, University of Dundee. [3]BHF/Centre for Cardiovascular Science, University of Edinburgh. [4]Department of Renal Medicine, Royal Infirmary of Edinburgh. [5]Renal Unit, Ninewells Hospital

Biography - Dr Rachael Duff

Rachael is an Internal Medicine Trainee currently based in the Queen Elizabeth University Hospital in Glasgow. The work presented was carried out as part of the Academic Foundation Programme, where she had a rotation in NHS Tayside in 2022 during her foundation year 2, in collaboration with the University of Dundee. She is interested in a future career in nephrology and is aiming to apply for specialty training in renal medicine later this year.

Abstract

Introduction: Chronic kidney disease (CKD) is a significant contributor to global morbidity and mortality. Age, sex and socio-economic status are considered to be influential in the development, progression and outcomes from CKD. This study investigated disparities in age, sex and socio-economic status in CKD and updated global prevalence estimates through systematic review and meta-analysis.

Methods: Five databases (MEDLINE/PubMed, Embase, Cochrane CENTRAL Library, CINAHL, Web of Science) were searched from 2014 to 2022, with 14,871 articles screened, 119 papers included and data analysed on 29,159,948 participants. Studies were included if they described CKD prevalence in participants over the age of 18 and were carried out in the general population. CKD was defined on the basis of albuminuria/proteinuria and/or an estimated glomerular filtration rate of <60ml/min/m^2. Random effects meta-analyses using generalised linear mixed models were conducted to determine overall prevalence, prevalence of stages 3 – 5 and prevalence in males and females. Influences of age, sex and socio-economic status were assessed in subgroup analyses, and risk of bias assessment and meta-regressions were conducted to explore heterogeneity.

Results: Overall prevalence of CKD was 13.0% (11.3 – 14.8%) and 6.6% (5.6 – 7.8%) for stages 3 – 5. Prevalence was higher in studies where all participants were over the age of 60 (19.3% for stages 1 – 5, 15.0% for stages 3 – 5) and meta-regression demonstrated association of age, body mass index, diabetes and hypertension with prevalence of CKD stages 3 – 5. The prevalence of CKD stages 1 – 5 was similar in males and females (13.1% versus 13.2%) but prevalence of stages 3 – 5 was higher in females (6.4% versus 7.5%). Overall prevalence was 11.4%, 15.0% and 10.8% in low, middle and high-income countries respectively; for stages 3 – 5 prevalence was 4.0%, 6.7% and 6.8%, respectively. Risk of bias of included studies was generally moderate or high, with 8% at low risk of bias, 44% at moderate risk of bias and 48% at high risk of bias.

Discussion: With nearly 30 million participants, this is the largest systematic review on CKD prevalence to date, with prevalence demonstrated to be persistently high globally. It has highlighted that important disparities related to age, sex and socio-economic status may exist, and addressing these concerns should be a priority for

policymakers. Future research should focus on targeted screening and treatment approaches, improving access to care and more effective data monitoring, particularly in low and middle income countries.

Figure 1: Pooled prevalence of CKD stages 1 - 5

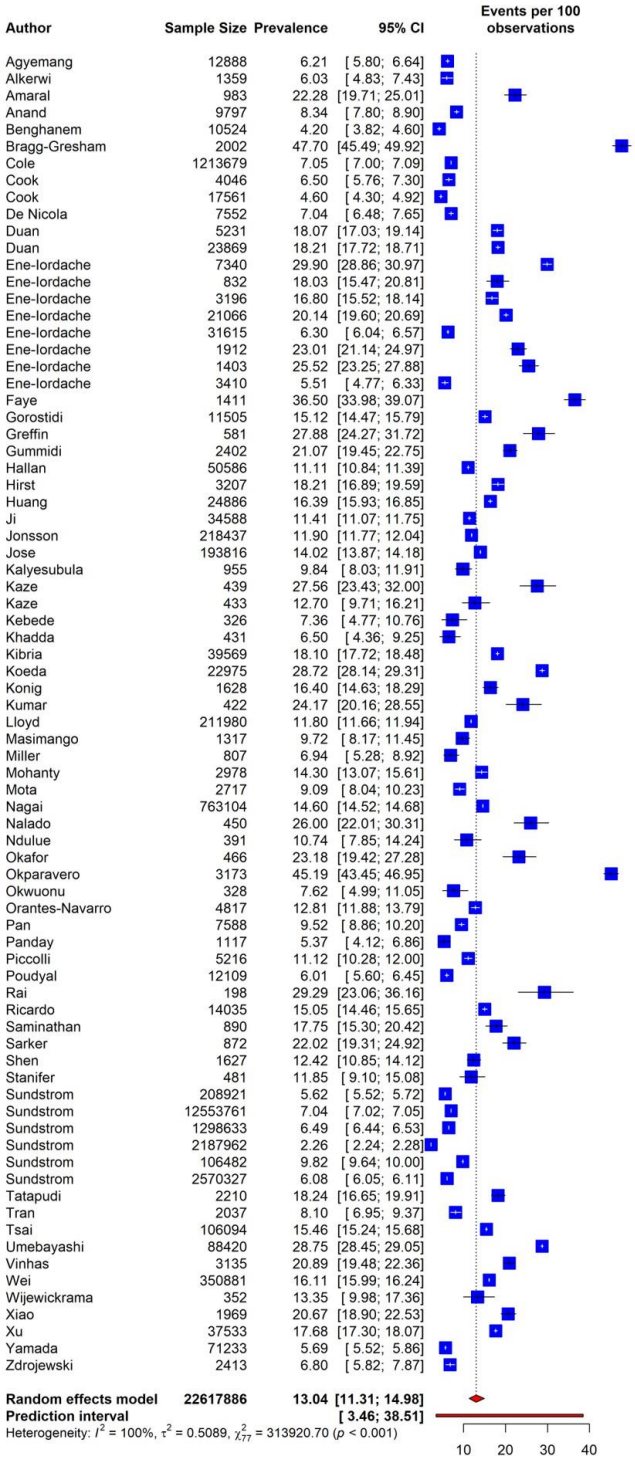
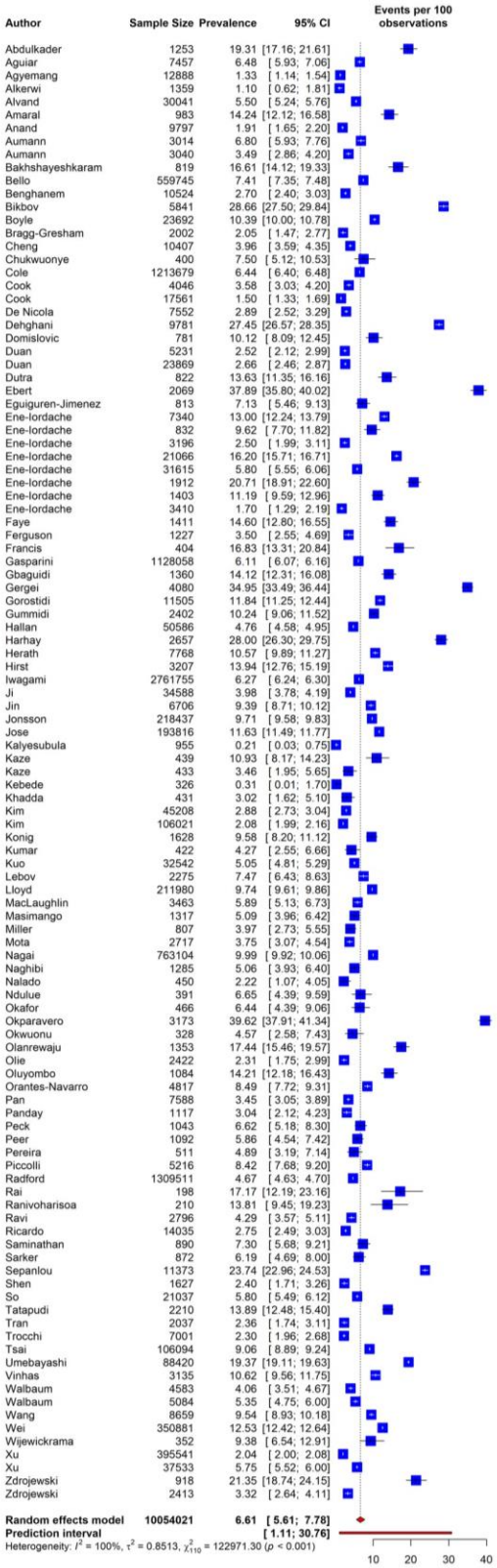


Figure 2: Pooled prevalence of CKD stages 3 - 5



Study Registration Number
PROSPERO ID: CRD42022311032

215: Tackling kidney inequalities: The development of the London Kidney Network (LKN) Health Inequalities in Kidney Care online learning module.

Ms Sarah Milne[1,2], Dr Ben Oliveira[3,2], Ms Susan Cummins[4,2], Ms Roseline Agyekum[5,6,2], Mr Andre Crawford[7], Ms Deepa Kariyawasam[5,2], Dr Gavin Dreyer[8,2], Ms Mariza Procopio[2]

[1]Royal Free London NHS Foundation Trust, London. [2]London Kidney Network, London. [3]Guy's and St Thomas' NHS Foundation Trust, London. [4]Camden & Islington Foundation Trust, London. [5]King's College Hospital NHS Foundation Trust, London. [6]King's College London, London. [7]Kings Health Partners, London. [8]Barts Health Kidney Department, London

Biography - Ms Sarah Milne

Sarah is Lead Nurse for Nephrology, and Clinical Service Line Lead, for Chronic Kidney Disease (CKD) and renal outpatients at the Royal Free London NHS Foundation trust. A senior kidney nurse with over 20 years' experience who has an interest in CKD prevention and early intervention, reducing health care inequalities, education and peer support. In 2020, Sarah was one of 16 multi-professional fellows accepted onto Health Education England first national Population Health Fellowship. She co-chairs the North Central London (NCL) Kidney network driving improvements in quality and outcomes for patients with CKD in NCL and is the education lead for the London Kidney Network, Health Equity Group.

Abstract

Introduction: The aim of the LKN health equity (HE) education group is to highlight the existing inequalities for people with kidney disease to everyone, clinical and non-clinical, involved in providing care across the whole patient pathway. Our group also supports the kidney workforce to address and reduce the impact of these inequalities in daily practice. Access to good quality training and education has been reported as pivotal towards highlighting and reducing the impact of health inequalities among high-risk groups. However, there are no specific resources for training staff working in kidney units to help understand and identify inequalities in kidney care. Accordingly, we developed an online education module to address the knowledge gap in both clinical and non-clinical staff.

Methods: To understand people's health inequalities training and education needs, the HE education group created a short online survey that was electronically distributed to all staff in the seven kidney units within the LKN. The survey was aimed at all clinical and non-clinical staff. We used the results of this to design a bespoke online education module focussing on the nature, causes and mitigation strategies for inequalities in kidney care.

Results: Of the 196 responses received, 62.7% (n= 123) were fully completed. Majority of respondents were nurses 42%, (n=52) 18% (n=22) Consultant grade medical staff, 11% (n=13) Dietitians, and 9% (n=11) in an administrator role, the remaining 20% (n=25) respondents were made up of other MDT members. 77% (n=94) of staff had not received any health equity training as part of their current role and 88% (n=106) expressed interest in health equity training. The preferred training format was self-paced e-Learning.

The LKN HEG education group worked with a learning technologist at Kings Health Partners Learning Hub to create an interactive e-learning module. The module content was developed with patient involvement and piloted by a wide range of stakeholders. This introductory course is aimed at all staff groups with consideration of literacy levels. The module includes a pre and post course knowledge check to assess learning, and participants are requested to complete a short module feedback survey at the end of the course. The module went live in late Autumn 2023 and the group are working with the LKN to advertise and encourage all staff in each of the seven kidney units to complete.

Discussion: Our module is ideally placed to help all staff identify and reduce inequalities in kidney care along the whole patient pathway. We will refine and update the content based on user and patient feedback. Preliminary feedback shows an increase in knowledge and skills following course completion. Promotion of the module and access to its content across all staff groups is a vital component of LKN efforts to reduce kidney health inequalities.

219: Noninvasive diagnosis of renal allograft acute cellular rejection through active Granzyme B in urine using a novel probe: a potential point of care test

Dr Jamie Scott[1], Ms Andrea Gonzalez Ciscar[2], Ms Rachael Boardley[2], Ms Emma Aitken[2], Mr John Asher[2], Mr Marc Clancy[2], Professor Colin Geddes[2], Dr Mike Dalrymple[1], Professor Marc Vendrell[1], Mr Stephen Knight[2]

[1]University of Edinburgh, Edinburgh. [2]Renal Transplant Unit, Glasgow

Biography - Mr Stephen Knight
Stephen is a senior surgical registrar in the West of Scotland. His interests include crowd-sourcing patient-level data, machine learning techniques, mobile data collection platforms and translational technology to measure postoperative surgical outcomes. During his PhD exploring global surgical outcomes, he helped lead GlobalSurg 3, a prospective international cohort study of early cancer outcomes of 15 000 patients across 82 countries. In addition, during the Covid-19 pandemic his work developing risk stratification scores to guide clinical management was published in the British Medical Journal and incorporated within UK national guidelines. The impact of his PhD research was recently acknowledged by the Royal College of Surgeons of Edinburgh through the award of the Syme Medal. He has received over £600 000 in research funding to date and recently received an ESOT mentorship award. He is currently the Principle Investigator for a study exploring the use of urinary markers to diagnose and manage acute cellular rejection in patients with renal allografts.

Abstract
Introduction: Acute rejection is a frequent complication of renal transplantation, requiring invasive allograft biopsy for diagnosis. Previous methods to develop a non-invasive test rely on amplification methods or have limited clinical utility beyond highly specialised laboratories. No point of care test for acute cellular rejection currently exists, which could reduce treatment delays and improve transplant outcomes.

Methods: We recruited 61 consecutive patients undergoing investigation for acute allograft dysfunction. All patients had previously demonstrated stable transplant function. Urine specimens were collected from each patient, with active Granzyme B (GzmB) measurements performed using a patented fluorescent probe. Total GzmB activity was correlated with allograft status, with results available within two hours. Serial measurements from patients with biopsy confirmed acute cellular rejection were taken each week for four weeks following completion of IV methylprednisolone treatment. Ethical approval was gained (GN22RE301).

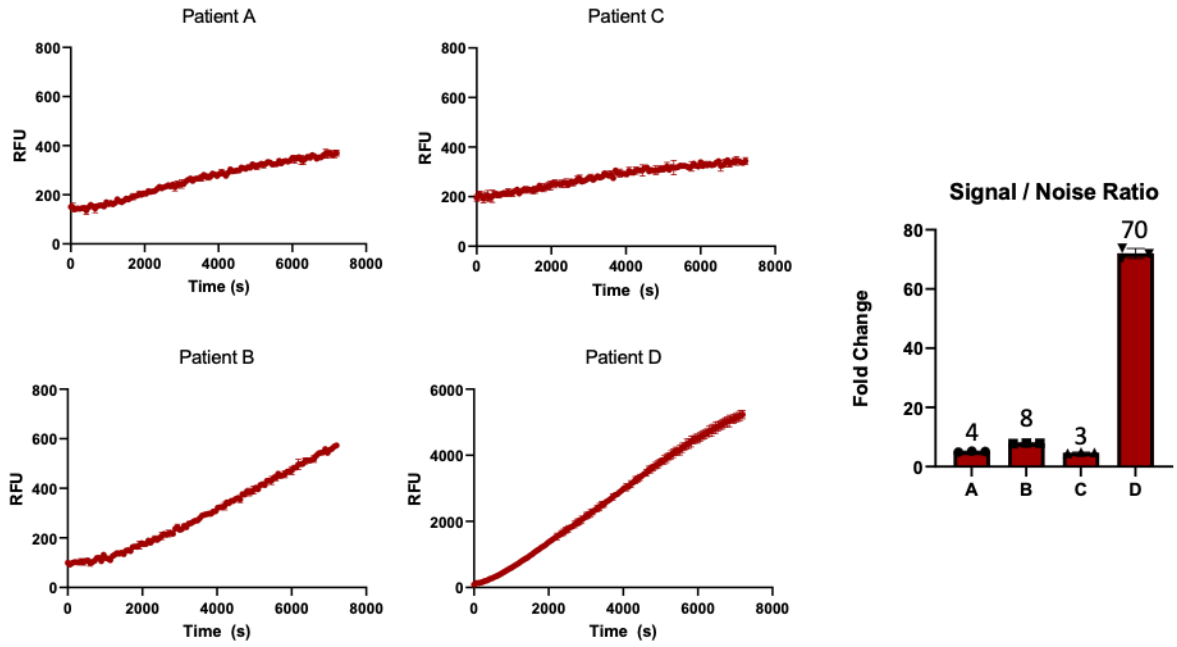
Results: Overall, 18 patients (29%) had biopsy-confirmed acute cellular rejection. No GzmB activity was measured in patients with BK nephropathy, urinary tract infection, or recurrent primary disease. Analysis demonstrated that acute cellular rejection could be predicted with a sensitivity of 77.8% and specificity of 88.4%, with a corresponding PPV of 73.7 and NPV of 90.5%. Accuracy was 85.3%. In patients with acute cellular rejection, probe GzmB measurements correlated with rejection severity in biopsy samples (Figure 1). A sequential reduction in GzmB activity was seen in patients with a corresponding fall in creatinine following treatment for acute rejection.

Discussion: We demonstrate the potential of a future point of care test to non-invasively diagnose acute rejection of renal allografts. We were able to identify acute cellular rejection with high specificity from patient urine samples, which correlated with severity and treatment response. This technology produces a result within two hours and can be delivered by the bedside with a device similar in size to a urine dipstick analyser. Further

research will now be focused on patients with low pre-probability of acute rejection in clinic to determine performance.

Funding: KRUK Stoneygate Award

Figure 1. Measured Granzyme B activity for the first four recruited patients (A-D). Two patients (B and D) demonstrated acute cell-mediated rejection on allograft biopsy, with signal correlating with severity of rejection (B: Banff classification 1A, D: Banff classification 2A)



515: Impact of kidney function trajectory and acute kidney injury on cardiovascular risk: a novel data-linkage study

Dr Peter Gallacher[1], Mr David Yeung[1], Dr Gavin Chapman[1,2], Dr Robert Hunter[2,1], Dr Eve Miller-Hodges[2,1], Dr Samira Bell[3], Professor Neeraj Dhaun[1,2]

[1]BHF/University Centre for Cardiovascular Science, University of Edinburgh. [2]Department of Renal Medicine, NHS Lothian. [3]Division of Population Health and Genomics, University of Dundee

Biography - Dr Peter Gallacher

I am a SCREDS Clinical lecture in General Practice (GP), GP trainee, and BHF-funded early career researcher with specific expertise in advanced epidemiological principles and statistical modelling. My current research interests involve cross-specialty collaboration between primary care, cardiology and renal medicine, and includes the advanced analysis of routine healthcare data and development of novel epidemiological methods, which I believe will directly inform future healthcare policy and improve the outcomes of patients with kidney disease.

Abstract

Introduction: Cardiovascular disease (CVD) is the commonest complication of kidney disease and CVD risk increases as eGFR declines. Previous studies investigating this relationship have utilised single measures of creatinine, relied on conventional disease modelling, or failed to account for the impact of acute kidney injury (AKI). Here, we evaluated how long-term changes in kidney function and AKI modify CVD risk following incident CVD events.

Methods: All patients aged ≥18 years and resident in NHS Fife/Tayside who underwent routine kidney function testing, were not on dialysis, and were subsequently hospitalised with incident myocardial infarction (MI), heart failure (HF), or stroke between 01/01/2004-31/12/2018 were eligible for inclusion in this retrospective data-linkage study. eGFR slopes were estimated using linear mixed-effects models – adjusted for age, sex, and socioeconomic status – and compared before and after each CVD event. Joint models – accounting for competing risks and adjusting for the same variables – were constructed for each eGFR group at time of event (<30/30-59/60-89/≥90ml/min/1.73m^2) to estimate risk of CVD death using serial eGFR measures (following each CVD event) and accounting for AKI at time of event.

Results: There were 13,141 patients with incident MI (69±13 years, 36.4% women, 24.7% eGFR <60ml/min/1.73m^2, 4.4% 1-year CVD death), 10,595 patients with incident HF (75±12 years, 46.0% women, 44.8% eGFR <60ml/min/1.73m^2, 10.2% 1-year CVD death), and 9,838 patients with incident stroke (72±13 years, 49.9% women, 29.6% eGFR <60ml/min/1.73m^2, 4.5% 1-year CVD death). The median number of creatinine tests prior to MI, HF, and stroke was 11 [IQR 5-24], 21 [IQR 10-37], and 13 [IQR 6-26], respectively, and 19 [IQR 11-34], 24 [IQR 13-43], and 18 [IQR 10-33] after, respectively. Rates of eGFR decline were similar before and after each CVD event (MI: -1.45 [95%CI -1.50 to -1.40] *versus* -1.28 [95%CI -1.34 to -1.22] ml/min/1.73m^2/year; HF: -2.06 [95%CI -2.12 to -2.00] *versus* -1.80 [95%CI -1.93 to -1.68] ml/min/1.73m^2/year; stroke: -1.45 [95%CI -1.51 to -1.40] *versus* -1.26 [95%CI -1.34 to -1.17] ml/min/1.73m^2/year).

For MI, the adjusted joint model demonstrated independent associations between post-event eGFR slope and risk of CVD death (e.g., for those with an eGFR 30-59ml/min/1.73m^2/year at event: adjusted hazard ratio [aHR] *per* 2.5 ml/min/1.73m^2/year decline, 1.23 [95%CI 1.16-1.32], *P*<0.001), and between AKI at time of event and risk of CVD death (e.g., eGFR 30-59ml/min/1.73m^2 at event: aHR 1.22 [95%CI 1.04-1.43], *P*=0.013) across all eGFR groups. Similarly, for HF, there were independent associations between subsequent eGFR slope and risk of CVD death (e.g., eGFR 30-59ml/min/1.73m^2/year at event: aHR *per* 2.5 ml/min/1.73m^2/year decline, 1.21 [95%CI

1.17-1.26], *P*<0.001) and between AKI at time of HF and risk of CVD death (e.g., eGFR 30-59ml/min/1.73m^2: aHR 1.16 [95%CI 1.03-1.29], *P*=0.012) across all eGFR groups. For stroke, we found no independent associations between eGFR trajectory or AKI and risk of CVD death.

Conclusions: Following MI and HF, but not stroke, subsequent eGFR slope and AKI independently associate with risk of CVD death across all eGFR groups. This novel data-linkage study illustrates the prognostic importance of dynamic changes in kidney function and the impact of AKI on CVD risk.

Kidney networks: adding value by working together – showcasing CKD prevention

299: An external evaluation of an Integrated Care System virtual chronic kidney disease service

Dr Rupert Major, Mr Niraj Lakhani, Ms Reena Patel, Ms Maria Martinez, Professor James Burton, Dr Richard Baines, Professor Fahad Rizvi, on behalf of the programme's team

Leicester, UK

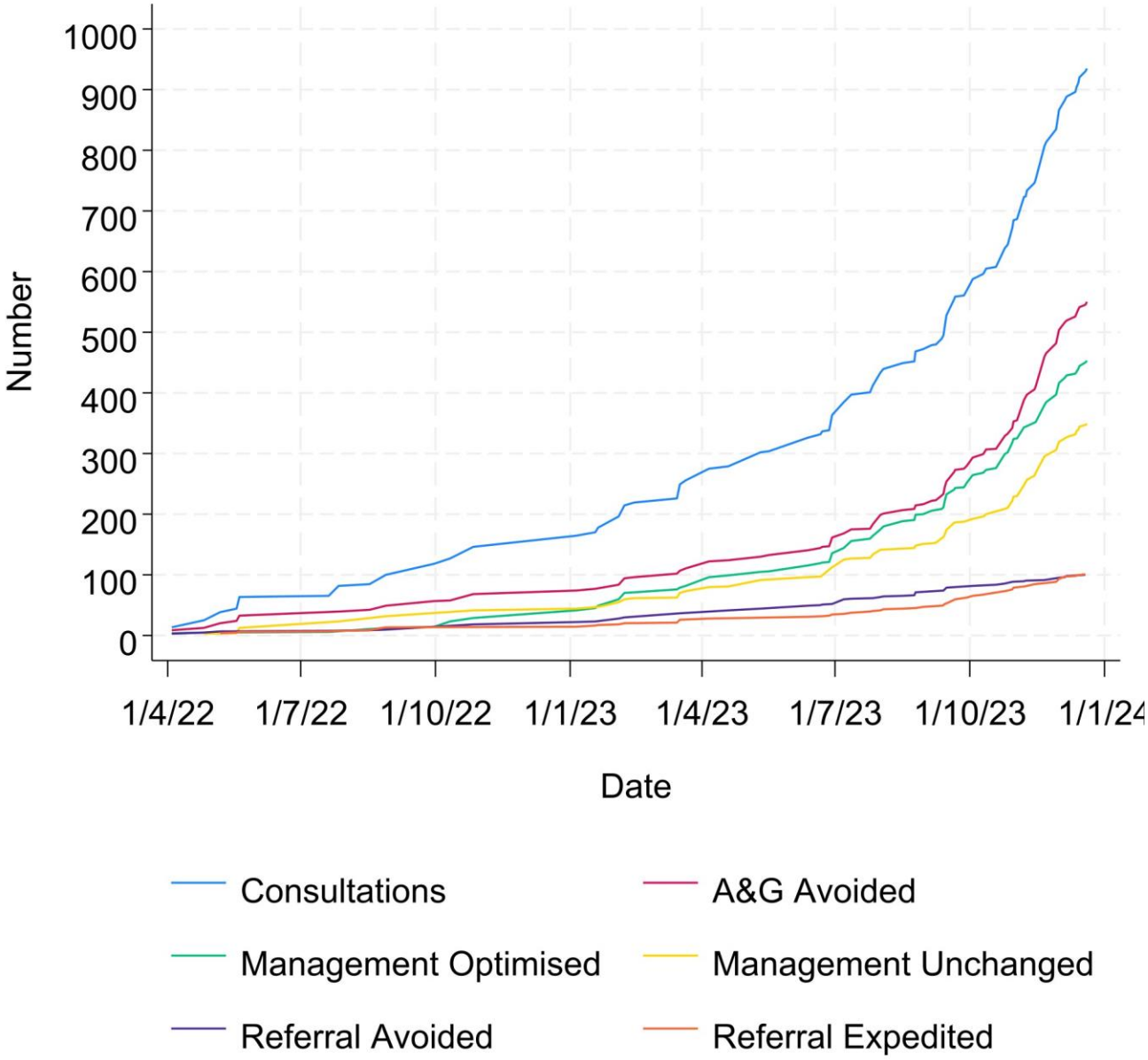
Biography - Dr Rupert Major
Associate Professor at University of Leicester and Honorary Consultant Nephrologist at University Hospitals of Leicester NHS Trust

Abstract
Introduction: Early diagnosis, risk stratification and increased use of evidence-based medications are essential to improve management of chronic kidney disease (CKD). Increased rates of urine proteinuria measurement, the use of The NICE recommended Kidney Failure Risk Equation (KFRE) and systematic medicine reviews are likely to address these problems. The vast majority of people with CKD are managed in a traditional primary care setting. The introduction of Integrated Care Systems (ICS) in England provides the opportunity to revolutionise CKD and other chronic disease management.

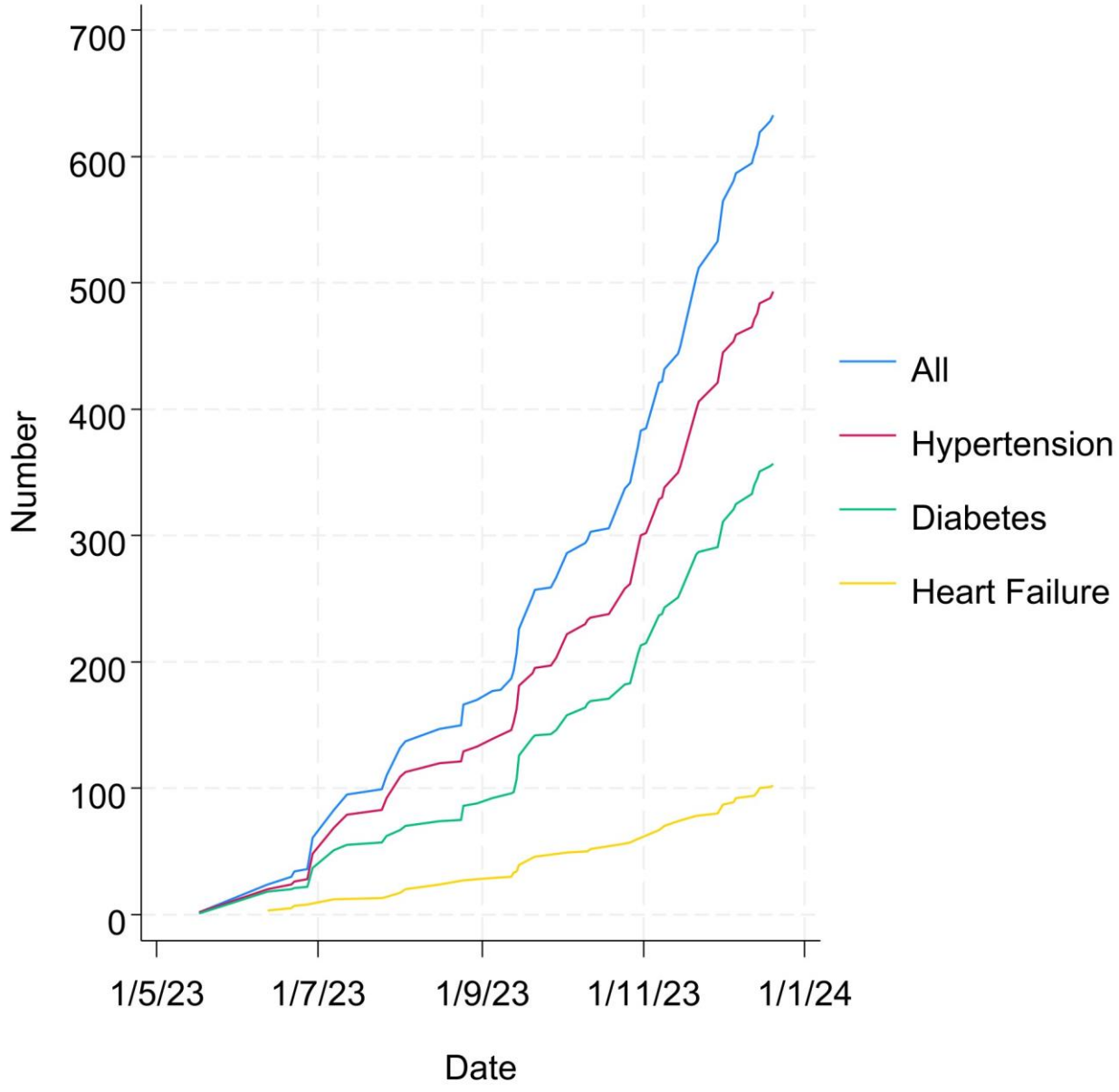
Methods: We implemented a virtual CKD service in an ICS serving 1.1 million people including areas of high levels of deprivation, ethnic diversity, and urban and rural populations. An independent, external evaluation of the programme was performed.

Results: The programme commenced in 2021 focusing on a public kidney education programme of educational videos. In April 2022 virtual clinics were piloted in four Primary Care Networks. The programme was expanded in May 2023 to make virtual clinics available to all PCNs.

As of December 2023, 14 out of 26 PCNs, representing primary care service for an estimated 700,000 people, are participating in the programme's clinics. Up until December 2023, 935 patient discussions have occurred with 453 (48.4%) involving medicines optimisation, 101 leading to referrals being expedited and 100 avoiding formal referrals (Figure 1).



Individuals with CKD reviewed in the virtual clinics also had high prevalences of hypertension, diabetes and heart failure (Figure 2).



The programme's external evaluation, including primary and secondary care costs, showed a predicted benefit of £1,200 per clinic. Immediate benefits were from treatment of patients away from secondary care and reduction in clinical time used for creating and responding to Advice and Guidance (A&G) requests. Further longer-term financial benefits in relation to reduction in hospitalisation and kidney replacement therapy were predicted by the economic modelling. With all PCNs participating, the annualised net benefit of the programme over five years is predicted to be £455,000 per year, or a benefit-cost ratio of 2.76.

Discusssion: An integrated care model for CKD can lead to high levels of engagement between primary and secondary care. Overall, an external economic evaluation of the programme has suggested that for every £1 invested in the programme £2.76 would be returned in benefit. This benefit is is gained in the short-term from

the reduction of secondary care-based assessment and in the longer term in relation to medicines optimisation leading to reduced need for future kidney replacement therapy.

240: A 'nudge' to improving uACR screening in Northland, New Zealand.

Dr Walaa Saweirs[1,2], Mrs Tracey Saweirs[1], Mrs Rian Gale[1]

[1]Te Whatu Ora, Whangarei. [2]University of Auckland, Auckland

Biography - Dr Walaa Saweirs

Walaa trained in Edinburgh. He was a Medical Research Council Research Fellow gaining a PhD on MHC Class II tetramer formation. He was part of the SIGN group that assisted in the development of guidelines on early chronic kidney disease at the 2006 UK Consensus conference. He took up a Consultant post in Northland, New Zealand in 2009, maintaining his passion for early chronic kidney disease management, and contributed to the New Zealand Consensus statement on the management of CKD in 2014. Walaa helped establish a telehealth program in Northland incorporating multi-disciplinary links with the tertiary centre as well as within the renal unit between satellite centres and virtual clinics. He established a monthly virtual clinical educational meeting with primary care teams in northern Northland. He was involved in the inception of the Australia-New Zealand PD Academy in 2010 and remains an Academy lecturer. He was Chair of the New Zealand PD registry from 2016 – 2022. He was the Clinical Director for Nephrology in Northland from 2016 – 2021. Walaa is currently a full-time Nephrologist in Northland and Honorary Senior Lecturer at Auckland University. He is the clinical lead of the Northland Early CKD program that was initiated in February 2022.

Abstract

Early detection of CKD can reduce its burden and attendant complications. This is particularly relevant in high-risk populations e.g. Māori and Pasifika. The recent Deloitte-KHA report highlights the economic value of early detection with a net benefit of $45AUD for every $1AUD invested.

The Northland region of New Zealand has a high level of socioeconomic deprivation and a significant Māori population. Initial data suggested that uACR screening covered less than 25% of the at-risk population potentially leading to delayed recognition and management of CKD. Utilising a co-design approach, our aim was to increase the uptake of uACR screening to at least 50%. This was part of a region-wide Early CKD program launched in September 2022.

The four primary care teams within the co-design group participated in an ‘uACR nudge’ pilot (2 ‘active’ [practices 17 and 36] and 2 ‘control’ [practices 15 and 28]) utilising the reScript® software in conjunction with mentoring support, from March to December 2023. The ‘control’ practices did not have access to the reScript® software. Mentoring support was available for the whole region. The reScript® software is utilised for electronic prescriptions in 85% of primary care practices and gathers data from all Northland practices. It can screen patients to identify those determined to be 'at risk’. If an uACR has not been performed in >15 months in an ‘at risk’ individual a ‘nudge’ appears on the clinician’s work page (“Recommend kidney health check: Please consider urine ACR”) at the time a prescription is written. The 'at risk' group was defined as those with known diabetes or hypertension, those of Māori, Pacifika or Indo-asian ethnicity aged >40 years, other individuals >50 years, or those with a BMI >30.

Baseline data from the 39 primary care practices in Northland revealed that 47% of the population fell within the ‘at risk’ category. Of these, 80% had not had a check of their uACR within the previous 15 months, 34% had no eGFR check and 40% had no HbA1c check within the same period. The co-design practice means were comparable to the regional means (47% ‘at risk’, 81% without uACR, 36% without eGFR and 41% without HbA1c).

The uptake of mentoring support was sporadic. This is likely to be a reflection of practice priorities and workload. Furthermore, screening impetus may have improved following two regional teaching events in mid-June and the beginning of November 2023 (Chart 1).

In the first half of the period (March-June), there was a significant increase in uACR uptake in one of the active practices, rising from 26% to 42% of the 'at risk' population ($p < 0.001$). The regional mean uptake remained unchanged during the same period. By the close of the period, all pilot practices had a significant increase in uACR screening. There was a statistically significant increase in the regional mean, improving from 20% to 23% ($p < 0.001$) (Chart 2).

The 'nudge' appeared to aide the initial uptake of screening, however, the improvement in practices without the nudge indicates that other factors contributed. These factors are likely to include clinician engagement and CKD prioritisation within each practice. These may also partially explain the improvement in the two control-arm practices. The regional teaching events may have had an impact given the improved screening in the second half of the pilot.

Chart 1:

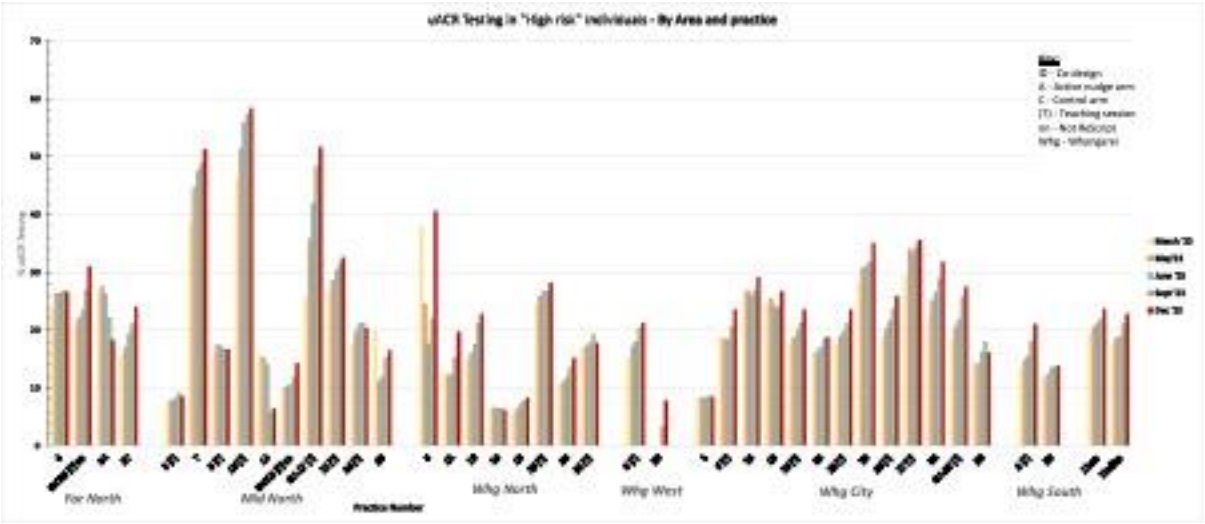
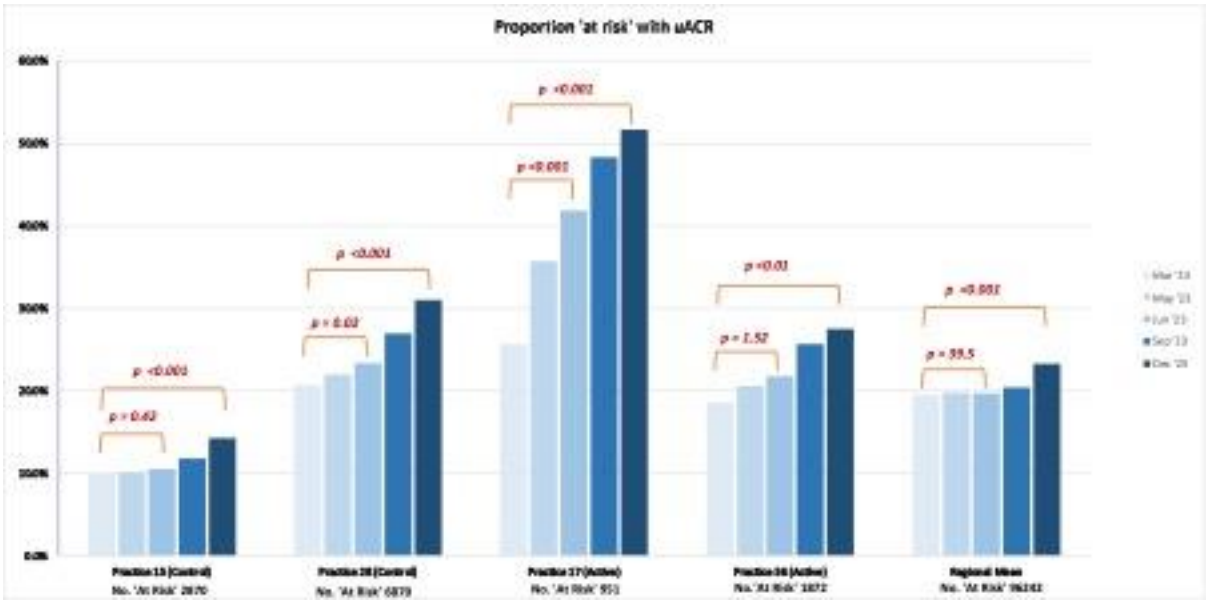


Chart 2:


Proportion 'at risk' with uACR
p <0.001
p <0.001
p <0.001
p <0.01
p <0.001
p = 0.02
p = 1.52
p = 59.5
p = 0.42

The Mental Capacity Act and kidney treatment: assessing capacity and the Court of Protection

441: Delirium-codes are more prevalent in younger hospitalized patients on dialysis compared to hospitalized people from the general population of the same age

Dr Anna Casula[1], Professor Charlotte Warren-Gash[2], Professor Daniel Davis[3], Professor Dorothea Nitsch[2,1]

[1]UK Kidney Association, Bristol. [2]London School of Hygiene & Tropical Medicine, London. [3]UCL, London

Biography - Dr Anna Casula

Anna Casula is a biostatistician with over fifteen years of experience at the UK Renal Registry. After obtaining a degree in Biology and many years working as a researcher in neuropharmacology, she has completed a master in Medical Statistics and has since been working at the UK Renal Registry, during which she has been involved in many research projects, and by working with multiple datasets on AKI, KRT and hospitalisation data, Anna has developed a keen interest in data quality improvement.

Abstract

Introduction: Delirium is an acute, fluctuating syndrome of encephalopathy causing disturbed consciousness, attention, cognition and perception. It is common in patients with predisposing factors (such as advanced age, or multiple co-morbidities). Kidney disease shares some of the same risk factors; patients with kidney disease may represent a high-risk population for delirium. We therefore set out to investigate the burden of delirium in hospitalised patients on dialysis.

Methods: Using UK Renal Registry data, we identified all the patients on dialysis on the 31st March 2018, and amongst these all admissions during the financial year 2018/19 using linked Hospital Episode Statistics (HES) for England. We used ICD10 F05 code to identify delirium. We compared the prevalence of coded delirium amongst hospitalised patients on dialysis with that reported overall in HES for the same time period (identified using the same ICD10 code), and derived prevalence ratios in defined age-strata.

Results: There were more patients on haemodialysis (n=11,371) than on peritoneal dialysis (n=1,460), and amongst patients on haemodialysis, there were more admissions (n=20,143, 5.5 per 1000 patient-years) than amongst patients on peritoneal dialysis (n=1,973, 4.7 per 1000 patient years). The crude prevalence of delirium amongst hospitalised patients on dialysis was 3.7% across all ages. The prevalence increased with increasing age, with approximately 6% of patients over 85 years affected. When stratified by dialysis modality and age, broadly similar estimates in prevalence of delirium were obtained, except for those aged 90 years or older in whom numbers for people on peritoneal dialysis were too low to obtain a reliable estimate.

When compared to the general population data from HES, prevalence ratios were elevated for those under 80 years, with the highest prevalence ratios seen for those under age 65 years. Prevalence ratios for delirium were lower in dialysis patients aged 80 or more years than seen for the general population of the same age.

Conclusions: Delirium appears to be recorded more commonly in hospitalised patients on dialysis compared to the general population in people aged less than 80 years. Further analyses need to investigate whether the associations seen are related to who is selected on dialysis at older age and/or whether younger patients on dialysis are more closely monitored when compared to other patients.

Table: Numbers of people on dialysis, stratified by modality (haemodialysis=HD, and peritoneal dialysis = PD) and age groups (in years), with numbers of admissions, numbers of admissions with delirium codes, derived percentages of admissions with delirium, and prevalence ratios compared to the corresponding HES data for the general population in the same financial year (2018/19). ** less reliable estimates due to small numbers*.

		Age 65-69	Age 70-74	Age 75-79	Age 80-84	Age 85-89	Age 90+	Total	85+
Dialysis	N people	2670	3153	3054	2537	1143	274	12831	1417
	N-days at risk	842,955	1,008,414	980,151	806,975	352070	81576	4,072,141	433646
	N admissions	4,874	5,649	5,015	4275	1870	433	22,116	2303
	N admiss with Delirium	116	187	194	190	106	32	825	138
	% admiss with delirium	2.38	3.31	3.87	4.44	5.67	7.39	3.73	5.99
Prevalence ratio dialysis/ general population		**2.50**	**2.06**	**1.37**	**0.93**	**0.76**	**0.68**		**0.68**
HD	N people	2356	2743	2703	2271	1041	257	11371	1298
	N-days at risk	753,000	891271	879588	729239	322294	77666	3653058	399960
	N admissions	4,478	5,122	4,533	3887	1718	405	20143	2123
	N admiss with Delirium	106	172	175	168	98	29	748	127
	% admiss with delirium	2.37	3.36	3.86	4.32	5.70	7.16	3.71	5.98
Prevalence ratio HD/ general population		**2.48**	**2.09**	**1.36**	**0.90**	**0.76**	**0.66**		**0.68**
PD	N people	314	410	351	266	102	*17**	1460	119
	N-days at risk	89,955	117,143	100,563	77736	29776	3910	419083	33686
	N admissions	396	527	482	388	152	*28**	1973	180
	N admiss with Delirium	10	15	19	22	8	*<5**	77	11
	% admiss with delirium	2.53	2.85	3.94	5.67	5.26	*	3.90	6.11
Prevalence ratio PD/ general population		**2.65**	**1.77**	**1.39**	**1.18**	**0.70**	*		**0.69**

131: Healthcare workload amongst people with chronic kidney disease: what impact do mental disorders have?

Dr Michael Sullivan[1], Dr Julie Langan-Martin[1], Dr Katie Gallacher[1], Dr Benjamin Elyan[1], Professor Angela Webster[2], Dr Jennifer Lees[1], Professor Patrick Mark[1]

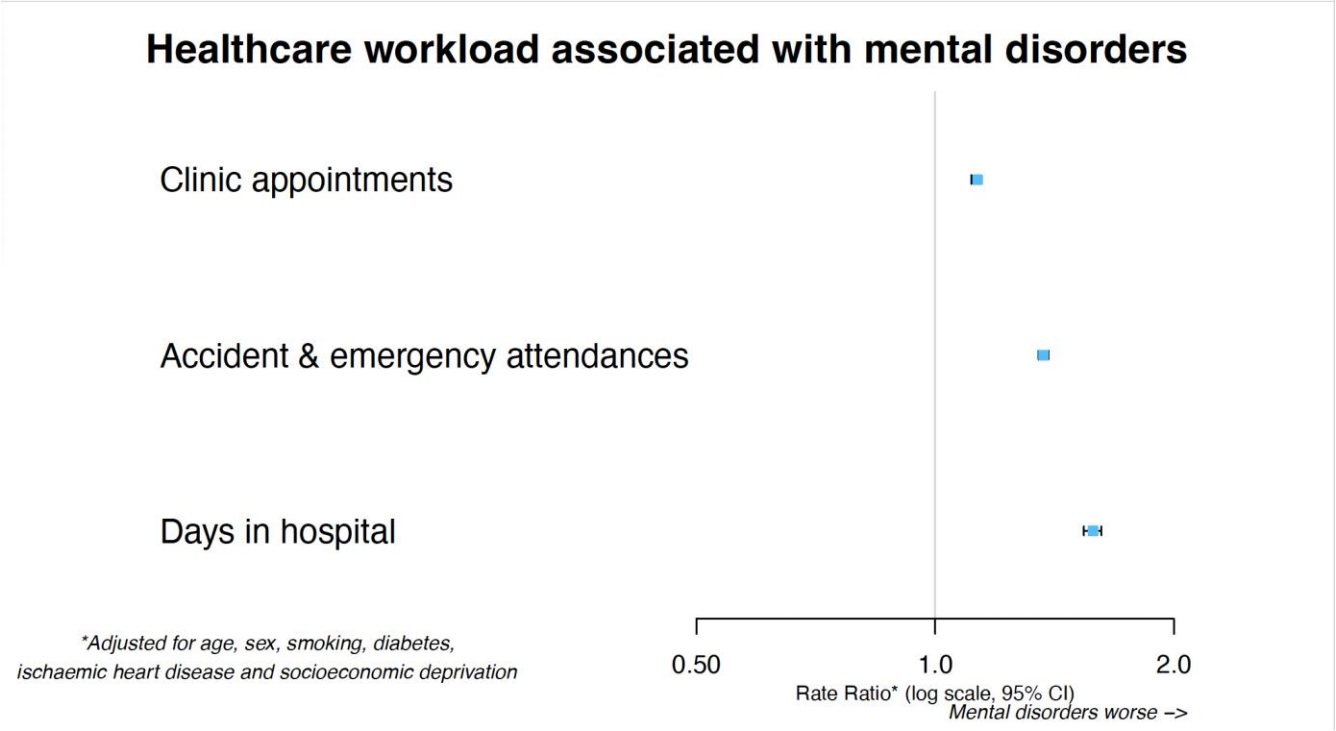
[1]Univeristy of Glasgow, Glasgow. [2]University of Sydney, Sydney

Biography - Dr Michael Sullivan
Dr Sullivan has an interest in using routine healthcare data to study risk factors for adverse outcomes in kidney disease.

Abstract
Introduction: People with chronic kidney disease (CKD) often experience a high healthcare workload in the form of medication management, contacts with healthcare services, and other tasks. Co-existing health conditions can increase healthcare workload, with mental disorders generating additional workload alongside physical conditions. We hypothesised that mental disorders in people with CKD would be common and that healthcare workload would be elevated for people with mental disorders.

Methods: Data were used from the Secure Anonymised Information Linkage Databank: primary care data for people living in Wales with linkage to hospital records. We studied adults over the age of 18 with CKD G3-5 not on kidney replacement therapy. We defined “mental disorder” as any primary care-recorded diagnosis of anxiety, depression, eating disorders, schizophrenia, and/or bipolar disorder. We estimated healthcare workload by quantifying visits to accident and emergency (A&E), days spent in hospital during emergency admissions (general hospital and psychiatric hospital), number of outpatient clinic appointments, locations of clinic appointments, and number of long-term medications prescribed. We estimated associations between mental disorders and healthcare workload using negative binomial models, making adjustments for age, sex, diabetes, ischaemic heart disease, smoking status, and socioeconomic deprivation.

Results: Of 173,388 people with CKD, mean age was 77 years, 54,537 (31.5%) had one or more mental disorder and 20,374 (11.8%) had two or more. Over a median follow-up period of 5.5 years, people with CKD and mental disorders spent a median 1.9 days in hospital (interquartile interval [IQI] 0.0 to 14.7) compared to people with CKD without mental disorders: 1.0 (IQI 0.0 to 9.9) days. People with CKD and mental disorders attended a median of 2.6 clinics (IQI 1.0 to 5.5) compared to people with CKD without mental disorders: 2.3 (IQI 0.8 to 4.9). The presence of any mental disorder was associated with more days spent in hospital: adjusted rate ratio (aRR) 1.58 (95% confidence interval 1.54-1.62), more A&E attendances: aRR 1.37 (1.35-1.39) and more clinic appointments: aRR 1.13 (1.11-1.14). The association with hospital days was strongest for people with eating disorders: aRR 3.70 (2.50-5.49). People with any mental disorder attended a similar number of locations for clinics than those without mental disorders: median 2 for both groups (IQI 1 to 3). However, people with schizophrenia, bipolar disorder or eating disorders attended more locations: median 3 (IQI 2 to 4). People with mental disorders took more medications (median 9: IQI 6 to 13) than those without mental disorders (median 7: IQI 4 to 10).



Discussion: Mental disorders are common amongst people with CKD and healthcare workload is greater for people with than without mental disorders. Although a proportion of the increased healthcare workload might be expected (such as people taking medications for their mental health), the additional days spent in hospital is a notable finding. This may reflect problems with how these people experience healthcare and it is likely to have an impact on their quality of life. Targeted work is required to understand the specific healthcare needs of people with CKD and mental health disorders.

Phosphate, calcium and PTH management – a bone of contention?

143: Exploring the real-life challenges to phosphate control in children with CKD – the IMPACT study

Mrs Louise McAlister[1], Ms Vanessa Shaw[2], Professor Kelly Lambert[3], Professor Rukshana Shroff[1]

[1]Great Ormond Street Hospital NHS Foundation Trust, London, UK. [2]UCL Great Ormond Street Institute of Child Health, London, UK. [3]University of Wollongong, New South Wales, Australia

Biography - Mrs Louise McAlister

Louise McAlister is a paediatric dietitian with some 33 years' experience; she has specialised in nephrology at Great Ormond Street Hospital (GOSH), London for the last 21 years. She provides dietetic support to children with acute and chronic kidney disease (CKD), renal tubular disorders, nephrotic syndrome and renal stones. GOSH is the largest paediatric renal unit in the UK, with 70 patients on chronic dialysis and 35 renal transplants annually. She has presented at paediatric nephrology conferences nationally and internationally, including BAPN, ESPN, IPNA and the European Peritoneal Dialysis meeting. She was invited as a clinical expert to join the Paediatric Renal Nutrition Taskforce and was first author for the clinical practice recommendations for the dietary management of calcium and phosphate in CKD, published in 2020. Amongst her other publications are chapters on the dietary management of renal tubular disorders and renal stones in the 5th edition of the textbook Clinical Paediatric Dietetics, 2020. Louise also contributed to a European consensus statement on calcium intake in children and adults with CKD, published in 2023.

Abstract

Introduction: Hyperphosphataemia is common in children with chronic kidney disease (CKD). Adherence to dietary advice and phosphate binders is estimated to be below 50%. Current strategies to address hyperphosphataemia are clearly ineffective.

The aim of this mixed-methods study is to explore the knowledge, challenges and priorities of children and young people (CYP) with CKD and their caregivers regarding a controlled phosphate (P) diet, and taking phosphate binders.

Methods: A purposive sample of CYP with CKD stages 4-5 and on dialysis (aged 8-18 years) and caregivers were recruited from three paediatric renal units within the United Kingdom.

Two surveys were developed for this study to assess P-related knowledge, educational preferences and perceived facilitators or barriers to adherence. The Phosphate Understanding and Knowledge Assessment questionnaires (PUKA-c and PUKA-a) for CYP and caregivers, respectively, were amended following feedback from stakeholders to ensure content validity.

Participants were invited to online focus groups (FGs) moderated by a dietitian. These followed a semi-structured format, exploring individual and shared experiences, learning style preferences and opinions on selected P-educational resources. The FGs were recorded with consent and transcribed verbatim. Inductive thematic analysis of the transcripts using the Framework Approach was undertaken.

Results: Eighty-four participants (44 CYP and 40 caregivers) were recruited, seventy completed PUKA questionnaires (39 CYP and 31 caregivers) and 46 attended FGs (25 CYP and 21 caregivers). Twenty-one (54%) CYP completing PUKA were male; 14 (38%) aged 8-12 years and 24 (62%) 13-18 years; 18 (46%) on dialysis and 30 (77%) on P-binders.

The internal consistency of the 13 PUKA knowledge questions was excellent (Cronbach's Alpha a = 0.96 and 0.98 for PUKA-a and PUKA-c, respectively). The knowledge scores were suboptimal, median score 72.7% (IQR 64.3-87.0%) for caregivers and 60.7% (IQR 50.0-72.4%) for CYP. There was a modest positive correlation [r=0.4 (p=0.03)] between the paired knowledge scores for the 28 dyads completing questionnaires.

From the questionnaires, 74% caregivers and 62% CYP reported they understood P-dietary advice; 42% caregivers and 31% CYP reported difficulties, of whom 72% caregivers and 64% CYP cited food restrictions as the main problem rather than taking P-binders (14% caregivers and 11% CYP).

Forty-six participants joined 13 FGs. Less than half (48%) CYP attending were male, 32% on dialysis, mean age 14 years [8-12 years (7), 13-18 years (18)]. Several themes were evident from FGs regarding the challenges of following controlled P-diets and taking P-binders. These include the widespread impact on family and social life necessitating constant adaptations to accommodate dietary restrictions; the desire for essential educational resources; a need for parental perseverance; and the need for dedication to implement P-control.

Discussion: The PUKA questionnaires reveal that despite adequate P-knowledge scores and reported understanding of dietary P-advice, CYP and caregivers want more help to increase personal agency. Further thematic analysis of FG transcripts provide deeper insights into this important area of treatment adherence in order to guide future dietetic support and communication methods. This data will help define the optimal strategy for educating, motivating and facilitating adherence to prevent adverse cardiovascular and bone outcomes.

Study Registration Number
ClinicalTrials.gov NCT05439980

577: Evaluation of vitamin D (25OH D) status in an ethnically diverse haemodialysis population and an insight of supplementation on renal mineral bone disease biochemistry.

Mrs. Zainab Mollabux[1], Professor Paul Cockwell[1], Ms. Yuki Heath[1], Ms. Jennifer Fryatt[2], Ms. Seema Jham[1], Ms. Jasvir Kaur[2]

[1]University Hospitals Birmingham, Birmingham. [2]Smethwick Dialysis Unit, Birmingham

Biography - Mrs. Zainab Mollabux
Specialist Dietitian (Renal)

Abstract

Introduction: Nutritional vitamin D deficiency is common in patients receiving long term renal replacement therapy with haemodialysis; however, monitoring is inconsistent. There is little evidence on the levels of vitamin D by ethnic group in a single geographical location and single unit where non-demographic confounders are limited, or on the impact of vitamin D supplementation on early changes in bone chemistry. Therefore, we audited vitamin D status in a single haemodialysis unit with an ethnically diverse population evaluated the impact of supplementation on mineral bone disease parameters in a subgroup.

Method: Vitamin D levels were assayed in a single month for all patients attending the unit. Results were classified as severely deficient 0 – 25 nmol/l, deficient 26-49 nmol/l, and sufficient 50 nmol/l or more. The results were discussed with the patients. For patients with a vitamin D level < 50nmol/l letters were then sent to the patient's GP requesting supplementation with 3200 IU colecalciferol daily for 12 weeks followed by a maintenance dose of 800 – 1000 IU per day There was no adjustment to any treatment with activated vitamin D, calcimimetics, or phosphate binders during supplementation. The impact of supplementation on mineral disease biochemistry markers (corrected calcium, phosphate, parathyroid hormone) was assessed for 17 patients.

Results: 54.3% of patients were severely deficient in vitamin D, 17.3% were deficient and 28.4% had sufficient levels (>50nmol/l). Median (range) by broad ethnicity status was significantly different by group: South Asian (n=82), 22.8 (<8.8-190.3); Black (n=43) 16.7 (<8.8-152.7), White (n=36) 43.4 (<8.8-133) (p=00003)

In the subgroup of patients analysed for post supplementation bone chemistry, prompt primary care prescription occurred in all and 15 of 17 confirmed concordance. There was no significant impact on bone chemistry of vitamin D supplementation: pre calcium 2.27 (1.91-2.39) mmol/l, post calcium 2.3 (1.82-2.51)mmol/l; pre phosphate 1.79 (1.06-3.51)mmol/l, post phosphate 1.74 (0.85-2.7) mmol/l; pre PTH 50.8 (4.8-140) pmol/l post PTH 58.8 (2.3-140) pmol/l.

Conclusion: Nutritional vitamin D deficiency in patients requiring haemodialysis is common. In this study most patients of South Asian and Black ethnicity had severe deficiency. There was no impact of vitamin D supplementation on short term changes in bone chemistry. There is an epidemiological link between vitamin D deficiency and adverse outcomes in the general population and nutritional vitamin D supplementation is widely used. However, it is not known if vitamin D supplementation in patients receiving haemodialysis improves outcomes, randomised controlled trials are in process. And little is known on the differential impact of vitamin D deficiency between ethnic groups in patients on long-term haemodialysis.

Biology and big data to transform lives in rare kidney diseases

205: Natural history of idiopathic nephrotic syndrome: The UK National RaDaR Idiopathic Nephrotic Syndrome cohort

David Pitcher[1], Jonathan Barratt[2], Fiona Braddon[1], Wu Gong[3], Bruce Hendry[3], Alex Mercer[4], Kate Osmaston[1], Retha Steenkamp[1], A. Neil Turner[5], Daniel P. Gale[6], Moin A. Saleem[7]

[1]UK Kidney Association, Bristol, UK. [2]University of Leicester & Leicester General Hospital, Leicester, UK. [3]Travere Therapeutics, Inc., San Diego, USA. [4]JAMCO Pharma Consulting, Stockholm, Sweden. [5]University of Edinburgh, Centre for Inflammation, Edinburgh, UK. [6]Royal Free Hospital, London, UK. [7]University of Bristol & Bristol Royal Hospital for Children, Bristol, UK

Biography - David Pitcher

David Pitcher is a statistician working for the UK National Registry of Rare Kidney Diseases (RaDaR) and currently undertaking a PhD at University College London. At RaDaR, he works as part of a team to help validate, analyse, and disseminate data related to rare kidney diseases. RaDaR aims to improve patient and clinician understanding of these rare diseases, to improve patient care and outcomes, and to help with recruitment to clinical trials. RaDaR has been enrolling patients since 2010 and is now a rich source of longitudinal data, enabling investigation into risk factors associated with disease progression. Previously, David worked for the Getting It Right First Time (GIRFT) programme, investigating centre variation in renal medicine, focussing on acute kidney injury (AKI). In this role, he jointly developed the AKI mortality indicator, a UK-wide case-mix adjusted model for mortality rates following an episode of AKI. Prior to GIRFT, he worked for 3 years at the UK Renal Registry, contributing to data analysis and writing of the annual report, which contains analyses of care provided to patients with chronic kidney disease at adult and paediatric renal units in the UK.

Abstract

Introduction: Idiopathic nephrotic syndrome (INS) is an important class of proteinuric renal disease leading to kidney failure (KF). Here we describe the natural history of INS and congenital nephrotic syndrome (NS) using the UK National Registry of Rare Kidney Diseases Idiopathic Nephrotic Syndrome (RaDaR-INS) cohort, including retrospective and prospective data from 4610 patients with NS not attributable to glomerulonephritis or systemic disorders recruited from 107 adult and paediatric kidney units across the UK since 2010.

Methods: Participant eligibility for the RaDaR-INS cohort included ≥12 months observation from disease onset and no KF (chronic kidney disease stage 5 or on renal replacement therapy) at or prior to disease onset. Disease onset date was defined as first database occurrence of kidney biopsy, primary diagnosis, or protein-to-creatinine ratio (PCR) ≥1.5 g/g. Participants were subcategorised into those with a genetic diagnosis (INS-genetic), biopsy-proven focal segmental glomerulosclerosis (FSGS-biopsy), biopsy-proven minimal change disease (MCD-biopsy), and those with no genetic or biopsy-proven diagnosis (INS-no genetic or biopsy diagnosis). Participants with a biopsy-proven MCD diagnosis and a subsequent biopsy-proven FSGS diagnosis were included in both MCD-biopsy and FSGS-biopsy categories and formed a category of their own (MCD progressing to FSGS). Longitudinal proteinuria, assessed as time-averaged PCR (TA-PCR), and eGFR slope were calculated over the full duration of follow-up or until KF. Kidney survival was calculated from disease onset to event (KF or death) and censored at last follow-up.

Results: Of the 4066 patients meeting eligibility, median age at disease onset was 28 years (IQR, 6-51), with children (<18 years) representing 39% of the study population. Median proteinuria was 6.4 g/g (IQR, 3.1-10.8; n=923), while mean eGFR was 118 mL/min/1.73 m2 (SD, 49; n=240) and 69 mL/min/1.73 m2 (SD, 34; n=906) in children and adults, respectively. Median follow-up duration was 8.2 years (IQR, 4.3-13.1), with KF/death events

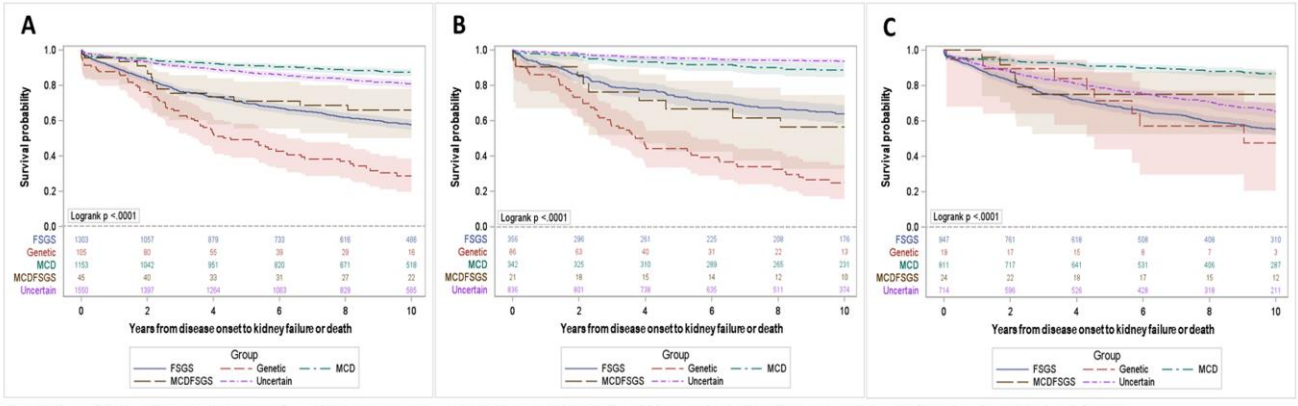
occurring in 30% of patients. Mean TA-PCR was greater in children than adults (5.0 g/g [SD, 13.9] vs 1.9 g/g [SD, 2.5]), as was annual rate of loss of eGFR (−7.4 mL/min/1.73 m2 [SD, 21.8] vs −3.1 mL/min/1.73 m2 [SD, 10.2]). Characteristics at disease onset and clinical outcomes in the INS cohort subcategories are presented in Figure 1. Kaplan-Meier survival plots for each subcategory, also further divided into children and adults, illustrate the poor survival probability in patients with FSGS, particularly INS-genetic patients who are predominantly diagnosed in childhood (Figure 2). While INS with no genetic or biopsy diagnosis presenting in childhood exhibits disease course and outcomes similar to MCD-biopsy patients, those diagnosed in adulthood have a more rapid disease course similar to FSGS-biopsy patients.

Discussion: The RaDaR-INS cohort represents a large study population with lengthy follow-up data. These analyses illustrate the difference in disease progression and survival rates in patients with INS with different causes or histological descriptions, highlighting in particular an unmet need for effective treatments for patients with NS and FSGS.

Figure 1: Characteristics at disease onset and clinical outcomes in patients with INS categorised by diagnosis.

Category		INS-genetic		FSGS-biopsy		MCD-biopsy		INS-no biopsy/genetic diagnosis		MCD progressing to FSGS	
		n	%	n	%	n	%	n	%	n	%
Age at disease onset		**105**	**100**	**1303**	**100**	**1153**	**100**	**1550**	**100**	**45**	**100**
	Median (Q1, Q3)	0.4 (0.1, 7.5)		35.5 (15.3, 53.4)		34.6 (13.3, 54.6)		13.6 (3.8, 45.9)		20.3 (4.9, 37.9)	
	Pediatric at disease onset	86	82	356	27	342	30	836	54	21	47
Gender		**105**	**100**	**1303**	**100**	**1153**	**100**	**1550**	**100**	**45**	**100**
	Female	53	50	552	42	519	45	639	41	19	42
Ethnicity		**105**	**100**	**1303**	**100**	**1153**	**100**	**1550**	**100**	**45**	**100**
	Asian	26	25	142	11	158	14	192	12	6	13
	Black	5	5	87	7	39	3	67	4	4	9
	Other	6	6	39	3	37	3	58	4	.	.
	White	59	56	920	71	812	70	888	57	14	74
	Not stated/missing	9	9	115	9	107	9	345	22	3	7
UPCR at disease onset		**26**	**25**	**336**	**26**	**323**	**28**	**254**	**16**	**16**	**36**
	Median, g/g (Q1, Q3)	28.5 (6.6, 37.8)		5.7 (2.9, 9.5)		6.6 (3.4, 10.3)		6.9 (3.1, 12.7)		5.0 (1.9, 10.5)	
Serum albumin at disease onset		**52**	**50**	**529**	**41**	**485**	**42**	**478**	**31**	**20**	**44**
	Median g/l (Q1, Q3)	15 (10, 27)		26 (19, 34)		21 (15, 29)		26 (17, 38)		21 (17, 29)	
eGFR at disease onset		**32**	**31**	**439**	**34**	**375**	**33**	**317**	**21**	**17**	**38**
	Mean, ml/min/1.73m2 (SD)	96 (62)		71 (41)		84 (38)		84 (45)		77 (32)	
Length of follow-up		**105**	**100**	**1303**	**100**	**1153**	**100**	**1550**	**100**	**45**	**100**
	Median, years (Q1, Q3)	4.1 (2.1, 8.6)		7.4 (2.7, 13.1)		9.1 (5.4, 14.6)		8.3 (5.0, 12.6)		9.7 (3.8, 16.7)	
Kidney failure or death event		**105**	**100**	**1303**	**100**	**1153**	**100**	**1550**	**100**	**45**	**100**
	Yes	78	74	637	49	168	15	343	22	18	40
Survival rate, estimate (95% CI)		**105**	**100**	**1303**	**100**	**1153**	**100**	**1550**	**100**	**45**	**100**
	1-year	0.88 (0.8, 0.93)		0.90 (0.88, 0.92)		0.96 (0.95, 0.97)		0.96 (0.95, 0.97)		0.96 (0.83, 0.99)	
	2.5-year	0.70 (0.61, 0.78)		0.80 (0.78, 0.82)		0.94 (0.92, 0.95)		0.92 (0.90, 0.93)		0.78 (0.63, 0.87)	
	5-year	0.49 (0.39, 0.58)		0.70 (0.67, 0.72)		0.91 (0.89, 0.93)		0.87 (0.86, 0.89)		0.71 (0.56, 0.82)	
	10-year	0.29 (0.20, 0.38)		0.58 (0.55, 0.61)		0.87 (0.85, 0.89)		0.81 (0.78, 0.83)		0.66 (0.50, 0.78)	
	15-year	0.16 (0.08, 0.26)		0.49 (0.45, 0.52)		0.84 (0.81, 0.87)		0.72 (0.69, 0.75)		0.59 (0.42, 0.73)	
eGFR slope, total		**65**	**62**	**835**	**64**	**849**	**74**	**851**	**55**	**40**	**89**
	Mean, ml/min/1.73m2 (SD)	-27.6 (34.7)		-6.5 (15.6)		-2.3 (9.9)		-3.3 (15.1)		-8.1 (14.0)	
	Median, ml/min/1.73m2 (Q1, Q3)	-17.1 (-36.9, -5.0)		-2.9 (-7.3, -0.4)		-0.9 (-3.4, 0.7)		-1.7 (-5.4, 0.5)		-2.4 (-12.1, -0.4)	
Time-average proteinuria, total		**55**	**52**	**809**	**62**	**823**	**71**	**864**	**56**	**39**	**87**
	Mean, g/g (SD)	20.3 (28.0)		3.6 (5.5)		2.2 (6.5)		2.8 (10.8)		6.3 (9.2)	
	Median, g/g (Q1, Q3)	7.8 (1.9, 29.1)		1.9 (0.7, 4.1)		0.8 (0.2, 2.0)		0.9 (0.3, 2.9)		2.1 (0.5, 8.3)	

Figure 2: Kaplan-Meier survival plots (incl. 95% CI) for patients with INS categorised by diagnosis. (A) all patients, (B) children, and (C) adults



Categories: FSGS = FSGS-biopsy; Genetic = INS-genetic; MCD = MCD-biopsy; MCDFSGS = MCD progressing to FSGS; Uncertain = INS-no genetic or biopsy diagnosis.

Clinical updates in glomerular disease

259: Efficacy and safety of ravulizumab in a phase 2 randomized controlled trial in IgA nephropathy

Jon Barratt[1], Jose L. Rocha[2], Dario Roccatello[3], Katherine Garlo[4], Kara Rice[4], Richard Lafayette[5]

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Biography - Jon Barratt

As the Mayer Professor of Renal Medicine, Professor Jonathan Barratt leads the Renal Research Group within the College of Life Sciences University of Leicester. His research is focussed on a bench to bedside approach to improving our understanding of the pathogenesis of IgA nephropathy a common global cause of kidney failure. Jonathan is the IgA nephropathy Rare Disease Group lead for the UK National Registry of Rare Kidney Diseases (RaDaR) and a member of the steering committee for the International IgA Nephropathy Network. He works closely with pharmaceutical companies interested in new treatments for IgA nephropathy and is Chief Investigator for a number of international randomised controlled Phase 2 and 3 clinical trials in IgA nephropathy and was a member of the FDA and American Society of Nephrology Kidney Health Initiative: Identifying Surrogate Endpoints for Clinical Trials in IgA Nephropathy Work group.

Abstract

Background: IgA nephropathy (IgAN) is the most prevalent primary glomerular disease, often progressing to end-stage kidney disease. Complement activation leads to glomerular damage by immune complex deposition and release of pro-inflammatory cytokines. Terminal complement inhibition specifically targets the pathophysiology of IgAN and may provide improved renal outcomes.

Methods: This primary analysis of a phase 2 RCT (NCT04564339) evaluated ravulizumab (IV; weight-based dosing Q8W) vs placebo in adults with primary IgAN. Eligible patients (18–75 years) with biopsy-confirmed IgAN, proteinuria ≥1g/d, on stable maximally tolerated RASi with stable blood pressure ≥3 months were enrolled. The primary endpoint was % change in proteinuria from baseline to week 26 based on 24-hour urine. Secondary endpoints included spot UPCR and change in baseline eGFR at week 26, safety, and PK/PD.

Results: 66 patients were randomized 2:1 to ravulizumab (n=43) or placebo (n=23). Mean age was 40.1 years, 46% were female, and 21% were Asian. At 26 weeks, proteinuria reduction was greater with ravulizumab vs placebo ; 40.3% vs 10.9% (treatment effect 33.1%, 90% CI, 14.7%, 47.5%; p=0.0012). In ravulizumab-treated patients, proteinuria reduction was rapid and sustained through week 26 (**Figure 1**) and eGFR remained stable. Ravulizumab was well-tolerated with a safety profile similar to that of placebo and no new safety concerns **(Table 1**).

Conclusions: This analysis supports clinically meaningful efficacy of ravulizumab based on rapid and sustained proteinuria reduction, providing proof-of-concept for a phase 3 trial of ravulizumab as a potential treatment for IgAN.

Presented at ASN Kidney Week 2023. More information can be found at www.asn-online.org: Barratt J, et al. Efficacy and Safety of Ravulizumab in a Phase 2 Randomized Controlled Trial in IgA Nephropathy [Abstract]. J Am Soc Nephrol 34, 2023: Kidney Week Abstract Supplement, pg B8.

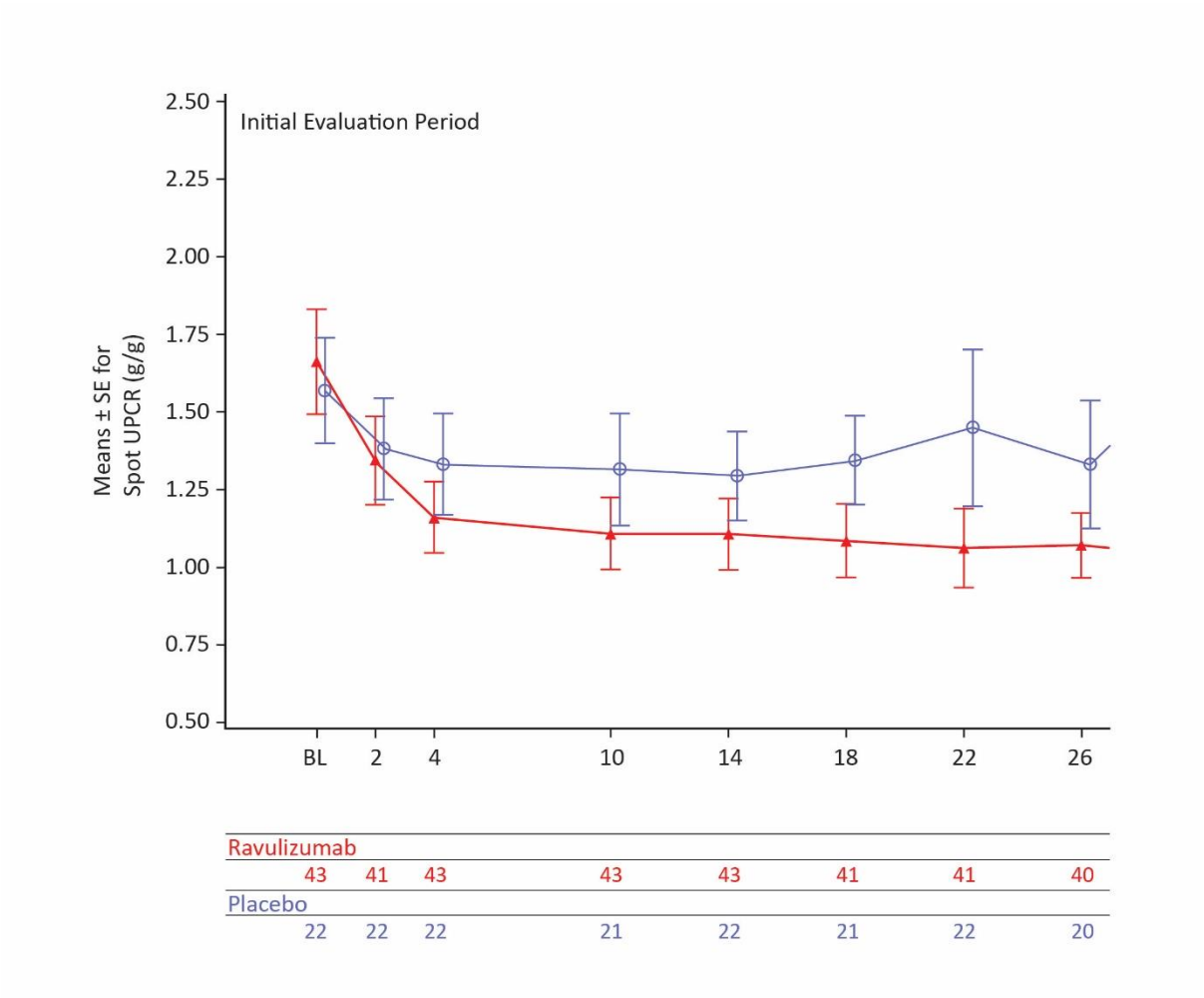

Figure 1: Proteinuria for patients treated with ravulizumab and patients treated with placebo up to 26 weeks

Table 1: Treatment-emergent adverse events up to 26 weeks

	Ravulizumab **N=43**	**Placebo** **N=23**
Any adverse event, n (%)	32 (74.4)	19 (82.6)
Investigator-assessed as related to study drug	9 (20.9)	6 (26.1)

Serious adverse event, n (%)	1 (2.3)*	0 (0.0)

*COVID occurred in one patient as an SAE that led to hospitalization and was investigator-assessed as unrelated to study drug and resolved during the study. AEs of special interest included meningococcal infections; there were no AEs of special interest. No AEs or SAEs leading to withdrawal from the study occurred and no deaths were reported.

Study Registration Number
NCT04564339

420: Long-term outcomes following rituximab therapy in primary membranous nephropathy

Dr Jessica Selwood, Dr A Nikolopoulou, Dr Tom Cairns, Dr Marie Condon, Professor Jeremy Levy, Dr Maria Prendecki, Dr Stephen McAdoo, Professor Megan Griffith

Imperial College Healthcare NHS Trust, London

Biography - Dr Jessica Selwood
I am a trainee in renal medicine and currently in my ST5 year at Hammersmith hospital, Imperial College Healthcare NHS Trust.

Abstract
Introduction: Short term outcomes for primary membranous nephropathy (MGN) treated with rituximab suggest remission rates of 60% [1], but little data exists on long term outcomes. This study examines the long-term outcomes for patients treated with rituximab beyond 1 year. Variables examined included remission, relapse, and long-term clinical outcomes, including renal function.

Methods: A single-centre, retrospective cohort study of 65 patients with primary MGN treated with rituximab with a follow-up period from 1 – 17 years. Patients treated with cyclophosphamide in addition to rituximab were excluded from the study.

Results: Demographics for the cohort are shown in figure 1.

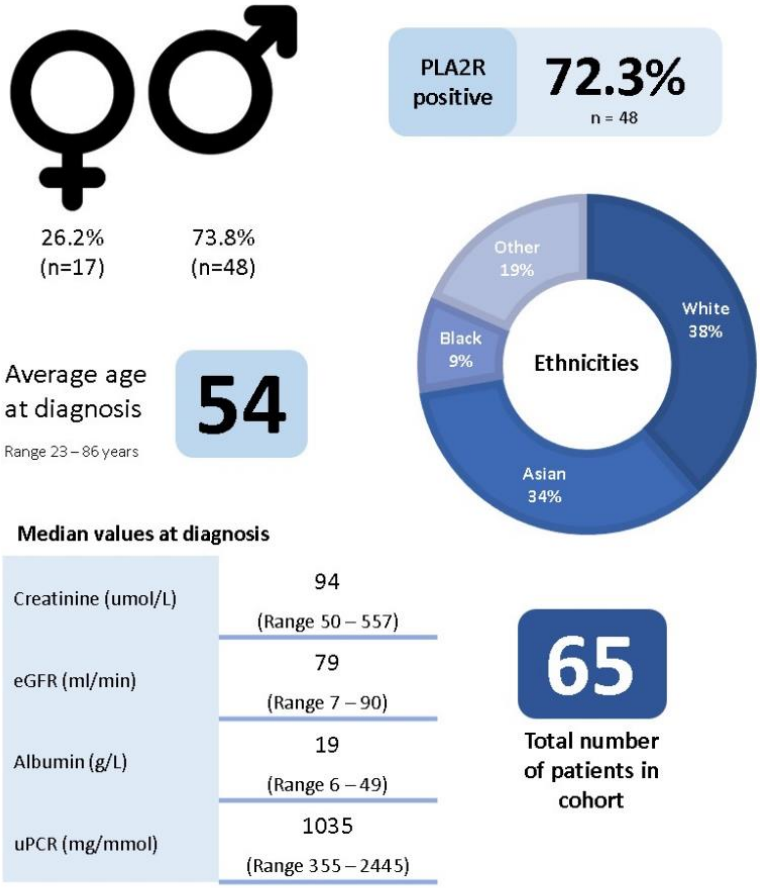

Figure 1: Demographics of cohort

31/65 patients (47.7%) received rituximab first line for nephrotic syndrome, and 34/65 patients (52.3%) received rituximab second or third line as treatment for relapse or after failure of other therapies. The standard dosing regimen for rituximab consisted of two 1 gram doses at least 2 weeks apart.

54/65 (83%) patients achieved partial remission at a median time of 6.9 months (range 14 days – 56.4 months), with 28/54 patients (51.9%) going on to achieve complete remission at a median time of 11.4 months (range 53 days – 91.5 months). 11/65 patients (17%) did not achieve remission.

18/54 patients (33.3%) relapsed having achieved remission, comprising 8/28 (28.6%) patients who were in complete remission and 10/26 (38.5%) patients in partial remission. Median time from remission to relapse was 714 days (range 27 days – 4165 days). 14/18 patients who relapsed (77.8%) were APLA2R positive at diagnosis, with 9/14 (64.3%) testing serologically positive at relapse. 5/14 were serologically APLA2R negative at relapse, however PLA2R staining on renal biopsy available for 2/5 patients showed evidence of positivity.

Follow-up periods and median eGFR at 1, 2, 5 and 10 years are shown in figure 2.

Length of follow up post-rituximab	Initial eGFR for each group (ml/min/1.73m^2)	Overall median eGFR (ml/min/1.73m^2)	Median eGFR (ml/min/1.73m^2) in rituximab as first line	Median eGFR (ml/min/1.73m^2) in rituximab as second or third line
Cohort at diagnosis (n=65)	-	79 (Range 7 – 90)	71 (Range 13 – 90)	84 (Range 7 – 90)
1 year	75 (Range 18 - 90) n=8	63 (Range 7 – 90)	63 (Range 7 – 90)	57 (Range 12 – 45)
2 years	79 (Range 13 - 90) n=33	51 (Range 8 – 90)	49 (Range 8 – 90)	52 (Range 16 – 90)
5 years	82 (Range 13 - 90) n=22	47 (Range 11 – 90)	39 (Range 11 – 90)	50 (Range 22 – 90)
10 years	30 (Range 7 - 88) n=5	36 (Range 16 – 90)	No patients at 10 years follow up	36 (Range 16 – 90)

Figure 2: Median eGFR over time

5/65 patients (7.7%) progressed to end stage kidney disease. 3/54 (5.6%) who achieved remission, subsequently progressed, compared to 2/11 (18.2%) who had not responded and remained nephrotic.

6/65 patients (9.2%) died >1 year after their first dose of rituximab, with causes of death displayed in figure 3.

	Cause of death	In remission at time of death
1.	Acute subdural haemorrhage	Yes
2.	Sepsis	Yes
3.	Hypoxic cardiac arrest	No
4.	Cause not documented	No
5.	Ruptured AAA	On dialysis, non-responder to rituximab
6.	Covid pneumonitis	No

Figure 3: Causes of death in MGN patients treated with rituximab

Discussion:

- Rituximab can be an effective treatment for MGN, however only 52% of the cohort achieved complete remission, and a significant number of patients go on to relapse.
- There is a suggestion that partial remission appears to be a risk factor for relapse compared with patients in complete remission.

- Non response is a risk factor for progression to ESKD, however there is a significant decline in GFR in some patients despite initially achieving remission.
- Work needs to be done on enhancing treatment to achieve higher rates of complete remission and prevention of progression of CKD. This may require increased frequency of dosing of rituximab or combination with alternative immunosuppressive agents.
- PLA2R on current serological assays is not always a sensitive predictor of relapse in some patients.

References

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Building beyond the Renal Services Transformation Programme - improving psychosocial support

514: DEVelopment of a Supportive Intervention to Support InfOrmal Caregivers of PeopLe with End-Stage Kidney Disease (ESKD) ReceiVing HaEmodialysis (EVOLVE Study)

Mr Michael Matthews[1], Professor Joanne Reid[2], Dr Clare McKeaveney[2], Professor Helen Noble[2]

[1]Ulster University, Londonderry. [2]Queen's University, Belfast

Biography - Mr Michael Matthews

Michael Matthews completed his BSc in Health Studies in Palliative Care (Queen's University, Belfast). He graduated with a Diploma in Specialist Renal Nursing (Queen's University, Belfast), completed a Post Graduate Certificate in Health and Social Care in Diabetes (Ulster University), and a Post Graduate Certificate in Professional Education (Queen's University). He graduated with an MSc in Nursing (Queen's University, Belfast). Most of Michael's experience has been within the sphere of renal nursing, having held several appointments including senior nurse, clinical research nurse and practice educator. He is currently pursuing a PhD Course of Study, having secured a scholarship from the Northern Ireland Kidney Research Fund. His research interests include the needs of informal caregivers of patients undergoing haemodialysis and the development of supportive interventions. Michael is currently employed as a lecturer in Adult Nursing in Ulster University, and continues to pursue further research in the area of the development of supportive interventions in informal caregiving.

Abstract

Introduction: Patients with end stage kidney disease (ESKD) receiving haemodialysis experience multiple symptoms, which can present physical and emotional challenges for both patients and their informal caregivers. Caregivers can experience anxiety, depression and social isolation, negatively impacting their overall wellbeing and resulting in caregiver burden. The needs of this group of caregivers has been largely neglected with little emphasis placed on supportive interventions that could assist them in their caregiving role.

Methods:

- Purposive sampling technique used to recruit informal caregivers and healthcare professionals across two health and social care trusts.
- Semi-structured interviews completed with 27 informal caregivers.
- Two focus groups completed with various members of healthcare professionals involved in the care of patients undergoing haemodialysis and their informal caregivers.
- Thematic analysis utilised to analyse data collected from semi-structured interviews and focus groups.
- Data management assisted by using the qualitative research software package NVivo, version 11 (QSR 2015).

Results:

Theme One - Impact of informal care provision

Caregiving had a negative impact on the emotional and psychological well-being of those caregivers participating in the study. They reported that they felt overwhelmed by the responsibilities of their care giving role, that they had little time for themselves, and that they experienced feelings of inadequacy and isolation. This first theme was comprised of three sub-themes - feelings of being overwhelmed, feelings of isolation and feelings of distress and anxiety.

Theme Two - The negative impact of a lack of education and knowledge about the complexities of renal care

The participants attested that taking on new practical roles and responsibilities proved challenging. Such responsibilities came from assisting with personal care needs, and managing food and fluid requirements, to the administration of medications and additional household tasks which caused caregivers to feel overwhelmed. These issues were explored across four core elements - lack of knowledge of medication management, difficulties in providing personal care needs, lack of knowledge of the renal diet and lack of knowledge of the complexities of renal care.

Theme Three - The benefits of spiritual beliefs, stress management and peer support in relieving the caregiver burden

Participants acknowledged the positive elements associated with their caring role. They highlighted the importance of adopting a positive attitude. Focusing more on the these positive aspects helped them deal with challenges and stressful situations to provide ongoing motivations to sustain them in their role. The factors associated with influencing a more positive caregiving experience were discussed through consideration of three core elements - spiritual beliefs, peer support, and stress management through mind body practices.

Discussion: This qualitative research study highlights the high level of burden, unmet practical needs and lack of psychological support given the complexities of experiences for caregivers of patients with ESKD undergoing haemodialysis. The expectations and demands of caregivers of this patient group continue to grow as the number of people with multiple co-morbidities accepted unto haemodialysis increases year on year. The findings from this study identify opportunities in terms of practical, psychological and social support. In doing so, healthcare providers could potentially develop and implement a suitable supportive intervention to facilitate a more positive caregiving experience through the provision of knowledge, skills and assistance, thereby enabling informal caregivers to carry out their caregiving role more effectively, and providing a more positive experience not only for informal caregivers but for their loved ones.

References

QSR (2015) NVivo 11 Software. Available at http://www.qsrinternational.com.

Study Registration Number

IRAS ID - 274023

Beyond the bloods: can we help people feel better?

366: Potentially modifiable factors influencing longitudinal health-related quality of life for people with chronic kidney disease in the NURTuRE-CKD cohort

Dr Thomas Phillips[1,2], Mr Scott Harris[1], Dr Olalekan Lee Aiyegbusi[3], Ms Melissa Benavente[4], Prof Paul Cockwell[5], Prof Philip A Kalra[6], Prof Paul Roderick[1], Prof David Wheeler[7], Prof Maarten Taal[4,8], Prof Simon Fraser[1]

[1]University of Southampton, Southampton. [2]University Hospital Southampton, Southampton. [3]University of Birmingham, Birmingham. [4]University of Nottingham, Nottingham. [5]Queen Elizabeth Hospital, Birmingham, Birmingham. [6]University of Manchester, Manchester. [7]University College London, London. [8]Department of Renal Medicine, Royal Derby Hospital, Nottingham

Biography - Dr Thomas Phillips

Tom Phillips is a renal registrar based in the Wessex Deanery currently working as a research fellow at the University of Southampton and University Hospital Southampton. He has an interest in health-related quality of life for people with chronic kidney disease and large data-based studies. He is attached to the Kidney Research UK funded project NURTuRE-CKD examining health-related quality of life outcomes with University of Southampton as sponsor. He is also a data science fellow in the Research and Development department of University Hospital Southampton.

Abstract

Introduction: Factors affecting poor health-related quality of life (HRQoL) for people with chronic kidney disease (CKD) have been previously described in literature, and worse HRQoL is associated with CKD progression and death. Little emphasis has been placed on which factors may be potentially modifiable, and longitudinal HRQoL outcome analyses in non-dialysis dependent CKD cohorts are few in number. Baseline analysis of the NURTuRE-CKD cohort identified several associations between these factors and HRQoL and these associations can now be examined with longitudinal data.

Methods: The NURTuRE-CKD cohort study recruited 2996 participants with non-dialysis dependent CKD between 2017-2019, collecting biochemical, anthropometric, sociodemographic, medical history and patient reported outcome measure (PROM) data. Face-to-face follow-up repeated these measures. Longitudinal worsening overall HRQoL was the main outcome of interest, represented by mapped EQ-5D-3L index value and visual analogue score (VAS). Multivariable linear mixed effects models were fitted in R using the lmer and lmerTest packages. Models for index value were fit separately for each independent variable of interest and collated, as well as fitting models with all variables of interest. Models were adjusted for available confounders, repeated measures and follow-up time. P-values were adjusted for multiple testing using false discovery rate correction.

Results: 2054/2996 (68.6%) had complete HRQoL data at follow-up, of whom most had CKD stage G3a-G4 (n=1597, 77.8%). 1817 (88.5%) were white and 1196 (58.2%) were male. Mean age was 63.7 (SD±14.5) years and the mean number of comorbidities was 3.7 (SD±2.2). Median (IQR) time between baseline and follow-up was 518 (410) days. At follow-up, mean mapped EQ-5D-3L index value was 0.72 (SD±0.3) and mean VAS score was 70.4/100 (SD±20.6). 1595 (77.7%) reported problems in at least one EQ-5D-5L dimension, with 255 (12.4%) developing issues since baseline. 1203 (58.6%) reported worse HRQoL index values at follow up and 910 (44.3%) reported worse VAS. The dimension with the highest number of newly reported issues at follow-up was 'usual activities' with 301 (14.7%). Multivariable linear mixed methods models showed independent associations with worse HRQoL (*Figures 1&2*) for those on ten or more medications (β-0.118, CI -0.137 to -0.100, p<0.001), current smokers (β-0.036, CI -0.067 to -0.006, p=0.0.012), obesity (β-0.059, CI -0.080 to-0.039, p<0.001), haemoglobin of

<100g/L (β-0.044, CI -0.073 to-0.016, p=0.014), hospital anxiety and depression scale scores of 8 or above for anxiety (β-0.146, CI -0.161 to-0.130, p<0.001) and depression (β-0.202, CI-0.219 to -0.186, p<0.001), worse health literacy (β-0.099,CI -0.136 to -0.063, p<0.001), and pain (β -0.148, CI -0.161 to -0.135, p=<0.001), weakness (β-0.106, CI -0.120 to -0.092, p<0.001) and shortness of breath symptoms (β -0.074, CI -0.087 to -0.060, p<0.001).

Discussion: Potentially modifiable factors influencing longitudinal worsening of HRQoL for people with CKD include polypharmacy, smoking, obesity, anaemia, depression and anxiety, limited health literacy, pain, weakness and shortness of breath symptoms. This highlights the need for high quality randomised controlled trials to test interventions addressing these factors with reported HRQoL outcomes. Further work in this cohort is required, examining a third timepoint for HRQoL and linked clinical outcome data.

	Multivariable linear mixed effects models fit for each factor vs. longitudinal mapped EQ-5D-3L index§			**Multivariable linear mixed effects with all variables in model vs. longitudinal mapped EQ-5D-3L index§**			**Multivariable linear mixed effects with all variables in model vs. longitudinal EQ-5D-5L visual analogue scale§**		
Risk factors	*Estimates*	*95% CI*	*p*	*Estimates*	*95% CI*	*p*	*Estimates*	*CI*	*p*
Renin-angiotensin inhibitor	0.013	-0.006 to 0.032	0.191	0.012	-0.004 to 0.029	0.273	0.775	-0.736 to 2.287	0.57
Prednisolone	-0.021	-0.046 to 0.005	0.157	0.022	-0.001 to 0.044	0.134	-0.309	-2.362 to 1.745	0.885
On 10 or more different medications	-0.118	-0.137 to -0.100	**<0.001**	-0.064	-0.083 to -0.046	**<0.001**	-5.071	-6.736 to -3.405	**<0.001**
Smoking status [Current smoker]	-0.036	-0.067 to -0.006	**0.012**	-0.005	-0.033 to 0.024	0.764	-0.544	-3.175 to 2.088	0.885
Body mass index (BMI, kg/m2) [Underweight]	0.012	-0.058 to 0.081	0.796	0.013	-0.057 to 0.082	0.764	0.087	-6.312 to 6.486	0.979
BMI [Overweight]	-0.014	-0.033 to 0.005	0.253	0.008	-0.011 to 0.027	0.556	0.478	-1.274 to 2.230	0.867
BMI [Obese]	-0.059	-0.080 to -0.039	**<0.001**	-0.029	-0.048 to -0.009	**0.015**	-2.393	-4.201 to -0.586	**0.036**
Haemoglobin <100 g/L	-0.044	-0.073 to -0.016	**0.014**	-0.025	-0.057 to 0.008	0.271	-5.668	-8.688 to -2.648	**0.001**
Nephrotic range proteinuria (>220 mg/mmol)	0.007	-0.017 to 0.031	0.464	0.024	0.000 to 0.048	0.124	0.387	-1.836 to 2.610	0.885
Serum bicarbonate <20 mmol/L	-0.018	-0.043 to 0.007	0.297	-0.011	-0.038 to 0.015	0.556	0.44	-2.024 to 2.905	0.885
Parathyroid hormone (PTH) [Raised (7.2-15.7pmol/L)]	-0.011	-0.031 to 0.009	0.512	0.008	-0.012 to 0.027	0.556	2.311	0.511 to 4.110	**0.038**
PTH [High (15.8-56.0 pmol/L)]	-0.013	-0.037 to 0.011	0.538	0.004	-0.019 to 0.027	0.764	2.261	0.392 to 4.131	0.052
PTH [Very high (>56.0pmol/L)]	-0.027	-0.058 to 0.004	0.336	0.004	-0.025 to 0.033	0.793	-0.309	-2.320 to 1.701	0.885
Serum phosphate >1.5 mmol/L	-0.022	-0.048 to 0.004	0.339	0.014	-0.016 to 0.043	0.533	-0.601	-3.342 to 2.139	0.885
Hospital anxiety and depression scale anxiety score >7	-0.146	-0.161 to -0.130	**<0.001**	-0.086	-0.104 to -0.068	**<0.001**	-5.131	-6.783 to -3.479	**<0.001**
Hospital anxiety and depression scale depression score >7	-0.202	-0.219 to -0.186	**<0.001**	-0.149	-0.168 to -0.129	**<0.001**	-12.636	-14.474 to -10.798	**<0.001**
Single-item literacy screener score >2	-0.099	-0.136 to -0.063	**<0.001**	-0.023	-0.063 to 0.017	0.413	-0.34	-4.036 to 3.356	0.931
Integrated palliative care outcome scale (IPOS) pain symptoms present	-0.148	-0.161 to -0.135	**<0.001**	-0.123	-0.138 to -0.108	**<0.001**	-4.898	-6.301 to -3.495	**<0.001**
IPOS weakness or lack of energy symptom present	-0.106	-0.120 to -0.092	**<0.001**	-0.047	-0.064 to -0.031	**<0.001**	-6.853	-8.389 to -5.318	**<0.001**
IPOS shortness of breath symptom present	-0.074	-0.087 to -0.060	**<0.001**	-0.017	-0.032 to -0.002	0.084	-3.055	-4.472 to -1.637	**<0.001**
				R^2 of model	0.697		R^2 of model	0.479	

p-values in **bold** denote statistical significance of <0.05 - all p-values adjusted using false rate discovery (FDR) correction

BMI reference category = Normal weight (BMI 18.5 to 24.9 kg/m2), smoking status reference category= non-smoker, PTH reference category = PTH low to normal (0 to 7.1 pmol/L), IPOS symptoms binary

§ model includes fixed effects of time*, age*, sex*, ethnicity, education attainment*, index of multiple deprivation*, comorbidity number*, eGFR at baseline and follow-up* and cognitive impairment on 6-item cognitive impairment test*, random effects of recruitment region and within subject (* denotes significant association with HRQoL outcome in combined model above)

Figure 1. Multivariable linear mixed effects regression models examining associations between potentially modifiable factors and overall HRQoL represented by repeated EQ-5D index values and VAS. Models are adjusted for known confounders in dataset and time

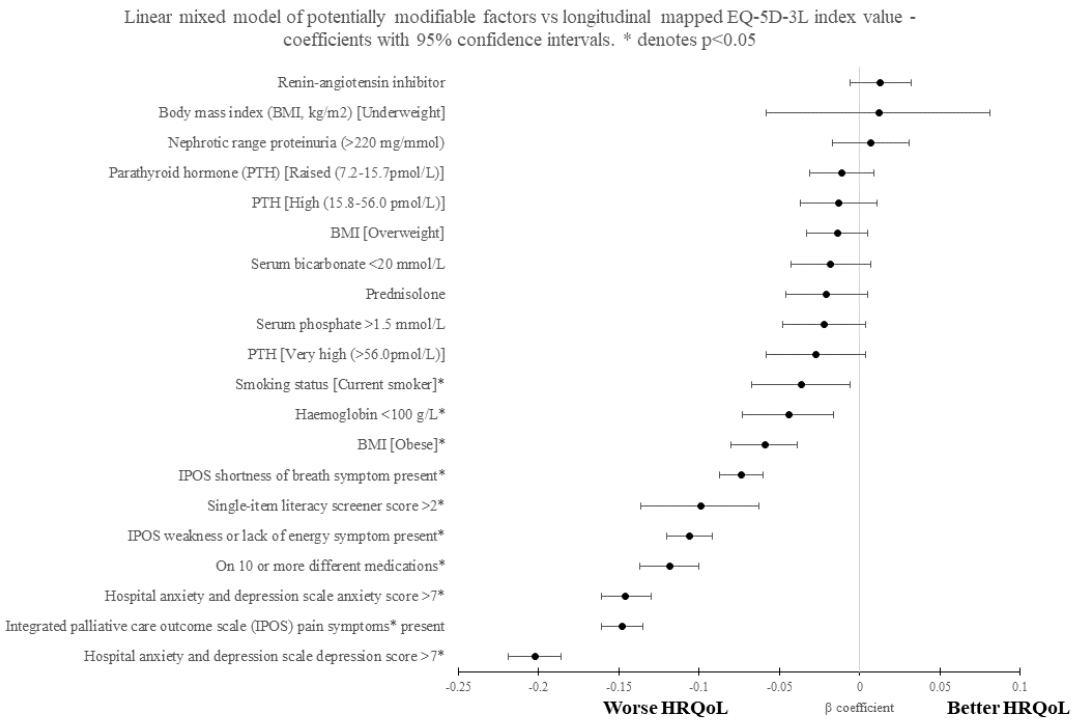

Figure 2. Forest plot of linear mixed models with mapped EQ-5D-3L index value as dependent variable – each independent variable was adjusted for known confounders in its own model and collated in this plot

107: The interplay between sleep quality and symptom experience in CKD

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Biography - Ms Ella C Ford

Ella Ford is a Research Assistant at the University of Leicester within the Kidney Research Lifestyles Team in collaboration with University Hospitals Leicester. She studied BSc Psychology at Nottingham Trent University, and MSc Health Psychology at the University of Nottingham.

Abstract

Introduction: Poor sleep quality is often reported by people living with chronic kidney disease (CKD), presenting challenges such as increased fatigue and decreased quality of life. Understanding how CKD symptoms relate to poor sleep could help identify people who experience, or may be at risk of experiencing, poor sleep quality. Determining the relationship between common CKD symptoms and sleep quality could provide insight into potential opportunities to intervene and influence this relationship, as well as possible strategies for improved symptom and sleep management. Here, we report the results of a multicentre survey study on sleep quality and symptoms experienced by people with CKD across the disease trajectory, compared to their significant others (SOs) without CKD.

Methods: People living with CKD and their SOs, from nine hospital sites in England, were invited to complete an online survey between February and October 2023. The survey included the Pittsburgh Sleep Quality Index (PSQI) and the Kidney Symptom Questionnaire (KSQ). Higher scores on the PSQI are indicative of worse sleep quality; participants with scores of ≥6 are categorised as having poor sleep. The KSQ consists of 13 items, regarding the frequency of CKD symptoms experienced, measured on a Likert scale from 0 ('never') to 4 ('everyday'). Participants were classified as experiencing the symptom if they reported experiencing it at least '1-2 times a week'. Two KSQ items relating to sleep were excluded from the analyses. Data were analysed using linear regression, Chi-squared, and Mann-Whitney U tests, as appropriate.

Results: Out of the 367 respondents to the survey, 338 completed the PSQI: 291 CKD (mean age 60.14(±14.2) years; 46% female; 173 (59%) non-dialysis; 66 (23%) kidney transplant; 34 (12%) haemodialysis; 18 (6%) peritoneal dialysis), and 47 SOs (mean age 62.66(±11.0) years; 68% female). The proportion of poor sleepers was significantly higher for people with CKD (60%) than SOs (45%) (P=0.046). The median number of symptoms experienced by people with CKD (5 symptoms) was significantly higher than for SOs (2 symptoms) (P=0.001). The top four most commonly reported symptoms for people with CKD were 'feeling cold' (62%), 'the need to urinate more often' (59%), 'pain in bones/joints' (55%) and 'loss of muscle strength/power' (55%). Table 1 displays the association of each symptom (experienced or not experienced) with sleep quality for people with CKD. For all symptoms, those who experienced the given symptom had worse predicted sleep quality than those who did not.

Table 1: Linear regression analyses results for PSQI score in people living with CKD

Symptom Experienced	B	CI	β	p
Itching	1.57**	(0.69, 2.44)	0.20**	0.001
Loss of appetite	3.07**	(2.14, 3.99)	0.36**	0.001
Pain in bones/joints	2.26**	(1.36, 3.15)	0.29**	0.001
Poor concentration/alertness	2.86**	(1.99, 3.72)	0.37**	0.001
Loss of libido	1.64**	(0.70, 2.57)	0.21**	0.001
Loss of muscle strength/power	2.63**	(1.77, 3.49)	0.34**	0.001
Shortness of breath	1.49*	(0.58, 2.39)	0.19*	0.001
Cramp/muscle stiffness	1.76**	(0.86, 2.64)	0.22**	0.001
Restless legs	2.41**	(1.52, 3.29)	0.30**	0.001
Feeling cold	1.85**	(0.95, 2.75)	0.23**	0.001
Need to urinate more often	1.46*	(0.55, 2.36)	0.18*	0.002

B and β represent the difference in PSQI score of participants who experience the symptom compared to participants who do not
All analyses were adjusted for age and gender
Significance (*) $p < 0.050$ (**) $p < 0.001$

Discussion: We found relationships between experiencing common CKD-related symptoms and poorer sleep quality in people with CKD. Our results illustrate that optimal CKD management should include an assessment of both symptom burden and sleep quality. Poor sleep quality may cause or worsen some symptoms such as 'poor concentration'. Conversely, musculoskeletal symptoms may impact sleep quality, rendering standard approaches to sleep hygiene insufficient. It is pivotal for multi-disciplinary teams and sleep services to work together to provide people with CKD the relevant information, or referrals, they may require to optimise sleep and symptom management and improve their quality of life.

Study Registration Number
ISRCTN84422148

Transforming kidney transplant services: delivering pre-emptive transplantation

359: Kidney Transplantation in Older People (KTOP): quality of life longitudinal mixed methods findings

Dr Lina Johansson[1], Dr Amarpreet Thind[1], Dr Shone Surendran[2], Miss Nicola Evans[3], Dr Annabel Rule[1], Prof Nicola Thomas[4], Dr Michelle Willicombe[5], Prof Edwina Brown[1]

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Biography - Dr Lina Johansson

Lina is a Clinical Academic Renal Dietitian working at Imperial College Healthcare NHS Trust

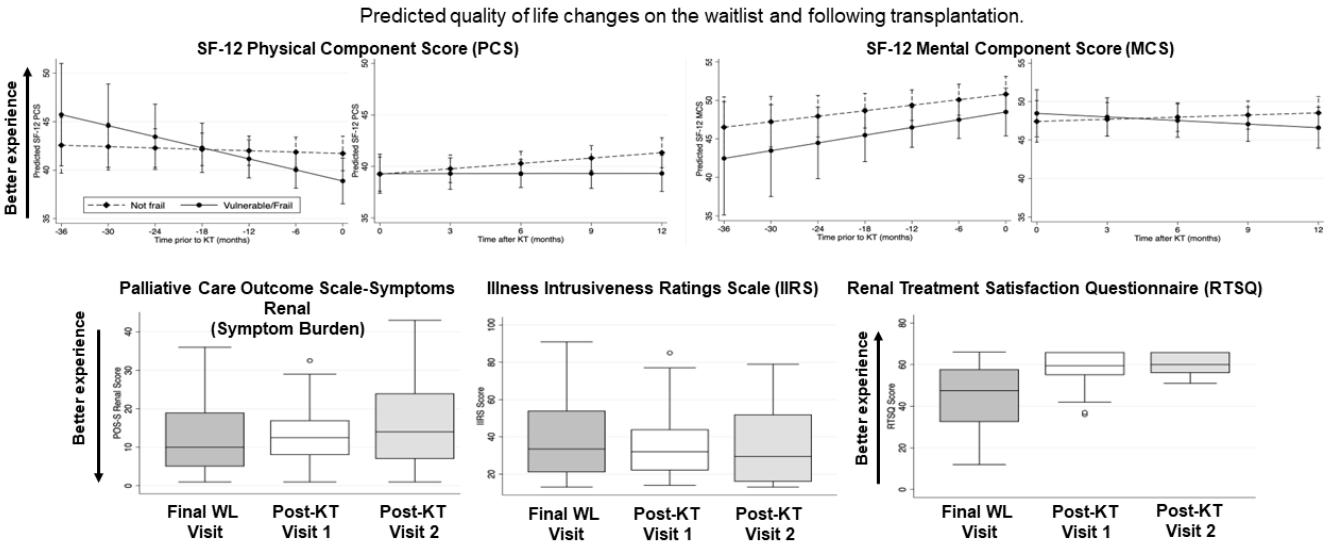
Abstract

Introduction: The Kidney Transplantation in Older People (KTOP) study is a longitudinal, single-centre study with a mixed methods design seeking to determine the impact of frailty on outcomes including the understanding of the lived experience of transplantation in older people.

Methods: The study included participants aged ≥60 year who were active on the KT waitlist (WL). Questionnaires assessing frailty, cognition, quality of life (QoL) and patient experiences were completed on the WL (12, 24 months) and following KT (3, 12 months) in the quantitative study. Questionnaires included SF-12 Physical Component Score (PCS) and Mental Component Score (MCS), Palliative care Outcome Scale for Renal (symptoms), Renal Treatment Satisfaction Questionnaire and Illness Intrusion Ratings Scale. Participants identified as frail or vulnerable to frailty (Edmonton Frailty Scale score ≥6) were invited to take part in semi-structured interviews at baseline (waitlist), and at 3 and 12 months post-KT for the qualitative study. Descriptive and mixed-effect analysis was used for the quantitative data, and the qualitative interviews were analysed by thematic analysis within a longitudinal context. The qualitative data is utilized to present an in-depth explanatory account and richer understanding of the experiences of older, frailer people undergoing KT.

Results: 210 participants were recruited to the quantitative study, 68 of whom were frail/vulnerable and 120 were transplanted. Twenty-one participants were recruited for the qualitative study from this frail/vulnerable sample, 10 of whom were transplanted.

The survey data from dialysis (wait-list) and post-transplantation QoL are illustrated below.



The themes and sub-themes encompassing quality of life are listed in the table.

Time pointc	Themes: *subthemes*		
Waitlist on dialysis	**Burden of dialysis** • *Physical impact* • *Emotional impact* • *Compromised quality of life*	**Living with frailty** • *Physical impact* • *Emotional impact*	**Personal & socio-cultural resources** • *Coping mindset* • *Faith as a source of resilience* • *Family involvement*
3 months post-transplant	**Burden of transplant procedure** • *Physical impact* • *Emotional impact* • *Returning to normal living* • *Misleading expectations*	**Living with frailty** • *Physical impact* • *Emotional impact* • *Lack of mobility*	
12 months post-transplant	**Living with a transplant** • *Physical impact* • *Emotional/stress impact* • *Compromised quality of life* • *Returning to normal living*	**Living with frailty** • *Physical impact* • *Emotional impact* • *Limited mobility*	

Discussion: The quantitative data presents some positive factors that impact life post-KT, as vulnerable/frail older people saw stabilisation in physical health (SF-12 PCS) and improvement in Renal Treatment Satisfaction. This contrasts with a concurrent dip in mental health (SF-12 MCS), an increase in symptoms and an initial worsening of illness intrusion post-KT. The findings that emerge suggest a complex and contrasting picture of the impact of KT on QoL in older vulnerable/frail people.

The qualitative data offers an explanatory account drawing on the diversity of patient lived experiences which expresses a more nuanced account of QoL findings. Transplantation is revealed to be a physically and emotionally demanding procedure without consistent improvements in frailty. Much valued time free from dialysis is balanced against feelings of loss of the dialysis network and the unexpected demands of life post-KT. Family/social networks, spiritual beliefs and positive mindset, where present, help older, frailer people cope with the sometimes turbulent transplant journey.

Conclusion: Older, frailer people have a stabilization in their physical health but a more nuanced change in QoL following transplantation, that differs person to person. Services, when involved in decision-making regarding waitlisting for KT, would benefit from considering the individual's personal and socio-cultural resources as these have significant influences on QoL post-transplantation.

200: Increasing pre-emptive transplant and listing rates in the South West region through a collaborative Quality Improvement (KQIP) Programme

Dr Richard Powell, Michaela Dicks, Allie Wilson, Ranjit Klare

South West Transplant Workstream, South West Region

Biography - Dr Richard Powell
Richard is a consultant nephrologist based in Plymouth and is the clinical lead for the SW Transplant QI workstream.

Abstract
Introduction: Pre-emptive kidney transplantation has been shown to improve patient outcomes and there has been a national focus to encourage this through the Transplant First initiative. NHS Blood and Transplant data showed that pre-emptive listing and transplant rates in the South West (SW) region had fallen over recent years, and this was identified as a key area for improvement through the SW Renal Operational Delivery Network and Kidney Quality Improvement Partnership (KQIP) programme starting in April 2022.

Our SMART aim was for at least 35% of living kidney donor (LKD) transplants to be performed pre-emptively by 2025, which would bring our region in line with the national average. Secondary aims were to increase pre-emptive listing to at least 60% and perform 30 additional LKD transplants annually across the region. Our plan was to achieve this through a multicomponent approach, with individual units designing QI projects to improve specific aspects of local transplant pathways and services.

Methods: Quality Improvement (QI) training was provided by the KQIP team, following an established 10-step plan including the use of process mapping, driver diagrams, PDSA cycles and measurement strategy. Individual support was also provided by the KQIP and SW Renal Network teams. Virtual regional meetings also facilitated constructive discussion between units. Data analysis was coordinated by the SW Renal Network, who developed a regional dashboard to share real-time data throughout the region, including key metrics such as eGFR at referral and pre-emptive referral, listing and transplant rates.

Results: We achieved our regional aim of at least 35% of all living donor kidney transplants being performed pre-emptively by the end of 2023, which was earlier than expected. There has also been a significant increase in the number of living donor transplants being carried out across the region, with the same number performed in the first 6 months of the 2023-24 financial year (28) as the whole of the previous 12 months.

We have also seen an increase in the number of patients being referred to transplant centres pre-emptively (over 60% regionally). The pre-emptive listing data will be available for the past 12 months in time for presentation at UKKW 2024.

Discussion: This collaborative QI Programme has led to an improvement in pre-emptive listing and transplant rates through a combination of local projects working together to achieve a common regional goal. There remain ongoing challenges and barriers to increasing LKD transplant rates further within our region, particularly relating to workforce resilience and theatre allocation, which are being addressed at a service level.

We found that the regional dashboard provided extremely valuable real-time benchmarking data, and this will be continued through the SW Renal Network. Regional meetings also enabled colleagues to share ideas and build relationships, as well as foster a culture of innovation and collaboration. One example of this was the

agreement of shared recipient referral criteria between the two transplanting centres in our region, which helped to reduce delays in transplant assessment. We hope that this approach will continue to develop further and that learning can be shared nationally.

Figure 1: Driver diagram

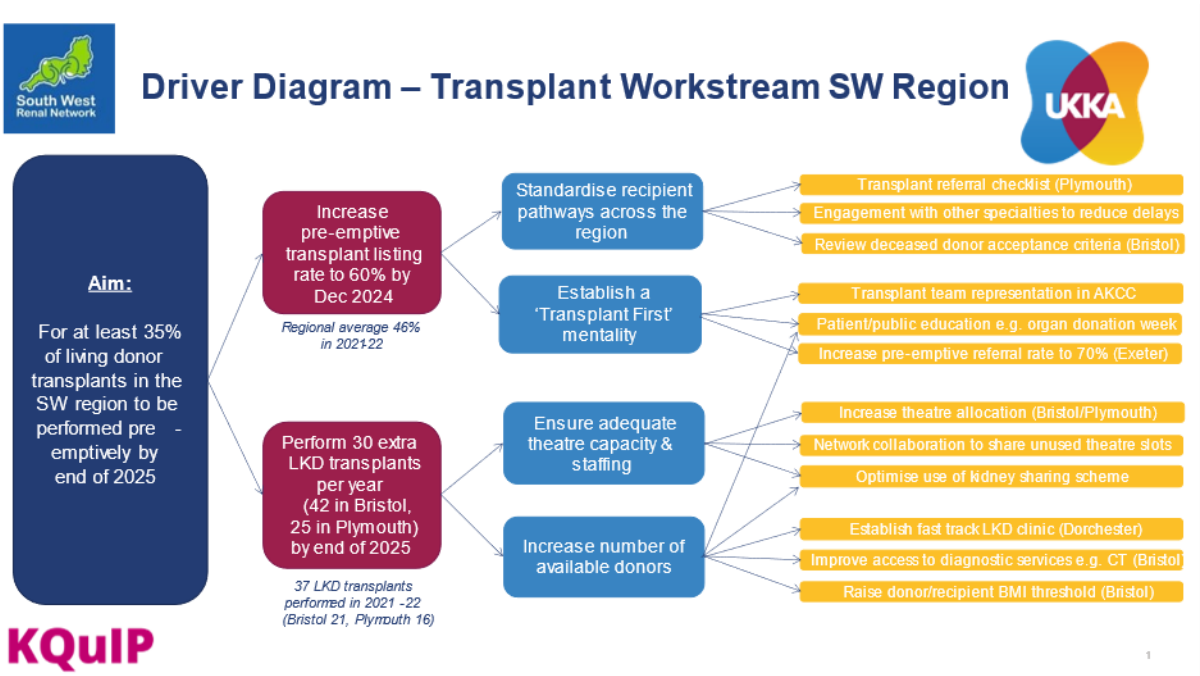


Figure 2: Pre-emptive referral data

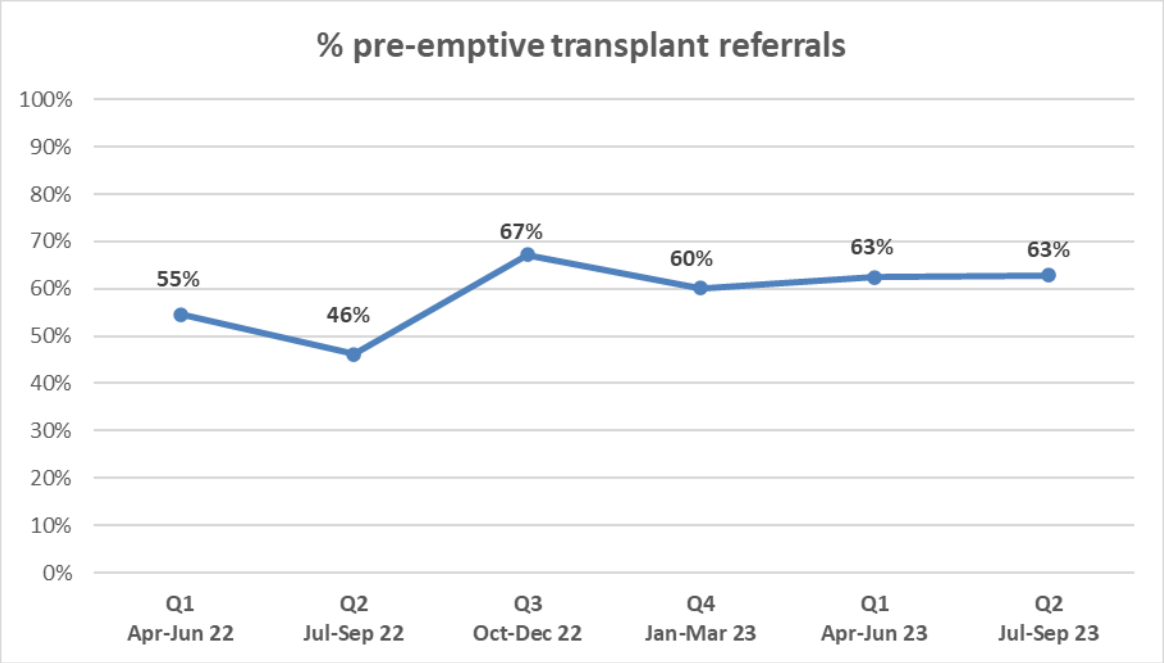
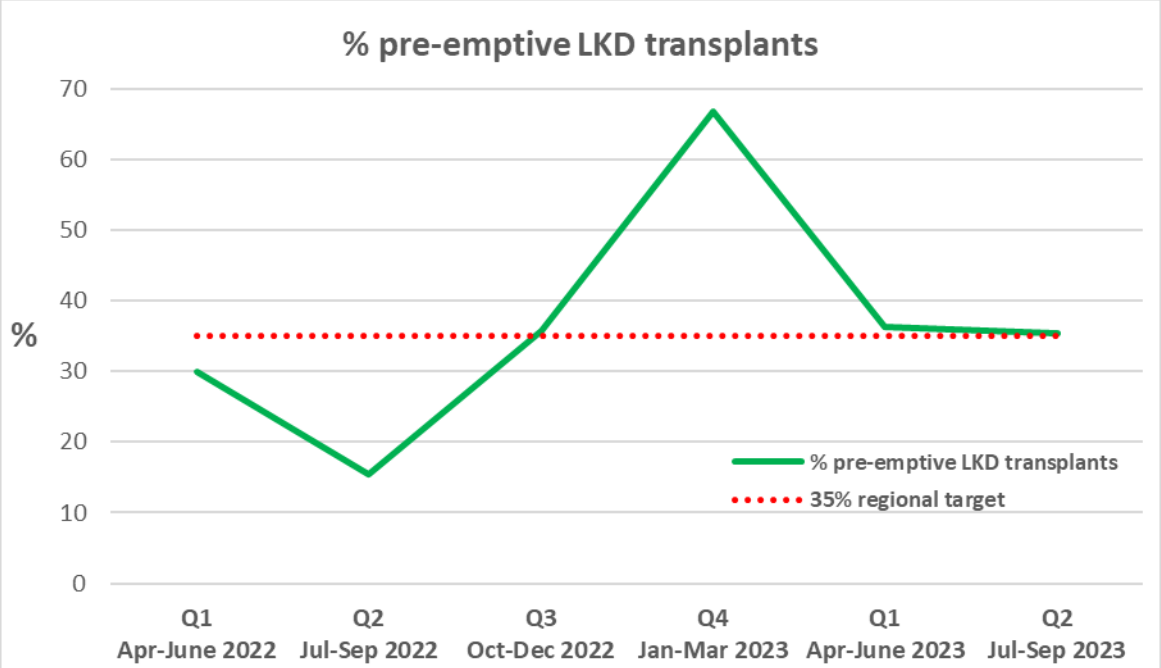


Figure 3: Pre-emptive LKD transplant data



How can I start to develop an integrated CKD service in my area?

407: Kidney Failure Risk Equation, providing routine community laboratory reporting – the Lancashire experience.

Dr Beng So[1], Dr Shonagh Haslam[1], Dr Martin Myers[1], Dr Sumantra Mukerji[2], Dr Nimalendran Muttucumaru[3], Ms Julie Southern[4], Ms Amanda Balshaw-Greer[5], Mr Michael Aitchison[1], Mr Timothy Howcroft[1], Dr Mohamed Elsayed[1]

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Biography - Dr Beng So

Dr. So is Clinical Director for Renal Medicine at Lancashire Teaching Hospitals NHS Foundation Trust. He is also the North West Kidney Network CKD workstream lead for Lancs & South Cumbria, Associate Clinical Information Offcer and past Topol Digital Fellow. He has a passion for CKD epidemiology and early detection on which he gained a Doctor of Medicine in 2018.

Abstract

Introduction: The 2021 CKD NICE guidance (NG203) recommended the adoption of the UK calibrated four-variable Kidney Failure Risk Equation (KFRE). To identify patients with 5-year risk of progressive renal failure greater than 5% who are likely to benefit from specialist Nephrology assessment in Secondary Care. Embedding the KFRE into clinical laboratory information management systems (LIMS) has been challenging. Here we described a successful trial, implementing routine KFRE reporting to primary care practices in the North West of England.

Methods: Following the publication of NG203, we examined the feasibility of implementing KFRE within our region. A local workgroup consisting of General Practitioners, Specialist Nurses, Clinical Biochemist, Clinical Scientist and Nephrologist convened to consider and prototype various solutions.

Due to U&E laboratory reporting being cluttered, we were not keen to add text to it to avoid alert fatigue. In addition, U&E are often indiscriminately requested, and unless complex rules placed, would produce multiple differing KFRE estimates for a single urine albumin creatinine ratio (uACR). Adding a KFRE 'order set' to our Order Communications System resulted in duplicate requests for estimated Glomerular Filtration Rate (eGFR) and uACR which would have to be received simultaneously to trigger a report.

We therefore concluded that the uACR should be the trigger for automated KFRE reporting. When a uACR sample is received in the laboratory, the algorithm running in Swisslab™ looks back for the most recent eGFR and if it is <60 ml/min/1.73m², triggers the KFRE calculation and generates a report. KFRE was not reported if no eGFR available in the previous 12 months or uACR was undetectable. Three General Practice locations were selected to pilot. The trial included 7 months of running in the background for fine tuning before real time reporting direct to GP electronic patient record systems.

Results: During background reporting, 1817 uACRs were received. Of which 80.7% did not generate a KFRE as there were no eGFR < 60 ml/min/1.73m² within 1 year. 1.3% had uACRs below the assay threshold for detection. Leaving 18% of uACRs where a KFRE calculation was triggered. Of these 1.5% generated a risk estimate of > 5% in 5 years with 16.5% < 5%.

Since 6th November 2023, KFRE reports have been reported live for these same three practices. Some additional changes to the wording of reports were made based on feedback. Final evaluation, adjustment and education are in progress prior to widespread roll out.

Discussion: Utilising the uACR as the trigger for proving KFRE estimates, in our LIMS was the more elegant solution for delivering routine reporting to primary care. It is more advantageous over KFRE order sets and eGFR triggers. The uACR is primarily requested for kidney failure risk assessment and we believe primary care clinicians requesting uACR are therefore primed to assimilate the KFRE estimate and act appropriately. Whilst multiple uACR requests could also lead to multiple KFRE results, this scenario was much less likely, as uACR requesting rates are much lower. We also feel using uACR to trigger KFRE will also encourage increased uACR testing.

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524: Involving people affected by Chronic Kidney Disease (CKD) in early pathway transformation

Miss Sadie Myhill[1], Mr Kabelo Murray[2], Miss Livi Bickford-Smith[3]

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Biography - Miss Sadie Myhill

Sadie joined Imperial College Health Partners as Senior Engagement and Involvement Lead in March 2021, with a focus on developing and delivering strategic patient, public and staff engagement programmes. She has extensive experience of designing qualitative insight activities. Prior to joining ICHP, Sadie held roles at Cancer Research UK and the British Heart Foundation; collaborating with internal and external partners to embed involvement into their plans.

Abstract

Introduction: 15% of the UK population over 35 have CKD, but only 2 in 10 people with the disease are currently diagnosed. A lack of early-stage symptoms, and low patient awareness, results in large numbers presenting with late-stage complications.

AstraZeneca, Imperial College Health Partners, North West London Applied Research Collaborative, Imperial College Health Care Nephrology Department, and the London Kidney Network collaborated to improve the diagnosis and early management of CKD in North West London.

Through a cohesive patient and clinical engagement strategy we were able to develop meaningful and sustainable relationships, using an iterative co-design process to develop solutions that considered the needs and experiences of patients, clinicians and the health system.

A significant issue in public health is breakdowns in communication and a conjoined lack of trust; clinicians do not have enough trust in the patient experience and patients do not trust that clinicians will listen to them. Bringing these stakeholders together, and facilitating collaboration between them as key partners in improving care outcomes and experiences, was core to our approach.

Methods: Our engagement had four key phases:

1. **Discovery:** the process started with extensive interviews with five patients at risk of CKD, seven patients at various stages of CKD and eleven clinicians from primary and secondary care. These diverse perspectives gave rich insights into the existing pathway and helped identify areas of greatest challenge and opportunity.
2. **Codesign:** through three ideation workshops participants co-designed pathway improvements. These sessions brought together fifteen patients and clinicians, enabling everyone to hear and learn from different perspectives whilst shaping and refining their ideas.
3. **Testing and evaluation:** the recommendations were taken forward and simple versions of the solutions were tested in GP practices to get early evidence of their impact. Ongoing clinician and patient feedback are an integral part of this phase.
4. **Strategic representation:** from the outset the project had an expert with lived experience of CKD on the project steering group to offer ongoing input into decision-making processes.

Results: Through the codesign process several patient-facing resources were developed:

- A patient education pack available on the NWL ICS website and as hand-outs in primary care practices.
- A simple invitation process and protocol to enable patients to be invited from primary care to a 'Know Your Kidneys' virtual education session.
- Signposting to wider support options, including peer support and Kidney Care UK resources.
- Reworded messaging sent to patients when their annual testing is due.

Another success of the project was the interactions facilitated between the stakeholder groups. Patients felt safe sharing their personal experiences and clinicians expressed increased empathy towards understanding these experiences.

"I felt genuinely heard and felt that my experiences and views as a patient were validated by hearing the experiences and thoughts of others from different cultures, backgrounds, ages and hospitals…it felt like a genuine partnership, and that I was an equally valued member."- **Patient participant**

Discussion: A goal of participatory approaches is creating sustainable relationships and lessening the 'distance' between clinicians and patients. Across our engagement activities we developed a genuinely collaborative approach to building this shared understanding.

We recommend exploring the impact engagement and codesign can have in improving how clinicians and patients interact with CKD and pathways to treatment.

Lessons from international collaborations and clinical experience abroad

510: Early Detection and Management of Community Acquired Acute Kidney Injury using point of care creatinine in a primary health care centre in Nigeria.

Dr Dimitrios Poulikakos[1,2], Dr Vivean Laurent-Ordu[3], Mrs Dorathy Emem Model[3], Mrs Oluo Doris Chiemela[3], Dr Siyeofori Dede[4], Prof Kinikawo Green[4], Dr Adaeze Oreh[5], Prof Pedro Emem-Chioma[6], Dr David Lewis[1], Prof Ibi Erekosima[1,2]

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Biography - Dr Dimitrios Poulikakos

Dr. Dimitrios Poulikakos is the Clinical Director for Renal Services in Northern Care Alliance NHS Foundation Trust and was appointed as a Consultant Nephrologist in August 2015. He graduated from the University of Athens, completed his MD (Res) at St George's University of London in cardiac risk stratification in Chronic Kidney Disease. He currently holds a senior honorary senior lecturer post at the University of Manchester.

Abstract

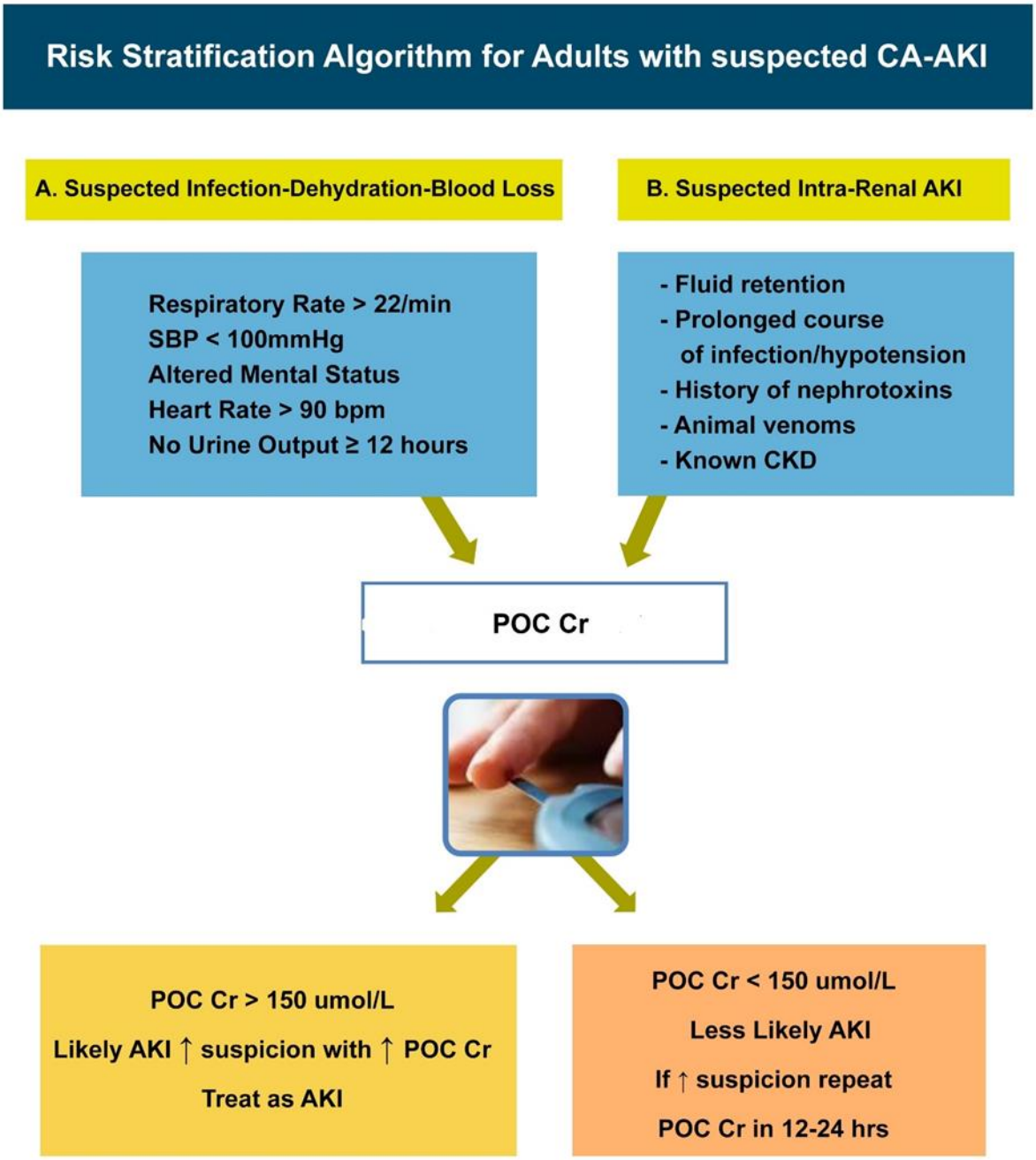
Introduction: Community acquired Acute kidney injury (AKI) and leads to poor outcomes in low and middle-income countries due to delayed diagnosis however its epidemiology is poorly studied due to lack of biochemical diagnosis. Supported by the International Society of Nephrology, we evaluated the accuracy of point of care creatinine (POC Cr) technology using capillary samples[1] and its use implementing a clinical algorithm to select patients at risk of AKI for POC Cr testing in the Hospital Emergency Department in Port Harcourt in Nigeria. In this phase of the project POC Cr was used in a large primary care health centre for early detection and management of community acquired AKI.

Methods: The study is conducted in Ozuoba Model Comprehensive Primary Health Care Centre. The centre has 4148 patient attendances per month (20.3% medical, 18.8% obstetrics and 60.8% paediatrics) with 11.1% considered acute requiring short admission at the centre usually for intravenous fluids. Historically, decision making is based largely on clinical judgement and renal function tests when requested from external laboratories are reported in > 48 hours. During this project POC Cr was offered on high-risk patients based on the clinical algorithm from the previous stage (Figure 1) and patients with detected AKI were offered short admission for intravenous fluids and antibiotics.

Results: To date 54 patients have been screened with POC Cr. Median age is 25.5 years , minimum 2 months, maximum 85 years, interquartile range (48-10), 62% are females, 57% presented with malaria diagnosis and 9% with gastroenteritis. Mean (standard deviation) of POC Cr was 105 (54) umol/L. There were 5 cases (9%) of AKI (Cr > 150 umol) detected in patients aged 5 months, 13 months, 7 years, 19 years and 31 years. All were treated with short admission and intravenous fluids and were discharged after clinical improvement. Knowledge of the presence of AKI altered management in all patients prompting short admission.

Conclusion: Community acquired AKI is common in young patients with malaria and early biochemical diagnosis can improve outcomes. The study continues to recruit and aims to investigate the characteristics of community acquired AKI in Africa and to contribute to the design of optimal and sustainable pathway for early detection and management of AKI.

Figure 1



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248: Promoting physical activity in peritoneal dialysis: understanding provisions and best practice from around Europe

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Biography - Dr Courtney Lightfoot

Courtney is a mixed methods researcher working with the Leicester Kidney Lifestyle Team at the University of Leicester. Her role involves the development, evaluation, and implementation of complex (digital) health interventions to support people with kidney disease to better (self-)manage their health and lifestyle behaviours. Her work focuses on helping people with kidney disease to live well by empowering them to take a more active role in their health and healthcare.

Abstract

Introduction: Many people receiving peritoneal dialysis (PD) have low levels of physical activity and impaired physical function which limits independence and increases the risk of adverse health events. The provision of physical activity and exercise for people with PD differs around the world. Learning and understanding how healthcare professionals from different countries support people to be active is important and may facilitate best practices. This study aimed to understand exercise perceptions and practices of PD clinicians across Europe.

Methods: We conducted an international survey exploring exercise-related perceptions and practices of PD clinicians across Europe. Individuals providing clinical care to people receiving PD were recruited via professional kidney networks including the UK Kidney Association, European Dialysis Transplant Nursing Association, and European Renal Care Association. Participants completed a 13-item web-based survey about current practices and perceptions on advising exercise to people receiving PD. The survey was developed through expert consensus with 20 international PD clinicians, exercise professionals, and people receiving PD. Questions exploring practices had “yes”, “no”, and “don’t know” responses, whilst questions exploring perceptions used 5-point Likert scale from “strongly agree” to “strongly disagree”. Data were analysed using frequency analysis and logistic regression to determine the proportion of participants agreeing with the statements provided and recommendations associated with confidence in prescribing exercise.

Results: 265 participants completed the survey (116 nephrologists, 132 nurses, 10 exercise professionals, 5 dietitians, and 2 others) from 35 different countries (**Figure 1**). Most participants had >5 years of experience (n=202, 76%), with only 9% (n=25) having <2 years’ experience. 67% (n=176) of participants worked in programs with ≤50 patients, 33% (n=89) with >50 patients.

Nurses (n=203, 77%) and nephrologists (n=194, 74%) were reported as the main providers of exercise advice. Most participants reported providing recommendations for lifting (n=139, 53%), swimming/water sports (n=169, 62%), activity following catheter insertion (n=184, 69%), and fall prevention (n=160, 60%). Almost all participants (n=262, 90%) agreed that it is important for people receiving PD to be physically active, with 86% (n=229)

promoting physical activity participation. Less than a third (n=82, 31%) perceived their patients to be physically active, with 82% (n=216) of participants reporting that their patients could perform more exercise. Most participants agreed that their patients would benefit from a structured exercise program (n=241, 91%), and an exercise professional (n=214, 81%); however, only 12% (n=31) had access to an exercise professional. 60% (n=160) of respondents were confident in prescribing exercise; those confident in prescribing exercise were almost twice as likely to provide recommendations on lifting (OR:1.7, P=0.043) and fall prevention (OR:1.9, P=0.016).

Discussion: The majority of healthcare professionals across Europe recognise the importance of physical activity for people receiving PD and promote its participation. Whilst it is perceived that structured exercise programs would be beneficial for people receiving PD, very few patients have access to an exercise professional. Incorporating exercise professionals and structured exercise plans into standard practices of care, alongside developing the confidence of other healthcare professionals in prescribing exercise, could increase physical function, maintain independence, and improve life participation.

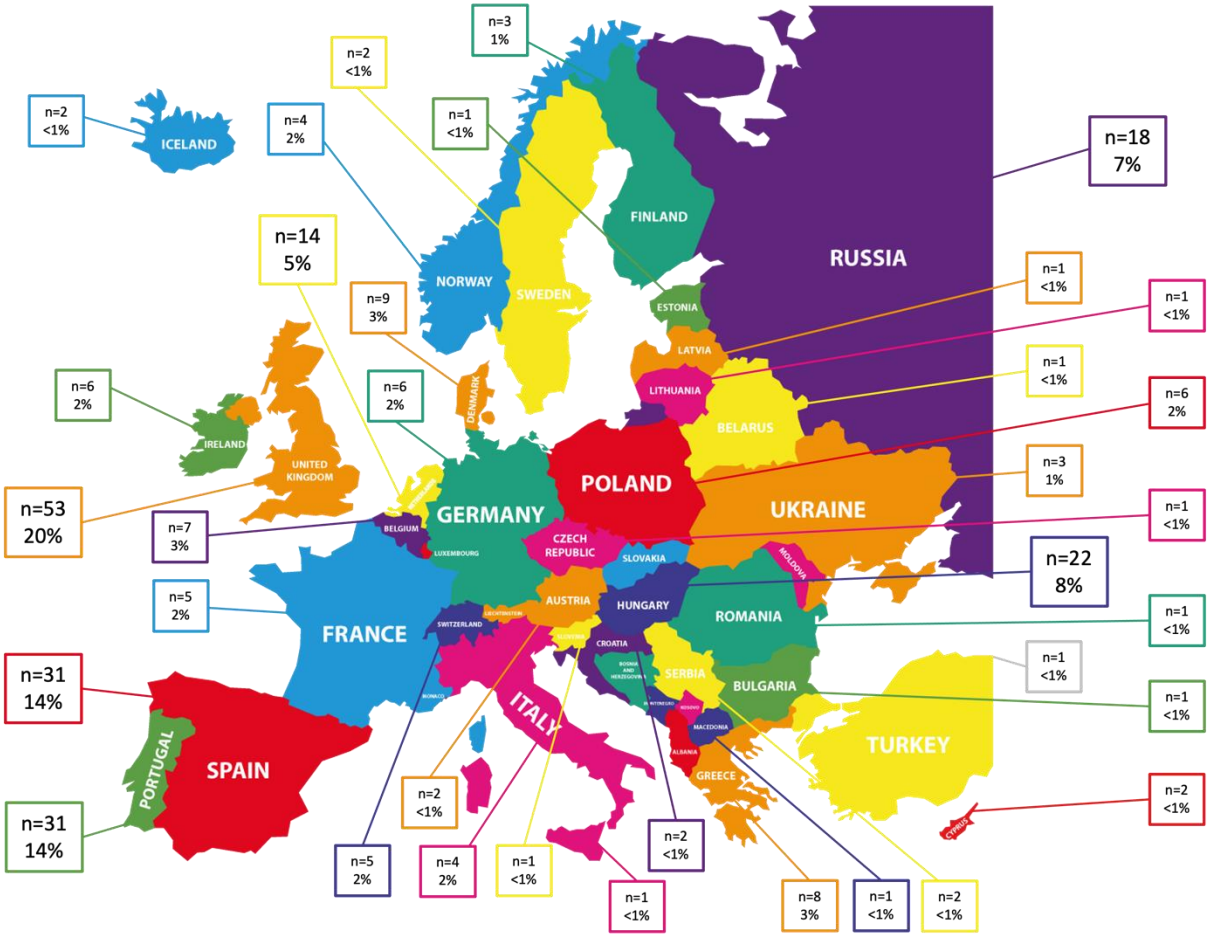

Figure 1. Number and proportion of participants by country

Kidney health inequalities: community engagement and research - moving the dial further along

576: Health Inequalities in kiDney Disease: mEeting the urgent need to identify Early disease in high-risk commuNities (HIDDEN-CKD): Community Participants Perspectives.

MS Rachel Musomba[1,2], Ms Roseline Agyekum[3], Dr Kathryn Griffiths[3], Ms Neerja Jain[4], Dr Shone Surendran[5], Mr Denis Onyango[1], Dr Kate Bramham[3]

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Biography - Ms Rachel Musomba

Rachel Z Musomba has a Public Health background with Quality Management training from McGill University, Montreal Canada. She is currently pursuing a PHD in Public Health and Epidemiology at the London School of Hygiene and Tropical Medicine. Rachel is also a renowned researcher with over 15 years of clinical and programming experience. She has made significant research contributions in the areas of anti-retroviral therapy and long term conditions with peer-reviewed publication. She is currently working as a Project Manager at the Africa Advocacy Foundation, UK. Her areas of specialisation include ; Community Public Health engagement, kidney health, HIV and Long-Term Conditions.

Abstract

Background: We have undertaken a community kidney health screening using urine albumin creatinine ratio (uACR) testing among 1000 African and Caribbean communities in England churches, mosques and public spaces. Several factors, including accessibility and acceptability are critical for successful implementation of this approach. However, there is limited qualitative appraisal of community engagement practices. Our study aimed to explore participant perspectives on testing to inform future optimisation of this approach.

Methods: 30 Participants provided informed consent (IRAS 302730) for one-to-one interviews and were purposively selected across outcomes and backgrounds. Interviews were audio recorded, transcribed verbatim and analysed thematically supported by NVivo 20 software.

Results: Overall, median age of study participants was 56 years (interquartile range 22–71 years), 53% (N = 16) were female and 60% (N=18) had abnormal kidney test results. Four main themes were generated: (I) community testing as an easy process compared to routine GP services, (2) appropriate approaches for community mobilisation and participant education (3) Peer educator strategies used for community engagement including peer-educators being friendly, welcoming, responding to participants' questions, giving advice and explaining results using simple bilingual languages. However, there were negative perceptions, (4) which showed challenges faced during events; participants linked this to a lack of clarity in the information provided about the results.

Conclusions: Attendance of community kidney testing was overwhelmingly positive. However high levels of communication, convenience and awareness were necessary to ensure participant's engagement with the kidney testing. Participants' perspectives need to be understood and community leaders or stakeholders should be involved to maximise participation and engagement.

Table 1. Showing participants' perspectives about community kidney testing using urine albumin creatinine ratio (uACR)

Participants perspectives	Themes	Codes	Quotations
Positive	Community testing as an easy process compared to routine GP services	▪ Easy access to services ▪ Readily available services ▪ Early diagnosis ▪ Faster services ▪ Good time with providers than GP ▪ Convenient	**Record 06 Female,** "You know, they have time to talk to me, compared to the GP, when you go to the GP, they only have 5-10 minutes with you, but the champions, they were able to explain to me the kidney, all the procedures, how to test and teaching me, informing me about the kidney problems which we were facing. So that's why I agreed to do the test because they have more time compared to the GP. So they were more empowering, you know, and not rushing." **Record 03 Male,** "For me, it was easier because I was tested there and then and I get the results and then I walk away. By making an appointment and you take the test and they say, "Come back the next day," or, "We shall call you to give you the results." **Record Male 2a**, "it was okay. That was my first time of being under such an exposition and was an eye-opener. I really was a happy that I was part of it. And it was also my first time of going through such… that kind of test because I've never done it before. And I was also happy that I was able to do it". **Record 04 Female**, "Yes, this one was more easy to do that, more accessible, because they come into the community, whereby sometimes getting an appointment at the GP nowadays really takes long. So when it comes to the community, it is accessible, it is near you" **Record 05 Female**, "When I'm going to book an appointment with a GP, it's very, very stressing, like it takes time, the GP is not always available, so this is very easy because the people are coming to you, and you don't have to go to the GP, go through documents, go through all that stuff, for just an appointment. The GP situation is very, like… this is easier, I will go for this rather than go to the GP." **Record Female 2a**, "Oh, definitely community is faster, quicker and is very convenient." **Record 04 Male**, "I mean, the type of work we do here is… people don't have enough time. So I would encourage you guys to move so much in the communities, some people don't know exactly what you are talking about like I was." **Record 04 Male**, "What I'm saying is some people work Monday to Saturday, so some people just don't have time to check on their health conditions and all of that. So I would think that your people could be engaging within communities and churches." **Record 06 Female,** "For me, my opinion is most of us African community, we are busy, most of us we work, we have got to work, so we don't really have time to put ourselves to do those things, you know, like maybe go to the hospitals often. Because we come here as migrants, so what we just do is work, work, work, work." **Record 03 Male,** "Because these tests were very local to our community, and they were free, so they were just available."

	Appropriate approaches for community mobilisation and participant education	▪ Inclusive for African ▪ Relevant information on the leaflets ▪ Church announcements ▪ Convincing health talk ▪ Bilingual services ▪ Integrated services with church days ▪ Community support	**Record Female 2c**, "I feel like we don't have enough knowledge." **Record Male 2a**, "Yeah. I knew that they were… a disease that has to do with the kidney, yeah. But it was my first time of listening to teaching about it like that." **Record 07 Female**, "we actually believe that we are so strong that even if you feel that your body is somehow not well, that we think we can manage without seeking for help, we can manage without being tested….people, they are reluctant to go to their GPs for testing, and even if they go, they don't say it out because they think they are very strong and they can actually manage it". **Record 01 Female,** "Oh, because it was… like I say, on this day, it was in our church hall, so the team was doing the kidney test, and then there was another station for blood pressure and then there was another one for eye tests. So I said to myself, "Why not? I'm already here." It was a community day, I thought to myself, "Why not?" you know? So that's how I ended up getting involved". **Record 07 Female,** "I just heard it through the announcement in the church that the people were going to come and do some testing and they were so interested, so I participated." **Record 03 Male**, "Yes, because when you came and talked to the whole congregation, it crept into my mind and I said, "Ah, why don't I take it? After all, it's free, and it's available for me, I don't need to go and make an appointment anywhere," so it was easier for me to take."
	Peer educator strategies used for community engagement.	▪ Clearly gave results ▪ Support from community members ▪ Good peer-educator team	**Record Male 2d**, "More available, more flexible ." **Record Male 2f**, "I just want to say thank you, the testing was nice, and I've also learned from you, because I didn't know much about kidneys, and I didn't have much of it, but now I know." **Record 07 Female**, "I just want to thank them for the good work that they have done, and also they've actually encouraged me to go to my GP, which is a great achievement, I just want to say thank you for the community champions because of their professionalism and also the delivery of the good work that they have done, especially in my life. Thank you." **Record 06 Male,** "I think being in a community, it was good because you get support from the community and the different people you know, rather than in a hospital or with people who don't know about you, you feel like a machine. Yeah, so in the community, you feel you are being catered for or looked after."
Negative	Challenges faced during events.	▪ Crowding ▪ Darkness/nighttime ▪ No trust in the results ▪ Communication ▪ Distracted attention ▪ Insufficient privacy	**Record 03 Female**, "It's just at the time when we did it, it was dark, we were outside, and it started getting dark and we had to move inside, and we were in a tent, but yeah, it was fine, and it wasn't one person, there were a lot of people who needed it done". **Record 03 Female**, "To be honest, I can't even remember what the result was, because I tend to just block out anything negative that is too negative. And at the time, we were just rushing and so, no, I didn't do anything about it".

			Record Female 02a,"Maybe communication. Yes, communication, sometimes the way we communicate, the results, we are tired, so a bit of improving on communication." Record 03 Female, "It's nice to know, but I'm not sure how accurate it is. **Record Male 02d**, "I wasn't comfortable with the female nurses that were on the ground, so I decided to take it home and do it." "I think your team is more females, and if you would have more males on board, you can break that gender gap that sometimes some people are not comfortable here, so I think that could be all part of it." **Record Male 2d**," I wanted to have that privacy, having the test from home". **Record 01 Male**, "Ah, why am I doing this?" and, "There are lots of people around," … very private, ….ahhh…someone seeing you bringing back the container …So, yeah, it was scary at the beginning.

Study Registration Number
IRAS 302730

608: Identifying language barriers and their effect on patient outcomes in low clearance clinic: results from a single-centre retrospective review

Dr Abdulrahman Al-Mohammad[1], Dr Amy Needleman[1], Ms Yeun Gyeong Woo[2], Dr George Riding[1], Dr Sarah Fox[1], Dr Sandra Johnson[1], Dr Colley Crawford[1]

[1]Royal Free London NHS Foundation Trust, London. [2]University College London, London

Biography - Dr Abdulrahman Al-Mohammad

Abdulrahman Al-Mohammad is a junior clinical fellow in renal medical education at the Royal Free Hospital, London. He completed his foundation training in the North Central and East London Foundation School and has interests in nephrology, research and health inequalities.

Abstract

Introduction: Language barriers can negatively impact healthcare outcomes.[1] Patients with advanced progressive CKD are managed at our tertiary renal centre through a dedicated 'low clearance' clinic, where they receive education regarding CKD treatment and complications, renal replacement therapy (RRT) options, and maximum conservative management (MCM). We hypothesised that language barriers in this setting could result in miscommunication, with a consequent negative impact on treatment and patient outcomes.

Methods: We conducted a retrospective analysis of all patients from our low clearance clinic who started RRT or died before RRT commencement in 2022. We predicted that patients with language barriers were more likely to present to low clearance clinic with worse renal function, start their RRT early, die earlier, have an unplanned start to their dialysis, have haemodialysis over peritoneal dialysis or transplant, and use a catheter for their haemodialysis.

Data collection consisted of:

1. All patients: age, eGFR (2021 CKD-EPI Creatinine Equation) and Clinical Frailty Score (CFS) at first low clearance clinic contact;
2. RRT starters: age, eGFR and transplant waiting list status at start of RRT; mode of RRT, type of vascular access and whether RRT was initiated in an unplanned fashion; death within 3 months and 12 months of initiating RRT;
3. Deceased before RRT: age at death; decision made for MCM; death within 3 months and 12 months of first low clearance clinic contact.

Results: A total of 389 patients were identified, of whom 203 initiated RRT and 186 died without commencing RRT. 53 patients (13.6%) required an interpreter as they did not speak English. A total of 18 languages were recorded. We did not identify any patients with limited English proficiency through review of their electronic health record.

No significant differences on univariate analysis were found in any metric except for younger age at first low clearance clinic contact (66.6 years vs 68.7 years; $p < 0.01$). Surprisingly, patients requiring an interpreter had a higher percentage of AVFs (55% vs 39%) and planned starts to RRT (76% v 69%) than patients without a language barrier. Further results are shown in Table 1. We are currently analysing hospitalisations and presentation to A&E as other outcomes of interest.

Discussion: Overall, the outcomes for patients using interpreters compared very favourably to those without a language barrier. These findings were consistent with results from a previous study at our centre which did not find a significant association between interpreter use and treatment pathway (supportive care, RRT or death before treatment decision).[2] That patients using interpreters do not appear to be significantly disadvantaged in the outcomes studied is surprising and may relate to both our methodology and to patient factors.

Clinical experience suggests that a significant percentage of our patients have mild language barriers, i.e. not sufficient to warrant interpreter use. In our review, clinicians only mentioned language barriers when an interpreter was required. As such, patients with more mild forms of language barrier were likely misallocated to the no language barrier group.

Whereas clinicians often spend more time explaining topics to patients requiring an interpreter, they may overestimate the understanding of patients fluent in English with whom they might spend less time. In addition, patients who require an interpreter may be less likely to dissent against clinician advice if they do not feel able to effectively communicate their concerns.

Table 1 Baseline data and key patient outcomes by language barrier

	All patients		*P*-value
	No language barrier	Interpreter required	
Age at presentation, years (mean ± SD)	68.7 ± 15.3	66.6 ± 17.3	0.005
eGFR at presentation, mL/min/1.73 m²	19.8 ± 7.5	19.1 ± 6.6	0.493
Clinical Frailty Score at presentation (mean ± SD)	3.7 ± 1.7	3.9 ± 1.6	0.580
Sex			0.012
Female (%)	123 (37%)	29 (55%)	
Male (%)	213 (63%)	24 (45%)	
Ethnicity			
White (%)	146 (43%)	11 (21%)	
BME (%)	127 (38%)	31 (58%)	
Not stated (%)	63 (19%)	11 (21%)	
Duration in low clearance clinic, months (mean ± SD)	34.1 ± 33.1	29.7 ± 24.2	0.544
	Initiated RRT		*P*-value
	No language barrier	Interpreter required	
Age, years (mean ± SD)			
at presentation	59.9 ± 14.4	56.7 ± 15.9	0.274
at start of RRT	62.2 ± 14.9	59.2 ± 16.3	0.313
Sex			0.048
Female (%)	57 (33%)	15 (52%)	
Male (%)	117 (67%)	14 (48%)	
eGFR, mL/min/1.73 m²			
at presentation	18.5 ± 7.2	18.2 ± 7.3	0.862
at start of RRT	7.9 ± 3.4	7.0 ± 2.4	0.188
Clinical Frailty Score at presentation (mean ± SD)	3.1 ± 1.4	3.2 ± 1.4	0.728
Duration in low clearance clinic, months (mean ± SD)	28.0 ± 29.1	30.1 ± 27.4	0.695

Transplant waiting list status at time of RRT			0.564
Active/transplanted (%)	45 (26%)	13 (45%)	
Workup ongoing (%)	34 (19%)	6 (21%)	
Excluded (%)	95 (55%)	10 (34%)	
Mode of RRT			0.811
Haemodialysis (%)	107 (62%)	18 (62%)	
Peritoneal dialysis (%)	49 (28%)	7 (24%)	
Renal transplant (%)	18 (10%)	4 (14%)	
Vascular access			0.194
AV fistula (%)	42 (39%)	10 (56%)	
HD catheter or AVG* (%)	65 (61%)	8 (44%)	
Fashion of RRT start			0.453
Planned (%)	120 (69%)	22 (76%)	
Unplanned (%)	54 (31%)	7 (24%)	
RRT start within			0.850
3 months of first LCC	15 (9%)	3 (10%)	
3-12 months of first LCC	46 (26%)	8 (28%)	
Death within			0.262
3 months of first LCC	8 (5%)	0 (0%)	
3-12 months of first LCC	12 (7%)	2 (7%)	

	Deceased		*P*-value
	No language barrier	Interpreter required	
Age, years (mean ± SD)			
at presentation	78.2 ± 9.6	78.6 ± 9.7	0.843
at death	81.6 ± 9.6	59.2 ± 9.5	0.838
eGFR at presentation, mL/min/1.73 m²	21.3 ± 7.6	20.1 ± 5.6	0.470
Clinical Frailty Score at presentation (mean ± SD)	4.6 ± 1.6	4.8 ± 1.4	0.683
Sex			0.104
Female (%)	66 (41%)	14 (58%)	
Male (%)	96 (59%)	10 (42%)	
Duration in low clearance clinic, months (mean ± SD)	40.7 ± 35.8	29.2 ± 20.1	0.777
Opted for Maximum Conservative Therapy			0.725
Yes (%)	102 (63%	16 (67%)	
No (%)	60 (37%)	8 (33%)	
Death within			0.411
3 months of first LCC	7 (4%)	1 (4%)	
3-12 months of first LCC	39 (24%)	2 (8%)	

*eGFR calculated according to 2021 CKD-EPI Creatinine Equation; BME, black and minority ethnic; * one patient received an AV graft; LCC, low clearance clinic*

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The kidney biopsy makes it to the 21st century: what next?

186: International renal biopsy practice is influenced by human and systemic factors

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Biography - Dr Michael Toal
Dr Toal is a Clinical Research Fellow at Queen's University Belfast and Renal Medicine/General Internal Medicine trainee in the Northern Ireland deanery. He is currently in his second year of a PhD investigating strategies to improve diagnosis and risk stratification in glomerulonephritis. Through this work he has recruited over 1000 nephrologists from 84 countries for the largest international study of renal biopsy practice ever undertaken. Dr Toal has held a teaching role within the university since 2016 and has recently completed a Postgraduate Diploma in Clinical Education. He holds several non-clinical roles including OSCE examiner, interview panellist for Internal Medical Training, question writer for both the MRCP(UK) Renal Medicine SQG and ESE Nephrology for the online resource 'Study prn'. He is the team doctor for Transplant Sport Northern Ireland and has attended the British Transplant Games in this capacity.

Abstract
Introduction: Renal biopsy is an invasive investigation but crucial for diagnosis of many diseases. Patients often require at least one day in hospital and the potential risks of the procedure include life-threatening haemorrhage (1). There is substantial variation in biopsy practices between and within countries, and by social deprivation classes, however the reasons behind these discrepancies remain unclear (2,3). There is limited research into renal biopsy practice with available studies restricted to single countries (4,5).

Methods: A questionnaire for nephrologists was developed using an iterative design with several cycles of refinement, including feedback from a pilot study of over 30 nephrologists to produce the final version. A propensity-to-biopsy score was derived from participant responses to simulated cases and relative biopsy contraindications, which categorised respondents into one of five categories (least likely to most likely to biopsy) for instant feedback on completion. Dissemination occurred through international nephrology societies (including UKKA) and social media platforms (Twitter/X).

Results: 1093 respondents from 84 countries completed the questionnaire, including 213 from the UK. To the researchers' knowledge, this is the largest study of its kind with the broadest international representation. Biopsy propensity was generated as a score from 0-44, with a higher score signifying an increased propensity to perform a biopsy. The mean score was 24.1.

A decision to perform a renal biopsy was most likely for nephrotic or nephritic syndrome cases, but least likely in the setting of reduced kidney size. Propensity-to-biopsy scores were significantly higher in males ($p<0.001$), who had a greater tolerance for relative contraindications to biopsy. Propensity was highest in respondents aged 30-39 years and lowest in respondents aged 50-59 years ($p<0.001$). Respondents in the latter group were more likely to have encountered a severe complication of nephrectomy or patient death than the former group.

When countries with over 20 respondents were analysed, the mean score ranged from 22.4 (Finland) to 26.2 (Mexico) ($p<0.001$). No significant difference was observed between the four UK nations (mean score = 23.2). Not all nephrologists perform renal biopsies and the propensity score was significantly higher in individuals who had performed more than 20 biopsies within the last year (25.6) compared to none (23.5) ($p<0.001$). Propensity-

to-biopsy was lowest in the group who had no experience of complications and was not adversely affected by previous serious complications including death.

Discussion: Renal biopsy practice is variable and influenced by the inherent characteristics of nephrologists and the environment in which they work. Older nephrologists had more experience of a biopsy complication through the course of their career, however complication severity did not appear to reduce propensity-to-biopsy, which was lowest in individuals who had never had a complication. Nephrologists who performed more procedures had an increased propensity-to-biopsy, suggesting that this may be affected by personal control over access to the procedure. Awareness of these influences is important to ensure that patients are not disadvantaged and can receive timely investigations and treatment.

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Implementing strategies to support people to live well with kidney disease: utilising the RSTP toolkit

89: Implementation of therapy support in the Advanced Kidney Care Clinic: A Quality Improvement project

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Biography - Dr Hannah Young

Hannah Young qualified as a Physiotherapist in 2005 and joined the Leicester Kidney Lifestyle Team in 2011 to develop and implement a programme of exercise delivered during haemodialysis. In 2013, Hannah was awarded an MSc in Physiotherapy with distinction from the University of Nottingham. In her role as a Specialist Physiotherapist at the University Hospitals of Leicester NHS Trust, she has led projects designed to develop, test and implement novel rehabilitation strategies for people living with advanced kidney disease. Most recently she has established a therapy service within the existing advanced kidney care clinic to proactively supports people to maintain or improve their physical and mental wellbeing. In 2021 she completed an NIHR Doctoral Fellowship, hosted by the University of Leicester. This work focused upon understanding frailty, falls and the role of exercise in haemodialysis patients. The same year she moved to Leicester Diabetes Centre. Her research interests include frailty, cardiorenal metabolic multi-morbidity, physical activity, physiotherapy, and rehabilitation and has a particular passion for mixed-methods research and clinical trials. In 2023 she was awarded an advanced NIHR fellowship to develop and test a tailored 24-hour health behaviour programme for people living with frailty and multiple long-term conditions, and their carers.

Abstract

Introduction: Access to specialist physiotherapy (PT) and occupational therapy (OT) services within renal services in the UK is variable, driving inequitable care and outcomes. The integration of therapy services into advanced kidney care clinics (AKCC) may build physiological and psychological resilience and improve outcomes. The Renal Service Tranformation Programme recommends that people with CKD have access to specialist assessment and reablement at key junctures in the journey, such as the onset of advanced CKD. The aim of this quality improvement (QI) project was to introduce a therapy clinic which proactively supports patients to maintain or improve their physical and mental wellbeing.

Methods: In May 2023 we introduced a therapy clinic within the AKCC at the University Hospitals of Leicester. A specialist PT and OT completed a person-centred assessment to support the development of a care plan in partnership with patients and family. Interventions were tailored to the individual's needs, goals and circumstances.

We used Plan-Do-Study-Act cycles to iteratively test and improve the service. We collected data relating to physical activity, geriatric impairment, physical function and psychological distress using validated outcome measures and screening tools.

Results: We present data collected up to the 24th of August 2023. Of 124 individuals screened across a single list in 11 clinics, n= 118 (95%) were appropriate for the service. Of this cohort, 31% received a holistic assessment and intervention. Of those assessed, n=22 (60%) were male. Their mean age was 70±2 years and 76% were White British. Their mean eGFR was 14ml/min/1.73m2 (IQR 11- 15). Assessment revealed that 32% had fallen in the last year and were at high risk of future falls (mean FRAT score 3±1). 49% were classified as frail. The mean sit-stand in 5 second score was 13.2 (IQR 11-15) seconds. 14% reported significant psychological distress. The mean weekly time spent undertaking moderate to vigorous physical activity was 0 (IQR 0-65) minutes and 0 (IQR 0-0) people were achieving the UK guidelines of two days a week of strength training. Participants received 2±0.8 interventions. Anonymous feedback revealed that the service was highly valued by patients and the MDT.

Conclusions: This QI project reveals high levels of inactivity, frailty and functional impairment within patients routinely seen in the AKCC. The integration of a therapy service within the existing clinic is feasible, with longer term evaluation needed to demonstrate effectiveness. Work is underway to secure longer-term funding and to refine and upscale the service.

564: An exploration of inpatient referrals to Renal Clinical Psychology: Reasons for referral and equality and diversity issues

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Nottingham University Hospitals NHS Trust, Nottingham

Biography - Dr Emma Coyne
Emma is a Consultant Clinical Psychologist and has working in renal psychology for 15 years. She is involved in research in a number of areas including developing renal psychosocial care, acceptance and commitment therapy interventions, young adult transition and mental capacity and dialysis.

Abstract
Introduction: Quality of life and well-being of people with kidney disease is adversely affected by psychological distress, depression and anxiety (Guerra et al, 2021). Inpatient admissions are adversely impacted by Kidney conditions with 1 in 5 individuals admitted to the hospital in emergency being affected by acute kidney injury (AKI) (Kidney Care UK, 2023). There is a need for access to psychosocial care at key transition points within the patient journey (Coyne et al, 2023; NHSE, 2023).

Renal psychologists are highly trained doctoral level professionals. They aim to reduce distress, improve psychological well-being and improve health outcomes for patients. They apply psychological theory and models to the context of physical health, illness and renal disease across the lifespan. This specialist knowledge base is used to design, implement and evaluate psychological services into kidney care. A full clinical psychology service includes both inpatient and outpatient referrals.

Over the last 15 years the numbers of inpatient referrals has increased significantly. Qualitatively the service had noted an increase in the complexity of referrals, particularly those with AKI and those with longer term admissions to hospital.

Methods: An audit was conducted using data from inpatient renal referrals to Adult Renal Clinical Psychology gathered between January 2023 to December 2023 from NHS databases and cross checked with discharge summaries. The data consisted of patient demographics, number of referrals, primary reason given for referral, treatment modality, length of stay and referring consultant nephrologists. Descriptive statistics were conducted through Microsoft Excel

Results: The total number of patients referred were 90 with 157 number of referrals. 51 were male and 39 were female. The majority were from a white ethnic background (73%). The most frequent referrals were related to people with AKI and patients currently receiving haemodialysis. The age group data showed referrals typically from 51-65 years (30; 33.3%), over 65 years (20; 22.2%) and 18-30 years (17; 18.9%). The primary reasons for referral were low mood (42) and Anxiety (12) but there were multiple reasons for referral including post ITU stays, adjustment reactions and delirium. Patient length of stay was higher than the ward average and there were gender differences in referral patterns. Female Nephrologists were more likely to refer to Renal Psychology than male Nephrologists or Surgeons.

Discussion: The data shows that most adults referred to Renal Clinical Psychology were of white ethnic background in comparison to their ethnic minority peers. Barriers and perceptions of accessibility to the service are considered. Of those referred, the most frequent age group to be referred were 51-65 years. The increase in number of young adults referrals may well reflect the close work between Renal Psychology and the Renal

Young Adult worker who supports in identifying distress in this age group. Men were more likely to been referred than women which may reflect how male distress is perceived in a ward environment. Patient experiencing AKI and patients already undergoing haemodialysis were more likely offered psychological support. Gender differences in staff referral patterns may relate to perceptions of Clinical Psychology and may benefit further exploration to understand the reasons for these differences. Further recommendations for service development are considered including the use of more standardised screening of patient referrals, collection of intervention data as well as potential training for ward staff on which patients could benefit from referral to Renal Psychology.

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The UKKA and Kidney Care UK: Creating a new era of trusted, accessible patient information

479: "What compromises are you willing to make?": Descriptions of kidney failure treatment options in information resources and their influence on patient understanding and decision-making

Dr Ryann Sowden[1], Dr James Robb[1], Dr Chloe Shaw[1], Dr Anna Winterbottom[2], Dr Katherine Bristowe[3], Dr Hilary Bekker[2], Prof James Tulsky[4], Prof Fliss Murtagh[5], Dr Rebecca Barnes[6], Prof Fergus Caskey[1], Dr Lucy Selman[1]

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Biography - Dr Ryann Sowden

Dr. Ryann Sowden is Research Assistant at the University of Bristol and a Speech and Language Therapist. Her research interests include communication between clinicians and patients, media communication, health service development, global development and communication disability.

Abstract

Introduction: For patients over the age of 65 with comorbidities and/or poor performance status, and for patients over the age of 80, choosing whether to have conservative kidney management (CKM) or dialysis treatment can be complex, involving weighing up potential benefits against risks and considering possible impact on quality and length of life: the potential compromises that each choice carries. In choosing a treatment, patients often rely on information resources from renal units. We aimed to describe how information resources present living and dying with kidney disease in relation to CKM, haemodialysis and peritoneal dialysis, and consider implications for patients' treatment decision making.

Methods: Information resources were collected between June 2021 and January 2023 from four renal units in England and Wales with varied kidney failure treatment rates, as part of the OSCAR study (Optimising Staff-Patient Communication in Advanced Renal Disease). Physical and digital copies of information resources were collected from outpatient waiting areas, consultation rooms, and group patient education sessions.

We included documents which focused on the treatment options of CKM, dialysis (haemodialysis and peritoneal dialysis) and transplant. Documents were categorised as: Direct Treatment Option Information Resources, focusing directly on treatment options, either individually or in comparison (category A); and Indirect Information Resources, focusing on broader contextual information related to treatment options, such as lifestyle impacts and the logistics of receiving treatment (category B).

Document analysis of the information resources was informed by critical discourse analysis. We examined how documents describe and explain living and dying with kidney failure in relation to treatment options, and how treatment options were placed in context, identifying themes, 'frames,' and discourse

Results: 72 documents were identified across the four renal units, with 46 documents included after deduplication and screening (Figure 1). Analysis identified three global themes (see Table 1 for illustrative data extracts):

1) *How treatment options are constructed*. Dialysis was typically constructed positively (e.g. as "life saving") and CKM negatively (e.g. "this will result in death").

2) *Deciding is challenging*. Treatment decision-making was portrayed as a challenge which might require emotional support. as the importance of shared/informed decision-making and the right to decide were highlighted, however some resources presented the patient in a passive role.

3) *End of life and dying*. Information resources tended to present patients living with one treatment option choice (dialysis) and dying with another (CKM). Advance care planning, palliative care and descriptions of dying were presented in the context of CKM, implying these were not relevant topics for patients choosing dialysis.

Figure 1: Included information resources

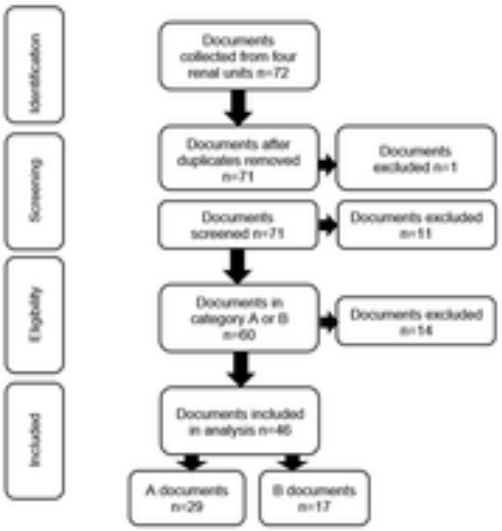

Table 1: Themes and illustrative data extracts

1) How treatment options are constructed	Treatment is dialysis	"Kidney failure, if left untreated, is fatal but modern medicine has provided us with a life saving treatment – DIALYSIS." A-3-11
	CKM is non-treatment	"Some people may decide not to have dialysis and this will result in death from kidney failure." A-1-10
2) Deciding is challenging	Emotional support needed	"Being diagnosed with kidney failure can be a very worrying time for patients and their families. It marks the beginning of a life-long 'career' as a kidney patient and starts a journey of decision-making about treatment choices." A-3-10.
	Explicit/implicit clinical values/principles	"Can I choose not to have dialysis treatment? Yes. You have the right to decide not to start treatment if you feel the burden of dialysis would outweigh the benefits to you and lessen your quality of life."A-1-18
	Autonomy in making a choice	"Your Nephrologist will ultimately decide when you need to start dialysis." A-2-05
3) End of life and dying	Living with the treatment option (associated with dialysis)	"How long can you live on dialysis? We do not yet know how patients on dialysis will live. We think that some dialysis patients may live as long as people without kidney failure." A-3-11
	Dying with the treatment option (associated with CKM)	"What support and help will there be as my kidney function gets much worse? Your doctors or nurse may suggest talking to specialists in end-of-life care. These doctors and nurses are known as the palliative care team and they will talk to you about how you would like to me looked after as your kidney function declines. These discussions are known as Advance Care Planning. They may involve your GP, your family and staff from your local hospice." A-2-01 [in CKM section of the resource]

Discussion: The information resources we identified typically presented unbalanced explanations of dialysis and CKM. CKM was frequently equated with death and dying, while the compromises associated with dialysis (a time-intensive and potentially painful treatment) are often minimised. Despite the focus on patients' "right" to choose a treatment option, it may therefore be challenging for a patient to choose CKM, even when this treatment choice is the best fit for their goals and values. Information resources regarding dialysis often exclude important information on implications of that choice for the end of life, and on the potential benefits of advance care planning.

Sustainable kidney care: a global initiative towards greener nephrology

261: Sustainable dialysis: What difference does it make?

Mr Gareth Murcutt

Royal Free London NHS Foundation Trust, London

Biography - Mr Gareth Murcutt
Gareth Murcutt has been the Renal Technical Manager at the Royal Free London NHS Foundation Trust since 1996. Before this he worked in renal technology within both the NHS, and the private sector in the UK and abroad. He has presented work on a variety of subjects at national and international conferences and served on many professional group committees over the years. During 2022/3 Gareth completed a Scholars Course in Sustainable Kidney Care funded by the UKKA SKC and delivered by The Centre for Sustainable Health. His focus has become evaluating processes within dialysis, developing and evaluating the carbon footprints, social impact and economic benefits of many different interventions. Within this project these goals are presented in a standardised form to enable extrapolation by other kidney care services.

Abstract
Kidney care and specifically haemodialysis is widely recognised as a carbon intensive, though life-saving treatment [1]. As such, making dialysis more sustainable has become an important subject of discussion amongst all members of the renal multiprofessional team. This project forensically analyses three different options, two of which have been published in case studies [2,3], in a format suitable for comparison by the wider kidney care community. It estimates many of the potential financial, social and environmental benefits of each of the three within a sustainable QI framework (SusQI).

To enable extrapolation of the data for other kidney care services all the options were evaluated within a theoretically standardised model of a 30-bedded dialysis unit running 3 shifts per day, six days per week. The first option was moving from single-use 5 litre individual acid concentrate containers to a central acid delivery (CAD) system [2]. Second was using the dialysis machine's ultrapure fluid to perform online priming, bolus giving and washback rather than purchasing and using bags of 0.9% saline solution. The third alternative evaluated, was a reduction in dialysate flow of 100ml/min in terms of acid concentrate, bicarbonate, energy and water usage and the associated savings [3]. The third option also allows for the calculation of savings by reducing/stopping the dialysate flow whilst waiting for patients to commence dialysis. Ongoing investigations include moving from 1:34 to 1:44 dilution acid concentrate and replacing a heat disinfection cycle with a rinse cycle.

Central Acid Delivery was found to provide the greatest potential annual emissions reduction of over 30,000 $kgCO_2e$ as well as saving £20,000, over 700 hours of staff time and 450,000 kgs of reduced manual handling. In terms of financial savings, online priming can deliver over £42,000 at 2023 UK National Framework prices as well as over 5,300 $kgCO_2e$. Even every 100 ml/min reduction in dialysate flow can produce yearly savings of £13,600 and almost 8,000 $kgCO_2e$ in the 30 bedded unit.

If kidney care services are to play their part in helping the NHS reach the Net Zero goal set by the UK government [4], then it is important that these options are considered by all dialysis units. It is acknowledged that not every alternative is suitable for all kidney care services, but presenting the data for a standardised dialysis unit allows them to be easily evaluated across the UK. It should also be noted that all three options also

deliver considerable potential financial savings, which should help with the development of any business cases required to support sustainable developments.

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344: Towards achieving sustainable health care in a renal centre - carbon saving is coupled with cost efficiency.

Dr Stephanie Choo[1], Dr John Stoves[2]

[1]St James's University Hospital, Leeds. [2]Bradford Royal Infirmary, Bradford

Biography - Dr Stephanie Choo

Dr Choo graduated from the University of Edinburgh in 2016 and subsequently completed foundation and core medical training in the South East Scotland and North East England deanery respectively. She moved to Yorkshire in 2020 to commence her speciality training in renal medicine. Since commencing her specialty training, she has developed a keen interest in sustainable healthcare and has recently been appointed as a sustainability fellow in Renal Medicine at Leeds Teaching Hospitals NHS Trust. During her upcoming time out of programme, her focus will be on improving the carbon footprint of in-centre haemodialysis. She also has keen interest in medical education obtaining a PG Diploma in Medical Education. Outside medicine, she enjoys gardening and exploring the scenic countryside and natural landscapes in the UK.

Biography - Dr John Stoves

Dr Stoves graduated from the University of Edinburgh and became a consultant in Bradford in 2003. He served as the renal clinical lead for Yorkshire and the Humber Strategic Clinical Network from 2013 to 2017. His main interests include renal care in the community, renal transplantation, transitional care for young adults with kidney conditions, metabolic renal stone disease, and polycystic kidney disease. He is involved in multiple multidisciplinary team quality improvement projects including the Tackling AKI Health Foundation project, the development of a cultural and health improvement officer post to support the care of South Asian patients in Bradford, and the national KQuIP initiative. He is also involved in postgraduate medical education, sustainable healthcare, and clinical research.

Abstract

Healthcare contributes 4% of global carbon dioxide equivalent (CO_2e) emissions [1], with kidney care contributing significantly and disproportionately to this. Renal medicine was one of the first specialities to actively develop a "green" community. Here, we summarise a series of comprehensive and impactful green initiatives across various aspects of kidney care delivery in a kidney unit from 2005 to date. Figure 1 provides a list of all implemented changes alongside carbon and cost savings. Financial and carbon estimates in haemodialysis related interventions are based on a 40 bed haemodialysis unit.

One of the first initiatives was the development of a CKD e-consultation service in 2005. This service aimed to facilitate prompt decision-making and streamline referrals to the kidney unit. In collaboration with primary care teams and supported by the hospital trust, the initiative utilised the SystmOne® IT system to enable electronic consultations. The outcomes included increased GP confidence in managing CKD in the community, fewer unnecessary clinic referrals, and significant carbon savings of 40kg CO_2e for each outpatient visit that was avoided [2].

The haemodialysis unit upgraded its water treatment system in 2009 when the renal technologists noted that two of the water plants wasted approximately 70% more reject water. For a capital outlay of £60,000, this resulted in £18,000 of actual cost savings per year and an annual estimated CO_2e savings of 8.42 tonnes [3]. In the same year, the unit implemented a central acid delivery system which significantly reduced acid and plastic canister wastage, resulting in an estimated savings per annum of 16.03 tonnes CO_2e / £22,900. The financial appraisal revealed a return on investment of 163% over five years [4].

The kidney unit invested the full value of a BJRM Innovation in Renal Medicine Award in a "Lighting Project." This project involved replacing outdated, less energy-efficient fluorescent light fittings with movement-sensitive 'T5' fittings, the improved lighting levels being accompanied by reduced maintenance costs and estimated annual savings of 2.3 tonnes of CO_2e / £612 [5].

In 2013, the haemodialysis team systematically reviewed dialysis prescriptions and started utilising the dialysate autoflow facility available on the Fresenius 5008 machine. This reduced water and acid consumption by 9% and enabled the use of smaller 650g bicarbonate bags, resulting in annual savings of 3.7 tonnes CO_2e / £11,524. The implementation process involved training the multi-professional team to ensure a smooth transition with no reduction in dialysis adequacy [6].

These initiatives illustrate the importance of environmental sustainability as a key pillar of renal care provision, and highlight the important association between sustainable healthcare, financial efficiency and enhanced patient care. Since the start of this journey 18 years ago, the cumulative estimated CO_2e and financial savings exceed 1,000 tonnes of CO_2e and £1.8 million respectively. Interventions to facilitate environmental sustainability may require upfront costs and staff investment of time and effort, but the dividend is long-term environmental protection, financial savings, enhanced quality of care, greater staff satisfaction, and enhanced service resilience. Sharing these experiences may help other institutions to integrate green initiatives into everyday service planning.

Figure 1: Summary of sustainable interventions in our renal unit from 2005-2023

Interventions	Capital outlay costs	Year introduced	Financial savings per year (estimated / actual) and estimated CO_2e savings per year	Cumulative estimated savings to date
Electronic consultations via: 1) E-consultation and E-referrals via SystmOne® as an alternative to paper hospital referral for advice and referrals 2) NHSAttend Anywhere 3) Virtual Renal Metabolic Stone 4) Young Adult Transition Clinics	None	2005 and 2020	Financial: Unable to quantify accurately. CO_2e: 40kg per outpatient visit avoided.	CO_2e: 280 tonnes (approximately 7000 appointments over 12 years)
Renal Unit Hub via Systm One ® - Two-way sharing of Electronic Health Records between the renal unit and general practice	None	2010	Unable to accurately quantify financial and CO_2e savings. However, this initiative resulted in reduced face to face hospital attendances for blood test monitoring and reduced paper communications to and from primary care teams (thousands of communications per annum)	
Use of online priming on haemodialysis machines (avoiding saline bags)	None	2010	Financial: £56,160 (Estimated) CO_2e: 7.1 tonnes	Financial: £730080 (13 years) CO_2e: 92.7 tonnes (13 years)
Upgrade of water treatment systems in the haemodialysis unit	£60,000	2011	Financial: £18,000 (Actual) CO_2e: 8.4 tonnes	Financial: £216,000 (12 years) CO_2e: 101.0 tonnes (12 years)
Central delivery of acid for haemodialysis	£43,900	2011	Financial: £37,488 (Estimated) CO_2e: 38.2 tonnes	Financial: £449,856 (12 years) CO_2e: 458.3 tonnes (12 years)
Use of 1:44 (instead of 1:34) haemodialysis acid concentrate solution	None	2011	Financial: £0 (Actual) CO_2e: 3.5 tonnes	Financial: £0 (12 years) CO_2e: 42.1 tonnes (12 years)
Lighting Project - installation of 85 fluorescent 'T5' light fittings to replace the order 'T8' light fittings	£5,000	2012	Financial: £612 (Estimated) CO_2e: 2.3 tonnes	Financial: £6,732 (11 years) CO_2e: 25.3 tonnes (11 years)
Systematic review of haemodialysis prescription to increase the use of dialysate autoflow facility	None	2013	Financial: £11,524 (Estimated) CO_2e: 3.7 tonnes	Financial: £115,240 (10 years) CO_2e: 37.2 tonnes (10 years)
Incremental and decremental haemodialysis (Average 25 patients per year on twice weekly haemodialysis)	None	2020	Financial: £121,725 (Estimated) CO_2e: 30.4 tonnes	Financial: £365,175 (3 years) CO_2e: 91.3 tonnes (3 years)

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Peritoneal dialysis related infection

586: Does the PD peritonitis risk increase in patients needing an extra connection for icodextrin? A review of data over 5 years in a single centre

Dr. Rehma Nanteza, Dr. Jenny Allen

Nottingham Hospitals NHS Trust, Nottingham

Biography - Dr. Rehma Nanteza
IMT3 Renal Medicine

Abstract
Background: PD peritonitis is a serious complication of peritoneal dialysis (PD) leading to significant morbidity, and it is the commonest reason for transfer to hemodialysis. PD peritonitis rates are high in the UK and rates in our unit are above the ISPD target of 0.4 episodes per patient year. Icodextrin is commonly used in PD patients to reduce glucose exposure and improve ultrafiltration. Icodextrin is produced by Baxter, and has compatible connections with the Baxter PD systems. Patients using a Fresenius PD system have to perform an additional connection to use icodextrin. Following root cause analysis assessment of cases of peritonitis within our unit, the use of Fresenius prescriptions with icodextrin was identified as a possible risk factor for peritonitis.

Method: We performed an observational study of incident PD patients over 5 years. We reviewed peritoneal dialysis prescriptions and recorded all episodes of peritonitis

Results: 338 patients commenced PD over the 5 year study period (November 2018 to November 2023). Of these 181 (53%) had at one or more episode of peritonitis within the 5 year follow up period. 82 patients had no documented prescription and were excluded from data collection. Of these 32 (39%) had peritonitis. Of the 256 patients with a documented prescription 149 (58%) had an episode of peritonitis. 97 (38%) patients used a Baxter system with icodextrin and 66 (26%) used a Baxter system without icodextrin, 33 (13%) used a Fresenius system with icodextrin and 60 (23%) used a Fresenius system without icodextrin. PD peritonitis amongst patients using a Fresenius system with icodextrin was most common, with 25 patients (76%) having an episode of peritonitis during the study. This compared to 31 patients (51%) using Fresenius system without icodextrin, 60 (61%) using Baxter system with icodextrin and 33 (50%) using a Baxter system without icodextrin.

Table 1 PD peritonitis Infections according to PD prescriptions, with or without Icodextrin and Fresenius

PD System	BAXTER without icodextrin	BAXTER with icodextrin	FRESENIUS without icodextrin	FRESENIUS with icodextrin
Peritonitis	33(9.7%)	60 (17.6%)	31(9.1%)	25 (7.3%)
No peritonitis	33(9.7%)	37(10.9%)	29(8.6%)	8(2.3%)

Conclusion: The incidence of peritonitis within our cohort was relatively high, reflecting poor peritonitis rates within our unit. PD patients using an extra connection in order to use icodextrin whilst on a Fresenius system were more likely to develop peritonitis. We hypothesise that this increased risk is due to the extra connection required for icodextrin use. The incidence of peritonitis was slightly higher in all patients requiring icodextrin, which may reflect a group of patients with more comorbidity including fluid overload, heart failure, frailty

(assisted PD), and those with a fast solute transfer rate. Our data supports the hypothesis that additional connections using different PD systems may increase the risk of peritonitis. This observation warrants further investigation. PD units who use Fresenius systems with icodextrin should be aware of a potential for increased risk of peritonitis in this group.

247: Single centre experience of using QuickCheck point of care device for diagnosing PD peritonitis: impact on diagnosis and management

Ms Christine Budd[1], Mr Edward Cornish[1], Dr Richard D'Souza[1], Dr Jennifer Williams[1,2]

[1]Royal Devon University Hospital Trust, Exeter. [2]University of Exeter, Exeter

Biography - Dr Jennifer Williams
Jennifer Williams is a clinical lecturer in renal medicine at the University of Exeter. Her work is focused on the diagnosis and management of diabetes in patients on peritoneal dialysis

Abstract
Introduction: Peritoneal dialysis (PD) associated peritonitis remains a significant complication resulting in significant morbidity, mortality and unplanned transfer to haemodialysis. ISPD stipulates 2 out of 3 criteria to diagnosis peritonitis; abdominal pain or cloudy fluid, white cell count (WCC) >100/uL, positive fluid culture. Traditionally our unit used a haemocytometer manual cell count and reported WCC as a range (<10, 10-100 or >250). QuickCheck is a point of care device providing rapid leukocyte counts which we have integrated into our care pathway for patients with suspected PD peritonitis. We reviewed the impact on diagnosis and treatment of PD peritonitis since the introduction of this new device.

Methods: During 2023 QuickCheck was used to rapidly confirm or rule out peritonitis and to quantitatively monitor the response to treatment in several individuals with confirmed peritonitis (as per most recent ISPD guidelines). The majority of patients had a paired sample sent to the laboratory for confirmation of WCC. Those patients for which the clinical index of suspicion was low and QuickCheck count was <100/uL did not have paired fluid samples. If QuickCheck count was >100/uL fluid was sent to the laboratory for WCC, culture and sensitivities and empirical antibiotic therapy was commenced.

Results: Over a calendar year in 2023 QuickCheck was used 65 times in 53 individuals.

Comparative results in *de novo* samples

	QuickCheck >100/uL	QuickCheck <100/uL
Laboratory WCC >100/uL	16 3/16 = culture negative	0
Laboratory WCC <100/uL	6 6/6 = culture negative	9

In addition:

- 14 patients had QuickCheck counts of <100/uL but no paired laboratory count. In all patients there was low clinical suspicion for peritonitis. 1/14 developed peritonitis within 3 months of this negative test (following a breach of catheter integrity).

- 3 patients had a QuickCheck count >100/uL but no paired lab sample. 2/3 were culture negative

6 patients who would not have met the criteria for diagnosis based on laboratory WCC, were diagnosed and treated for peritonitis based on QuickCheck results (red box). All of these patients presented with an absolute indication for cell count (cloudy/blood stained fluid). 100% were culture negative.

Discussion: Based on our experience, QuickCheck appears to be a highly sensitive method for diagnosing peritonitis with a negative predictive value of 100%.

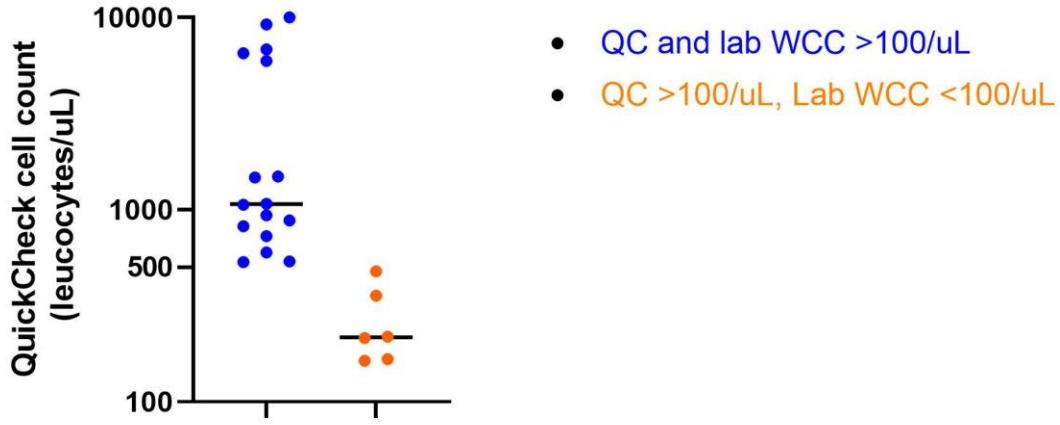
It was used efficiently to correctly rule out peritonitis in patients where the clinical suspicion was low and to monitor response to treatment in those with confirmed peritonitis.

We note very high culture negative rates and relatively lower WCC (Figure 1) in the group who were diagnosed with peritonitis based on QuickCheck but who would not have met criteria based on laboratory counts. This raises questions around how specificity is impacted when a new more sensitive test is applied to diagnostic criteria formulated on a different method.

We will continue to monitor the impact of this new diagnostic test on our local peritonitis rates and specifically culture negative rates.

Consideration should be given to how best to standardise diagnosis across units using cell count methods with differing degrees of sensitivity.

Figure 1 - Comparative QuickCheck counts



Failing kidney transplant: next steps in management in children and adults

227: A comparative analysis of the starting modality of kidney replacement therapy amongst UK children and the association with all-cause mortality

Dr. Camilla Pillay[1], Dr. Ruth Costello[1], Mr Patrick Bidulka[1], Dr. Maria Anna Casula[2], Dr. Shalini Santhakumaran[2], Dr. Lucy Plumb[2], Professor Dorothea Nitsch[1,2]

[1]London School of Hygiene and Tropical Medicine, London, United Kingdom. [2]UK Kidney Association, Bristol, United Kingdom

Biography - Dr. Camilla Pillay

I am currently undertaking higher specialty training in Nephrology and General Internal Medicine in the South London region. I have an interest in renal and dialysis epidemiology, with a focus on the design, implementation, and analysis of translational and epidemiological research in chronic kidney disease, pre-dialysis and dialysis care. Outside of training, I recently undertook and completed a MSc degree in Epidemiology at the London School of Hygiene and Tropical Medicine (2022-23).

Abstract

Introduction: Children receiving dialysis frequently experience a greater burden of health-related complications that interfere with physical and cognitive functioning and reduce life expectancy [1], when compared to those who receive a pre-emptive kidney transplant (PKT).

Whilst PKT has been associated with a lower risk of death in the short-term, few studies have compared the long-term survival of children to adulthood by their starting kidney replacement therapy (KRT) modality. Subsequently, there is insufficient prognostic information available for clinicians to counsel children and their caregivers before and after KRT onset.

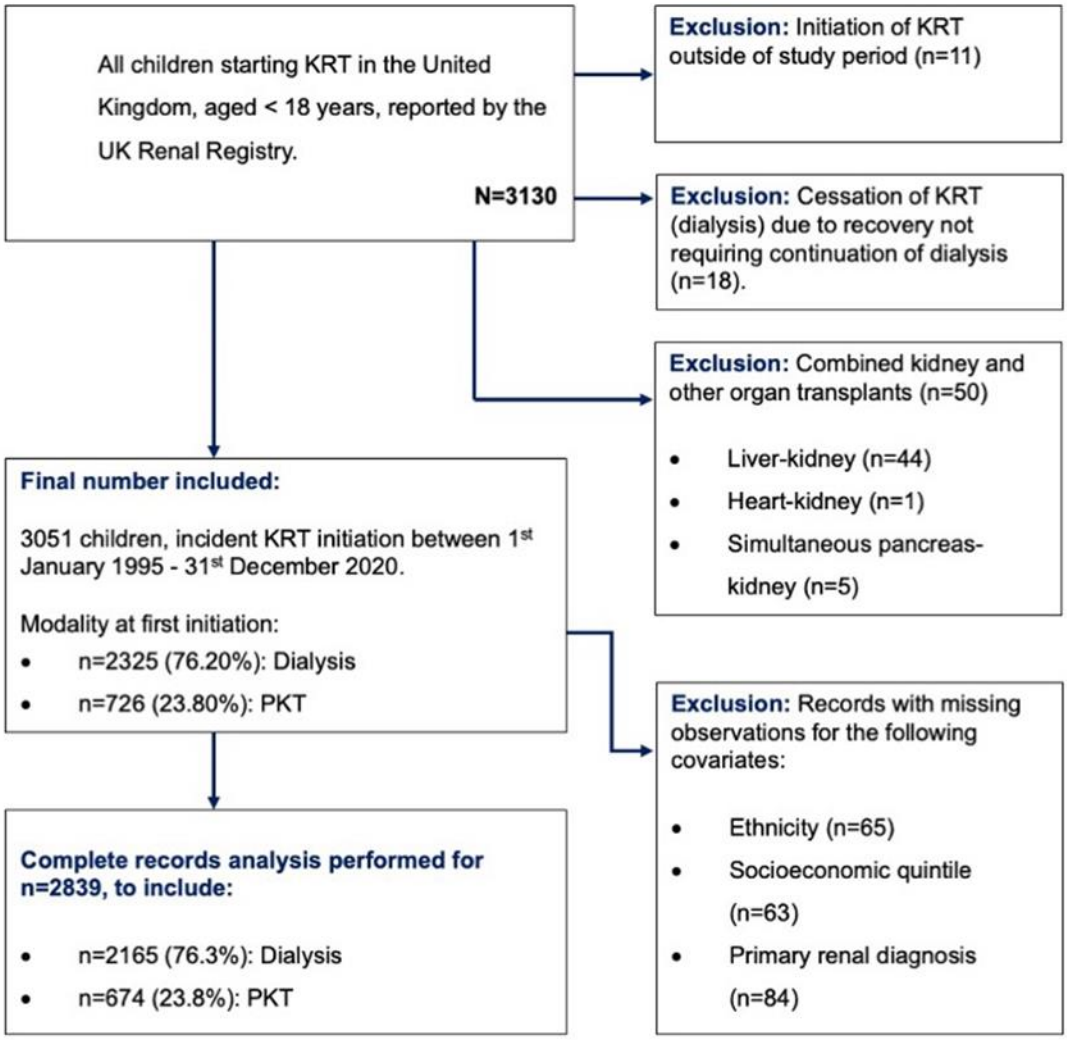
Our aim was to identify if dialysis as the first treatment modality amongst United Kingdom (UK) children was independently associated with higher all-cause death when compared to those receiving a PKT at KRT onset.

Methods: Using UK Renal Registry data, we undertook a historical cohort analysis of children (aged < 18 years) who started KRT between 1/1/1995 and 31/12/2020. The study population included children who had required chronic dialysis (haemodialysis or peritoneal dialysis for ≥ 3 months) additionally to those who received a PKT at KRT onset. Children who had received combined kidney and other organ transplants and those in whom dialysis was withdrawn following recovery of their kidney function were excluded.

Multivariable Cox proportional hazards analyses were performed, measuring the association between the starting modality of KRT received and all-cause death. Analyses compared the rates of death amongst children starting chronic dialysis to those receiving a PKT at KRT onset. Covariate-adjusted hazard ratios of death (HR, within 95% confidence intervals, CI) were stratified by age at KRT onset.

Results: 3051 children started KRT within the study period (Figure 1).

Figure 1. Flow chart showing the selection (inclusion and exclusion) of children in this study.



Children starting chronic dialysis were a younger median age at KRT initiation (10.8 years, IQR: 3.8-14.9) when compared to those pre-emptively transplanted (12.3 years, IQR: 7.7-15.3). Dialysis was most frequently initiated as the first KRT modality (compared to PKT) amongst children of Black (90.7%) and those of Asian, mixed, and other ethnic groups (83.3%) when compared to children of White ethnicity (73.3%).

Complete-records analyses were performed on 2839 children, followed to a median duration of 10.3 years (interquartile range, IQR: 4.9-16.4). Within these analyses, 281 deaths were recorded.

Children starting dialysis in the youngest age group had a 2-fold higher mortality (0 to < 9 years: HR 2.16, 95% CI: 0.99-0.74) when compared to those pre-emptively transplanted at KRT onset (Figure 2.).

Figure 2. Hazard ratios (HR) of all-cause death in association with the starting modality of KRT, stratified by age group at KRT onset.

Age at KRT onset (years)	**Number/proportion of deaths by starting modality of KRT** (n/N, %)	**Person-time** (years)	**Crude HR** [a] (95% CI)	**Adjusted HR** (95% CI) [a b]
0 to < 9	Dialysis: 107/790 (13.5)	8.3		2.16 (0.99-4.74)
	PKT: 7/179 (3.9)	1.9		1.0 (reference)
9 to < 14	Dialysis: 54/633 (8.5)	7.4	1.82 (1.30-2.54)	1.31 (0.74-2.33)
	PKT: 15/251 (6.0)	3.0		1.0 (reference)
≥ 14	Dialysis: 64/635 (10.1)	7.0		1.06 (0.63-1.79)
	PKT: 18/234 (7.7)	2.4		1.0 (reference)

p-value = p=0.6330 (likelihood ratio test for interaction between age group at KRT start and the starting modality at KRT initiation.

[a] Crude and adjusted analyses undertaken on 2722 children after exclusion of 117 children of Black ethnicity due to no deaths occurring amongst those pre-emptively transplanted in this ethnic group.

[b] Adjusted for: Age (continuous variable), Sex (reference: male); Time-period (reference: 1995-2007); Ethnicity (reference: White ethnicity); index of median deprivation quintile (continuous variable) and Primary renal diagnosis (reference: Congenital anomalies of the urinary tract diagnoses)

There was weak evidence for a difference in mortality in association with starting modality amongst children in other age groups (9 to < 14 years: HR 1.31, 95% CI: 0.74-2.33; ≥ 14 years: HR 1.06, 95% CI: 0.63-1.79).

Discussion: This study, integrating paediatric and adult registry datasets, is the first to provide estimates of long-term survival amongst UK children after KRT onset. Evidence for a difference in mortality by first KRT modality remains uncertain. Further work will assess whether comorbidity-related factors measured at KRT initiation may explain the differences in survival amongst children by their starting modality and inform an individualised approach to their care before and after KRT initiation.

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230: Successful sequential haploidentical maternal haematopoietic stem cell and kidney transplantation without requirement for long term immunosuppression

Professor Stephen Marks[1,2], Dr Giovanna Lucchini[2], Dr Austen Worth[2], Dr Kshitij Mankad[2], Dr Wesley Hayes[2], Dr Iona Madden[2], Dr Camille Laroche[2]

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Biography - Professor Stephen Marks

Stephen Marks is Professor of Paediatric Nephrology and Transplantation at University College London Great Ormond Street Institute of Child Health and President Elect of the British Association for Paediatric Nephrology. He is clinical lead for renal transplantation and Director of the National Institute for Health Research Great Ormond Street Hospital Clinical Research Facility at Great Ormond Street Hospital. He is theme lead for high intensity early phase clinical trials for NIHR GOSH Biomedical Research Centre. His research continues to date in the fields of renal transplantation (including innovative drug trials concerning new anti-rejection therapies and assessment of children post-renal transplantation), systemic lupus erythematosus and vasculitis.

Abstract

Introduction: Schimke Immuno-osseous Dysplasia (SIOD) is a rare autosomal recessive disease, occurring in 1 in 3 million caused by mutation of SMARCAL1 gene. Life expectancy mainly relies on management of end-stage kidney disease and prevention of recurrent and potentially fatal opportunistic infections.

Methods: A 5-year-old girl of non-consanguineous parents presented with SRNS secondary to focal and segmental glomerulosclerosis (FSGS), short stature, dysmorphism and normal development. Genetic analysis confirmed SIOD, and she commenced haemodialysis (HD) one year later. She had previously shown adequate vaccine responses, but further presented progressive T cell lymphopenia.

Results: Successful haploidentical haematopoietic stem cell transplantation (HSCT) followed by living related kidney transplantation (LRKT) from the same donor parent to allow tolerance of the allografts without maintenance immunosuppression therefore aiming to reduce the risks of possible fatal infections, deterioration of bone health, atherosclerosis and risk of fatal transplant associated graft versus host disease (TA-GVHD). At the time of HSCT, the patient was switched from HD to CVVH and pre-HSCT conditioning regimen was delivered according to the Stanford protocol and included 200cGy total body irradiation in single fraction. Special attention had been given to urothelium protection and infectious prophylaxis in view of future kidney transplantation. Stem cells graft was selectively depleted of αβ T-cells and CD19 B-cells to decrease GVHD risks. She developed mucositis requiring intravenous parenteral nutrition for 13 days, probable fungal chest infection and grade 1 acute cutaneous GVHD. Her blood pressure was stable under CVVH and she was converted back to HD on day +24 and discharged on day +40 from HSCT with 100% donor engraftment without systemic immunosuppression. She underwent successful high risk LRKT in view of vascular (small vessels and small size of 10.5kg and 89 cm with z-scores of -7.94 and -6.94 requiring mesh), immunological and pre-transplant hypertensive risks from her mother 6.25 months after HSCT with expected zero HLA mismatch and negative crossmatch. She did not receive any induction or anti-proliferative agents. Her renal function normalised on day 5. Even since the complete cessation of corticosteroids and tacrolimus after respectively four and five weeks post transplant, she remains with a normal estimated glomerular filtration rate of 130mls/min/1.73m^2, absence of proteinuria and normal serum albumin. She remains clinically stable now ten months post LRKT. She has good T-cell reconstruction but required antibiotic prophylaxis (including PJP prophylaxis) for six months post transplant as well as anti-viral prophylaxis with oral letermovir and aciclovir for four and 52 weeks respectively

post-LRKT. Aspirin prophylaxis was discontinued one month post transplant as there were no vascular anastomosis complications.

Discussion: Apart from being the first child in the United Kingdom to undergo these sequential procedures, it is the first described case of SIOD patient undergoing HSCT under CVVH prior to future kidney transplantation. This successful intervention led to the LRKT with minimal immunosuppression and enabled better blood pressure control and increased quality of life for this patient.

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Novel solutions to effective sustainable CKD prevention work with primary care

148: Empowering patients to take charge of their kidney health: A healthcare staff perspective in the UK.

Ms Naeema A Patel[1,2,3], Dr Matthew PM Graham-Brown[4,3], Professor Alice C Smith[1,2,3], Dr Courtney J Lightfoot[1,2,3]

[1]Leicester Kidney lifestyle Team, Department of Population Health Sciences, University of Leicester, Leicester, UK. [2]NIHR Leicester Biomedical Research Centre, Leicester, UK. [3]Department of Renal Medicine, University of Hospitals of Leicester NHS Trust, Leicester, UK. [4]Department of Cardiovascular Science, University of Leicester, Leicester, UK

Biography - Ms Naeema A Patel

Naeema is a final year PhD student at the University of Leicester. Naeema has a background in Health Psychology. Her research focuses on the evaluation and implementation of self-management resources for people with CKD. Naeema has a particular research interest in digital health interventions, healthcare service improvement, patient activation, addressing health inequalities and improving patient experiences and outcomes.

Abstract

Introduction: The NHS long-term plan identifies self-management as an essential part of the care strategy for patients with long-term conditions such as chronic kidney disease (CKD). Effective self-management has the potential to minimise the impact of CKD, slow disease progression and improve health outcomes, but evidence-based resources to educate patients and support self-management behaviour are lacking. Healthcare professionals (HCPs) and service providers have a critical role in encouraging and supporting self-management and it is essential to incorporate their views and perspectives in the development of resources and services. The aim of this qualitative study was to explore the views of professional stakeholders about the importance of self-management for patients with CKD.

Methods: Kidney HCPs and service managers, from our professional contact list, were invited to take part in a semi-structured interview conducted either face-to-face or via telephone. The interview topic guide explored their understanding and experience of self-management and current provision of specific education for kidney health (including lifestyle management). Interviews were audio recorded and transcribed verbatim. Data were analysed using thematic analysis.

Results: Forty-two participants (20 nephrologists, 6 kidney nurses, 10 allied health professionals [physiotherapist, dieticians, and pharmacists], and 6 service managers in kidney care or broader long-term conditions and quality improvement managers). Interviews lasted an average of 50 minutes (range: 38-79 minutes).

Five overarching themes were identified:

- **The role of self-management was perceived to be overlooked in CKD**.

Participants highlighted the need for earlier education to address the lack of knowledge and misconceptions, and current variation in the delivery of self-management education and support. A lack of awareness of CKD was felt to be a major barrier.

- **Understanding of self-management and related concepts**

Self-management was described in terms of empowering patients. Participants considered their role to be supporting patient autonomy in managing their health. The concept of patient activation was poorly understood and explained by participants.

- **CKD self-management should be part of self-management behaviours across multiple-long term conditions**

Participants contextualised CKD in relation to other long-term conditions, expressing the importance of risk factor management, and psychosocial and emotional support.

- **Ensuring self-management interventions can be highly personalised and responsive**

Understanding patients' personalities, needs and preferences, alongside competing health priorities was considered to help develop a collaborative approach to managing the patient's health(care).

- **Validity of information and peer champions**

Self-management interventions must have reliable information using multi-format approach. Having peer support and champions was perceived to be key for effective delivery.

Discussion: This study highlights the current challenges in supporting patients with CKD to actively self-manage. The findings emphasise the importance of patient education in CKD risk management, and that HCPs should prioritise patient understanding and information. Self-management interventions must be evidence-based and tailored responsively to individual needs, and peer support is likely to play an important role in supporting access and uptake for many patients. These critical factors must be incorporated into the design and delivery of CKD healthcare services to optimise patient management and outcomes.

558: Transforming outpatient care using MyRenalCare: Outcomes of the NHSX digital health partnership award project

Dr Robert Lewis, Dr Ahmed Elsolia, Dr Nicholas Sangala

Wessex Kidney Centre, Portsmouth

Biography - Dr Robert Lewis

Rob graduated in 1984 from Westminster Medical School, now part of Imperial College London. He trained as a nephrologist in London, working at St Bartholomew's, Kings College and Guy's Hospitals. He completed his higher medical degree (MD) at Guy's Hospital in 1996 and has been a consultant nephrologist at the Wessex Kidney Centre since 1997. Rob was Director of the service between 2001 and 2008 and took on the role again in 2016. His particular area of interest is early chronic kidney disease (CKD). He was founder member of the national CKD Strategy Group and helped develop the 2014 NICE guidelines for management of CKD in the UK.

Abstract

Introduction: A move towards digital healthcare is a key ambition of the NHS Long term plan. This ambition is largely predicated on the need to find new solutions at scale to meet the needs of the large and growing number of people living with chronic disease. In 2022 the Wessex Kidney Centre in partnership with Kidney Care UK, the University of Portsmouth and Ardia Digital Health Ltd won an NHSX grant to expand the use of MyRenalCare from 100 patients to 1000 and asses the financial, environmental and operational benefits.

Methods: Patients were invited to register online for MyRenalCare through information leaflets and posters created in collaboration with Kidney Care UK. The number of virtual consultations delivered using MyRenalCare were recorded using the hospital Patient Administration System (PAS) and patient initiated follow up (PIFU) data was recorded on MyRenalCare. The environmental impact was performed by a team of experts from the University of Manchester who conducted a full life cycle analysis using retrospective data from 331 patients over a 3-month period in 2022. A health economic analysis was conducted by the University of Southampton from an NHS and societal perspective using cost data from the NHS reference costs for outpatients, and unit costs of health and social care for staff costs. This analysis was based on data from the last quarter of 2022. Attitudes of patients and healthcare professionals towards digital technology was assessed by the University of Portsmouth (UoP) using the Technology Acceptance Model (TAM3). Usability of MyRenalCare from patient and healthcare professionals was assessed using a combination of interviews and a Think Aloud protocol conducted by researchers from the UoP.

Results: As of December 31st 2023, 1553 patients were using MyRenalCare (Table 1). In 2023, 1180 virtual appointments were delivered to 479 patients by 10 consultants using MyRenalCare, more than double the number of virtual appointments delivered in 2022 (Fig 1). There were 2510 PIFU requests submitted through MyRenalCare, with <10% requesting a face to face or telephone response and the vast majority were responded to by message, directly on MyRenalCare (Fig 2). Use of MyRenalCare to deliver virtual appointments reduced the miles travelled per patient by >50% and increased outpatient capacity by 33%. The health economic analysis revealed that use of MyRenalCare would save the NHS £1,476,268 per year if adopted by all consultants in the Wessex Kidney Centre with an additional £370,917 societal savings (time off work, travel, parking). Clinicians found MyRenalCare simple to use, a more efficient way of delivering care and communicating with their patients. The TAM assessment revealed that patients of all ages were prepared to use digital health if it was useful for their care.

Discussion: This project has demonstrated that the use of digital health, in this case, MyRenalCare is acceptable to patients of all ages and stages of CKD. MyRenalCare is able to reduce costs, increase capacity and have a positive impact on the environment whilst meeting key objectives of the NHS long term plan. More work is needed to assess scalability nationally and importantly impacts on health inequality.

Table 1

Patient Status	No. of patients	Min age	Average age	Max age
General Nephrology	824	18	57	93
Chronic Transplant	386	22	56	87
HomeHD	109	19	55	87
Kidney Donor	86	29	58	81
Acute Vasculitis	48	33	67	87
In Centre HD	33	27	54	77
APD	28	19	61	87
CAPD	21	33	60	81
Low clearance	18	35	66	83
Total	1553	18	57	93

Fig 1

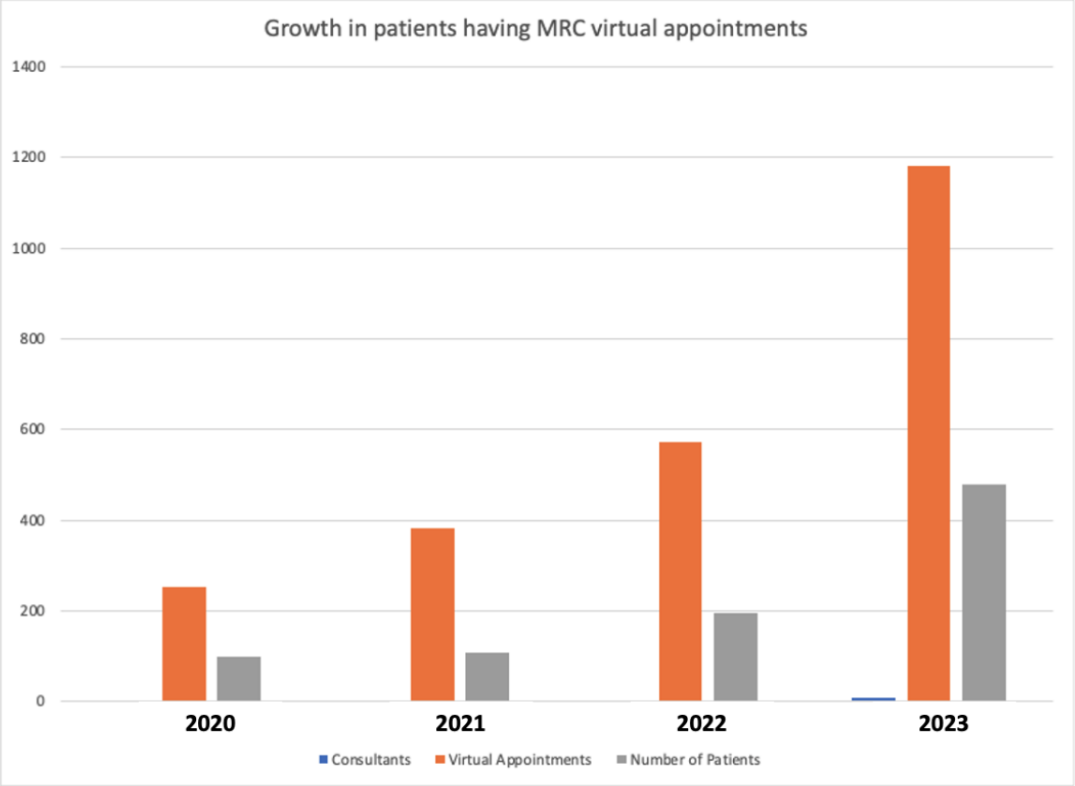
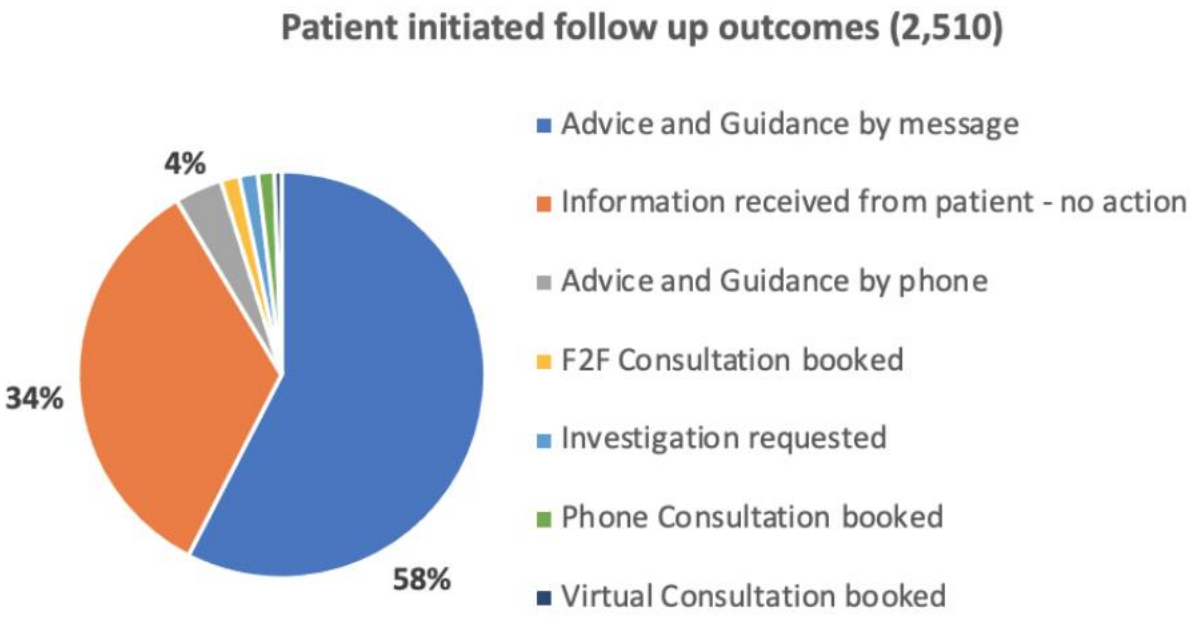


Fig 2


Patient initiated follow up outcomes (2,510)
4%
34%
58%
Advice and Guidance by message
Information received from patient - no action
Advice and Guidance by phone
F2F Consultation booked
Investigation requested
Phone Consultation booked
Virtual Consultation booked

New routes to protect damaged and aged kidneys

388: Novel Keap1-Nrf2 protein-protein interaction inhibitor UBE-1154 protects from kidney disease in a mouse model of Alport syndrome

Dr Shota Kaseda[1,2], Mr Jun Horizono[1], Mr Yuya Sannomiya[1], Mr Jun Kuwazuru[1], Dr Mary Ann Suico[1], Mr Ryoichi Sato[1], Mr Hirohiko Fukiya[3], Mr Hidetoshi Sunamoto[3], Ms Sakiho Oda[3], Mr Yuimi Koyama[1], Ms Aimi Owaki[1], Mr Haruki Tsuhako[1], Mr Masahiro Shiraga[1], Dr Bernard Davenport[2], Dr Tsuyoshi Shuto[1], Mr Kazuhiro Onuma[3], Prof Rachel Lennon[2], Prof Hirofumi Kai[1]

[1]Department of Molecular Medicine, Kumamoto University. [2]Wellcome Trust Centre for Cell-Matrix Research, University of Manchester. [3]Pharmaceutical Research Laboratory, UBE Corporation

Biography - Dr Shota Kaseda

Dr. Shota Kaseda obtained his bachelor degree in Pharmaceutical Science from Kumamoto University in 2017 and continued to pursue his MSc and PhD degrees at the Department of Molecular Medicine. After obtaining his PhD degree in 2022, he continued to work at Kumamoto University as the postdoctoral researcher, and he joined Wellcome Centre for Cell-Matrix Research, University of Manchester in 2023 as the Visiting Research Fellow. His research is focusing on the understanding mechanism of glomerular disease, especially Alport syndrome. He was awarded “JSPS Research Fellowships for Young Scientists” in 2019, “JSPS Overseas Challenge Program for Young Researchers” in 2021, and “AMED Scholarship Program for Young Researchers related to Drug Discovery and Development” in 2023.

Abstract

Introduction: Keap1-Nrf2 pathway is a key regulator of cellular defense and a promising therapeutic target for several diseases. We showed the efficacy of Keap1-Nrf2 protein-protein interaction (PPI) inhibitor UBE-1099 on progressive phenotype in mouse model of chronic kidney disease (CKD), Alport syndrome (Kaseda et al., 2022, PMID: 35721612). In the present study, we developed a more potent and safer Keap1-Nrf2 PPI inhibitor, UBE-1154, and evaluated its efficacy on Alport mice.

Methods: Development of UBE-1154 was performed by fluorescence polarization and Nqo1 induction test, which is a Nrf2 target molecule. Oral bioavailability of UBE-1154 was measured using C57BL6J mice, BALB/c mice and cynomolgus monkeys. Alport mice (C57BL6J Col4a5-G5X) or Nrf2 knockout-Alport mice were treated orally with UBE-1154 (0.3, 1, 3 mg/kg) or vehicle daily, starting at 6 weeks of age when mice first presented signs of renal insufficiency. We examined renal function and pathology at 22 weeks of age when mice reached end-stage renal disease. Moreover, effects of UBE-1154 and angiotensin receptor blocker (losartan; 6-11 weeks of age; 250 μg/mL, 12 weeks of age -; 125 μg/mL, free drinking water) on the survival of Alport mice were also studied. To clarify the molecular effect of UBE-1154, RNA sequencing of glomerulus and kidney tissues were performed.

Results: UBE-1154 inhibited the Keap1-Nrf2 PPI and induced Nqo1 activation. Oral bioavailability of UBE-1154 was very high (C57BL6J mice, 95%; BALB/c mice, 78%; cynomolgus monkeys, 107%) and UBE-1154 strongly induced Nqo1 expression in mice renal tissue. UBE-1154 dose-dependently ameliorated the renal dysfunction (GFR, plasma creatinine and BUN), glomerulosclerosis, renal inflammation, fibrosis and tubular injury in Alport mice These therapeutic effects were abrogated in the Nrf2 knockout-Alport mice. Although transient increase of albuminuria was induced by UBE-1154, the amount of albumin reabsorption in the proximal tubule was also decreased. Considering that filtered albumin is injurious to kidney cells, UBE-1154 appears to promote albumin excretion into urine in a protective manner. Compared with vehicle-treated Alport mice, UBE-1154 extended median life span by 3.9% at a dose of 0.3 mg/kg, by 9.4% at a dose of 1 mg/kg and by 22.7% at a dose of 3

mg/kg, whereas losartan increased median lifespan by 8.4%. Moreover, transcriptome analysis in the glomerulus showed that UBE-1154 induced the expression of genes associated with the cell cycle and cytoskeleton, which are not dysregulated in Alport mice. This may explain its unique mechanism of improvement such as glomerular morphologic change. In contrast, transcriptome analysis in the kidney tissue showed that UBE-1154 improved the dysregulation of immune and metabolic-related genes in Alport mice. These results suggest that the therapeutic mechanism of UBE-1154 is not due to improvement of initial lesions specific to Alport, but rather to improvement of subsequent lesions common to CKD.

Discussion: These results revealed the therapeutic effect of UBE-1154 on the progressive phenotype of Alport mice, as well as its unique effect on albuminuria, indicating a promising new therapeutic strategy for the treatment of Alport syndrome and CKD.

202: JAK inhibition protects renal function in experimental polycystic kidney disease by targeting extracellular matrix signalling and proliferation

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Biography - Dr Fiona Macleod

Dr Fiona Macleod is a post-doctoral research associate at the University of Queen Mary University London researching RNA-binding proteins and JAK/STAT signalling in polycystic kidney disease. Her project is funded by a Future Leaders Fellowship award to Dr Maria Fragiadaki (UKRI; MR/T04201X/2). Prior to her PhD in Molecular Medicine at the University of Sheffield, she completed her undergraduate degree (BSc) in Biomedical Sciences and Masters in Toxicology (MSc) at the University of Surrey, in which she also received the Toxicology Award and the Syngenta Award.

Abstract

Introduction: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common genetic cause of kidney failure. It is characterised by cyst development, inflammation and fibrosis. ADPKD is caused by mutations in PKD1 or PKD2 which disrupt multiple cell signalling pathways, including the evolutionary conserved Janus Kinase and Signal Transducers and Activators of Transcription (JAK/STAT) pathway. JAK/STAT signalling is altered in ADPKD and implicated in disease pathogenesis. Growth hormone (GH), a cytokine which induces JAK2/STAT5 signalling, is also aberrantly increased in ADPKD. Thus, we sought to elucidate the role of GH/JAK2/STAT5 signalling in ADPKD and how disruption of this pathway with a GH receptor antagonist (GHA) or small molecule JAK inhibitor (ruxolitinib) impacts disease.

Methods: RNA was extracted from whole kidneys of mice with Pkd1 deletion (Pkd1nl/nl) or wild-type littermate controls. RNA was also extracted from cultured human ADPKD renal epithelial cells (SKI-001) stimulated with either GH alone (500ng/mL), GH with ruxolitinib(1μM), or GH with GHA(2.5ng/mL), and its quality verified by bioanalyser. To measure differential gene expression *in vivo* and *in vitro,* we employed Illumina RNA sequencing analysis and bioinformatics analysis was performed.

Results: Stimulation of human ADPKD-derived cells with GH significantly induces STAT5 activation with subsequent elevation in proliferation and *in vitro* cystic growth. GH stimulation led to an upregulation of 106 genes ($p<0.001$). Extracellular matrix (ECM) organisation and IL-4/IL-13 signalling were enriched in GH-stimulated cells, indicating a profibrotic role of GH. Additionally, genes associated with key processes in ADPKD pathogenesis such as hypoxia and proliferation were highly expressed in response to GH.

Next, we wished to understand the cellular and molecular effects of GH inhibition in SKI-001, to achieve this we treated cells with two inhibitors, ruxolitinib or GHA. Both inhibitors were capable of abrogating some of the effects of GH, including in functional assays alongside profibrotic ECM and IL-4/IL-13 signalling RNA expression. Taken together, the RNA-sequencing profiles revealed that ruxolitinib is a potent and specific inhibitor of GH function in ADPKD-derived cells, having very little or additional effects on non-JAK/STAT pathways. Hence, we decided to use ruxolitinib in murine ADPKD models.

Pkd1nl/nl mice treated with ruxolitinib showed a significant reduction in fibrosis ($p<0.01$) and KW:BW ($p<0.05$), alongside reduced serum BUN ($p<0.05$). To understand the mechanism behind this, RNA-sequencing was performed which showed 679 downregulated DEGs with ruxolitinib treatment compared to vehicle controls (padj<0.05). Interestingly, KEGG pathway analysis revealed a reduction of GH signalling with ruxolitinib

treatment. Enrichment analysis showed significant downregulation of ECM signalling and proliferation-associated genes such as the STAT5-transcriptional target cyclin D1, highlighting these pathways as ruxolitinib targets contributing towards reduction in fibrosis and kidney volume.

Discussion: Growth hormone induces several pathways, with ECM remodelling and hypoxia being key players. In vivo inhibition of this pathway with the JAK2 inhibitor ruxolitinib significantly reduces fibrosis and protects renal function through reduction of proliferative signalling and fibrotic pathways involving ECM signalling and collagen synthesis. Taken together we show for the first time that GH antagonism is beneficial in the polycystic kidney.

Improving quality of life for older people having dialysis

228: Evaluating symptom burden and decision making in older people with advanced chronic kidney disease (CKD): a cross-sectional service evaluation

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Biography - Iqbal Lokman

Iqbal is a fourth-year medical student at the University of Manchester, currently on placement in Lancashire Teaching Hospitals NHS Foundation Trust. He is an international student from Malaysia, keen on surgery, obstetrics, and emergency medicine. Outside of medicine he enjoys playing badminton, dancing, and learning music.

Abstract

Introduction: The benefits of dialysis compared with conservative management (CM) are less certain in older people with advanced chronic kidney disease (CKD) living with frailty and multimorbidity. Symptom burden and quality of life may worsen following dialysis initiation; studies have reported that patients can experience dialysis decisional regret. We conducted a cross-sectional service evaluation to understand symptom burden, experience of shared decision making and decisional regret for older people receiving haemodialysis (HD) and CM in our trust.

Methods: People aged 65 and older receiving HD (for 3 to 12 months) or CM were recruited between April and May 2023 from our trust. Patients were approached on HD units or via telephone. Baseline demographic and clinical characteristic data were obtained from electronic patient records. A Clinical Frailty Scale (CFS) assessment was performed for each patient using the CFS app. Patients with a CFS score ≥5 were categorised as frail. Activities of daily living (ADL) were assessed using the KATZ ADL index. Patients completed questionnaires evaluating symptom burden (IPOS-Renal), experience of shared decision making (SHARED questionnaire) and decisional regret (Decision Regret Scale). Information about advance care planning (ACP) was recorded. Mann-Whitney U, independent samples T-tests, Chi-squared, and Pearson's correlation coefficient were calculated using Statistical Package for Social Scientists (SPSS).

Results: Twenty-five HD and 25 CM patients were included with mean age of 74.7 (SD=5.9) and 83.2 (SD=5.2) years old, respectively. Eleven (44%) HD patients and 9 (36%) CM patients were female. The most common co-morbidities were hypertension (n=32, 64%), diabetes (n=16, 32%) and ischaemic heart disease (n=14, 28%). There was no significant difference in frailty (HD n=15 [60%], CM n=17 [74%], p=0.307) or KATZ ADL score between the two groups (p=0.124)

There was no significant difference between mean total IPOS-renal scores (HD 13 [SD=8.5], CM 15 [SD=8], p=0.395). CM patients were significantly more affected by dyspnoea (p=0.014) and drowsiness (p=0.036). HD patients experienced more wasted time for appointments (p=0.001), mostly related to transportation issues.

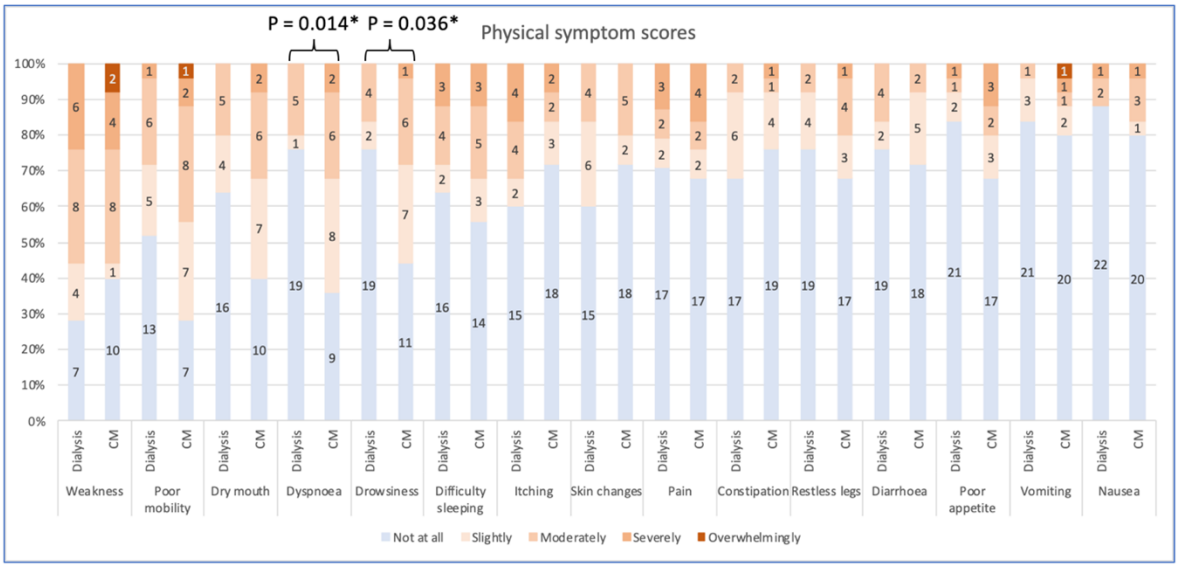

Figure 1: *IPOS-Renal physical symptom scores across both treatment modalities. For each physical symptom, the question is "How has each symptom affected you over the last week?" *: Mann-Whitney U test.*

CM patients had more discussions about other treatment options aside from the one chosen (p=0.036), had their opinions sought more (p=0.038) and felt welcome to consider different options (p=0.018). HD patients felt more informed that there was a preferred medical treatment for their advanced CKD (p=0.006).

HD patients regretted their treatment option more than CM patients (p=0.028). A moderately-negative correlation was found between shared decision making and regret (r= -0.455, p<0.001).

Finally, CM patients had more ACP decisions documented than HD patients (CM n=14 [58%], HD n=6 [26%], p=0.025).

Discussion: Symptom burden was similar between CM and HD patients (see *Figure 1*). HD patients felt less involved during decision making than CM patients and experienced more regret about their treatment choice. It is vital that all treatment options, including CM, are openly and impartially discussed with patients to truly ensure shared decision making and minimise the likelihood of decisional regret.

Unexplained CKD and kidney failure - paediatric, adult and genetic approaches

406: Developing a Personalised Human Proximal Tubular Cystinuria Drug Screening Model

Mr Mohammed Dakhakhini[1], Professor Richard Coward[2], Professor Gavin Welsh[3]

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Biography - Mr Mohammed Dakhakhini

Mohammed did his undergraduate degree in Medical Laboratory Technology from King Abdulaziz University in Jeddah, KSA in 2012. He studied various medical subjects and built a wide-based knowledge in areas such as Clinical Biochemistry, Haematology, Immunology, and Microbiology. He then worked for six years as a Medical Technologist II in the Clinical Biochemistry laboratory in the ministry of National Guard Health Affairs in Jeddah from 2013 to 2019. During his experience he mastered skills of results analysis and corelation, instruments maintenance, quality assurance, and was an active member of creating an alternative working plan to reduce the turn-around time of analysis and CAP preparation committee. In 2020, he perused higher education and got his master's degree (MSc) with a Distinction in Clinical Biochemistry from the University of Manchester. Having studied this extensive course allowed him to gain specialised knowledge in research and subjects such as Endocrinology, Paediatric Biochemistry, and Nutrition and Drug Monitoring. Currently, Mohammed is studying for his PhD at Bristol's medical school in the university of Bristol. His research tests possible treatments of the renal stone disorder 'Cystinuria' on a cellular level and is being supervised by Professor Richard Coward & Professor Gavin Welsh.

Abstract

Introduction: Cystinuria is a rare inherited renal stone disorder that effects 1 in every 2000 people in the UK. Even though drug treatment is available it still imposes huge disadvantages to patients through associated side-effects such as: weight gain, excessive fatigue, loss of taste, and breathing difficulties, all of which lead to poor quality of life. This fact necessitates the need for other therapeutic approaches that can treat the disorder without causing major side-effects. Cystinuria is generally caused by a mutation in one or both cystine channels of ***$b^{0,+}$AT*** or ***rBAT*** which are encoded by the ***SLC7A9*** or ***SLC3A1*** genes. Having these mutations leads to mis-localization of functioning ***$b^{0,+}$AT*** and ***rBAT*** proteins from the plasma membrane of proximal tubular cells (PTC) which translate into a disruption of Cystine re-absorption which in turn leads to urinary Cystine accumulation and stones. This research hypothesizes that repurposing established drug compounds (LOPAC 1280) to re-direct ***$b^{0,+}$AT*** and ***rBAT*** proteins back into the plasma membrane could be a new therapeutic approach. Previously, we investigated that in all tested mutated cell lines, both proteins were mostly trapped in the Endoplasmic Reticulum (ER).

Methods: We elected to study the commonest cystinuria mutation in the UK which is the *p.Met467Thr* mutation in ***$b^{0,+}$AT.*** A Green-fluorescent-protein (eGFP) tagged *p.Met467Thr* human PTEC line was studied. The IN-CELL Analyzer served as the primary working station, with settings optimized for precise measurements. A protocol has been optimised to systematically compare the Pearson's Correlation Coefficient (PCC) of ***$b^{0,+}$AT*** protein co-localization within the ER across different cellular conditions. Control drugs for validation were selected externally and included in the study, with their concentrations and incubation conditions optimized separately.

Results: A successful pilot study with 80 compounds from LOPAC 1280 drug demonstrated ***b$^{0,+}$AT*** protein localisation. Ongoing work encompasses the screening of all 1280 compounds in the mutated cell line (*p. Met467Thr*), aiming to identify additional drugs that can facilitate the translocation of ***b$^{0,+}$AT*** protein to the plasma membrane. This investigation is conducted using our optimized protocol, affirming its robustness in evaluating the impact of compounds on ***b$^{0,+}$AT*** protein co-localization within the ER. We are currently analysing the whole 1280 LOPAC library which will be completed in the next 3 months.

Discussion: We have now established a florescent personalised medicine human PTEC Cystinuria model to identify new treatments for this disease. This model can easily be used for other human Cystinuria gene mutations for a personalised medicine approach.

Viral complications of transplantation: a scientific update

502: Use of Uromune vaccine to prevent recurrent UTIs in Kidney Transplant Recipients

Miss Denise Cunningham, Miss Emma-Louise Kent, Professor Alan Salama, Ms Fiona McCaig, Ingrid Bruno-Snelling

Royal Free Hospital, London

Biography - Miss Denise Cunningham
Denise Cunningham is a specialist renal pharmacist with over 6 years of renal experience. She is responsible for the provision of a comprehensive, patient-centred clinical pharmacy service to all renal patients at the Royal Free London NHS Foundation Trust. Her major areas of interest are transplantation and auto-immune renal disease, she is a qualified non-medical prescriber running weekly acute and chronic transplant clinics. After graduating from The National University of Ireland, Galway with a BSc (hons) in biochemistry she went on to obtain a first class Master of pharmacy degree from Robert Gordon University. In 2012 She started her clinical pharmacy career at The Royal Free London NHS Foundation Trust where she gained extensive experience in a variety of specialist areas before focusing her interest on renal pharmacy. She is an active member of the Renal Pharmacy Group and was involved in the development of The National Institute of Clinical Excellence guidelines for Belimumab in Lupus nephritis and targeted release Budesonide in IgA disease. She has a keen interest in education and training and has been instrumental in setting up a pre-transplant patient education clinic at the Royal Free Hospital.

Abstract
Introduction: In kidney transplant recipients (KTRs), UTIs are common with the highest incidence in the first 12 months post transplantation. There are no current guidelines for treating recurrent UTIs in KTRs but patients are often given prolonged courses of antibiotics, which is contributing to worsening antimicrobial resistance patterns worldwide. Both single and recurrent episodes of UTIs are associated with graft loss, with the latter reaching up to 50% loss at 5 years at our institution. This is comparable to an episode of biopsy proven transplant rejection.

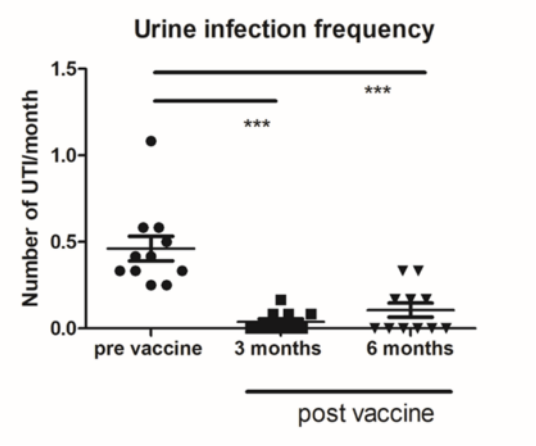
Although attempts at defining reversible risk factors for UTI are always undertaken there remains a cohort of KTR with recurrent UTI, despite treatment with both non-anti-microbial and antibiotic prophylaxis.

Methods: We have instituted an MDT-approved use of Uromune vaccination, in KTR with at least 3 proven infections per year with any of Klebsiella, proteus, enterococcius or E .coli (strains covered by the vaccine). We have collected biosamples, and data on need for antibiotics, hospital admission, drug tolerability, as well as quality of life assessed by EQ50.

Results: To date we have 15 patients dosed with vaccine, 3 discontinued it due to adverse symptoms (palpitations, abnormal taste), one died of longstanding metastatic cancer before treatment completion. We report on 11 who have completed 6 months of follow up.

Number (median (IQR)) of UTI/month pre-vaccine was 0.42 (0.25-1.1), in the first 3 months post vaccine 0 (0-0.17), and within 6 months 0 (0-0.33)($p<0.0001$, one way ANOVA) (Figure). New antibiotic prescriptions/month were significantly reduced following vaccination, 0.25 (0.08-0.6) pre-vaccine to 0(0-0.8) at 6 months ($p=0.02$). We found no significant changes in admissions to date.

Discussion: The vaccine was generally well tolerated and successfully reduced the incidence of UTI in the majority of patients. Longer follow up is required to understand durability and economic impact of vaccination. Future analysis of changes in urinary microbiome and immune responses to the specific bacteria is planned.



Exploring the provision of psychosocial care to the young adult population

99: Kidney replacement therapy decision-making experiences of young adults living with kidney failure

Dr Sarah Ofori-Ansah, Dr Michelle Evans, Professor Calvin Moorley, Professor Lesley Baillie

London South Bank University, Institute of Health and Social Care

Biography - Dr Sarah Ofori-Ansah
Sarah has kidney care experiences and her research interest includes interprofessional learning and decision-making experiences.

Abstract
Introduction: Young adults living with chronic kidney disease experience challenges as the disease progress and can become overwhelmed with the burden of the illness and its management. Young adults who progress to chronic kidney disease stage 5 or kidney failure must decide and select their preferred kidney replacement therapy choice. Kidney healthcare professionals work in collaboration with young adults to deliberate on available therapy options and support them to make an informed or shared decision about their preferred kidney replacement therapy. Evidence suggests that high proportion of young adults living with kidney failure commenced dialysis as their first kidney replacement therapy choice and less received pre-emptive kidney transplantation. However, little is known about young adults' decision-making experiences of selecting a kidney replacement therapy and how decision-making affects their well-being. This study explored the lived experiences of how young adults with kidney failure made decisions concerning selecting their kidney replacement therapy.

Methods: Young adults with kidney failure aged 18-30 years, who have made a kidney replacement therapy decision were purposefully recruited using social media. This qualitative study used interpretive phenomenology; semi-structured interviews were conducted to explore the experiences of eighteen young adults. Thematic analysis of the data was performed to provide an in-depth understanding of young adults experiences of selecting a kidney replacement therapy.

Results: Kidney replacement therapy decision-making was influenced by personal, environmental and psychosocial factors. Participants experienced a change in their self-identity and felt their life had been thrown off track which made their world turn upside down. The study also identified sub-optimal health literacy relating to information about chronic kidney disease and kidney replacement therapy options. Participants struggled to consistently engage in decision-making as equals and felt their voice was not always heard. The participants experienced challenges with communication of therapy implementation and lacked support transitioning from previous lives to the long-term dependence on their chosen kidney replacement therapy. Decision-making and the experiences of choice negatively impacted on participants' psychosocial and mental well-being, but the majority of the participants lacked psychosocial support.

Discussion: Young adults living with kidney failure have unmet information and decisional needs, and experienced inequalities during decision-making. Provision of better health education about options, supporting young adults to engage as an equal in decision-making and incorporating psychosocial support as part of the decision-making process could reduce the negative impact of decision-making experienced. An 'implement talk' phase has been added to the existing three-talk model of shared decision-making to update it to a four-talk model (team talk, option talk, decision talk and implement talk) to address some of the unmet decisional needs

of young adults. The updated four-talk model of shared decision-making could offer a more comprehensive approach to kidney therapy decision-making and support the implementation of chosen therapy. The model could also support young adults transitioning to long-term dependence on a kidney replacement therapy and reduce the psychosocial impact on young adults' well-being.

Pathology case discussions

297: Learning from an uncommon manifestation of a rare mitochondrial disorder

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[1]Newcastle University, Newcastle. [2]The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle

Biography - Dr Hannah Gillespie
Hannah is an Academic Clinical Fellow in Renal Medicine at Newcastle University

Abstract

Introduction: Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome is a maternally inherited mitochondrial disorder.[1] It is a multi-organ disease, with wide clinical manifestations, most often presenting in childhood. MELAS is most often associated with an adenine to guanine transition at position 3243 of mtDNA (m.3243A>G) in the MT-TL1 gene encoding $tRNA^{Leu(UUR)}$.[1,2] Here, we present a case of a patient with a rarer m.324A>T variant whose phenotype included nephrotic syndrome.

Case report: An 18-year-old boy, under the care of the Mitochondrial Disorders team, was referred to Adult Nephrology with new onset oedema, hypertension, and proteinuria. He was known to have MELAS, with a rare m.324A>T mitochondrial DNA pathological variant. He had longstanding gut failure and was TPN dependant. In addition he had bilateral sensorineural hearing loss, visual impairment, pubertal delay, gait ataxia, and a seizure disorder.

He had developed gradually worsening facial and limb swelling and increasingly lethargic. Investigations confirmed hypoalbuminemia (21 g/L), with preserved renal function (sCr 48 umol/L) but marked proteinuria of 10g/L. He was commenced on ace-inhibition and loop diuretics with reasonable effect.

All immunology, including phospholipase A2 receptor antibody, was negative. At biopsy, the appearances were unusual. Abnormal mitochondria were identified. Three segmental sclerosing lesions were present, with extensive segmental basement membrane thickening with the presence of double contouring and subendothelial granular deposits. This was in keeping with a membranoproliferative pattern of glomerular injury, rather than focal segmental glomerulosclerosis (FSGS).

Discussion: This case report has two important learning points. First, we present the unusual renal manifestations of MELAS syndrome in a young patient with a rare genetic variant. Most cases of MELAS have the m.324A>G variant and the corresponding phenotypes are usually Fanconi syndrome or FSGS. Our patient, with membranoproliferative glomerulonephritis, is one of only a handful of patients with a known m.324A>T variant,[3] and one of only three cases in the published literature associated with the clinical phenotype of MELAS.[4]

Second, there is an important practical learning point for the clinical teams who care for patients with mitochondrial disorders. Mitochondrial diseases have a wide range of renal phenotypes.[5] Regular monitoring of patients with known mitochondrial diseases for development of proteinuria (through dipstick testing or urinary protein quantification) and Fanconi phenotypes (such as glycosuria) may enable earlier detection and treatment of renal manifestations before they become otherwise clinically apparent. Recruiting such patients to RaDaR will allow disease progression and longitudinal outcome data to be established for such patients.

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297: IgG4-related disease presenting with nephrotic syndrome due to minimal change disease.

Dr Amy Needleman[1], Professor Michael Sheaff[2], Dr Ruth Pepper[1], Dr Rhys Evans[3]

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Biography - Dr Amy Needleman

Dr Needleman is currently a ST5 Renal Trainee in North Central London. Prior to this she completed her Internal medicine training in London and holds a PG Certification in Medical Education at the Royal College of Physicians.

Abstract

Introduction: IgG4-related disease (IgG4-RD) is a multisystem disease with lymphoplasmacytic inflammation and fibrosis. Affected tissues are infiltrated by IgG4+ plasma cells. IgG4 related kidney disease (IgG4-RKD) occurs in 12% of cases in the UK, usually consisting of tubulointerstitial nephritis (TIN)[1], with reduced excretory kidney function or mass lesion on imaging. One quarter of cases are associated with glomerular disease, predominantly membranous nephropathy. IgA nephropathy and membranoproliferative glomerulonephritis have also been described[2]. Here, we report a case of IgG4-RD presenting with minimal change disease (MCD).

Case presentation: A 67-year-old male of Asian background with hypertension and type 2 diabetes presented with a 4 month-history of systemic upset, 7kg weight loss and migratory joint pains. He was referred to renal with leg swelling, shortness of breath and significant proteinuria (uPCR 1042mg/mmol). His creatinine was 140µmol/L and bloods consistent with nephrotic syndrome (albumin 17g/L, cholesterol 9.3mmol/L). Further investigation demonstrated hypocomplementemia (C3 0.59g/L, C4 <0.02g/L) and raised IgG4 subclass levels (5.29g/L). Ultrasound showed cortical irregularity of both kidneys and a Positron Emission Tomography-Computed Tomography demonstrated multiple avid lymph nodes and uptake in the spleen, pancreas, and prostate (**Figure 1a**).

A diagnostic kidney biopsy demonstrated unremarkable glomeruli on light microscopy with no glomerular immunoglobulin staining (**Figure 1b**). Electron microscopy was consistent with minimal change disease (**Figure 1c**). Additionally, there was a plasma cell rich interstitial infiltrate with strong positive staining for IgG4 (52 IgG+ plasma cells/high power field and 60% IgG4/IgG ratio) fulfilling Raissan's diagnostic criteria for IgG4-RKD[3] (**Figure 1d**). A unifying diagnosis of MCD in the setting of IgG4-RKD was made.

He was treated with prednisolone 60mg daily, alongside conservative measures for the nephrotic syndrome (angiotensin converting enzyme inhibition, furosemide, atorvastatin and heparin). There was no significant glomerular response and he represented to hospital on day 17 with fever and an extremely tender, enlarging erythematous, macular rash on his thigh. A clinical diagnosis of necrotizing fasciitis was made. Despite antibiotics and multiple surgical debridements, he became septic requiring ventilation and kidney replacement therapy. Despite reduction in immunosuppression and intravenous immunoglobulin, he developed Enterobacter and Enterococcus bacteriaemia as well as candida fungaemia resulting in mitral valve endocarditis. This culminated in acute bowel ischemia and the patient died 52 days after initial presentation.

Discussion: Glomerular diseases may be primary processes or secondary to systemic disease (malignancies, infection, and allergy[4]) or medications. MCD is often primary, thought to result from T cell dysfunction and production of circulating permeability factor. Whilst MCD has been reported in Japan in a patient with known IgG4-RD[5], this is the first reported case of IgG4-RD presenting with MCD and the first case of IgG4-related MCD in a patient in Europe. This case highlights both the need to consider IgG4-RD as a secondary cause of MCD (particularly in patients with hypocomplementemia which is not associated with primary MCD) and supports an

increasing awareness of the broad range of glomerular pathologies associated with IgG4-RKD. Finally, the life-threatening complication of necrotizing fasciitis in this case reinforces a rare but serious consequence of corticosteroid therapy.

Figure 1

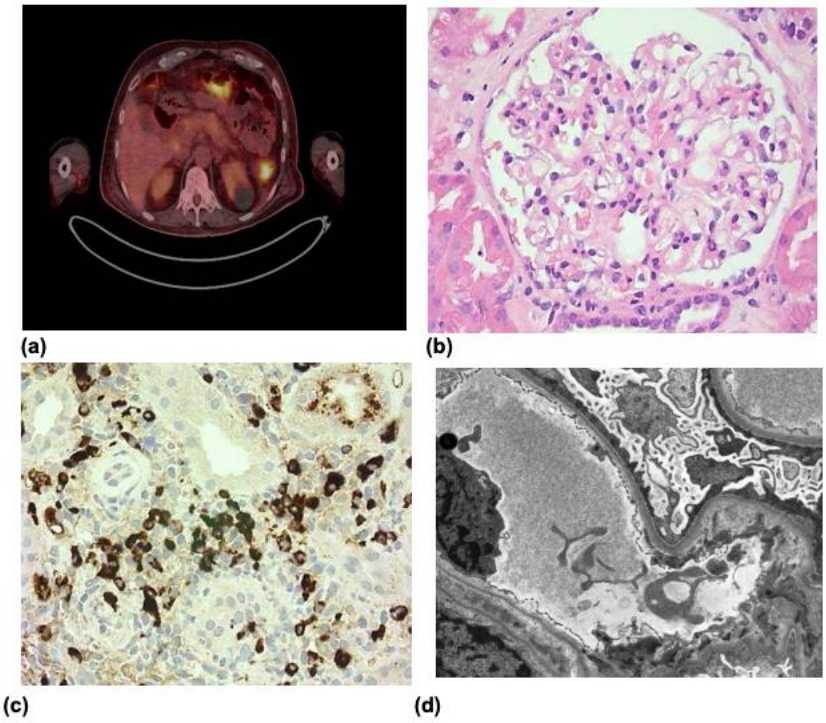

Figure 1: Imaging and histopathology demonstrating minimal change disease in the setting of IgG4-RD

a. PET-CT scan demonstrating splenic uptake and likely pancreatic uptake.
b. Light microscopy (H and E stain; magnification x400) demonstrating a histologically normal glomerulus
c. Light microscopy (IgG4 immunostain; magnification x250) demonstrating multiple IgG4+ plasma cells
d. Electron microscopy demonstrating complete foot process effacement of podocytes with microvillous transformation and an absence of electron dense deposits (x2500)

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332: IgA-dominant infection-related glomerulonephritis associated with Klebsiella Pseudomonas skin infection

Dr Daniel Yeong Hoong Thong[1], Dr Myint Thu Aye[2], Dr Mahzuz Karim[2], Dr Anna Paterson[3], Dr Sathia Thirunavukkarasu[3]

[1]Norfolk and Norwich University Hospitals Foundation Trust, Norwich. [2]Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich. [3]Cambridge University Hospitals NHS Foundation Trust, Cambridge

Biography - Dr Daniel Yeong Hoong Thong

I am a specialty registrar in renal and general internal medicine in the East of England deanery. My interests include learning about research advancements particularly in the field of glomerulonephritis as well as medical education.

Abstract

Case history: A 50 years old man was referred from the Emergency Department due to stage 3 acute kidney injury. He had a background of intravenous substance misuse and Hepatitis C infection. He was not on active antiviral therapy. He complained of a chronic discharging left shin ulcer and generalised malaise. On examination, there was cellulitis surrounding the ulcer, but he was haemodynamically stable.

Blood tests showed serum creatinine 594 µmol/L (baseline 83 µmol/L 2 years prior to presentation), urea 26.4 mmol/L, potassium 6.9 mmol/L, haemoglobin 83 g/L, white cell count 6.9 $x10^9$/L, and platelet count 225 $x10^9$/L. Urine dip showed 3+ blood, 2+ protein and 1+ leucocytes. Anti-neutrophil cytoplasmic antibodies, anti-glomerular basement membrane antibodies, and antinuclear antibodies were negative, C3 and C4 were normal, and there were no detectable cryoglobulins. Serum IgA level was raised at 4.16 g/L. There was no detectable serum paraprotein, and the serum free light chain ratio was normal. Three sets of blood cultures yielded no bacterial growth. Swab from the ulcer grew *Klebsiella pneumoniae* and mixed coliforms. Renal tract ultrasound was normal.

A kidney biopsy was performed. 2 of 16 glomeruli were obsolete, and 3 showed cellular crescents. The glomeruli showed mesangial hypercellularity and segmental endocapillary proliferation, with neutrophils seen in these areas. There was accompanying severe acute tubular injury with patchy focal mixed acute and chronic interstitial inflammation and occasional neutrophil casts within tubules. Immunohistochemistry revealed weak granular IgA deposition within the mesangium and some capillary walls, together with moderate punctate C3 in these areas. There was weak to moderate non-specific staining of the mesangium with C1q and IgM, but no significant IgG. Electron microscopy showed intramembranous, subendothelial, and occasional subepithelial hump-like electron dense deposits.

A diagnosis of IgA-dominant infection-related glomerulonephritis was made. He was commenced on intravenous antibiotics and required temporary haemodialysis. There was partial recovery of his renal function, his a creatinine on discharge was 437 µmol/L.

Discussion: IgA-dominant infection-related glomerulonephritis is an uncommon finding on kidney biopsy. It is differentiated from IgA nephropathy by the findings of neutrophilic endocapillary proliferation, stronger staining for C3 than IgA, and subepithelial hump-like deposits. It is typically associated with *Staphylococcal* infection, although in this case the cellulitis was caused by *Klebsiella pneumoniae*. Unlike classical post-infective glomerulonephritis, renal manifestations typically occur concurrently with the causative infection.

There is no established effective treatment for IgA-dominant infection-related glomerulonephritis. Management is supportive, and immunosuppression is not generally advised. Renal biopsy can confirm the diagnosis and inform prognosis. Outcome is usually poor, with renal function returning to pre-morbid levels in fewer than 20% of patients, and the majority being left with varying degrees of chronic kidney disease.

374: Navigating Complexity: A Case Report of Chronic Kidney Disease with Renal Stone Unravelling a Rare Metabolic Disorder

Dr. Alshymaa Eltahan[1,2], Dr. David Lewis[1], Dr. Seema Rana[3], Professor Darren Green[1,4]

[1]Salford Renal Department, Northern Care Alliance NHS Foundation Trust, Manchester, United Kingdom. [2]Faculty of medicine, Helwan university, Cairo, Egypt. [3]Salford cellular pathology department, Northern Care Alliance NHS Foundation Trust, Manchester, United Kingdom. [4]University of Manchester, Manchester, United Kingdom

Biography - Professor Darren Green

A consultant in nephrology and acute medicine, Honorary Professor of Cardiovascular Medicine, expert advisor to the National Institute for Health and Care Excellence and research lead for the UK Society for Acute Medicine. His research and clinical expertise are on the interaction between the heart and kidneys, primarily the management of heart failure in patients with CKD. He runs a regional specialist service for patients with complex cardiovascular disease involving CKD, heart failure and ARVD.

Abstract

Clinical Presentation: A 48-year-old female of Asian heritage was referred for renal assessment after experiencing recurrent acute kidney injury (AKI) with incomplete recovery between episodes. This was initially attributed to dehydration and interstitial nephritis stemming from long-standing vomiting, a manifestation of gastroscopy-proven erosive gastritis, compounded by the use of high-dose proton pump inhibitors (PPI). Her relevant medical history is of right nephrectomy in 1996 due to recurrent urinary tract infections (UTIs), and previous left renal calculus in 2019 with no visible stones on further CT imaging. Despite living with a single kidney, her baseline eGFR had been normal prior to referral. While unaware of her mother's medical history, her father was recently diagnosed with kidney disease (no clear history) and her sister Wilson's disease.

A kidney biopsy was undertaken given the incomplete eGFR recovery between episodes. The biopsy revealed adequate tissue including 24 glomeruli, no significant glomerular pathology was seen. There is 65% tubulointerstitial atrophy and fibrosis, and yellow to red-brown-tinged crystals within tubular lumina and epithelial cells, prompting a histiocytic reaction. These crystals were birefringent under polarized light and did not stain with Perl's and Von Kossa stain **(Image 1a-d)**. Immunofluorescence was negative for all immunoglobulins and complement fractions. No immune complex/substructure deposits were seen in the glomeruli on electron microscopy.

Blood tests assessing APRT activity indicated values within the carrier range. The patient and her family have been referred for comprehensive genetic testing for APRT genetic mutations.

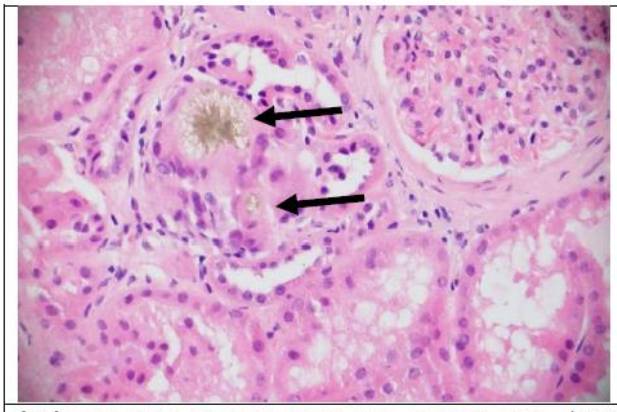
Treatment with Allopurinol 300mg daily resulted in a sustained eGFR improvement from 19 to 33 ml/min/1.73m^2 at 6 months after initiation.

Discussion: Adenine phosphoribosyl transferase (APRT) deficiency, also known as Dihydroxyadenineuria, is a rare autosomal recessive inherited condition leading to kidney stones. If left untreated, up to 25% progress to end-stage kidney disease (ESKD). Although inherited, half of patients present in adulthood and may do so with laboratory findings of CKD rather than specifically with stones**[1]**.

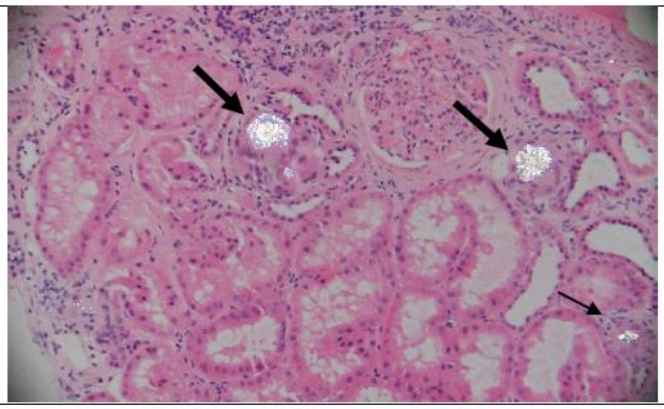
This case highlights the significance of precise diagnosis in calculi-related kidney diseases. Early intervention can alter the trajectory of specific conditions, averting progression to ESKD. This case is unusual in being a carrier of an autosomal recessive condition presenting with full manifestations of the disease.

Patient Consent: The patient has given verbal, documented consent for case publication.

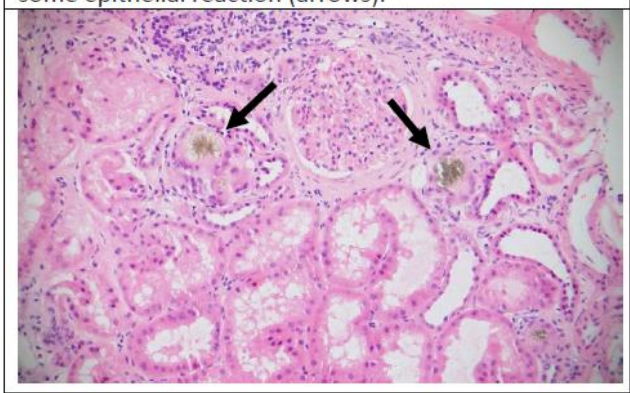
Acknowledgment: We thank all renal and pathology staff members at Salford Care Organisation who contributed to the diagnosis and management of our case.



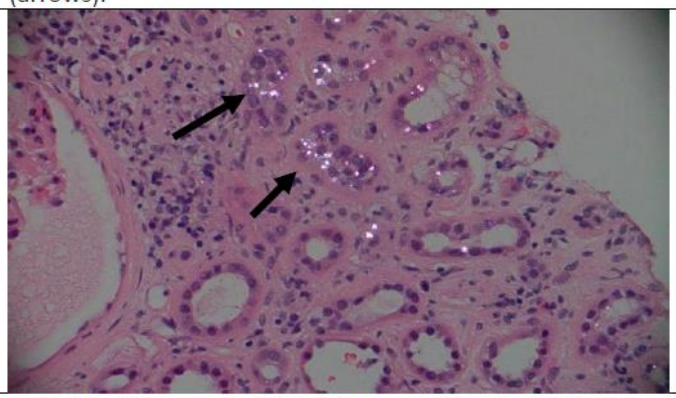
(1a): HE 40X magnification: HE stained slide (40X magnification) showing intratubular yellow to reddish brown tinged crystals within the lumen of tubule with some epithelial reaction (arrows).



(1c): HE with polarised light 20X magnification: HE stained slide under polarized light (20x magnification) showing birefringence in the crystals present in the lumen of tubules (arrows).



(1b): HE 20X magnification: HE stained slide (20x magnification) showing intratubular yellow to red brown tinged crystals within the lumen of tubules (arrows).



(1d): HE with polarised light 40x magnification : HE stained slide under polarized light (40x magnification)showing birefringence in the crystals present in the cytoplasm of tubular epithelial cells (arrows).

Image (1): Light microscopy examination of kidney biopsy.

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Poverty is everyone's business - the case for closer collaboration between health and social care

470: Using Social Prescribing To Address Health Inequalities In A Haemodialysis Population; A Pilot Study

Dr Rebecca Lau, Maisha Ahmed, Tadala Kolawole, Trishala Varma, Cassim Schott, Katie Gallagher, Dr Ben Oliveira, Dr Sajeda Youssouf

Barts Health NHS Trust, London

Biography - Maisha Ahmed
Maisha Ahmed is a Healthy Living Advisor in the renal unit at the Royal London Hospital, supported by funding from the Public Health team. Her role is to support patients who have newly started dialysis to navigate healthcare and other services. This involves triaging patients, signposting, and referring them to relevant hospital and community support services that best meet their needs, to deliver personalised care for all. Her background is in Psychology and she has a deep passion for supporting people with their mental health, to help them reach their potential and optimise well-being. She plans to start a formal counselling qualification under the aegis of the Barts Health Education Academy later this year.

Abstract
Introduction: Social determinants of health are known to have a greater impact on health outcomes than genetics or access to healthcare services. There is evidence that higher deprivation correlates with a greater risk of chronic kidney disease, and worse outcomes.

Barts Health is one of the largest renal services in the UK with 392 patients starting haemodialysis in 2023. It serves one of the most deprived areas of the UK. Late presentation to renal services is high at 30% and poor health literacy is common. Social prescribing can be used to mitigate the negative impact of these wider determinants. Along with the Barts Health Improvement team a successful bid was made to fund a fixed term post for a Healthy Living Advisor (HLA) to support new dialysis patients and address some of the wider determinants influencing their poor health outcomes.

Methods: All new patients (131 total) starting haemodialysis from September-December 2023 were screened by questionnaire, assessing self-reported difficulties in finance, housing, food and support network (see attached figure). An EQ5D score was calculated assessing each patient's quality of life. A folder of resources and services was compiled. From this assessment, the HLA gave advice, signposted or made relevant referrals. This data was then added to an online and secure database.

The HLA was supported by fortnightly meetings with the project team to discuss findings, identify learning, and refine the role.

Results: 131 patients (100% of those starting dialysis in this time) have so far been assessed by HLA. They had an average age of 60.8; 53% were female and 47% were male. 77% were unemployed or retired, 11% remained employed and 11% were on sick leave. 75% of patients lived in the first (25%) or second (50%) most deprived quintiles of deprivation, according to Indices of Multiple Deprivation tool.

Of the 131, 27% reported financial insecurity, 14% reported food insecurity, and 9% reported housing insecurity in the last 2 months. 73% of patients benefited from either simple advice, signposting to relevant services or an

onward referral to another service (see table). The most common area which required input was diet, the majority of which was via dietician referrals, but also included referrals to foodbanks for 10%. The second most common need was financial. This was often support on applying for benefits as well as signposting to grants for kidney patients.

Discussion: The lack of pre-dialysis care in patients presenting late to renal services is known to be associated with adverse outcomes. Improving outcomes in this cohort includes a need to address patient factors such as diet and financial concerns, in order to empower patients to manage their own health and wellbeing. . We have demonstrated that there is a high degree of financial, housing, social and food insecurity within our study population. Our HLA addressed this through simple advice, signposting or direct referrals to onward services. We aim to follow up the impact of this service through qualitative and quantitative assessment of the benefit of support given in the next phase of this project.

Do you have difficulty making ends meet at the end of the month?	No	95
	Yes	36
Do you ever have to miss a meal because you don't have food?	No	110
	Yes	18
In the past 2 months, have you been living in stable housing that you own, rent, or stay in as part of a household?	Yes	117
	No	11
If you were in trouble or felt alone, do you have family or friends you can rely on for support?	Yes	106
	No	23
Do you ever feel unsafe?	No	116
	Yes	13
Do your personal health issues impact your role as a carer	No	111
	Yes	16
Do you want to talk to someone who may be able to help?	No	77
	Yes	51

Figure 1 – Questionnaire used by the HLA to assess degree of self-reports financial, housing, social and food insecurity

Demographics		
No. of patients	131	
Average Age	60.08	
Gender	Female	53% (n=69)
	Male	47% (n=62)
Employment status	Unemployed	60% (n=78)
	Employed	11% (n=15)
	Sick Leave	11% (n=15)
	Retired	18% (n=23)
Indices of Multiple Deprivation Tool	**Quintiles**	
most deprived	**1**	**25% (n=33)**
	2	**50% (n=66)**
	3	**15% (n=19)**
	4	**8% (n=10)**
least deprived	**5**	**2% (n=3)**

Results Table Demonstrating Actions of the Healthy Living Advisor	
Healthy Living advisor Action	
No actions needed	32
Simple Advice Given	45
Signposting to Relevent Service	50
Referral made by HLA to Service	56
Type of advice / signposting / referral	Number
Finance	38
Housing	16
Social	16
Diet	46
Legal	2
Physical/Medical	39

Fun and practical quality improvement – past, present, and future of QI

493: The Design and Implementation of a Multispecialty, Multidisciplinary Acute Kidney Injury Quality Improvement Strategy.

Dr Sacha Moore[1], Dr Sharan Chugani[2], Lisa Fabb[2], Owain Brooks[2], Dr Tim Scale[2]

[1]Cardiff University & Swansea Bay University Health Board, Cardiff, UK. [2]Swansea Bay University Health Board, Swansea, UK.

Biography - Dr Sacha Moore

Qualifying in Medicine from the University of Southampton, Sacha completed the Academic Foundation Programme at North Wales Clinical Research Centre where he gained distinction and the Shergill Dissertation Prize in MRes Applied Biomedical Sciences Research. Having obtained MRCP(UK) and completed Internal Medicine Training, Sacha is a Welsh Clinical Academic Track Fellow and Specialty Registrar in Nephrology & General Internal Medicine. His main research interests lie in the cardiovascular sequelae of CKD, multimorbidity and AKI, and span basic science, translational and clinical research.

Abstract

Introduction: The recent NEPHwork acute kidney injury (AKI) audit confirmed the high in-hospital mortality (approximately 30%) associated with AKI stages 2 and 3, with the wider literature confirming community-acquired AKI also contributes to morbidity and mortality considerably. Moreover, the audit demonstrated significant variation in the timely delivery of pivotal investigations and interventions. The National Institute for Health and Care Excellence (NICE) Quality Standard 76, published in April 2023, further highlights the need for improvement in AKI care with particular attention to timely clinical reviews and appropriate follow-up. In response to this clear need for multifaceted improvement in AKI care, and bolstered further by shared learning at the UK Kidney Association AKI Strategy Meeting in September 2023, we report the design and implementation of an AKI quality improvement strategy.

Methods: A multispecialty, multidisciplinary AKI working group was established in mid-2023, meeting quarterly, encompassing nephrologists, acute physicians, emergency physicians, intensive care physicians, primary care physicians, critical care outreach nurses, pharmacists and biomedical scientists representing all health boards across Wales. The working group have generated a new agreed set of all-Wales AKI guidelines (a number of example pages in figure 1) to support AKI investigation and management in both primary and secondary care, including the creation of guidance on a mobile application.

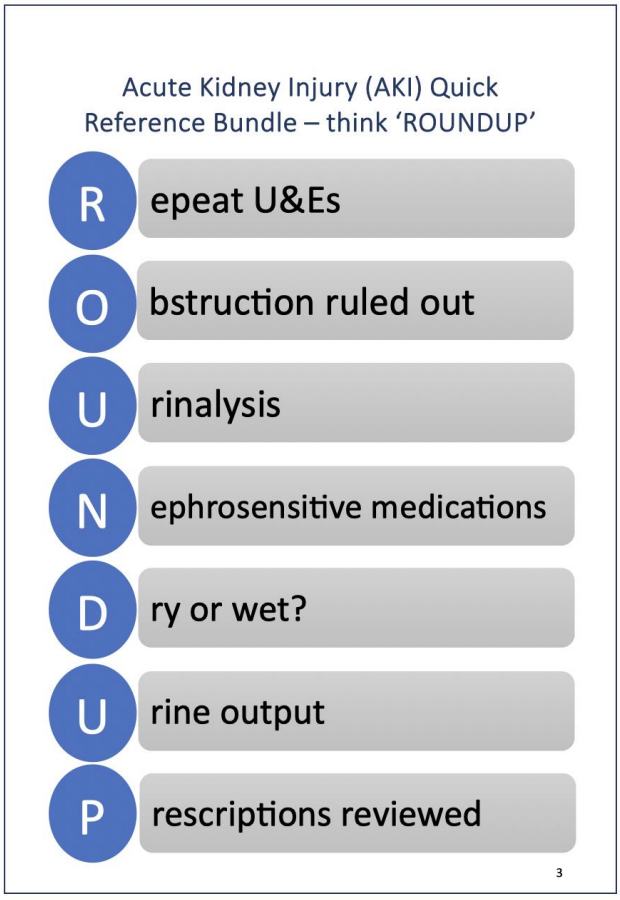
A programme of implementation has been designed to address key steps identified in the AKI care process map with PDSA cycles for each (as per example in figure 2). Implementation can be delivered at local sites by localised teams using this framework to support guideline usage. Areas for improvement include undergraduate medical education, postgraduate medical education, nursing education, allied health professional education, early pharmacist review pathway, implementation of the 'ROUND-UP' mnemonic and quick reference cards, and AKI hot clinic creation to support discharge and follow-up. Each area is targeted as its own quality improvement initiative to ensure clear run chart mapping of results, as well as mapping cumulative overall improvements in AKI care.

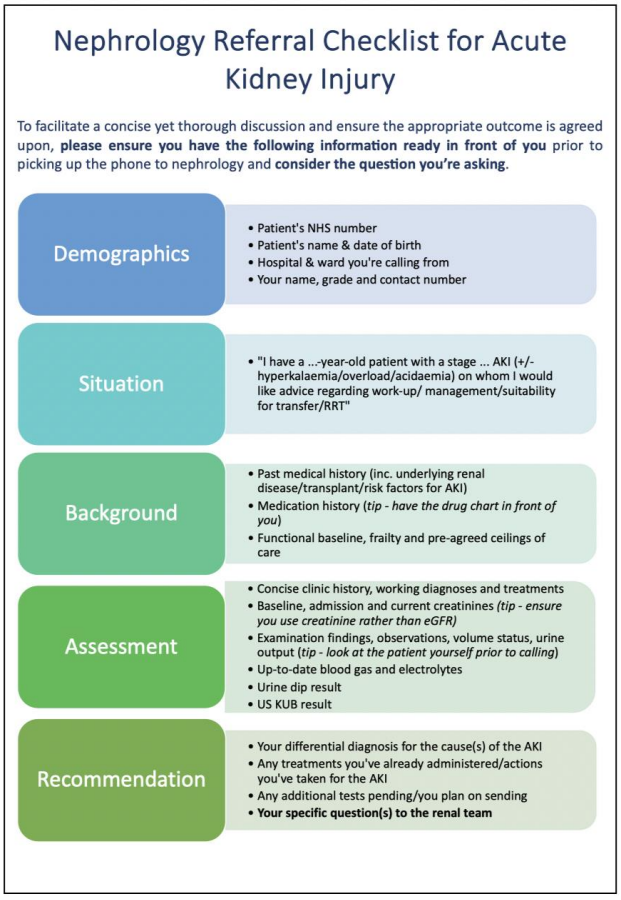
Results: Agreed outcomes include subjective improvement in knowledge and confidence in managing AKI across multiprofessional groups, evidence of improved application of ROUNDUP principles, and concordance with discharge and follow-up . The results of initial quality improvement measure implementation are expected imminently.

Discussion: Through a multispecialty, multidisciplinary approach, we have designed and commenced delivery of all-Wales AKI guidance with associated improvement strategies that are realistic and targeted to improve AKI care. Here, we report our strategy. This multidisciplinary approach ensures sustainability of change and interventions over time and the utilisation of expertise from across the professional spectrum.

With thanks to all members of the All Wales AKI Group for their work in guideline development.

Figure 1 - Example pages from the new All Wales AKI Guidelines





Diagnosis

Broadly, the pathophysiological mechanism of AKI can be divided into pre-renal, intra-renal and post-renal causes.

Pre-renal	Intra-renal	Post-renal
• Hypovolaemia • Hypotension • Hypoperfusion/ Renovascular	• Acute tubular necrosis • Glomerular inflammation • Interstitial inflammation	• Urinary tract obstruction

The most common cause is a pre-renal cause but, if this is sustained, the most common reason for a progressive or severe AKI is acute tubular necrosis (ATN). ATN will often result in an oliguric AKI that requires time and removal of the precipitant to allow for recovery (note a polyuric phase can occur during post-ATN recovery). AKIs are often multifactorial. Consider these potential causes when undertaking your clinical assessment and investigations.

Medication Review

There is no single approach to medications in AKI. A full medication review should be undertaken **in conjunction with a pharmacist** where possible, considering medications that may have contributed to the AKI alongside pre-existing medications which might need to be avoided/temporarily withheld/used with caution/therapeutic alternatives. The term 'nephrotoxic' is purposefully avoided and there is a **move towards the term 'nephrosensitive'**. The following are common medication culprits:

Consider avoiding	Consider temporarily withholding	Consider dose adjustment or switch to alternative
• Aminoglycosides *e.g. gentamicin* • NSAIDs *e.g. ibuprofen* • Trimethoprim (*n.b. may cause pseudo-rise in creatinine*) • Amphotericin	• ACEi *e.g. ramipril* • ARB *e.g. candesartan* • ARNI *e.g. Entresto* • Metformin • SGLT2 inhibitors *e.g. dapagliflozin* • MRA *e.g. spironolactone* • Diuretics *e.g. furosemide* ***if clinically dry***	• Anticoagulants *e.g. low molecular weight heparins, direct oral anticoagulants* • Opiates *e.g. switch morphine to oxycodone* • Gabapentinoids *e.g. gabapentin, pregabalin will accumulate* • Antimicrobials *e.g. dose reduce Tazocin, Aciclovir*

Investigations

The following investigations should be undertaken as standard in patients with AKI:

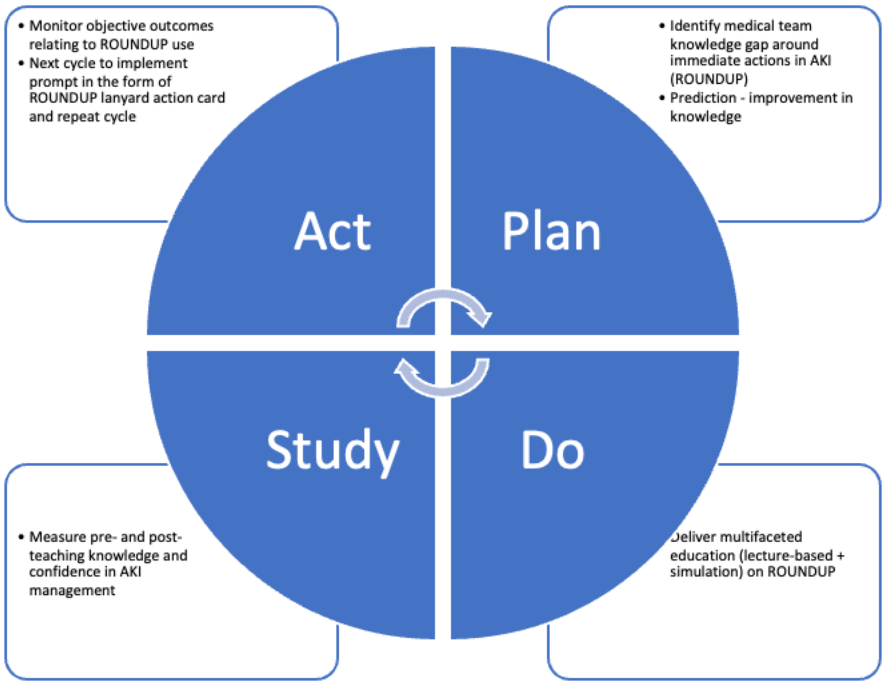
- **Blood tests** to include FBC, U&Es, LFTs, Bone Profile, CRP, Bicarbonate (if available).
- **Venous blood gas** (assessment of acid-base balance including lactate).
- **Urinalysis** (predominantly for blood & protein).
- **Blood cultures** and **urine MC&S** if clinical concern regarding infection/sepsis.
- **Bladder scan** (to exclude bladder outlet obstruction).
- **ECG** (for rhythm and in case of hyperkalaemia).
- **Chest x-ray** (for fluid overload/infection/pulmonary haemorrhage).
- **Urinary tract imaging** (US KUB or CT KUB if US not readily available) – perform within 6hrs if concern regarding obstruction/single kidney, or within 24hrs if high stage AKI/failure to response to initial treatment.

In those with a urine dipstick positive for blood and/or protein, or with unexplained or worsening stage 3 AKI, or with clinical concern regarding the possibility of intrinsic renal pathology (e.g. systemic symptoms), additional investigations may be warranted. **If advised to do so by a senior clinician**, some or all of the following investigations may be requested (frequently termed the 'renal screen'):

ANCA *(vasculitis)*	ANA, anti-dsDNA, C3, C4 *(SLE)*	Urinary ACR/PCR *(proteinuria quantification)*
LDH, blood film, reticulocytes, haptoglobin (*TMA, if thrombocytopaenia)*	Anti-GBM *(Goodpastures)*	Serum electrophoresis & free light chains (urine Bence Jones if FLC not available), immunoglobulins *(myeloma)*
CK *(rhabdomyolysis)*	HbA1c *(diabetes mellitus)*	Virology *(Hep B/Hep C/HIV nephropathy)*

Additional investigations including ENA, cryoglobulins, ASOT, ACE, anti-PLA2R and urinary electrolytes may be requested under specialist guidance.

Figure 2 - Example PDSA Cycle



"Get realist" – applying realist methodology to describe AKI e-alert interventions – interactive session

267: The Kidney-specific Psychosocial ASSessment and support (Kidney PASSPORT) feasibility trial: Learning from the Assistant Wellbeing Practitioner (AWP renal) role.

Dr Alex Hamilton[1], Dr Rebecca Bell[2], Professor Paul Farrand[3], Miss Sam Strickland[3]

[1]Royal Devon University Healthcare NHS Foundation Trust, Exeter, UK. [2]North Bristol NHS Trust, Bristol, UK. [3]University of Exeter, Devon

Biography - Dr Alex Hamilton

Alex is a Consultant in Renal Medicine at the Royal Devon University Healthcare NHS Foundation Trust and a Senior Clinical Tutor at the University of Exeter Medical School. He has an interest in transition and young adult care and preventative intervention for common mental health difficulties in CKD.

Abstract

Introduction: Psychosocial interventions for depressive and anxiety symptoms are effective in CKD, but studies mainly focus on people on dialysis. Little is known about the role of screening and prevention of common mental health difficulties in early CKD.

This trial assessed the research feasibility of an intervention to screen for psychological distress in CKD and deliver prevention approaches for sub-threshold symptoms. The intervention was facilitated by an Assistant Wellbeing Practitioner (AWP), a Band 3 healthcare assistant familiar with renal services and upskilled with specific competency-based training.

Methods: We conducted a mixed-methods, one-year, single-centre, prospective, single-blind, wait-list, randomised controlled feasibility trial. We anticipated screening 250 individuals to identify 100 eligible, with a 40% screening positivity rate, a 45% participation rate and 20% attrition rate, to give 36 participants in the feasibility study. Primary outcomes are shown in Table 1. Potential participants were screened using an online self-completion questionnaire. Participants were randomised to 6 months of immediate or wait-list intervention.

Data was collected using online self-report surveys, clinical research forms and semi-structured qualitative interviews. The trial was overseen by a steering committee and received the relevant ethics approvals. Funders included Kidney Care UK, the British Renal Society, the Royal Devon and Exeter Research Capacity Awards and the Exeter Kidney Unit development fund.

Results: We approached n=233 people. Feasibility outcomes are shown in Table 2. Due to logistical issues an extension was obtained and in total n=24 participants were recruited, agreed by the steering committee.

All clinical research forms were completed. The most common intervention components were self-management and liaison with the clinical team. The median (interquartile range) difference in baseline and post intervention PHQ-9 score was -5 (-7, 0), n=19, p=0.003) and GAD-7 score was -7 (-8, -2), n=19, p=0.0002).

Qualitative findings showed the AWP was seen as filling in the gaps left by other parts of the service. Key themes were accessibility, time availability, empathy, patient empowerment, and ability to empower the individual. Balance – especially family, work and health - was noted to be a challenge for participants. Importantly, the AWP was able to help participants overcome previous negative experiences.

The trial provided valuable learning regarding role implementation, including recruitment, training, work patterns, everyday practicalities, and supervision arrangements.

Discussion: We propose a novel intervention for screening and addressing early mental health problems in people with CKD. A single-centre feasibility design was appropriate. The screening positivity rate was lower than anticipated, informing samples for future trials. Outcome data collection via self-report surveys was not feasible. The intervention was well received, with the AWP being valued and self-help and clinical liaison being core elements. Significant reductions in depression and anxiety screening scores were observed.

Despite the rigorous design, limitations included slow initial recruitment impacting the sample size and AWP role vulnerability. Future work includes adapting the AWP training and role based on trial learning and considering suitability for other long-term conditions.

In conclusion, the AWP role shows promise in routine screening for and prevention of common mental health difficulties in CKD.

Table 1

Primary outcomes	Participant recruitment rate (calculated by assessing the proportion of those who screen positive, that complete the consent form) Participant retention rate
Secondary outcomes	Consent to screen rate Screening positivity rate Randomisation acceptability (assessed via qualitative interviews) Completion of self-reported outcome measures Adherence to the intervention

Table 2

Participant recruitment rate Participant retention rate	46% 87%
Consent to screen rate Screening positivity rate Randomisation acceptability Completion of self-reported outcome measures Adherence to the intervention	95% 24% Deemed acceptable 67%, 52%, 43% and 38% at the specified time points In the immediate group, 4/12 patients received the intervention compared to 11/12 in the delayed group. Of those not receiving the intervention, 2 were referred to talking therapy services, 1 did not start and 6 discontinued (3 lost to follow up and 3 deaths unrelated to the trial). There was a median of 7 AWP appointments (n=4 in immediate group and 11 in the delayed group).

Study Registration Number
ISRCTN82492510

Best science abstracts

477: Downregulation of urinary microRNA 133 predicts progression of IgA nephropathy

Dr Daniel Smith[1,2,3], Miss Sophie Hughes[1], Dr John Watkins[4], Dr Katherine Simpson[5], Professor Donald Fraser[1], Professor Timothy Bowen[1]

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Biography - Dr Daniel Smith

Daniel Smith is a post-doctoral researcher at the Wales Kidney Research Unit, working on the discovery and validation of microRNA biomarkers in urine through PCR based methods and their subsequent detection at point of care through development of electrochemical biosensors. Daniel completed his master's MChem in Chemistry at Cardiff University in 2013 before completing his PhD between the schools of medicine and chemistry in electrochemical microRNA detection in 2017. Since that time Daniel has been a key member of the Wales Kidney Research Unit and has developed his research to include not only the production of biosensors, but the discovery and validation of new microRNA biomarkers in urine and plasma through RT-qPCR based methodologies. Daniel has also been working part-time as a virtual lecturer in pharmacology at Queen Margaret University in Musselburgh Scotland since Jan 2021, and also in project management, taking up a part time position as an assistant project manager for the upcoming NURTuRE AKI program run by KRUK in 2022.

Abstract

Introduction: Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide and reliable diagnosis requires kidney biopsy. Around 30% of people with IgAN progress to chronic kidney disease (CKD) and then renal failure, which requires transplant or dialysis. Proteinuria analysis fails to identify up to 50% of progressive cases, and does not provide patient-specific information. Novel, non-invasive biomarkers for diagnosis and progression of IgAN are therefore highly desirable and have significant potential to improve clinical outcomes. We have described altered expression profiles of microRNAs (miRNAs) in people with delayed graft function following transplantation, acute kidney injury and diabetic kidney disease (DKD). Most recently, we identified a panel of urinary miRNAs that distinguish between rapidly progressing and stable DKD pathologies. Consequently, we hypothesised that urinary miRNAs could act as diagnostic IgAN biomarkers and distinguish between rapidly progressing and stable IgAN. Here we describe the first non-invasive miRNA biomarkers for IgAN diagnosis and prediction of IgAN progression.

Methods: Using Taqman low density array (TLDA) RT-qPCR technology, we analysed 754 urinary miRNAs and, in selected cases, followed up with individual RT-qPCR assays for miR-133a and miR-133b. TLDA ouput data were analysed using the online Thermo Fisher Scientific software in the Amazon Web Services cloud. Two-tailed, unpaired Student's t-tests were used to analyse statistical differences between the experimental groups. Urine miRNAs were analysed from 20 people with a stable IgAN phenotype (eGFR decline <2 mL/min/yr), 18 people with progressive disease (eGFR decline >2 mL/min/yr) and 20 unaffected individuals. MiRNA expression profiles were compared between IgAN (n = 38) and controls (20), as well as progressive (18) and stable disease (20). Predictive models were used to test the utility of our miRNA data to distinguish between people with IgAN and controls, or between people with stable and progressive IgAN phenotypes. Receiver operating characteristic (ROC) curves were plotted and area under the curve (AUC) values calculated.

Results: Comparison of TLDA urinary miRNA profiles between IgAN and unaffected individuals highlighted the biomarker potential of miR-191 ($p<0.005$), miR-657, miR-659 and miR-892b (all $p<0.0001$), with the latter three significantly upregulated in IgAN. The combined data for these transcripts showed 100% discrimination between people with IgAN and control individuals, with a 1.0 AUC following ROC curve analysis. Comparing TLDA profiles of stable and progressive IgAN phenotypes identified miR-133a and miR-133b (both $p<0.005$) as the most discriminatory biomarkers, both showing significant downregulation in the progressive IgAN phenotype. Individual RT-qPCR analyses of these transcripts yielded a combined AUC of 0.944.

Discussion: We have identified a novel urinary miRNA profile that identifies IgAN. We have also shown, for the first time, that detection of downregulated urinary miR-133 predicts IgAN progression. Three human genomic loci are sites for miR-133 transcription. Primary miRNAs transcribed from loci on chromosomes 18 and 20 give rise to mature miRNAs miR-133a1-3p and miR-133a2-3p, both of which have the identical nucleotide sequence 5'-UUUGGUCCCCUUCAACCAGCUG-3' and were therefore detected as miR-133a. A primary miRNA derived from a third locus, on human chromosome 6, yields mature miR-133b-3p with the sequence 5'-UUUGGUCCCCUUCAACCAGCU**A**-3', detected in this study as miR-133b. We are currently analysing these markers in an independent cohort of 196 IgAN and 37 non-IgAN urine samples as controls from the National Unified Renal Translational Research Enterprise (NURTuRE-CKD) biobank to support the findings described above.

440: Single-nucleus RNA sequencing uncovers diverse renal stromal cell types, states and dynamics during kidney growth

Dr Irina Grigorieva[1], Dr Yueh-An Lu[2], Dr Tanya Smith[1], Dr Barbara Szomolay[1], Dr Sumukh Deshpande[1], Dr Soma Meran[1], Professor Timothy Bowen[1], Professor Donald Fraser[1]

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Biography - Dr Irina Grigorieva

I am a Research Associate at the Wales Kidney Research Unit (WKRU) in Cardiff University. I have established an independent research niche within WKRU following my Marie Curie Fellowship at the Medical University in Vienna. My research focuses on molecular mechanisms underlying kidney development, repair and regeneration. I study transcription factors, long non-coding RNAs and matrix proteins that regulate renal stromal cell differentiation, heterogeneity and repose to injury using a variety of cutting-edge techniques including genetic models and lineage labelling, single-cell transcriptomics and multiplexed immunofluorescence imaging.

Abstract

Introduction: Renal stromal mesenchymal cells are essential for tissue homeostasis and mediate both recovery and progression of kidney damage. In development, stromal cells promote nephron progenitor differentiation and vasculature patterning. In mature kidney, they reside between the tubules providing optimum micro-environments and inductive signals to support tubular repair. However, stromal cells also drive excessive fibrosis and inflammation. Underlying these diverse responses are molecularly distinct stromal cell types, but their biological functions and factors that influence subtype differentiation are unknown. To better understand stromal-tubular cell interactions we have characterised stromal cell transcriptomes in growing mouse kidneys when tubular epithelial cells undergo extensive proliferation to increase nephron length. Our data provides a high-resolution atlas of stromal cell types, uncovers transient cell states associated with nephron growth and reveals novel rare stromal cell populations.

Methods: Kidneys were retrieved from 1, 2, 4, and 12-week-old mice (n=4 per group, 16 mice in total) and nuclei were isolated for single-nucleus library preparation (10X Genomics), RNA sequencing (Illumina NextSeq 550) and bioinformatical analyses (Seurat). Renal stromal cells were genetically labelled with fluorescent tdTomato by Foxd1-driven Cre-recombinase. Kidneys were evaluated histologically by multiplex immunofluorescence to validate distinct cell populations.

Results: Unbiased clustering analysis was performed on 68,775 nuclei obtained from whole kidneys. All expected cell types were identified in the primary analysis. Sub-clustering was performed on 10,509 *Pdgfrb*+ nuclei which uncovered 18 distinct stromal cell clusters. Differential gene expression analysis identified unique marker genes enriched in each cluster and pathway analysis (IPA) inferred functional roles of each subtype. Time-point analysis showed a marked decline in stromal cell abundance from 31.6% of total cells in 1-week-old kidneys to 3.5% in 12-week-old kidneys. This was inversely correlated with tubular epithelial cell number and was validated in kidney sections. Notably, stromal cell clusters were dynamic during kidney growth: two mega-clusters were identified at early time-points (comprising 38% of total stromal cells) and were enriched in pathways associated with ECM organisation (collagens and MMPs), signalling by MET and axonal guidance (Semaphorin and Netrin signalling), these clusters were absent at later time points and replaced by clusters rich in metabolic pathways such as oxidative phosphorylation. Other clusters did not show change in gene expression or abundance during kidney growth (e.g. *Ren1+* cells). RNA-velocity analysis revealed further

differentiation trajectories. Rare stromal cell populations were identified in mature kidney (clusters 11, 15, 16 and 17) with distinct expression profiles. Ongoing work is focussed on ligand-receptor analysis to identify pathways underpinning stromal-epithelial interactions, and spatial validation of stromal cell types in kidney sections to determine their abundance, localisation and temporal dynamics during kidney development, growth and disease progression.

Discussion: Our snRNA-seq analysis provided high-resolution insights into kidney stromal cell heterogeneity revealing 18 discrete cell clusters with unique transcriptomes in the growing mouse kidney. We have identified transient stromal populations and signalling pathways associated with tubular proliferation and nephron growth. This insight may help us to develop targeted therapies to promote tubular repair post kidney injury.

431: Spatial and single cellular profiling of human IgAN renal biopsies reveals cell-type specific disease signatures and cellular crosstalk within heterogeneous tissue.

Dr. Jessica Kepple[1], Dr. Joanna Hester[2], Dr. Fadi Issa[2], Dr. Rui Qi[1], Dr. Matthew Brook[3], Dr. Thomas Connor[3], Dr. Katherine Bull[1,3]

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Biography - Dr. Jessica Kepple

I graduated from the University of Florida, USA with a dual BS/BA in Microbiology and Anthropology. Subsequently, I completed my PhD in Molecular Biology and Physiology at the University of Alabama, Birmingham, USA as part of the prestigious Comprehensive Diabetes Research Center. Under the supervision of Dr Chad Hunter, I investigated various aspects of brown adipose biology. In particular, my research illuminated novel transcriptional co-regulators governing tissue function and applications of brown adipose as an islet transplantation site. Starting in November 2021, I will begin as a University of Oxford- Novo Nordisk Postdoctoral Research Fellow in the lab of Dr Katherine Bull and Professor Richard Cornell (NDM) and Dr Ramneek Gupta (NNRCO). The focus of my research is to identify early modulators of kidney disease in human renal transplant tissue. To complete this project, I am developing and utilizing integrated imaging 'omics' platforms that can be applied to renal biopsies to reveal causative pathways and possible drug targets. In addition to traditional snRNA-Seq transcriptomic methods, I employ spatial transcriptomic, LCM-target MS proteomics, and CRISPR-Cas9 edited renal organoids as methods to explore novel molecular factors driving renal disease.

Abstract

Background: IgA nephropathy (IgAN), arising from the aberrant deposition of IgA1 polymeric immune complexes within renal glomeruli, is the most common primary glomerulonephritis worldwide. Conventional histological MEST-C classification aids earlier risk prediction, but to improve classification and identify new therapeutic targets we need to better understand molecular disease pathways. Integrated spatial and single nuclei transcriptomic profiling of human renal biopsy tissue may provide novel insight into early cellular changes in key glomerular cell types including mesangial cells and podocytes within a spatial context.

Methods: Renal biopsy cores from IgAN patients and pre-implantation donor kidney controls were processed for clinical histology, single-nuclei RNA sequencing (snRNA-Seq), and spatial transcriptomics. SnRNA-Seq libraries were integrated and analyzed using R software to assess cell composition and differentially expressed genes between biopsy types. Glomerular and immune regions of interest were defined in formalin-fixed paraffin-embedded (FFPE) renal biopsy sections and profiled via the GeoMx Digital Spatial Profiler, with subsequent analysis of bulk gene expression using GeoMx data analysis suite and R.

Results: snRNA-Seq identifies all key glomerular and tubular cell populations in addition to immune cell types. IgAN kidneys have relative reductions in podocyte cell numbers compared to mesangial cells, indicating podocyte loss, and increased immune cells compared to controls. Differential gene signatures associated with IgAN include cell cycling in podocytes, cytoskeletal rearrangement in immune cells, and extracellular matrix remodeling in mesangial cells. The spatial analysis provides an enriched glomerular gene expression dataset, demonstrating altered gene pathways associated with immune cell crosstalk and extracellular matrix accumulation in IgAN diseased glomeruli, with distinct differences between early and late disease and between glomeruli within the same biopsy. Immune signaling changes include increased lipid antigen presentation in

IgAN glomeruli. Deconvolution of spatial transcriptomic data reveals enrichment in specific immune cell populations including NK cells, B cells, T cells, and macrophages in severely diseased tissue.

Discussion: Multiomic cellular profiling allows us to reveal novel cell-type specific disease signatures in patient biopsies and highlights cellular crosstalk, and both inter- and intra-sample heterogeneity. Using conventional renal biopsy cores, we identify major renal cell types and infiltrating immune cells and highlight differential immune signaling and glomerular podocyte loss. This approach is scalable, and results will be integrated to identify novel therapeutic targets and improve disease stratification and classification.

85: Evaluation of a proteomic signature, coupled with the kidney failure risk equation, for predicting end stage kidney disease in a chronic kidney disease cohort

Mr. Carlos Raul Ramirez Medina[1], Dr. Ibrahim Ali[2], Dr. Ivona Baricevic-Jones[2], Prof. Moin Saleem[3], Prof. Anthony Whetton[4], Prof Nophar Geifman[5]

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Biography - Mr. Carlos Raul Ramirez Medina
Research Associate at the University of Manchester. MSc in Health Data Science. BSc. Computer Science.

Abstract

Introduction: Early identification of patients at high risk of developing end-stage renal disease (ESRD) is crucial for optimising patient care, implementing targeted prevention strategies, and allocating resources effectively. While the Kidney Failure Risk Equation (KFRE) has emerged as a more accurate tool for ESRD risk than static eGFR-based thresholds, it lacks insights into individual patient-specific biological mechanisms driving ESRD. This study aimed to evaluate the KFRE in a UK-based advanced CKD cohort and explore whether the incorporation of a proteomic signature could enhance the prediction of developing ESRD within 5-years.

Methods: Using the Salford Kidney Study biobank, a UK prospective cohort of over 3,000 non-dialysis CKD patients recruited since 2002, we identified 433 patients meeting our inclusion criteria: (1) a minimum of four eGFR measurements over a two-year period and (2) a linear eGFR trajectory. Plasma samples were obtained and analysed for novel proteomic signals using SWATH-Mass-Spectrometry (MS), generating a digitised proteomic profile for each patient. The 4-variable UK-calibrated KFRE was calculated for each patient based on their baseline clinical characteristics. ESRD was defined as (1) initiating long-term haemodialysis or peritoneal dialysis, (2) receiving a renal transplant, or (3) initiating follow-up in a conservative care clinic within five years from baseline. The Boruta machine learning algorithm was used for feature selection (of proteins most contributing to differentiation between patient groups). Logistic regression was employed for estimation of ESRD prediction by (1) proteomic features; (2) KFRE; and (3) proteomic features alongside KFRE. Statistical analysis and machine learning approaches for discovery were performed using the computing environment R.

Results: SWATH maps (on 433 patients with 943 proteins quantified) were generated and investigated in tandem with available clinical data to identify potential progression biomarkers. Through differential expression analysis and supervised machine learning algorithms for feature selection, we identified a set of proteins (SPTA1, MYL6 and C6) that, when used alongside the 4-variable UK-KFRE, modestly improved the prediction of 5-year risk of ESRD (AUC= 0.75 vs AUC=0.70). Functional enrichment analysis using the identified proteomic signature revealed Rho GTPases and regulation of the actin cytoskeleton pathways to be statistically significant, inferring their role in kidney function and the pathogenesis of renal disease.

Discussion: The proteomic analysis of an advanced chronic kidney disease (CKD) cohort identified that proteins SPTA1, MYL6 and C6, when used alongside the 4-variable UK-KFRE achieve an improved performance when predicting a 5-year risk of ESRD. Specific pathways implicated in the pathogenesis of podocyte dysfunction were also identified, which could serve as potential therapeutic targets. The in-depth proteomic characterisation of this CKD cohort identified potential therapeutic targets and is a step forward in understanding the pathogenesis

of renal disfunction. The findings of our study carry implications for comprehending the involvement of the Rho family GTPases in the pathophysiology of kidney disease, advancing our understanding of the proteomic factors influencing susceptibility to renal damage.

390: Sparsentan has direct effects on the glomerular capillary wall to attenuate increased permeability after exposure to nephrotic syndrome plasma

Michael Crompton[1], Judy Watson[1], Elizabeth Colby[1], Wilmelenne Clapper[2], Celia Jenkinson[2], Bruce Hendry[2], Radko Komers[2], Moin Saleem[1], Gavin Welsh[1], Rebecca Foster[1], Simon Satchell[1]

[1]University of Bristol, Bristol, UK. [2]Travere Therapeutics, Inc, San Diego, USA

Biography - Michael Crompton

Michael Crompton completed his BSc (Honours) in Molecular Biology with Biochemistry at the University of Durham in 2007. In 2008, he worked as an Associate Scientist in the Transgenic Technologies group at GlaxoSmithKline R&D. In 2010, he undertook a PhD in the Genetics and Pathobiology of Deafness group at MRC Harwell and the University of Oxford with Prof. Steve Brown, identifying a mutation in Nisch that causes otitis media in a mouse model via LIMK1 and NF-κB pathways, which he completed in 2014 (funded by Medical Research Council). Michael continued his research in hearing loss as a post-doctoral Research Associate in the UCL Ear Institute, University College London with Dr Sally Dawson, investigating the genetic basis of otosclerosis (funded by Action on Hearing Loss). In 2019, he moved to Bristol Renal, Translational Health Sciences, University of Bristol as a post-doctoral Research Associate with Prof. Simon Satchell and later with Dr Becky Foster. Since then, he has been interested in investigating mineralocorticoid receptor-mediated glycocalyx damage (funded by Kidney Research UK), endothelial glycocalyx restoration to prevent proteinuria-associated damage (funded by British Heart Foundation) and glomerular endothelial glycocalyx in nephrotic syndrome (funded by Travere Therapeutics, Inc).

Abstract

Introduction: The glomerular endothelial glycocalyx (eGlx), a luminal layer of proteoglycans, glycoproteins and glycolipids, forms the first part of the glomerular filtration barrier (GFB). Nephrotic syndrome (NS) describes a group of pathologies of the renal glomerulus that result in proteinuria and is associated with glomerular endothelial dysfunction. Current treatments are broad and non-specific. Sparsentan is a single-molecule dual endothelin type-A and angiotensin II type 1 receptor antagonist that has received accelerated approval in the United States for the reduction of proteinuria in adults with IgA nephropathy at high risk of disease progression. Our validated glomerular permeability assay directly measures the albumin permeability (Ps'_{alb}) of capillary loops within individually trapped glomeruli [1]. This ex vivo assay is independent of haemodynamic factors and tubular albumin handling – factors known to affect urine protein concentrations. This work examines whether sparsentan could reduce glomerular albumin permeability in NS, by preserving the eGlx to maintain the GFB.

Methods: Human NS plasma samples were collected under ethical consent from 3 patients that had undergone plasma exchange from periods when they were in relapse (RL), or subsequent remission (RM). Adult male Sprague Dawley rats (175-200 g) were perfused with 4% Ringer BSA solution. Glomeruli were isolated on ice by graded sieving from the cortex of each kidney. Glomeruli were incubated, in the presence of AF488-conjugated BSA (AF488-BSA, 30 µg/ml) and R18 (36.5 µg/ml), with 10% plasma from NS patients for 1 hour, and simultaneously treated with sparsentan (0.1 µM, 1 µM and 10 µM) or vehicle. The glomerular Ps'_{alb} assay was used to measure changes in albumin permeability. We applied a fluorescence profile peak-to-peak confocal imaging technique to treated glomeruli to assess glomerular eGlx thickness [2].

Results: Human NS patients in RL had a significantly greater proteinuria compared to RM (RL, 10,000 ± 1,354 mg/g; RM, 95.3 ± 59.7 mg/g, $P = 0.017$). Incubation of rat glomeruli with RL plasma induced a significant increase in Ps'_{alb} (RM+vehicle, $6.0 \times 10^{-7} \pm 0.12 \times 10^{-7}$ cm/s; RL+vehicle, $10.9 \times 10^{-7} \pm 0.84 \times 10^{-7}$ cm/s, $P < 0.001$) with a

significant reduction in glomerular eGlx thickness (RM+vehicle, 210 ± 21.2 nm; RL+vehicle, 109 ± 7.9 nm, P = 0.027), compared to rat glomeruli incubated with paired RM plasma. Sparsentan-treated RL incubated glomeruli were protected from both the increase in Ps'_{alb} (RL+spars 10 µM, $6.3x10^{-7} \pm 0.19x10^{-7}$ cm/s, $P < 0.001$) and the loss in glomerular eGlx (RL+spars 10 µM, 222 ± 8.5 nm, P = 0.013), to a level comparable to RM incubated glomeruli. The effect of sparsentan on Ps'_{alb} was dose dependent (RL+spars 1 µM, $8.0x10^{-7} \pm 0.46x10^{-7}$ cm/s; RL+spars 0.1 µM, $9.6x10^{-7} \pm 0.22x10^{-7}$ cm/s) with Ps'_{alb} changes correlating inversely with glomerular eGlx thickness (r^2 = 0.75, $P < 0.0001$). In RM glomeruli, sparsentan alone had no effect on Ps'_{alb} compared with vehicle (RM+spars 10 µM, $6.2x10^{-7} \pm 0.25x10^{-7}$ cm/s, P = 0.590), suggesting no effect on otherwise healthy capillaries.

Discussion: We have shown that dual inhibition of endothelin and angiotensin receptors, with sparsentan, preserves the glomerular eGlx resulting in normalised glomerular permeability in NS. These findings suggest that the direct action of sparsentan on the GFB could help maintain barrier integrity in NS, in particular by glycocalyx protection.

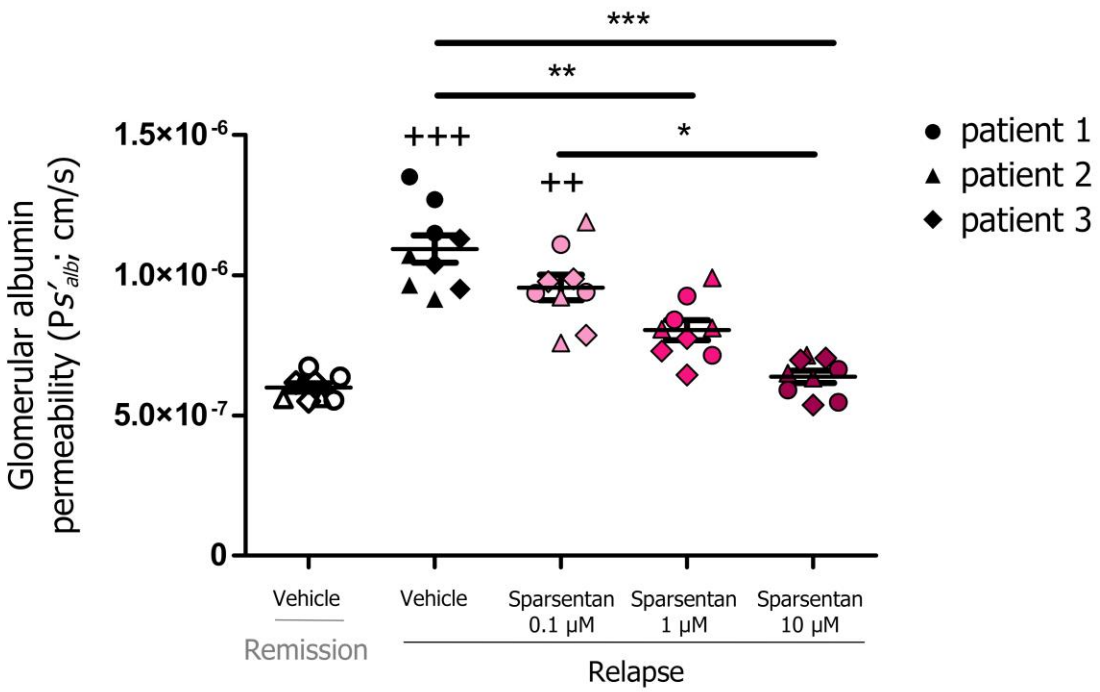

Figure 1. Sparsentan dose-dependently attenuates increases in rat glomerular albumin permeability resulting from incubation with human nephrotic syndrome plasma. Each point on the graph represents a rat. ++, P<0.01 vs. Remission+Vehicle; +++, P<0.001 vs. Remission+Vehicle; *, P<0.05; **, P<0.01; ***, P<0.001.

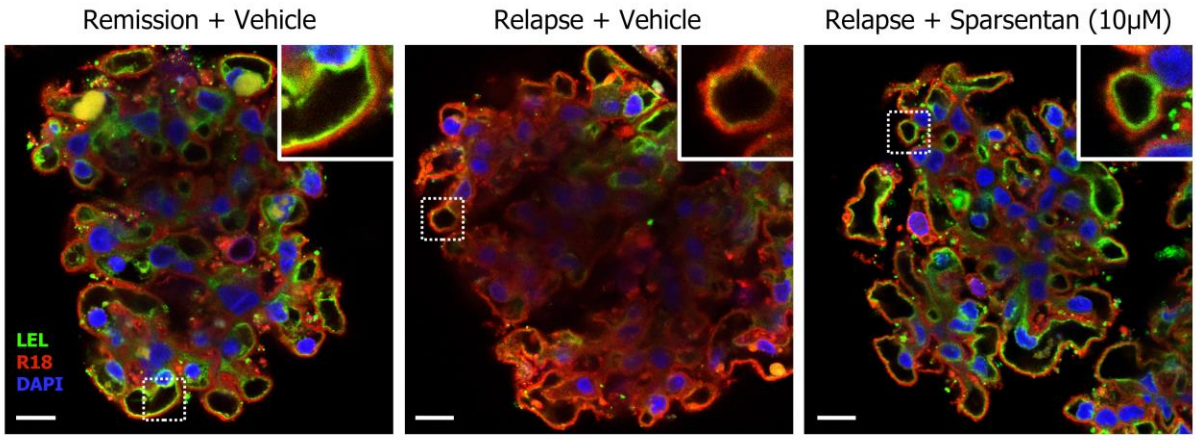

Figure 2. Fluorescence confocal imaging of rat glomeruli exposed to human nephrotic syndrome plasma confirms that glomerular endothelial glycocalyx damage is prevented by sparsentan. Representative images show glomerular capillaries labeled red (R18) and the luminal glomerular endothelial glycocalyx labeled green with Lycopersicon Esculentum Lectin (LEL). Scale bar = 10 μm.

This work was funded by Travere Therapeutics, Inc.

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436: Genetically induced senescent cells recruit leukocytes, promote fibrosis, and permit their own clearance from healthy young kidneys.

Dr Marie-Helena Docherty[1], Mr Maximilian Reck[2], Mr Ross Campbell[1], Dr David Baird[1], Dr Laura Denby[2], Dr Katharine Mylonas[1], Dr David Ferenbach[2]

[1]Queen's Medical Research Institute (QMRI), Edinburgh. [2]Centre for Cardiovascular Science (CVS), Edinburgh

Biography - Dr Marie-Helena Docherty

I'm a renal SpR in the RIE. I have just completed my PhD looking at cellular senescence, the development of fibrosis and mechanisms pertaining to the clearance of senescent cells.

Abstract

Increasing evidence links senescent epithelia to progressive fibrosis and functional loss in experimental and human kidney disease. Whether senescent cells themselves are sufficient to initiate and sustain progressive kidney fibrosis is not known.

We hypothesised that induction of targeted epithelial senescence in the absence of other renal injuries would be sufficient to initiate and sustain fibrosis.

We generated a Pax8creERT2;mdm2 fl/fl mouse ('TG') via a cross of two established stains and treated these and wild type (WT) mice with tamoxifen by oral gavage to induce epithelial restricted senescence via mdm2 deletion. Markers of fibrosis (Collagen I) and growth arrest (p21cip1) were quantified by immunofluorescence (IF), and total collagen by picrosirius red staining. Full transcriptomic analysis was undertaken using scRNA-seq (10X).

Tamoxifen dosing resulted in p21cip1 induction in renal epithelia in TG but not in wild WT mice by IF (10.45 ± 2.9 *vs* 3.15 ± 0.7, $p<0.05$; Fig. 1). On scRNA-seq, TG (but not WT) kidneys contained transcriptionally distinct, cdkn1a+ epithelia, recruited leukocytes and increased activated myofibroblasts. IF confirmed increased renal fibrosis at D7 in TG *vs* WT (Collagen 1 1.1 ± 0.3 *vs* 3.1 ± 0.5, $p<0.005$; Fig. 1). However, by D42 scRNAseq analysis demonstrated clearance of cdkn1a+ senescent epithelia, normalisation of leukocyte counts and resolution of myofibroblast activation in TG kidneys, with confirmation at a protein level by IF – showing no difference in p21cip1 levels between WT and TG mice (2.4 ± 1.4 *vs* 4.1 ± 1.1, $p=0.7$; Fig. 1) and no progressive fibrosis. This was not the case with senescent cells induced by injury where D42 post ischaemia-reperfusion injury (IRI) scRNAsequencing data clearly demonstrated the persistence of senescent epithelia.

Our results demonstrate that epithelial senescence induction is profibrotic in the absence of injury to other cell lineages. Of importance, mechanisms in the healthy adult kidney allow detection and physiologic clearance of senescence and prevent ongoing fibrosis. These mechanisms appeared only to be present in the context of senescent epithelia induced by loss of MDM2, and not present post-injury; where senescent epithelia persisted and were not cleared.

Understanding how these pathways are lost with ageing and chronic injury may lead to new routes to promote clearance of profibrotic senescent epithelia.

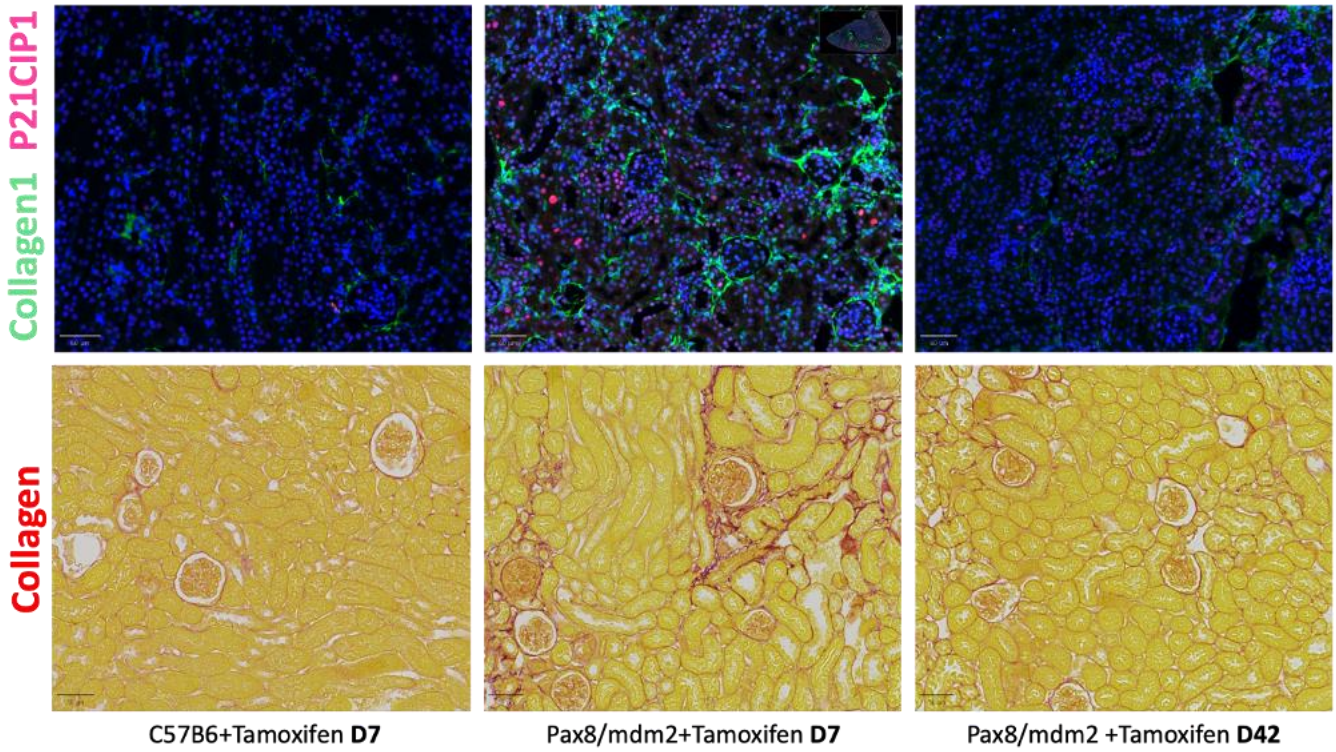

Figure 1. Induction of senescent epithelia (p21cip1) and fibrosis at D7 in a young female TG mouse *vs* WT control. Paired D42 images from the same TG mouse demonstrating clearance of p21cip1 and reduction in fibrosis.

Meeting the challenges of kidney supportive care

312: Kidney Supportive Care – Staff education. Development of a bespoke kidney supportive care education package.

Mrs Sarah Mackie[1,2], Dr Stuart Deoraj[3], Dr Dominique Wakefield[4,2], Dr Tina Thompson[5,2], Dr Hatty Douthwaite[1], Mrs Kate Shepherd[1,2], Ms Tatjana Rudolphy[6,2], Mr Jack Chilton[4], Dr Heather Brown[4,2], Dr Katie Vinen[1,2]

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Biography - Mrs Sarah Mackie

Sarah is a senior nurse with 30 years' experience, predominately in the field of kidney care, with a focus on maintaining excellent standards of care in busy and challenging environments. An innovator who has implemented new services to improve standards and access to care for patients. Additionally, she has a longstanding passion for education.

Abstract

Introduction: London has 2929 patients with an eGFR <15ml/min under a kidney clinicians care [1] , and 6909 patients receiving dialysis, with 23% aged 75 or older and 4.7% aged 85 or older [2.] Many also face increased frailty and vulnerability, making the provision of high quality, holistic care challenging, relying on effective communication, empathy and a clear understanding of the patient's needs.

As part of the kidney supportive care workstream within the London Kidney Network (LKN), a bespoke education training package has been developed. It addresses a knowledge gap identified in a survey of 253 kidney care professionals, 61% of whom were nurses, 21% doctors, 10% unspecified and 8% allied healthcare professionals. Notably, 63% lacked prior training. 85% of those surveyed also expressed interest in receiving support and training. The study package consists of two eLearning modules, covering kidney supportive care and advanced care planning (ACP) and is accessed through King's Health Partner's (KHP).

Existing staff education tools for kidney disease predominantly focus on palliative and end-of-life care, with limited emphasis on the needs of patients in the later stages of kidney disease. Our work aims to educate kidney professionals in the tools required to enhance patient quality of life, as the primary goal of care. This may include those who forgo dialysis, or those who are on renal replacement therapy, such as dialysis or transplantation, who require additional support to meet their frailty needs. Older patients, especially, require excellent frailty care, symptom management, and tailored support for dialysis, ensuring a genuine opportunity for future planning.

Methodology: The staff education package is composed of three key elements: eLearning content (figure 1), an ACP 'at a glance' tool (figure 2), and two concise infographic videos (figure 3). The content has been peer and patient endorsed and has undergone successful piloting. The two modules require a total of 90 minutes for completion and are designed for all kidney clinicians, encompassing a staff total of over 2250 across the 7 London kidney units, who stand to benefit from this initiative.

In order to facilitate effective learning and engagement, and to assist staff in translating knowledge into practice, the modules feature a diverse range of interactive elements.

In-person meetings were conducted with 120 members of staff, from the seven London kidney units to actively promote and disseminate information about the supportive care education module.

Results: The education package uses a combination of text resources and concise infographic videos developed in collaboration with an animation company. Additionally, the package is supplemented by case studies, exercises, videos and quizzes, with links to further resources.

Finally, as part of region-wide quality improvement, data monitoring on module performance and completion will guide ongoing development and ultimately sustainably improve patient care.

Conclusions: A follow-up staff survey 12 months post module launch, revisiting confidence and knowledge together with a review of completed ACP's and Clinical Frailty Scales (CFS), will aid in evaluating and demonstrating success. National interest has also prompted plans for broader implementation, aiming to improve workforce knowledge and consequently the patient experience.

Figure 1: Example of eLearning page

[Link to eLearning module, via KHP]

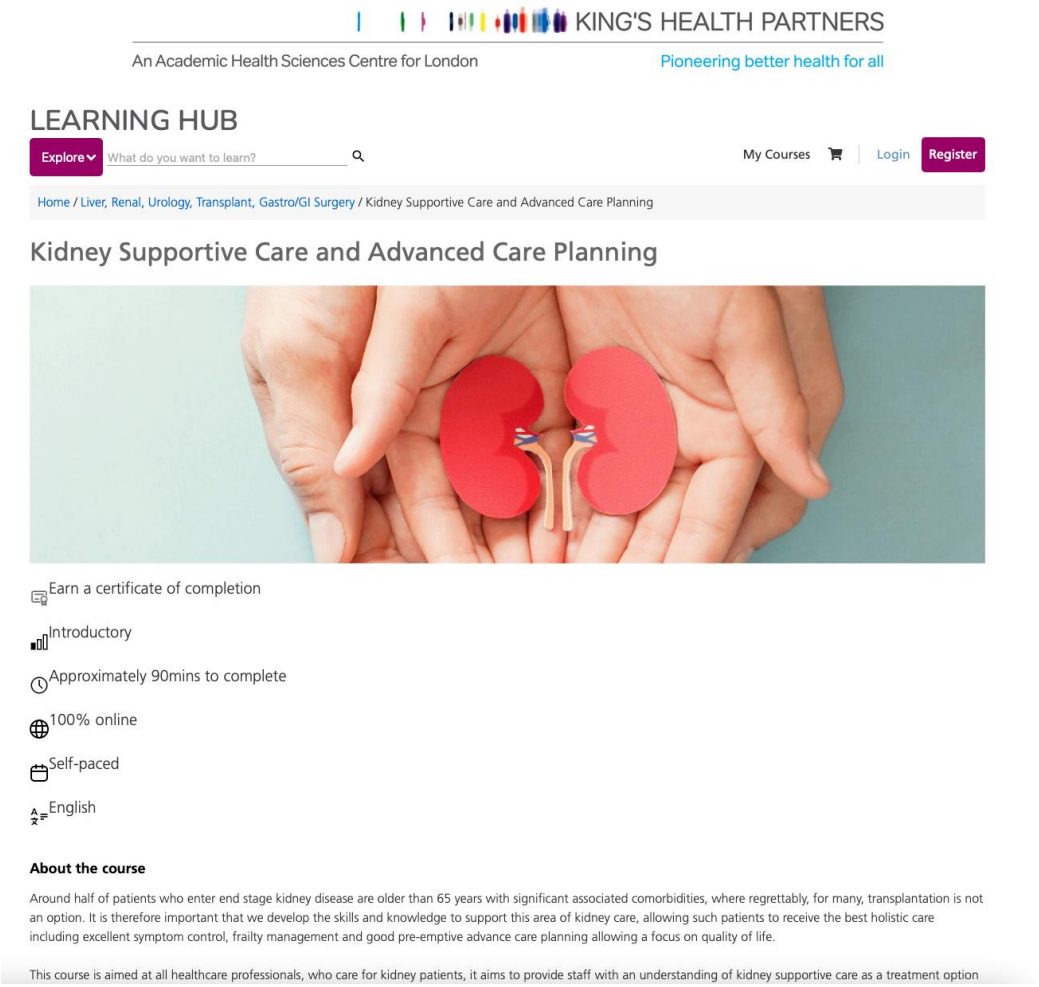
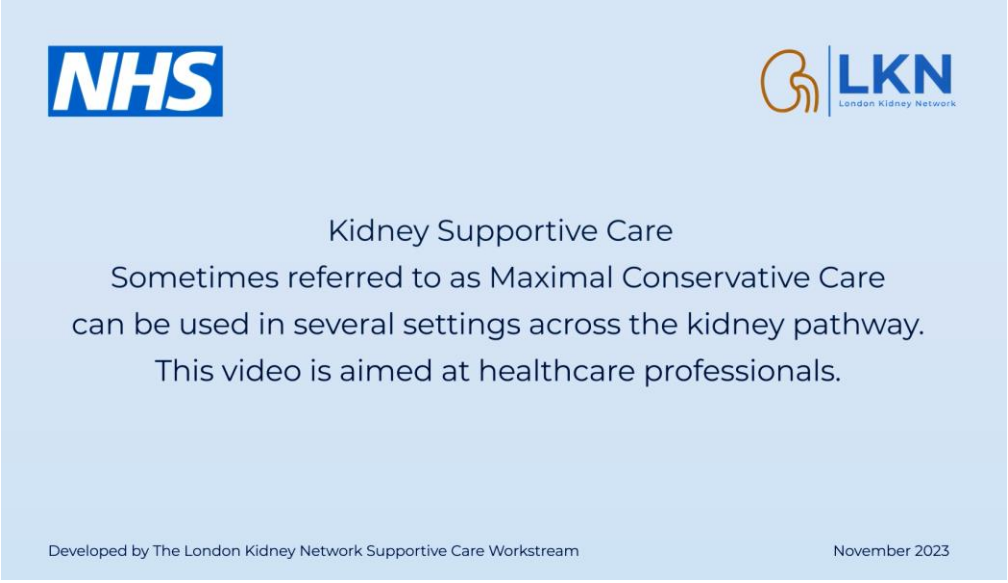


Figure 2: LKN ACP 'at a glance' tool

Figure 3: Example of infographic videos.

[Link to infographic videos, via LKN website]



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https://ukkidney.org/sites/renal.org/files/25th%20Annual%20Report%20Final%202.6.23.pdf

Accessed 28th December 2023

268: Prescribing patterns in older people with advanced chronic kidney disease approaching the end of life.

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Biography - Dr Matthew Letts

Dr Matthew Letts is currently undertaking a competitively awarded NIHR Academic Clinical Fellowship in Renal Medicine: his specialty training in renal and general internal medicine is being undertaken at North Bristol NHS Trust, and his research training is being undertaken at the University of Bristol with the Renal Population Health Sciences group (led by Prof Fergus Caskey and Assoc Prof Pippa Bailey). Dr Letts is working on exploring prescribing patterns for elderly people with chronic kidney disease, with a focus on de-prescribing; and also working with Dr Jemima Scott, carrying out a mixed-methods investigation into the reasons for disparities in cardiac care of people with and without chronic kidney disease.

Abstract

Introduction: Advancing age and chronic kidney disease (CKD) are risk factors for polypharmacy[1] – the regular daily intake of >5 medications. Polypharmacy is a key action area for the World Health Organization in its effort to reduce global medication-related harm[2]. Deprescribing, the systematic review and rationalisation of potentially inappropriate medications, is a proposed way of addressing polypharmacy. Deprescribing is particularly relevant near the end of life, when preventative treatments provide less benefit. Prescribing practices for elderly people with advanced CKD in the last years of life are currently unknown. The aim of this study was to describe prescribing and deprescribing patterns in such a cohort.

Methods: The EQUAL study is an international, prospective cohort study of people ≥65 years with an incident estimated glomerular filtration rate (eGFR) of ≤20ml/min/1.73m^2.[3] We analysed data from participants who died during follow up, including 3-6 monthly study-visit-collected prescribed oral medications (POMs). Generalized additive models were used to explore trends leading up to death in the total number of POMs, and the proportion of participants taking specific medications. Data are presented for medications: a) identified as targets for deprescribing in the elderly with CKD (statins, proton-pump inhibitors (PPIs) and antihypertensives – alpha-blockers, beta-blockers, calcium-channel blockers (CCBs), diuretics and renin-angiotensin-aldosterone inhibitors (RAASis))[4,5]; b) used for symptom control in kidney failure (opioids and gabapentinoids)[6]; and c) prescribed to >30% of the cohort (allopurinol, aspirin, vitamin D)[7].

Results: Data from 563 participants were analysed, comprising 2,793 study visits (median follow-up time 2.2 years (interquartile range (IQR) 1.1-3.8) pre-death), and 22,200 POMs. At baseline, mean age was 77.8 years (standard deviation (SD) 6.7), median eGFR 18.1mls/min/1.73m^2 (IQR 15.0-21.2), and 87.2% were experiencing polypharmacy. The number of POMs increased over the time approaching death (Figure 1) – 7.3 (95% confidence interval (CI) 6.9-7.7) at 5 years pre-death, 8.3 (95% CI 8.0-8.6) at 2.5 years pre-death, and 8.7 (95% CI 8.4-9.1) at death. At their final study visit 90.1% were experiencing polypharmacy. Trends in the proportion of individuals prescribed specific medications differed by POM class (Figure 2). Opioids, diuretics and PPIs increased in the last years of life; statins, RAASis, alpha-blockers and CCBs decreased; and allopurinol, beta-blockers and gabapentinoids remained stable. Aspirin and vitamin D showed phasic patterns, increasing then decreasing.

Discussion: Elderly people with advanced CKD experience increasing levels of polypharmacy as they approach the end of life. Although there is evidence that certain medication classes are being deprescribed, this is outweighed by increased prescribing of other agents. Previous analyses of EQUAL decedents have shown that blood pressure decreases pre-death[8] – we show this is despite reductions in most classes of antihypertensives. Our work suggests a high reliance upon pharmacological interventions (both symptom-directed and preventative) for older people with CKD who are approaching death. We cannot ascertain whether this reflects personalised prescribing, aligned with individuals' preferences and prognoses; however, high levels of polypharmacy potentiate risks of side effects, medication burden and drug-drug interactions, and indicate a role for enhanced medication review in this setting.

Figure 1. Trajectory of the total number of prescribed oral medications (POMs), with 95% confidence interval.

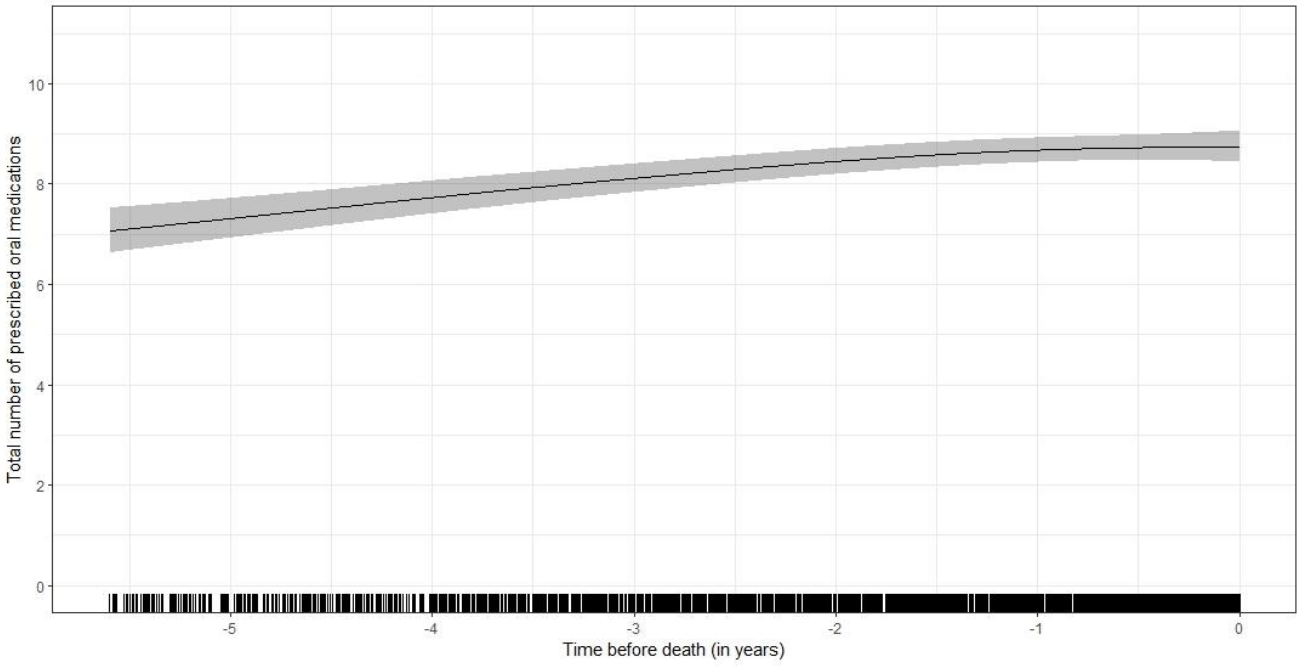
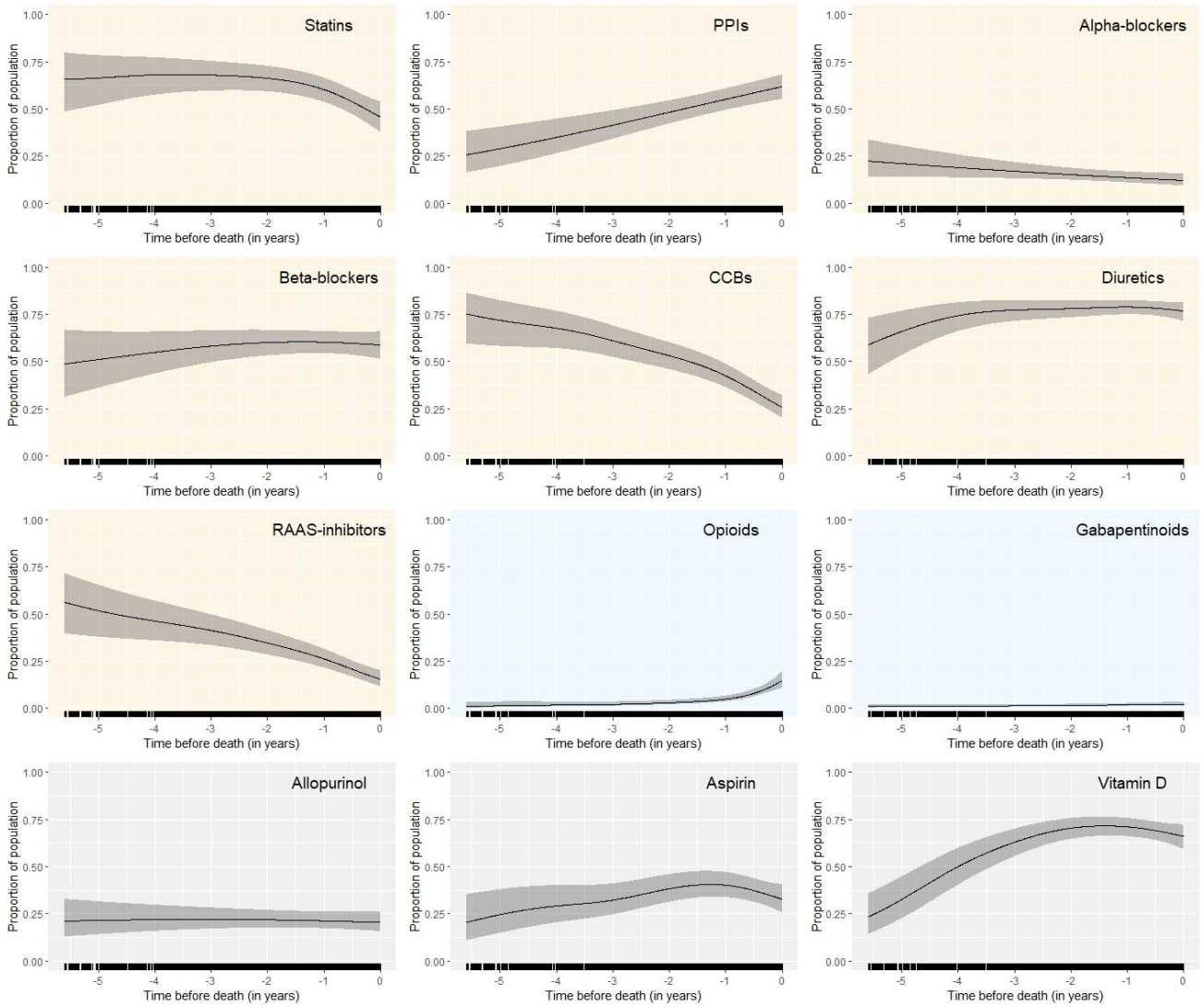


Figure 2. Trajectories of the proportion of participants prescribed certain classes of POM, with 95% confidence intervals: targets for deprescribing (yellow), those used for symptom control (blue), and those prescribed to >30% of the cohort (grey).



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Getting the right vascular access for patients - facilitating the flow

472: Optimising the timing of referral for vascular access - a retrospective analysis using eGFR and KFRE thresholds

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Biography - Dr Rupert Major
Associate Professor, University of Leicester. Honorary Consultant Nephrologist, University Hospitals of Leicester NHS Trust

Abstract
Introduction: The optimum timing for referral for arterio-venous fistula (AVF) formation remains unclear. eGFR thresholds, such as eGFR of 15 ml/min/1.73m2, have been suggested historically but with sparse evidence for their use. More recently, the Kidney Failure Risk Equation (KFRE) has been proposed for this use. Previous studies have suggested that a two year kidney replacement therapy (KRT) risk of more than 40% may be optimal to allow for adequate time for AVF formation and maturation whilst minimising referrals.

Methods: We performed retrospective analysis of a single Network's data for individuals with advanced CKD over the last decade. Anonymised data for individuals with an eGFR of ≤30 ml/min/1.73m2 were analysed. We performed the analysis using several different models to account for the completeness of proteinuria data and the presence of acute kidney injury at the time of potential decision making. Analysis was performed of the following thresholds to refer for AVF formation:

- eGFR of 12, 13, 14, 15 ml/min/1.73m2
- KFRE two year risk of 20%, 30%, 40%, 50%

Follow-up started at the first point the individual met each threshold, and continued until commencing KRT, dying or two years had elapsed.

The following were calculated for each model and threshold:

- Percentage progressing to KRT, dying prior to KRT and surviving for two years
- Individuals meeting referrals threshold per KRT case i.e. potential referrals and procedures per KRT case
- Median, 25th and 10th percentile times to KRT i.e. time from referral for 50%, 25% and 10% of population to reach KRT

Results: 4,918 individuals were identified for the analysis. Mean age was 69.7 (SD 14.4) years with 2,801 (57.0%) males. 3,312 (67.8%) individuals were White and 1,319 (27.0%) South Asian. Mean eGFR was 23.3 ml/min/1.73m2 and two year KFRE risk of 9.6% (SD 11.3). 491 (10.0%) individuals required KRT and 1,033 (21.0%) died within 2 years of follow-up from their first result in the dataset.

Summary results for the model for complete urine protein data and excluding episodes of acute kidney injury are shown in Table 1. For this model, referral at all eGFR thresholds down to 12 ml/min/1.73m2 and for a KFRE of >30% would lead to at least two referrals being required for every KRT case. Compared to an eGFR of 15

ml/min/1.73m2, a KFRE threshold of 40% identified a lower number of people who died prior to reaching the need for KRT and had a lower referral to KRT ratio (1.6 compared to 2.9). The median, 25th and 10th percentiles were similar for both thresholds. Results were similar across the different models,

	eGFR				KFRE 2 Year			
	15	14	13	12	20%	30%	40%	50%
n	1494	1338	1177	999	1242	877	624	387
Deaths (%)	23.5	24.2	24.0	24.4	18.3	16.9	13.9	12.4
KRT Cases (%)	35.0	38.1	42.4	46.2	35.6	49.3	63.0	72.1
Referrals per KRT case	2.9	2.6	2.4	2.2	2.8	2.0	1.6	1.4
Time to KRT, Days								
Median	278	270	246	236	338	311	267	232
25th Percentile	160	139	124	120	198	189	159	126
10th Percentile	74	62	51	43	99	98	65	62

Conclusions: Use of eGFR thresholds down to 12 ml/min/1.73m2 would potentially lead to at least two referrals for AVF formation per case of KRT within 2 years. Compared to a 15 ml/min/1.73m2 threshold, a KFRE of more than 40% threshold would potentially lead to a reduction in referrals, a lower number of referrals per KRT case and a lower proportion of deaths prior to commencing KRT. The time to allow for AVF creation and development would remain similar for both thresholds. The measurement of urinary protein, to allow for KFRE calculation, should continue even in advanced kidney disease to allow for timing of vascular access formation and prognosis. Multi-centre, collaborative studies are required to firmly establish the best threshold for considering referral for AVF formation.

371: Assessing Vascular Access Thrombectomy Service Adherence to GIRFT Recommendations: Single Centre Experience

Dr Alshymaa Eltahan[1,2], Zulfikar Pondor[1], Dr. David Lewis[1], Dr. Maharajan Raman[1], Paula Gleave[1], Dr. Dimitrios Poulikakos[1,3], Dr. Rosemary Donne[1,3]

[1]Salford Renal Department, Northern Care Alliance NHS Foundation Trust, Manchester, United Kingdom. [2]Faculty of medicine, Helwan university, Cairo, Egypt. [3]University of Manchester, Manchester, United Kingdom

Biography - Dr. Rosemary Donne

Dr Donne is a consultant nephrologist at Salford Care Organisation, Northern Care Alliance and lead for the advanced kidney care and vascular access services. She is also KQIP national co-lead and has a strong interest in using quality improvement methodology to improve patient care, including work in vascular access, pre-emptive transplantation and home dialysis

Abstract

Introduction: Studies showed that early thrombectomy of dialysis vascular access (VA) is associated with better outcomes **[1],** especially for native VA **[2].** Timely treatment of VA thrombosis within 24-48 hours is recommended by GIRFT to minimize access loss and requirement for dialysis line insertion **[3]**. Our centre has approximately 430 HD patients but has no on-site vascular surgery or vascular access interventional radiology (IR) service. Wait time for elective VA surgery or fistuloplasty is >8 weeks and VA surveillance is based on routine clinical monitoring. VA prevalence is 62% AV fistula (AVF), 2% AV graft (AVG), 36% central venous catheter (CVC). Fistula thrombectomy is provided at another centre, with increasing waiting times over recent years due to shortage of interventional radiologists. This study evaluates adherence to GIRFT recommendations for patients at our centre requiring thrombectomy and will identify potential local strategies to reduce fistula thrombosis and CVC use.

Methods: In a 24-months' retrospective cohort analysis of maintenance HD patients with permanent VA, we obtained data on:

1) Time between the date of confirmed VA thrombosis and thrombectomy procedure

2) Clinical success rate defined as delivering at least one HD session after thrombectomy

3) Requirement for Central Venous Catheter (CVC) insertion

4) CVC-related infections (exit site, or bacteremia)

5) Post-intervention primary patency rate at 3 and 6 months (time from date of index procedure until the next access thrombosis or reintervention) **[4]**

6) Requirement for hospital admission with total inpatient admission days and inpatient cost

7) Complication free days (CFD)-extended over one year (days without serious vascular access events, radiological or surgical intervention, VA infection, hospitalisation or use of central venous catheter)**[5].**

Results: 44 patients with permanent VA developed VA thrombosis. The median waiting time for thrombectomy was 8 days **(Fig. 1)**. Post-intervention primary patency rate was 71% at 3-months and 60% at 6-months **(Fig. 2).** 61% of patients required hospital admission with a 12-day median length of stay, with total inpatient admission days of 403 days over 2 years (2022-2023), and total cost of £246,065 **(Fig. 3&4).** The median CFD-extended was 356 days, ie. 9 days/patient/year with VA-related complications **(Fig.5).**

Discussion: This study shows that our centre's VA thrombectomy service falls far outside the GIRFT recommendation of intervention within 24-48 hours. The high associated rates of CVC use, inpatient bed days and avoidable costs place a heavy burden on patient outcomes and NHS resources. The ideal solution of an on-site thrombectomy service is difficult to achieve due to lack of vascular IR support. In response to this study, we now aim to reduce thrombosis rates by training additional interventional nephrologists in elective fistuloplasty, implementing a robust VA surveillance to improve early detection of malfunctioning VA suitable for elective intervention and improving staff education on fistula care.

Acknowledgment: Many thanks to Jayne Moore and Jonathan Allsopp (Finance department and member of CIPFA) for providing the detailed inpatient cost.

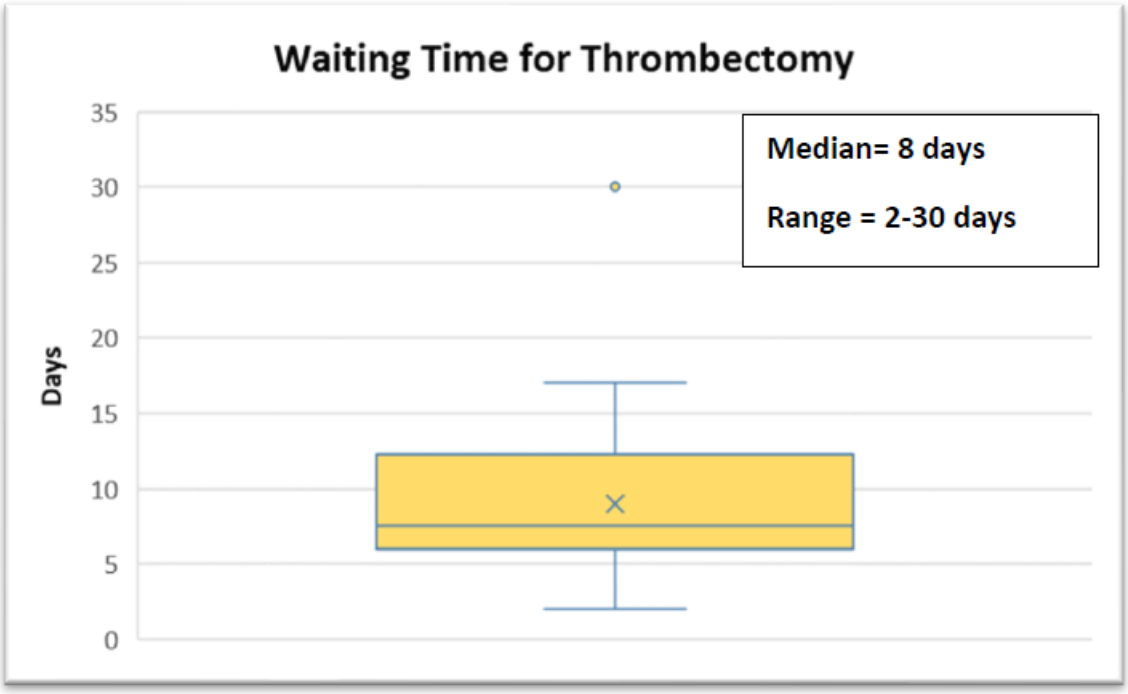

Figure (1): Thrombectomy interval.

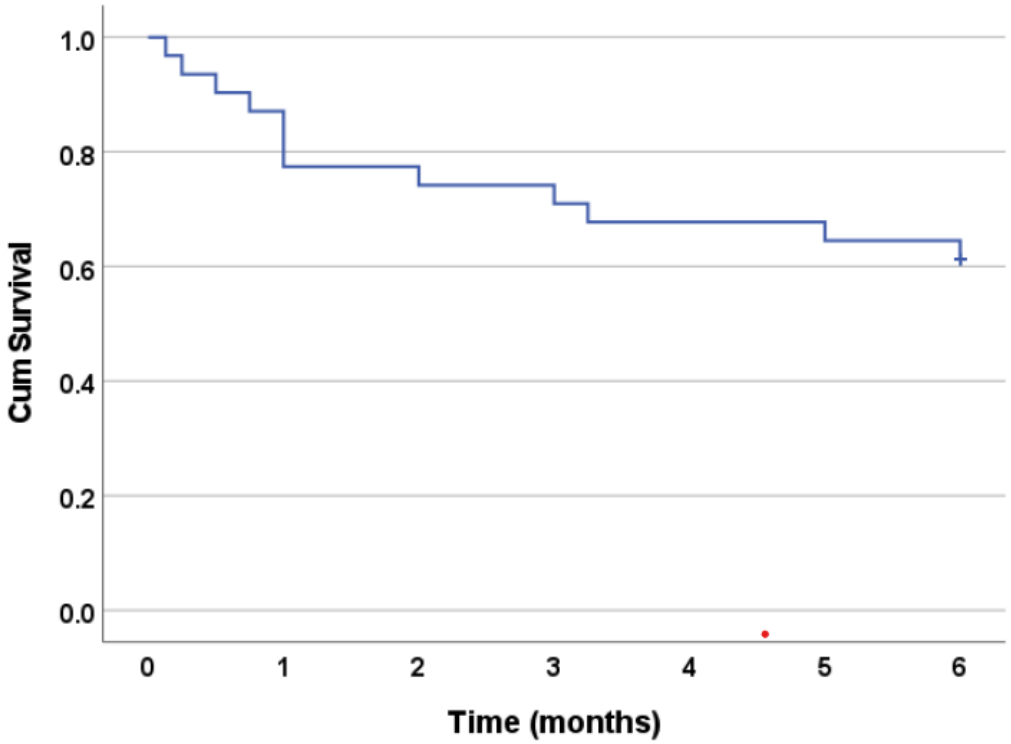

Figure (2): Kaplan-Meier curve for post-intervention primary patency rate from the index thrombectomy episode at 3 and 6 months with patency rate 71% and 60%, respectively.

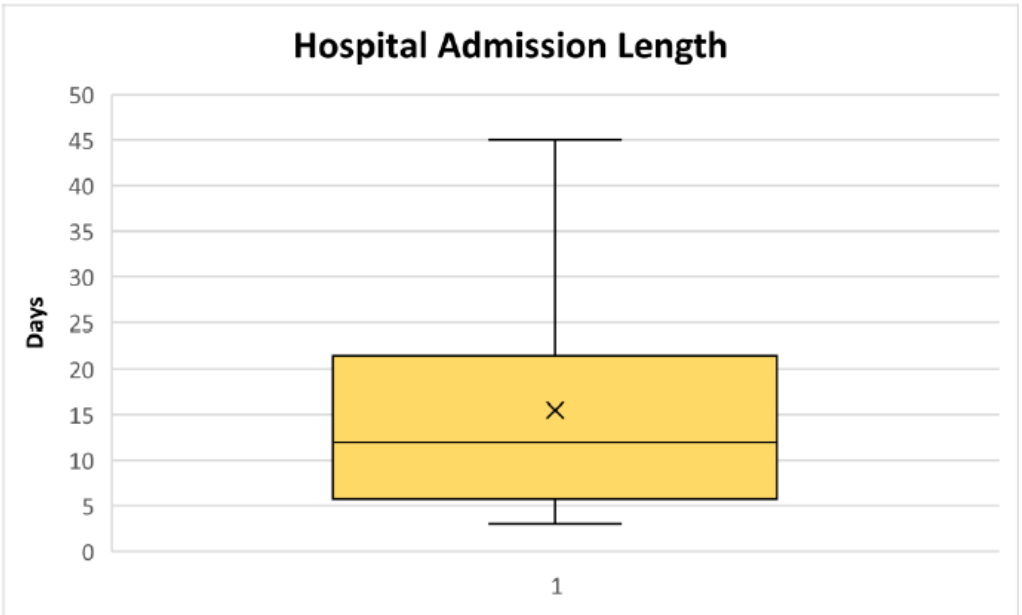

Figure (3): Length of hospital admission, median = 12 days, Range = 3-45, total admission days 403 days over 2022-2023.

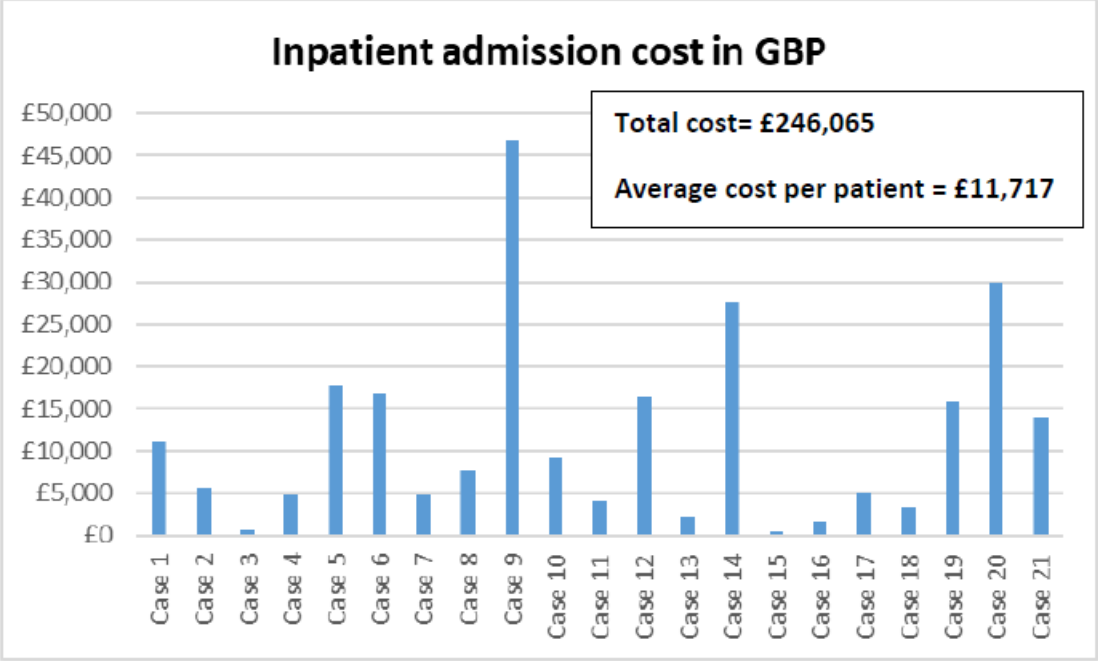

Figure (4): Inpatient admission cost per patient.

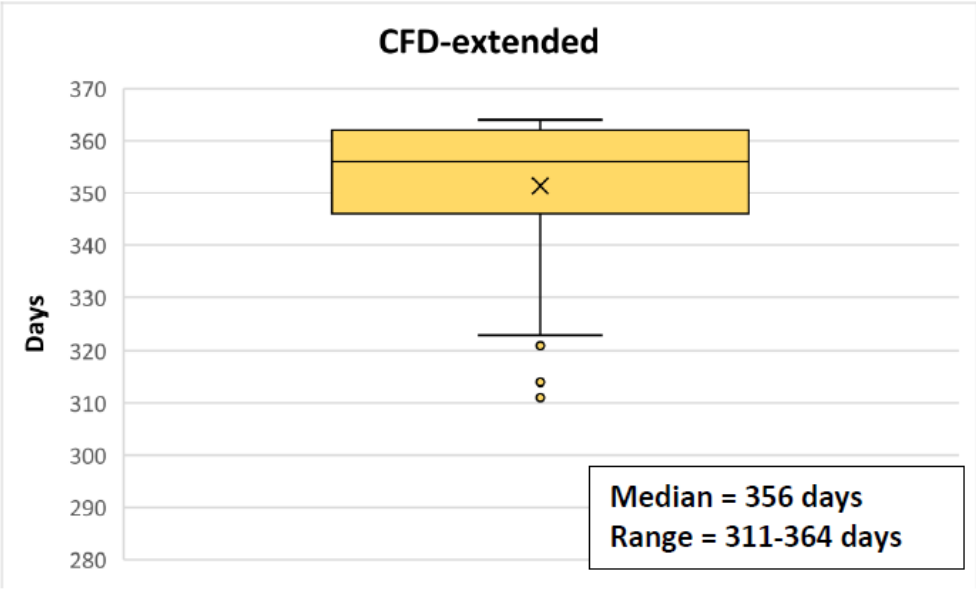

Figure (5): CFD-extended (days without serious vascular access events, radiological or surgical intervention, VA infection, hospitalisation or use of central venous catheter)

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Healthcare data for patient benefit

453: NURTuRE-CKD: Outcomes by primary renal diagnosis

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Biography - Dr Thomas McDonnell

I graduated from Bristol medical school in 2014. Undertaking my foundation years followed by a junior clinical fellowship in Renal medicine at Aintree hospital, Liverpool. I then moved to Adelaide, Australia and worked for two years in Flinders Hospital emergency department and Intensive care unit. On returning to the UK I completed 3 years internal medicine training in South Manchester. I then secured a Nephrology training position in the North West with one day a week research. It was during this year that my interest in research peaked publishing two cross sectional studies focusing on glomerular diseases and two literature reviews. I was then provided with the opportunity to undertake a PhD with the university of Manchester. After my ST4 year, in August 2023, I came out of program to work as a research registrar at Salford Hospital. My research is focused on the NURTuRE-CKD study, examining CKD progression with a specific emphasis on how novel biomarkers can enhance prediction accuracy and offer deeper insights into the mechanisms of CKD. I am also passionate about education and training. As an IMT I was regional representative and education lead for South Manchester and i'm currently Trainee communication lead for Salford hospital.

Abstract

Introduction: Chronic kidney disease (CKD) represents a major global healthcare challenge, affecting approximately 850 million people worldwide(1), and is an independent risk factor for the progression to kidney replacement therapy (KRT) and all-cause mortality(2). However, CKD encompasses various causes, each with unique pathophysiology and rates of progression(3). Here we describe the outcomes from NURTuRE-CKD, an ongoing, multicenter prospective cohort study of 2996 non-dialysis CKD patients, by primary renal diagnosis, aiming to describe the differing rates of progression, ESKD and mortality by CKD cause and provide insights into those at greatest risk.

Methods: Patients with an eGFR of 15–59 mL/min/1.73 m^2 or eGFR ≥60 mL/min/1.73 m^2 with a uACR >30 mg/mmol were enrolled, in addition to 86 controls. The full study design and methods of NURTuRE-CKD have previously been reported (4). Outcomes and serial eGFR data were sourced from the UK Renal Registry. ESKD was defined as initiation of KRT or eGFR<15 mL/min/1.73 m^2. Rate of progression was determined via eGFR slope. ERA diagnostic categories were used for primary renal diagnoses, with ‘glomerular diseases’ split into glomerulonephritis (GN) and vasculitis. The Chi-squared test was used to compare categorical variables, and the Kruskal-Wallis test for continuous variables. A multivariable Cox proportional hazards regression analysis

predicting the time to ESKD by primary diagnosis was undertaken, using vasculitis as the reference category. Model 2 included adjustments for baseline eGFR

Results: Table 1 depicts both the baseline characteristics and outcomes by the 8 diagnosis categories. Average follow-up duration was 53.8 months, not significantly different between the groups, but all other baseline variables differed significantly. The hypertensive/renovascular group were oldest and familial group youngest at 71 and 53 years, respectively. At baseline the diabetic nephropathy (DN) group had the lowest eGFR 28 ml/min/1.73m^2 and highest uACR 88.3 mg/mmol. However, the familial group had the steepest *pre-enrolment* eGFR decline slope.

Delta eGFR during the follow-up period was steepest in the familial group and DN groups at -3.4 and -3.0 ml/min/1.73m^2, respectively, whereas the vasculitis group had slowest progression -0.7 ml/min/1.73m^2. Overall rate of ESKD was 24.7%; lower in the vasculitis (14%), systemic disease (17.7%) and tubulointerstitial (18.8%) groups, and higher in the DN (36.7%) and familial (31.6%) groups. All-cause mortality was greatest in the DN group at 40.4%. Despite being the fastest progressors defined by eGFR slope, the familial group had the lowest mortality rate (5.2%), but they were of younger age and had a high rate of kidney transplantation (10.1%).

Unadjusted HRs for ESKD, were significantly higher for all diagnoses except tubulointerstitial and systemic diseases compared to the vasculitis group; DN evidenced the highest hazard ratio at 3.15 (2.18-4.55). When adjusted for baseline eGFR, HRs for the glomerulonephritis 2.04 (1.89-4.03), diabetes 1.5 (1.04-2.16) and familial 2.76 (1.89-4.03) remained significantly higher.

Discussion: Rates of progression and incidence of clinically meaningful outcomes differ between CKD causes in NURTuRE. Those with DN and familial conditions had faster eGFR decline and had higher rates of ESKD, with associations persisting despite controlling for baseline eGFR. Recognising that CKD progresses at different rates is crucial, not only for providing personalised care, but also key to understanding differing pathophysiologic mechanisms of progression. NURTuRE-CKD will also explore novel biomarkers, with the aim of illuminating mechanisms of progression, improving risk prediction and highlighting novel drug targets.

Table 1 – Baseline variables and outcome by primary renal diagnosis.

	DN (344)	Familial (327)	Glomerulonephritis (435)	HTN/Renovascular (268)	Miscellaneous/Unknown (968)	Systemic (64)	Tubulointerstitial (325)	Vasculitis (264)	Total (2996)	P value
Follow-up (months)	53.1 (47.8-58.4)	52.6 (48.2-58.2)	54.0 (49.6-58.0)	54.9 (49.3-58.5)	53.5 (49.3-57.4)	55.6 (49.6-58.6)	54.2 (49.4-58.0)	53.3 (49.8-57.8)	53.8 (49.3-58.0)	0.436
Age	67 (59-74)	53 (46-64)	58 (45.5-69)	71 (63-79)	69 (59-76)	68 (60-76)	61 (49-71.5)	68 (58-73)	65 (53-74)	*
Male	222 (64.5%)	154 (47.1%)	291 (66.7%)	183 (68.3%)	564 (58.3%)	38 (59.4%)	167 (51.4%)	134 (50.8%)	1753 (58.5%)	*
White	291 (84.6%)	280 (85.6%)	355 (81.4%)	228 (85.1%)	875 (90.4%)	59 (92.2%)	284 (87.4%)	241 (91.3%)	2613 (87.2%)	*
Diabetes	X	28 (8.8%)	55 (12.9%)	84 (31.6%)	302 (31.7%)	19 (30.2%)	61 (19.4%)	36 (14.2%)	922 (31.4%)	*
BMI	31.7 (27.3-36.1)	27.2 (24.2-30.3)	28 (24.9-31.3)	28.6 (25.9-31.9)	28.9 (25.4-33.4)	28.7 (25.7-31.7)	27.5 (24.6-31.6)	28.3 (25.1-32.3)	28.5 (25.2-32.7)	*
HTN	319 (92.7%)	286 (90.2%)	386 (90.4%)	246 (92.5%)	800 (84.0%)	43 (68.3%)	222 (70.5%)	201 (79.4%)	2503 (85.2%)	*
ACEI/ARB	264 (76.7%)	257 (78.6%)	371 (85.1%)	178 (66.4%)	557 (57.5%)	47 (73.4%)	149 (45.8%)	159 (60.2%)	1982 (66.2%)	*
Statin	290 (84.5%)	124 (39.1%)	256 (59.3%)	166 (62.4%)	580 (60.9%)	34 (53.1%)	139 (44.3%)	151 (57.2%)	1740 (58.9%)	*
Smoking	180 (53.6%)	134 (41.4%)	210 (48.4%)	155 (58.1%)	506 (53.1%)	36 (56.3%)	139 (44.0%)	112 (42.9%)	1472 (49.8%)	*
Albumin (g/L)	39 (35-41)	44 (40-46)	40 (36-43)	41 (38-44)	42 (38-45)	39 (34-43)	42 (38-45)	41 (38-44)	41.0 (37.0-44.0)	*
Bicarb (mmol/L)	24 (22-27)	25 (23-27)	25 (23-27)	25 (23-27)	25 (23-27)	25 (23-27)	24 (22-26)	25 (23-28)	25.0 (22.9-27.0)	*
Hb (g/L)	117 (106-128)	130 (119-142)	130 (118-143)	128 (116-142)	125 (113-139)	120 (113-129)	129 (118-141)	125 (112-137)	126.0 (114.0-139.0)	*
PO43- (mmol/L)	1.16 (1.02-1.33)	1.13 (0.99-1.25)	1.1 (0.97-1.28)	1.09 (0.94-1.23)	1.11 (0.98-1.26)	1.08 (0.96-1.27)	1.09 (0.98-1.22)	1.04 (0.94-1.17)	1.1 (1.0-1.3)	*
PTH (pmol/L)	37 (15-95)	11 (6-41)	11 (5-40)	24 (10-71)	16 (8-60)	40 (13-99)	17 (6-60)	11 (6-49)	16.5 (6.9-58.0)	*
BNP (ngl/L)	445 (168-1129)	131 (63-277)	164 (65-398)	452 (202-1601)	334 (117-814)	592 (175-1845)	157 (76-367)	195 (129-457)	238.0 (98.1-677.0)	*
CRP (mg/L)	3.15 (1.34-6.12)	1.73 (0.79-4.52)	1.75 (0.85-3.67)	2.97 (1.29-6.85)	2.65 (1.16-6.76)	2.85 (1.16-6.39)	2.61 (1.16-5.38)	2.52 (0.95-5.69)	2.5 (1.1-5.6)	*
Trop (ngl/L)	30.3 (18.3-52.2)	8.9 (5.4-14.9)	13.2 (8-23.9)	23 (14-36.9)	19.5 (10.8-32.9)	20.2 (10.4-55.3)	12.2 (6.8-20.9)	16.4 (9.7-26.3)	16.7 (9.1-30.2)	*
ACR (mg/mmol)	88.3 (20.9-228)	5.8 (2.3-25.1)	103.1 (31.9-221.9)	12.1 (3.2-55.4)	16.6 (2.1-79.9)	8.8 (1.9-172.4)	12.1 (2.5-43.1)	16.1 (3.8-55.1)	21.5 (3.5-100.9)	*
eGFR- EPI (mls/min/1.73m²)	28 (21-39.6)	37.7 (28.5-52.9)	39.4 (28.4-52.7)	30.4 (21.6-39.3)	31 (22-43.8)	33.8 (25.4-48.1)	34.6 (26.3-48)	42.5 (31.7-52.3)	34.3 (24.3-47.3)	*
Pre-slope (mls/min/1.73m²)	-2.9 (-5.1 to -0.7)	-3.3 (-5.1 to -2.0)	-2.1 (-4.5 to -0.2)	-1.5 (-3.2 to +0.3)	-1.2 (-2.9 to +0.4)	-1.4 (-4.6 to +1.3)	-0.5 (-2.3 to +1.1)	-0.2 (-1.9 to +1.8)	-1.7 (-3.5 to -0.1)	*
Post-slope (mls/min/1.73m²)	-3 (-5.5 to -0.8)	-3.4 (-5.2 to -2)	-2.4 (-5 to -0.4)	-1.7 (-3.3 to -0.2)	-1.7 (-3.4 to -0.2)	-1.3 (-4.1 to -0.2)	-1.1 (-3.2 to 0.5)	-0.7 (-2.7 to 0.9)	-1.97 (-4.0 to -0.3)	*
Dialysis	76 (22.1%)	47 (14.4%)	58 (13.3%)	35 (13.1%)	107 (11.1%)	9 (14.1%)	21 (6.5%)	16 (6.1%)	369 (12.3%)	*
eGFR < 15 (mls/min/1.73m²)	114 (33.7%)	97 (30.0%)	97 (22.5%)	59 (22.3%)	210 (22.2%)	8 (12.9%)	58 (18.2%)	27 (10.2%)	670 (22.7%)	*
Transplant	12 (3.5%)	33 (10.1%)	32 (7.3%)	5 (1.9%)	35 (3.6%)	1 (1.6%)	10 (3.1%)	3 (1.1%)	131 (4.4%)	*
ESKD	124 (36.7%)	102 (31.6%)	106 (24.5%)	66 (25.0%)	222 (23.4%)	11 (17.7%)	60 (18.8%)	37 (14.0%)	728 (24.7%)	*
Death	139 (40.4%)	17 (5.2%)	51 (11.7%)	76 (28.4%)	230 (23.8%)	20 (31.3%)	31 (9.5%)	50 (18.9%)	614 (20.5%)	*

Categorical variables expressed as number (%). Continuous variables expressed as Median (IQR). * Indicates P value of <0.001

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Study Registration Number

NCT04084145

178: Healthcare resource utilisation among adult patients with chronic kidney disease by KDIGO categorisation in England (CIPHER): Clinical Practice Research Datalink 2010-2019

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Biography - Dr. Paul Cockwell

Paul Cockwell is a consultant physician and nephrologist at Queen Elizabeth Hospital, University Hospitals Birmingham, professor of nephrology at the University of Birmingham, and medical director for Long-term Conditions and Prevention for Birmingham and Solihull Integrated Care System. Paul is president of UK Kidney Association, the representative professional body for UK renal health care professionals. He helped lead the development in Birmingham of one of the largest and most comprehensive renal services in Europe and developed a large integrated clinical research infrastructure supporting multiple outputs. He publishes widely in chronic kidney disease, paraprotein associated kidney disease and patient reported outcome measurements.

Abstract

Introduction: Chronic kidney disease (CKD) is associated with high clinical burden for patients and substantial economic costs for healthcare systems. Detailed estimates of healthcare resource utilization (HCRU) for patients with CKD in the UK are limited, particularly by stage of CKD. This study assessed outpatient and non-elective inpatient HCRU by stage of CKD in England.

Methods: This non-interventional study utilised data from primary care electronic health records from Clinical Practice Research Datalink (CPRD) AURUM and Hospital Episode Statistics (HES) admitted patient care (APC). Patients aged ≥18 years registered in CPRD with eligible linkage to HES between January 1, 2010 and December 31, 2019 with 2+ eGFR measurement during the period were identified. CKD was defined by eGFR <60 ml/min/1.73m^2 and/or presence of a uACR measurement ≥3 mg/mmol, both confirmed by a second measurement 90-365 days later. Start of follow-up (index) was set to the earliest date during the study period that CKD was confirmed. Follow-up for HCRU ended at earliest of death, administrative censoring, or 31st December 2019. Patients with end-stage kidney disease (eGFR<9 ml/min/1.73m^2) at index were excluded. Number of HCRU events for each HCRU category was estimated as rates per 1,000 person years (PY) for each calendar year based on cumulative number of events. Event rates were calculated as number of outcomes/total time at risk. Confidence intervals (95%) were calculated assuming a Poisson distribution. Age- and sex-adjusted rates were calculated to compare rates across CKD stages.

Results: Of 6.1 million adult patients meeting study inclusion criteria, 743,945 adults (12.2%) with CKD were identified. Mean age (SD) was 76.1 (11.5) years, 55.2% were female, and 89.8% White, contributing a total of 3,055,600 years of follow-up. Most (60.9%) patients had stage 3a CKD (eGFR 45-<59 ml/min/1.73 m^2). Among patients with uACR measurements (44.4%), 48.0% were A1 (<3 mg/mmol), 44.4% A2 (3-30 mg/mmol), and 7.6% A3 (>30 mg/mmol). Overall, per 1000 PY, there were 24,763 primary care visits, 475 non-elective all-cause hospitalisations, 4,950 attended (722 unattended) outpatient visits, including 308 (43 unattended) outpatient nephrology visits and 368.1 attended (61.2 unattended) cardiology visits. For all HCRU categories, greater KDIGO risk category at index was associated with higher HCRU. For example, after age and sex adjustment, patients with CKD stage 3b had a mean of 0.53/PY non-elective all-cause hospitalisations compared to 0.77/PY for patients with CKD stage 4. Additionally, a mean of 5.18 outpatient visits per PY was observed for patients

with CKD stage 3b, of which 0.91 were nephrology outpatient visits compared to 8.39 outpatient visits per PY for stage 4, of which 2.65 were nephrology outpatient visits. Generally, both lower eGFR and higher uACR were individually associated with higher HCRU.

Discussion: This study demonstrates high HCRU for patients with CKD, with increasing rates of HCRU with lower kidney function and greater kidney damage. Patients with more advanced CKD contribute at a disproportionally higher rate of outpatient healthcare encounters and non-elective hospitalisations. Efforts to prevent the development and progression of CKD and improving clinical outcomes will reduce frequency and cost of HCRU.

Patient acuity and workforce challenges in haemodialysis units; a collaborative approach

352: Improving transition onto haemodialysis: a novel trainee-led clinic giving better outcomes to patients and better training to registrars

Dr Joseph Cairns, Dr Clare Castledine

Royal Sussex County Hospital, Brighton

Biography - Dr Joseph Cairns
KSS Renal trainee ST7

Abstract
Introduction: Starting haemodialysis (HD) is a precarious time with high mortality and worse outcomes in unplanned starts.

An audit of our unit demonstrated median time to first consultant clinic review after HD start was 51 days (n=50). Two patients died before review and there were 31 emergency admissions within 60 days of HD start.

Running an HD unit is in the UK training curriculum. A 2018 survey of nephrology trainees revealed only 40% within 2 years of completion felt, “somewhat/very confident to run an HD unit”.

Methods: A trainee led clinic with 1 hour slots 2-3 weeks following in or outpatient HD start was co-designed with patients and the renal MDT. Consultations focused on symptoms, psychological and emotional impact of starting HD, modality choice, vascular access, transplant prospect, medication review, HD adequacy and fluid status exam. Pre-specified data were collected from hospital records and compared with patients starting HD prior to the clinic start using Mann Whitney U tests.

Results: Between November 2022 and September 2023 97 patients commencing HD were seen in the clinic. Patient characteristics (age, gender, ESKD aetiology), route onto HD (planned vs unplanned), modality prior to HD start and dialysis access in use at start were similar to the baseline audit. Time to first review reduced from 51 to 18 days (p=<0.001). On-call SpR reviews were reduced (0.94/patient to 0.58/patient), and were less likely to be related to routine dialysis issues (60% to 29%). 20 (21%) were referred for permanent vascular access, 18 (19%) for a home therapy, 17 (18%) for transplant assessment, 7 (7%) for renal counsellors/peer-support group, 12 (12%) for welfare advisor. 40 (41%) needed medication changes. 53 (53%) had a first target weight set or had target weight adjusted.

Discussion: Earlier formal medical review of patients improves time to target weight review, referrals to the wider MDT, tailoring of immunosuppression and stopping of medications no longer indicated. Trainees gain experience of managing HD patients outside a bleep-based, trouble-shooting setting. Future data collection is ongoing to explore reduction in hospital admissions and improvements in trainee confidence in managing HD patients.

445: The Dialysis unit is on fire – learning from crisis

Dr Stephen John, Annette Dodds

University Hospitals Birmingham, Birmingham

Biography - Dr Stephen John
Consultant Nephrologist and Clinical Service Lead for Nephrology (HGS) at University Hospitals Birmingham.

Abstract
Introduction: Dialysis is a 'mission-critical' service, where therapy interruption carries significant risk of patient harm. Home therapies are vulnerable to equipment breakdown, care-giver illness and delivery failure; whilst in-centre haemodialysis (HD) can be interrupted by staff sickness, stock issues and equipment failure either at bedside or unit level. Effective response to these challenges is an important component of service management. We describe our learning from a recent fire in an in-centre HD unit.

Details: Our Trust provides one of the largest HD services in the UK, with over 1400 people on therapy in many units across a wide geographic area. The majority are off-site, with two on-site units capable of both in- and out-patient treatment. In early January 2024, an electrical fire underneath one of our on-site units led to a full evacuation of our out-patient area during a full afternoon session; smoke ingress and damage to our HD water and dialysate (CDS) circuits. This required rapid intervention from a mixed team of departmental nursing, medical, technical and operational staff; combined with site estate and fire teams. Whilst the fire was extinguished rapidly, we were left with immediate concerns including re-deployment of patients / staff into other units, the safety of running our in-patient area with a damaged circuit, the clinical risk of shutting down our entire on-site service, identification of repairs required and teams to effect these, stock ordering for extended CDS down-time and effective communication between all parties.

We managed to repair the damaged sections of water circuit within a few days, with no significant unit downtime. Our CDS repair was more complex, but completed within a week. A comprehensive strategy for team debrief and wellbeing was instituted, critically including psychological support for colleagues affected, which we were able to deliver in-house due to prior staff training.

We have identified a number of potential improvements to practice to assist if a similar event occurs in the future. These include 'grab bags' (equipment to safely care for patients with AV access needles / central lines in an evacuation area), fire protection for HD supply circuits, prospective planning for HD supply circuit repairs, regular checking of alternative back-up HD solutions and designing HD circuits with redundancy. Fire evacuation drills are important, as all staff had attended trust fire training but did not necessarily feel equipped to manage the evacuation. This event, whilst unexpected, underlines the fallacy of HD services operating at near 100% capacity, as the majority in the UK currently do, leaving little scope for flexibility in the face of emergency. Our service has 'spare capacity' via some unused twilight sessions, thus staff/patients from the affected unit could be transferred; other UK services run all units on 3 sessions / day leaving no obvious solution in such situations.

Conclusion: This event demonstrates multiple learning points. The resourcefulness of our staff, and their willingness to contribute to solutions were outstanding. We recommend that all HD services have business continuity plans that are both 'on-paper' and practised, including damage to HD supply circuits. Portable equipment to care for patients outside the HD unit is needed; segmentation of HD circuits contributes to service

resilience; fire protection to the same is underappreciated but vital. Team well-being needs prioritisation after any critical incident, which also contributes to learning both locally and for the wider renal community.

Value in kidney health: using health economics to advance kidney care

298: Cost-effectiveness of bioimpedance guided fluid management in patients undergoing haemodialysis: the BISTRO RCT

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Biography - Dr Mandana Zanganeh

Dr Mandana Zanganeh is an Assistant Professor in Health Economics and a Member of the Centre for Health Economics at the University of Warwick (CHEW) in the UK. Dr Zanganeh currently works on various funded clinical trials, involving trial-based and modelling-based studies at Warwick Clinical Trials Unit (CTU). She joined CTU in May 2021, having previously worked with a multidisciplinary team at Warwick Evidence preparing technology appraisal reviews, commissioned by the National Institute for Health and Care Excellence (NICE). Her research interests include: economic aspects of healthcare; economic evaluations alongside clinical trials; methodological concerns surrounding the conduct of economic evaluation alongside randomised controlled trials; resource use and cost (e.g. using HES data); health technology assessment and systematic reviews. Dr Zanganeh has published her research in front-line health economics and medical journals. She presents her work at various international health economics conferences. She has completed a Medical degree at Tehran Azad University of Medical Sciences, an MSc in Public Health at Anglia Ruskin University, and a fully-funded PhD in Health Economics at University of Birmingham.

Abstract

Introduction: The BISTRO randomized controlled trial (RCT) investigated the effect of bioimpedance spectroscopy added to a standardized fluid management protocol on the risk of anuria and preservation of residual kidney function (primary trial outcomes) in incident haemodialysis patients. Despite the economic burden of kidney disease, the cost-effectiveness of using bioimpedance measurements to guide fluid management in haemodialysis is not known. Therefore, the objective of this study was to assess the cost-effectiveness of bioimpedance guided fluid management (BGFM) against current fluid management (CFM) without bioimpedance.

Methods: Within-trial economic evaluation (cost-utility analysis) carried out alongside the open-label, multicentre BISTRO RCT. Four-hundred and thirty nine adult haemodialysis patients, with >500 ml urine/day or residual glomerular filtration rate >3 ml/min/1.73m2, were recruited from 34 UK outpatient haemodialysis centres, both main and satellite units, and their associated inpatient hospitals. The study intervention was the incorporation of bioimpedance technology-derived information about body composition into the clinical assessment of fluid status in patients with residual kidney function undergoing haemodialysis. Bioimpedance measurements were used in conjunction with usual clinical judgement to set a target weight that would avoid excessive fluid depletion at the end of a dialysis session.

The primary outcome measure of the BISTRO economic evaluation was incremental cost (using Hospital Episode Statistics (HES) data on episodes of care provided in hospital and case report forms (CRF) for other cost categories) per additional quality-adjusted life-year (QALY) (EQ-5D-5L) gained over 24 months following randomization. In the main (base-case) analysis, this was calculated from the perspective of the National Health Service and Personal Social Services (NHS & PSS). Sensitivity analyses explored the impact of different scenarios, sources of resource use data (CRFs) and value sets (e.g., SF-12 converted to SF-6D).

Results: The BGFM group was associated with £382 lower average cost per patient (95% CI: –£3319 to £2556) and 0.043 more QALYs (95% CI: –0.019 to 0.105) compared to the CFM group. The probability of BGFM being cost-effective was 76% and 83% at commonly cited willingness-to-pay threshold of £20,000 and £30,000 per QALY gained, respectively. The results remained robust to a series of sensitivity analyses.

Discussion: Compared with current fluid management, bioimpedance-guided fluid management produced a marginal reduction in costs and a small improvement in QALYs. Results from both the base-case and sensitivity analyses suggested that use of bioimpedance is likely to be cost-effective.

Study Registration Number
Trial registration ISCCTN Number: 11342007

534: The Utility and Cost-effectiveness of Embedding Geriatric Expertise in a Tertiary Referral Renal clinic

Dr Andrew Mooney[1,2], Dr Sam Relton[2], Dr Anna Winterbottom[1,2], Dr Dan Howdon[2], Dr Gin Aylett[1]

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Biography - Dr Andrew Mooney

Dr Mooney has been a Consultant Nephrologist since 1999 and Honorary Clinical Associate Professor in Leeds since 2013. He works full-time for the NHS but maintains a research programme with over 60 peer-reviewed publications and 3500+ citations. He has been invited speaker at multiple national and international meetings, was Lead Clinician for the NICE Renal Replacement Therapy guideline, and co-written guidelines for the European and UK Renal Associations. He has also held a UK Arts Council theatre-production project grant and won awards for his dancing, but whatever he is doing, he would always rather be at home with his family.

Abstract

Introduction: The demographic of people receiving dialysis is changing with an increasing prevalence of frailty, co-morbidity and geriatric syndromes. To address this, we initiated routine, embedded, consultant geriatric review of a selected group of patients (frail/living with frailty syndromes, age>80 preparing for dialysis, undecided between treatment options, patient/family judged by MDT to have unrealistic perception of treatment benefit) in our renal low clearance (pre-dialysis) clinic alongside our already-established palliative care service to support decision-making about treatment options for end stage kidney disease.

Participants and Methods: Starting in 2018, 77 patients were reviewed before suspension enforced by the Covid-19 pandemic in March 2020 and a further 56 since resumption between July 2021 and January 2023. We present the short-term results of all 133 patients immediately following geriatric review, plus long-term outcome data for the first 77 patients for whom we have 3 years' follow up, including health economic analysis and ANOVA of frailty and treatment choice.

Results Initially the cohort included 10 patients who had already chosen conservative management (CM) of their renal failure, but after one PDSA cycle only patients choosing dialysis or undecided about treatment choices underwent review in the service (mean age 78 [range 62-92]; 70% male).

Following geriatric review, the number of patients uncertain about their future renal treatment plan changed from 43 to 3; the number choosing to have dialysis reduced from 80 to 44 and the number choosing CM increased from 10 to 74. The number of advance care plans made among the group reviewed by the geriatrician increased from 0 to 77, and the number of DNACPR records increased from 6 to 43; there were increased referrals to falls, memory and continence clinics. Overall, 57% of patients left clinic with a different management plan.

36 months after geriatric review, the survival rate in the group choosing dialysis was 46% and in the CM group was 33%; the majority of deaths were unrelated to renal failure.

ANOVA indicated that clinical frailty scores impacted outcome more than treatment choice; the costs of providing this review (average £193 per patient) were highly likely to be more than off-set by reductions in unnecessary fistula formation alone (average £288 per patient).

Conclusions: Routine, protocol-supported geriatric review in a tertiary referral renal service is cost effective and associated with increased dialysis decision-making, reduced dialysis uptake, increased advance care-planning, increased CPR decision-making plus recognition and appropriate referral of geriatric syndromes. Outcomes in the group suggest little difference in survival among those choosing dialysis vs CM, and that frailty is more indicative of prognosis than treatment choice.

Complement inhibitors and vasopressin-2 antagonists: recent advances in renal disease

498: Clinical characteristics and long-term outcomes of 287 C3 glomerulopathy and immune complex MPGN patients from the UK National Registry of Rare Kidney Diseases (RaDaR)

Dr Sherry Masoud[1,2], Mr Lewis Downward[1], Dr Katie Wong[1,2], Clare Proudfoot[3], Dr Nicholas Webb[3], Edwin Wong[4], Daniel Gale[1,2]

[1]National Registry of Rare Kidney Diseases, Bristol. [2]UCL Department of Renal Medicine, London. [3]Novartis AG, Basel, Switzerland. [4]National Renal Complement Therapeutics Centre, Newcastle

Biography - Dr Sherry Masoud

RaDaR Research Fellow, PHD student- UCL Department of Renal Medicine Interested in glomerulonephritis, genetics, histopathology and epidemiology

Abstract

Introduction: Primary membranoproliferative glomerulonephritis (MPGN), is a rare kidney disorder which can be further divided into immune-complex MPGN (IC-MPGN) and C3 glomerulopathy (C3G) based on relative complement and immunoglobulin staining on biopsy specimens. There is limited literature on the natural history and long-term outcomes of this disorder. The aims of this study were to:

1) Describe the demographics, clinical characteristics, and long-term outcomes of patients with IC-MPGN and C3G

2) Investigate potential biomarkers as predictors for disease progression and long-term risk of kidney failure (KF)

Methods: Adult and paediatric patients with diagnostic biopsy reports that could be classified or reclassified as C3G or IC-MPGN within RaDaR were included. RaDaR contains data on MPGN patients from kidney units across the UK, with automated collection of retrospective and prospective laboratory data. Follow-up time was from diagnosis, defined by biopsy date, until KF, death or last available test result. Kidney failure was defined as initiation of dialysis, kidney transplantation or sustained eGFR ≤15mL/min/1.73m^2 for ≥4 weeks. Annualized rate of eGFR loss (eGFR slope) was calculated for the first 24 months and over full duration of follow-up. A linear mixed model was used to estimate each patient's intercept and slope of eGFR using a minimum of four observations. Analyses of time to KF were conducted using Kaplan–Meier estimates with log-rank tests for comparisons and Cox regression. The latter was used to investigate the association of early (within 24 months of diagnosis) changes in urine protein:creatinine ratio (UPCR), eGFR and eGFR slope and long-term risk of KF.

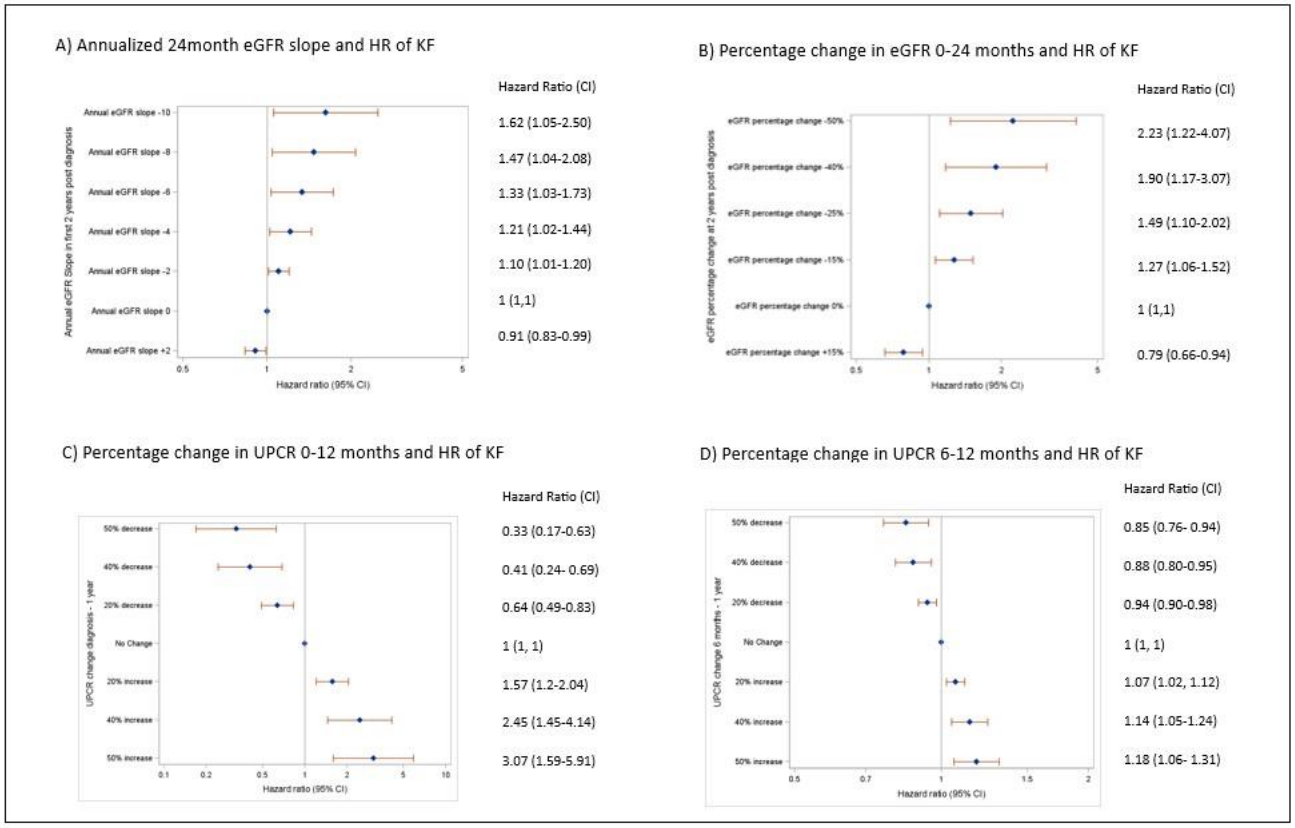
Results: Our cohort included 135 patients with C3G and 152 patients with IC-MPGN diagnosed between 1987 and 2020. At the time of diagnosis 153/287 (53%) of the cohort were paediatric (<18 years old). Both groups had significant proteinuria at baseline (Table 1). Median eGFR was 70mL/min/1.73 m^2 (IQR 30-92) and 58mL/min/1.73 m^2 (IQR 40-110) for C3G and IC-MPGN respectively. Median time to KF was 9.3 years for C3G and 12 years for IC-MPGN but the difference was not statistically significant (p= 0.31). KF was significantly associated with changes in UPCR between 0-12 months and 6-12 months (HRs adjusted for eGFR) (Figure 1). Similarly, a 50mg/mmol reduction in time-averaged UPCR between 0-12 months and 6-12 months was also strongly associated with a lower risk of KF (HR adjusted for eGFR [95% Confidence Interval] 0.66 [0.53-0.83] and 0.71 [0.59-0.85] respectively). Both annualized 24 month eGFR slope, and percentage change in eGFR at 24 months were also significantly associated with KF events (Figure 1).

Discussion: We present one of largest studies describing the demographics, clinical characteristics, and long-term outcomes of 287 with IC-MPGN and C3G. Consistent with other studies we found no statistically significant difference in time to KF for C3G and IC-MPGN patients (1). We also demonstrate the value of short-term changes in proteinuria and eGFR (within 24 months of biopsy diagnosis), for predicting long-term risk of kidney failure.

Table 1. Baseline Characteristics and Clinical Outcomes of UK patients with C3G or IC-MPGN

	C3G		IC-MPGN	
	N	(%)	N	(%)
Age at diagnosis (years)				
Median (IQR)	14 (9 - 34)		23 (9 - 55)	
Pediatric	82	(61)	71	(47)
Sex				
Male	65	(48)	79	(52)
Ethnicity				
White	100	(74)	120	(79)
Median follow up duration				
Median (IQR), years	5.8 (2.9-11.4)		6.8 (1.8- 11.4)	
UPCR (Median IQR, mg/mmol)				
Diagnosis	412 (126 - 700)		466 (167 - 820)	
6-month	150 (71 - 436)		92 (28 - 253)	
12-month	128 (25 - 413)		78 (18 - 311)	
eGFR at diagnosis				
Median (IQR), mL/min/1.73 m^2	70 (30 - 92)		58 (40 - 110)	
Serum albumin at baseline				
Median (IQR), g/L	31 (23-38.5)		28.5 (22-36)	
Complement C3 levels at diagnosis				
Median (IQR), g/L	0.26 (0.12, 0.47)		0.64 (0.20, 0.94)	
Complement C4 levels at diagnosis				
Median (IQR), g/L	0.19 (0.14, 0.30)		0.14 (0.09, 0.23)	
Kidney Failure event				
Yes	85	(63)	107	(70)
No	50	(37)	45	(30)
eGFR slope				
Mean (95% CI), mL/min/1.73m2/year	-4.9 (-7.0, -2.9)		-3.3 (-4.6, -2.1)	

Figure 1. Forest Plots of UPCR and eGFR changes within 24 months of diagnosis and hazard ratio of kidney failure for IC-MPGN and C3G combined



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110: Efficacy of 12-week pegcetacoplan in kidney transplant recipients with recurrent C3 glomerulopathy (C3G) or immune complex membranoproliferative glomerulonephritis (IC-MPGN)

Dr Andrew Bomback[1], Dr Erica Daina[2], Professor John Kanellis[3], Professor David Kavanagh[4], Professor Matthew C. Pickering[5], Professor Gere Sunder-Plassmann[6], Dr Patrick Walker[7], Dr Zhongshen Wang[8], Dr Zurish Ahmad[8], Professor Fadi Fakhouri[9]

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Biography - Dr Andrew Bomback

Dr Bomback is a nephrologist specialised in glomerular diseases and resistant hypertension. He received his undergraduate degree from Harvard University and his medical degree from Columbia University College of Physicians and Surgeons. He completed residency in Internal Medicine and fellowships in Nephrology and Clinical Epidemiology at the University of North Carolina. In 2009, he returned to Columbia University as an associate at the Centre for Glomerular Diseases and is currently Assistant Professor of Medicine at Columbia University Medical Centre. Dr Bomback is a member of the Columbia Doctors Hypertension Centre, a multi-disciplinary centre of excellence that provides high quality care and state-of-the-art diagnostic testing for patients with hypertension. Dr Bomback has published >100 peer-reviewed articles and book chapters on the subjects of chronic kidney disease, glomerular diseases, and hypertension. He is an editor of the National Kidney Foundation's Primer on Kidney Diseases. Dr Bomback's research interests focus on novel therapies for glomerular diseases, the role of aldosterone in chronic kidney disease and obesity/metabolic syndrome. He currently serves as principal or co-investigator on clinical trials of new treatments for IgA nephropathy, membranous nephropathy, lupus glomerulonephritis, hereditary nephritis, C3 glomerulopathy, and focal segmental glomerulosclerosis.

Abstract

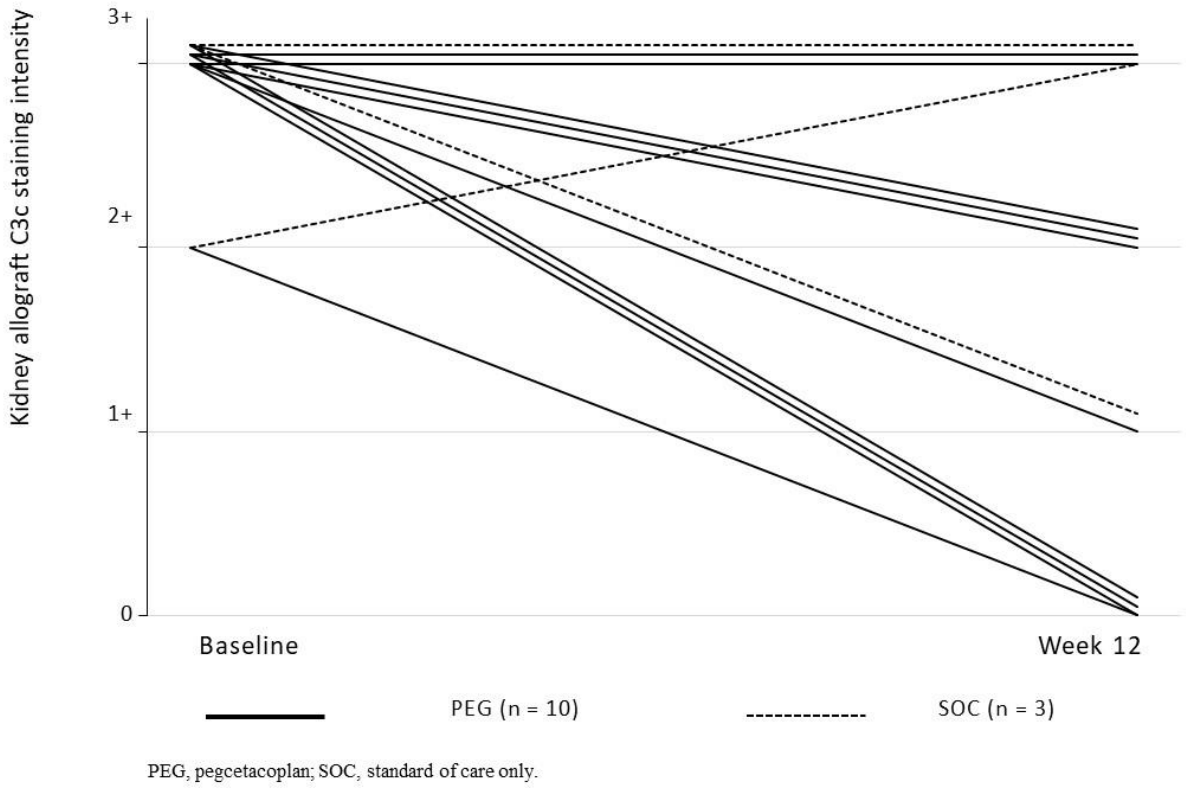
Introduction: Excessive deposition of C3 breakdown products in the kidney can lead to inflammation and damage of the kidney, often causing kidney failure. Pegcetacoplan (C3 inhibitor) may prevent C3 glomerulopathy (C3G) or immune complex membranoproliferative glomerulonephritis (IC-MPGN) progression. The Phase 2 NOBLE trial (NCT04572854) is the first prospective, multicentre, open-label, randomised controlled trial to evaluate the efficacy and safety of pegcetacoplan vs standard of care (SOC) in kidney transplant recipients with primary C3G or IC-MPGN recurrence.

Methods: Adult patients were randomised 3:1 to subcutaneous pegcetacoplan 1080 mg twice weekly plus SOC (n=10) or SOC only (n=3). Primary endpoint: reduction in renal biopsy C3c staining (≥2 orders of magnitude [OOM]) from baseline to Week 12 (W12). Additional W12 endpoints: changes in estimated glomerular filtration rate (eGFR), urine protein to creatinine ratio (uPCR), C3G activity score, serum C3, and serum sC5b-9.

Results: 9 (69.2%) patients had C3G and 4 (30.8%) had IC-MPGN. At W12, 5 (50%) pegcetacoplan patients had ≥2 OOM reduction in C3c staining (4 had 0 intensity); 8 (80%) had ≥1 OOM reduction (**Figure**). 9 (90%) pegcetacoplan patients had reduced C3G activity scores at W12. In subgroup (≥1000 mg/g), uPCR decreased with pegcetacoplan (–39.2%) at W12. The eGFR remained stable, serum C3 increased, and sC5b-9 decreased with pegcetacoplan (**Table**). There were no discontinuations/deaths due to treatment-emergent adverse events.

Conclusion: As early as W12, pegcetacoplan reduced C3c staining and proteinuria with stable eGFR, targeted the pathophysiology of C3 dysregulation, and was well tolerated in kidney transplant recipients with recurrent C3G or IC-MPGN.

Figure. Individual changes in C3c biopsy staining



PEG, pegcetacoplan; SOC, standard of care only.

Table. Clinical and biomarker changes in C3G and IC-MPGN

		uPCR (mg/g)		uPCR (mg/g)[a] (Patients with ≥1000 mg/g at Baseline)		Serum C3 (mg/dL)		Serum sC5b-9 (ng/mL)		eGFR (mL/min/1.73m²)	
		PEG[b] (n=9)	SOC[c] (n=3)	PEG[b] (n=5)	SOC[c] (n=2)	PEG[b] (n=9)	SOC[c] (n=2)	PEG[b] (n=10)	SOC[c] (n=3)	PEG[b] (n=9)	SOC[c] (n=3)
Baseline	**Mean[d] (SD)**	1506.7 (1097.23)	2314.8 (2170.68)	2349.3 (595.15)	3217.3 (2129.81)	56.1 (33.83)	103.0 (67.88)	651.4 (1024.68)	145.3 (41.28)	51.8 (13.18)	53.3 (11.37)
Week 12	**Mean[d] (SD)**	1048.7 (1293.10)	2412.9 (1980.32)	1582.9 (1559.20)	3150.3 (2140.18)	291.1 (92.11)	89.5 (53.03)	123.4 (82.26)	228.7 (162.54)	53.7 (23.11)	47.3 (11.85)
Change from baseline	**Mean[d] (SD)**	−458.0 (956.06)	98.1 (286.08)	−766.4 (1182.82)	−67.0 (10.37)	235.0 (83.71)	−13.5 (14.85)	−528.0 (955.19)	83.3 (121.33)	1.9 (21.74)	−6.0 (2.65)

C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex membranoproliferative glomerulonephritis; PEG, pegcetacoplan; SD, standard deviation; SOC, standard of care; uPCR, urinary protein-to-creatinine ratio.

[a]Measured by triplicate first-morning spot urine.

[b]Patients received subcutaneous pegcetacoplan 1080 mg twice weekly plus standard of care. Of 10 patients, 8 (80%) had C3G, and 2 (20%) had IC-MPGN. The mean (SD) age of the patients was 39.8 (12.59) years.

[c]Patients received standard of care only (SOC). Of 3 patients, 1 (33%) had C3G and 2 (67%) had IC-MPGN. The mean (SD) age of the patients was 44.3 (24.03) years.

[d]Means were calculated only using non-missing values.

Study Registration Number

NCT04572854

Navigating implementation of patient reported experience and outcome measures

403: Developing a core outcome set for pharmacist interventions in chronic kidney disease: results from an international survey and e-Delphi consensus study

Mr Ashkon Ardavani[1], Dr Ffion Curtis[2], Dr Patrick Highton[1], Professor Kamlesh Khunti[1], Dr Thomas Wilkinson[3]

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Biography - Mr Ashkon Ardavani
I am a final year NIHR-ARC EM PhD student at the University of Leicester and a GPhC-registered pharmacist. My PhD is investigating the role of pharmacists in managing people living with chronic kidney disease.

Abstract
Introduction: Research has demonstrated the benefits of interventions delivered by pharmacists in people with chronic kidney disease (CKD). However, significant variation exists for reported outcomes and the inconsistency in outcome measures used limits effective interpretation of the evidence. A core outcome set (COS) is a collection of outcomes that are standardised and agreed upon, where various stakeholders such as researchers, healthcare professionals, and patients provide input on outcomes which they think as a minimum should be reported for all trials for a specific therapeutic area. The Standardised Outcomes in Nephrology (SONG) initiative was launched to improve consistency in reporting of outcomes for trials in nephrology. Whilst SONG has developed COS for trials relevant for disease stage, population, and diagnoses, no COS that is intervention-specific (i.e. outcomes in pharmacy research in CKD) exists. The aim of this study was to develop a COS for pharmacist interventions in CKD.

Methods: This study consisted of two phases: Phase 1) an online survey of key stakeholders, and Phase 2) an e-Delphi survey. Phase 1 generated a long list of outcomes that was supplemented with outcomes identified from a systematic review. In Phase 2, an e-Delphi study, participants ranked these outcomes in terms of importance using the 9-point Likert scale over two rounds. Outcomes deemed 'important' (scored 7-9) by ≥75% were used to inform a provisional COS. We aimed to recruit a diverse range of participants from each of the following stakeholder groups: pharmacists, researchers, other healthcare professionals (HCPs), people living with CKD, and their family members/carers.

Results: 110 participants took part in Phase 1, and 90/110 (81.8%) took part in Phase 2 (e-Delphi). Participants were asked to rank a total of 65 outcomes. 42/90 (46.7%) participants completed Round 1 of the e-Delphi survey and 30/42 (71.4%) participants completed Round 2. Of these, in Round 2, n = 21/30 (70%) identified as someone living with kidney disease; n = 3/30 (10%) as a family member/carer; n = 5/30 (16.7%) as a researcher; n = 3/30 (10%) as another HCP, and n = 6/30 (20%) as a pharmacist. Participants were from a range of countries including the United Kingdom, the United States, and Spain.

No outcomes in either round were deemed to be of no importance. Following Round 2, 25 outcomes reached the ≥75% threshold to form a provisional COS (Table 1) that can be categorised under four outcome domains.

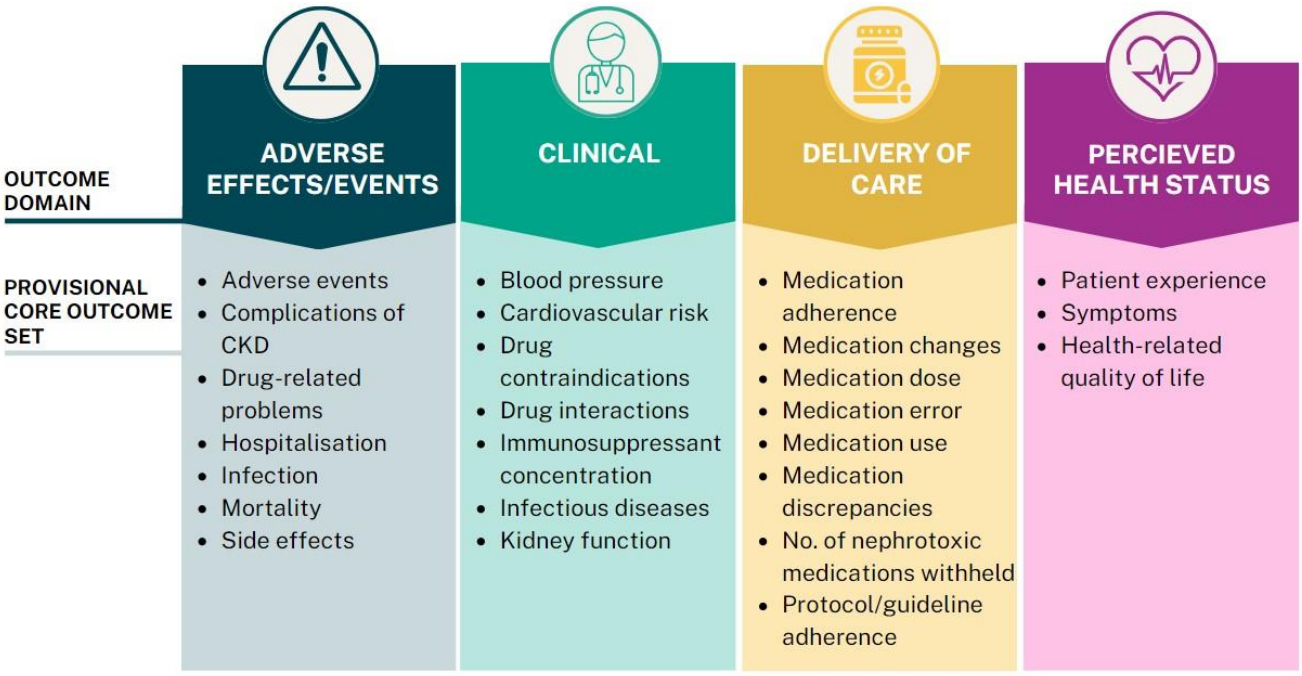

Figure 1. Provisional core outcome set with outcome (n=25) categorised under four domains

Discussion: The findings of this study will help establish a COS in CKD in relation to pharmacy research, where outcomes included will reflect those that are important to different stakeholder groups, including people with living experience of CKD, and be consistently reported in trials, helping reduce waste in research and improve interpretability of interventions. This study has important clinical implications and addresses a key gap for achieving consensus and improving the consistency of outcomes reported.

Study Registration Number

ClinicalTrials.gov (NCT05987280).

Blood purification: have we reached the end of the road with the tools that we have?

566: The CompAct-HD trial reports a persistent inflammatory profile in patients undergoing haemodialysis, acutely exacerbated with each haemodialysis treatment

Dr Duha Ilyas[1,2], Dr Elizabeth Blackburn[3], Dr Andy Herbert[3], Dr Leonard Ebah[1], Ms Jennifer Mackie[3], Dr Thomas Lindsay[1], Professor Sandip Mitra[1]

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Biography - Dr Duha Ilyas
Duha Ilyas is a nephrology trainee and Clinical Research Fellow currently a PhD student conducting clinical research in Manchester looking at the role of inflammation as a consequence of haemodialysis and patient outcomes.

Biography - Dr Elizabeth Blackburn
Elizabeth Blackburn is a biochemist with a particular interest in structural biology, enzymology and protein recognition in an immunological context. Her research as been focussed on the cyclophilin family of proteins, large bacterial virulence factors and the complement system. In her laboratory, use of robotic automation and multiplexing has facilitated the exploration of multiple biomarkers from small volumes of clinical samples.

Abstract
Introduction: Inflammation induced by haemodialysis (HD) treatment has been recognised for several decades. Despite significant advances in technology, there is evidence that incompatibility between the dialyser, a foreign surface, and the patients' blood, results in activation of the immune system. With each session, blood-membrane interaction leads to a repetitive activation of the innate complement system and a subsequent inflammatory response in patients. It is now widely acknowledged that the consequences of long-term inflammation include fibrosis and accelerated cardiovascular disease, a common cause of mortality in patients with renal failure.

The aim of the CompAct-HD trial is to characterize complement activation and biomarker response to blood-membrane-circuit interaction during HD.

Methods: For a single session, six timed intradialytic blood samples were collected from HD patients during standard treatment with ultrapure water and high flux "biocompatible" membranes. Complement activity potential was determined from timepoint 1 and inflammatory biomarkers from timepoints 2 to 6. Single time point samples were also collected from 7 healthy donors for comparison.

Highly multiplexed assays enabled to determine 30 biomarkers of inflammation, including cytokines, chemokines, growth factors and complement proteins, from a single blood sample.

All data analysis was performed using Microsoft© Excel Version 16.80 and GraphPad Prism 10.1.0.

Results: 354 patients were recruited from 8 dialysis units across Greater Manchester, United Kingdom. An interim analysis was performed on 150 HD patients receiving standard care as well as 7 healthy donors.

Dialysis appears to generate an acute inflammatory response, that is, within 15 minutes of commencing treatment which does not appear to resolve by the end of the session.

This heightened inflammatory state was observed in HD patients in comparison to healthy donors (Figure 1) with most pronounced changes seen in cytokines IL-1b, IL-10, IL-12p40 and TNF-a during dialysis. Established markers such as IL-6 also showed a 6-fold increase at the 75th percentile. Similarly, an exaggerated intradialytic response was observed in complement proteins, including the terminal complex C5b-9 and anaphylatoxin C5a with spikes of up to 7-fold and 10-fold respectively (Figure 2).

A session of haemodialysis was shown to cause a relative increase in complement proteins and inflammatory biomarkers in patients. The magnitude of response seen in patients was variable (Figure 3) with the greatest rise seen in the top quartile (above the Q3 boundary).

Discussion: Our findings evidence a sharp inflammatory response to modern day HD treatment across a large cohort of dialysis patients. When compared to healthy donors, we observed heightened levels of inflammation in patients with end stage renal failure that is further exacerbated with each session of dialysis therapy.

In summary, our study shows that haemodialysis has a significant role to play in the chronic inflammatory state of patients with end stage renal failure. Furthermore, here we describe potential targets, in both cytokine and complement proteins, which could be the key to downregulation of inflammation. By narrowing our focus towards targeted therapeutics, we have an opportunity to deliver a more biocompatible treatment and ultimately improve outcomes for patients undergoing haemodialysis.

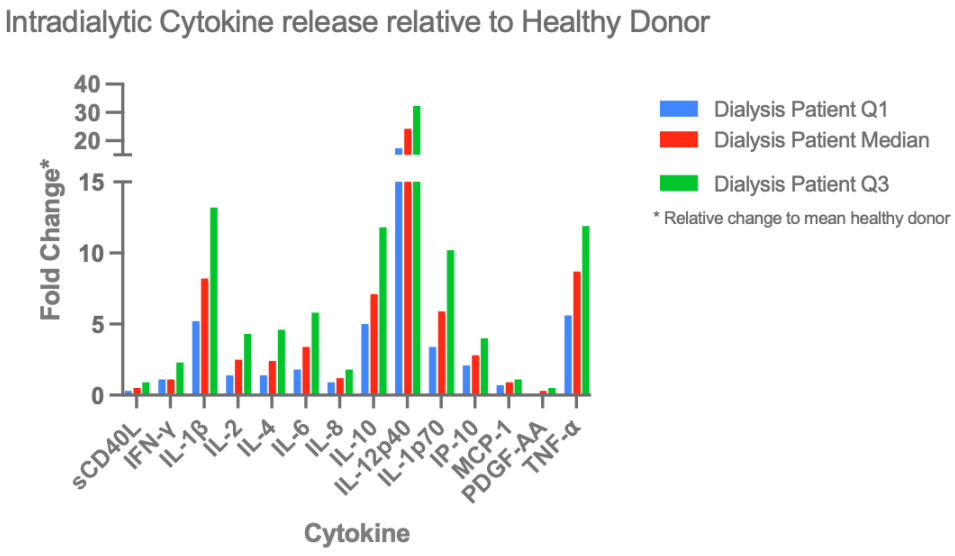
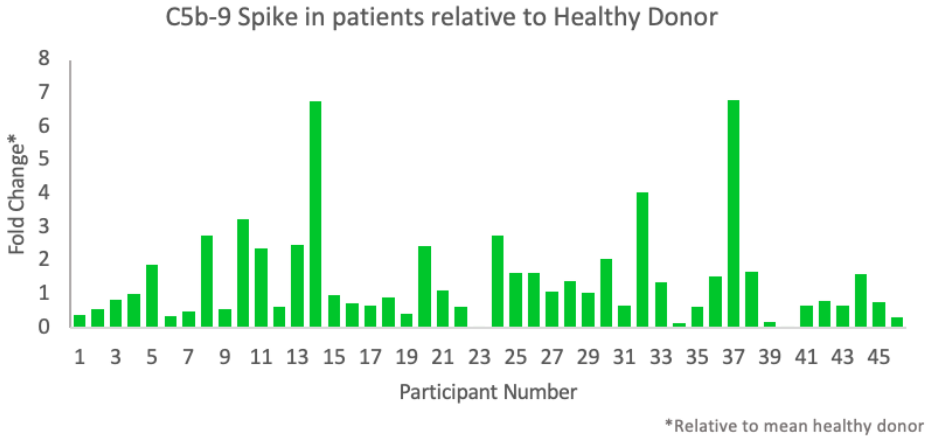


Figure 1: Average of peak cytokine release measured during a haemodialysis session for 150 haemodialysis patients. All measurements scaled to single point healthy donor values showing relative inflammation across all cytokines. The most pronounced changes are observed in IL-1β, IL-10, IL-12p40 and TNF-α with patients in the top quartile (75th percentile) with increases of up to 32-fold relative to healthy donors.



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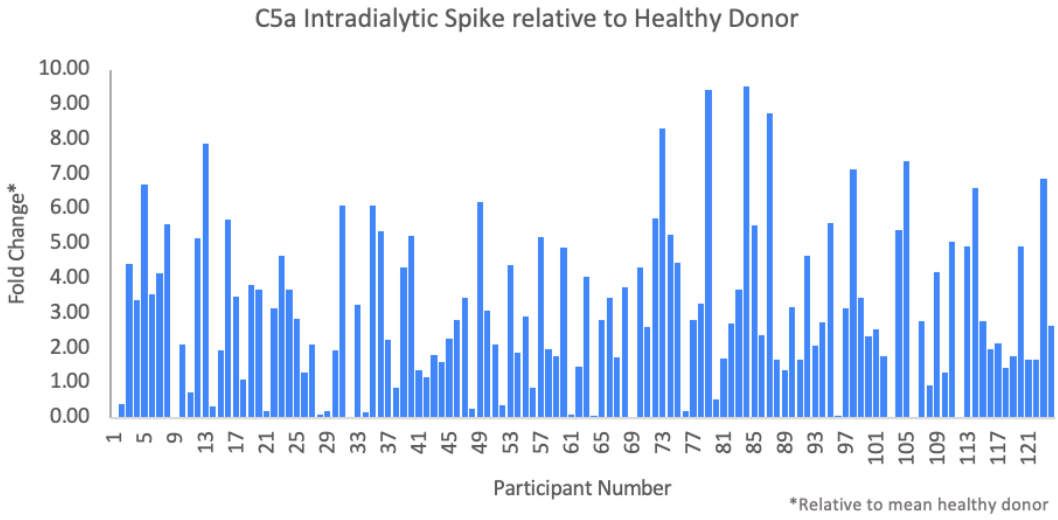
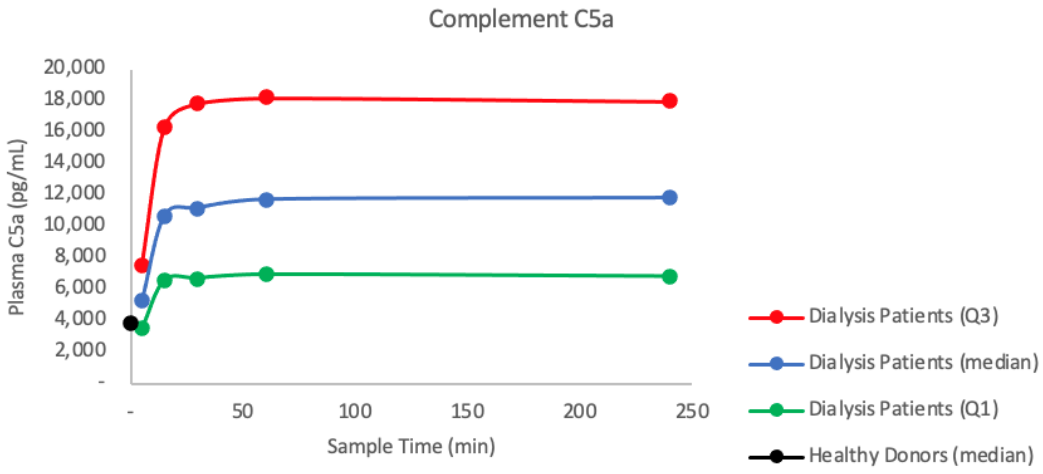


B.

Figure 2: A. A sub-analysis of 48 patients shows a relative intradialytic spike of C5b-9 (terminal complement complex) when scaled to the average healthy donor. Overall, a rise in levels was detectable with increases of up to 7-fold in some patients during one session of dialysis. B. Intradialytic spike of C5a when scaled to healthy donor showed increases of up to 10-fold.



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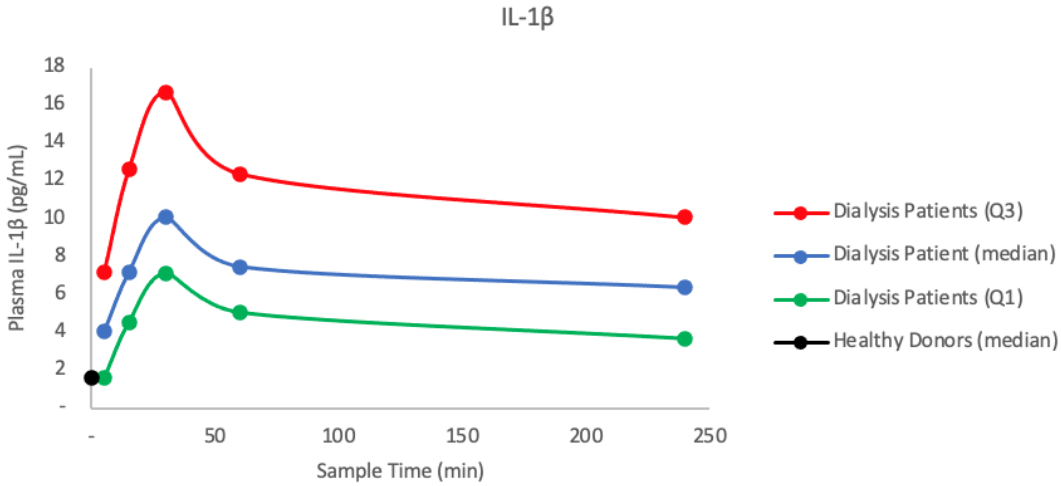

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Figure 3: A. Levels of C5a measured during HD showed an acute response that occurs within the first hour of treatment and remains elevated for the remainder of the dialysis session. B. Levels of IL-β show an acute rise within 30 minutes of commencing HD followed by a gradual fall, however, do not return to baseline levels on completion.

Body composition and its response to intradialytic exercise in kidney failure: a combined analysis of the PEDAL and CYCLE-HD randomised controlled trials

Dr Khai Ping Ng[1], Prof Jamie MacDonald[2], Mr Robin Young[3], Dr Daniel March[4], Dr Matthew Graham-Brown[4], Prof Tom Mercer[5], Dr Sharlene Greenwood[6], Prof James Burton[4], Prof Indranil Dasgupta[7]

[1]Renal medicine, University Hospitals of Derby and Burton. [2]Institute for Applied Human Physiology, Bangor University. [3]Robertson Centre for Biostatistics, University of Glasgow. [4]Cardiovascular Science, University of Leicester. [5]Centre for health, activity and rehabilitation research, Queen Margaret University. [6]Renal medicine, King's College Hospital. [7]Renal medicine, University Hospitals Birmingham

Biography - Dr Khai Ping Ng
Consultant nephrologist

Abstract
Background: Patients with kidney failure on hemodialysis (HD) are at high risk of sarcopenia obesity, highlighting the need for effective nutrition and exercise strategies to improve long-term outcomes. This post-hoc analysis of the PEDAL and CYCLE-HD studies aimed to 1) determine the clinical utility of fat tissue index (FTI) and lean tissue index (LTI) in comparison to body mass index (BMI) and 2) assess the effect of a 6-month intradialytic exercise intervention on FTI and LTI compared to usual care.

Methods: BMI, FTI and LTI were *a priory* secondary endpoints in both the PEDAL and CYCLE-HD trials. BMI was classified as per World Health Organisation (WHO) definitions. FTI and LTI were determined by Bioelectrical Impedance Analysis (BIA) and classified as per the MONDO study [1], that found an FTI of 4-15kg/m^2 and an LTI of 15-20kg/m^2 were associated with best survival.

Results: Across both studies, 298 participants had BIA measurement at baseline; with 209 at baseline and 6-months. Mean age was 58±15 years, 65% male, median HD vintage 1.3 years (IQR 0.5-3.4) and mean BMI of 28.3±6.3kg/m^2. BMI correlated with FTI (r=0.79; p<0.0001). Of those with healthy BMI (n=198), 17% were over-nourished by FTI (>15kg/m^2) and 74% undernourished (LTI <15kg/m^2). Conversely, among those with an FTI of 4-15kg/m^2, 14% were categorised as overweight or obese by BMI. There was no significant correlation between BMI and LTI; 24% had BMI ≥30kg/m^2 and LTI <15kg/m^2 (sarcopenic obesity); only 16% had both FTI of 4-15kg/m^2 and an LTI of 15-20kg/m^2. With intradialytic exercise, there was no significant difference between the groups in change over 6 months for LTI (-0.33, CI -1.08-0.41; p=0.4) or FTI (0.16, CI -0.69-1.00; p=0.7), regardless of compliance.

Conclusion: This study highlighted issues of body composition misclassification using conventional BMI cut-offs in HD patients. Only a minority of patients had both LTI and FTI within the range associated with best survival. The majority of patients had hidden sarcopenia with nearly 75% with normal BMI being sarcopenic. 6-months of intradialytic exercise did not improve body composition, suggesting alternative interventions are required to target fat and lean tissue mass and enhance patients' survival.

References

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Expanding access to home dialysis

225: Peritoneal dialysis nursing workforce: how does variation within a regional network effect quality of care?

Ms Katie Durman[1], Ms Babakang Shakoane[2], Ms Fatima Moreira[3], Ms Gloria Munoz-Figueroa[4], Dr Bhrigu Raj Sood[4], Ms Marizia Procopio[5], Dr Richard Corbett[6]

[1]Barts Health NHS Trust, London. [2]Kings College Hospital NHS Foundation Trust, London. [3]Royal Free NHS Foundation Trust, London. [4]Epsom and St Helier University Hospitals NHS Trust, Surrey. [5]London Kidney Network, London. [6]Imperial College Healthcare NHS Trust., London

Biography - Ms Katie Durman

I have held the position of Clinical Lead Renal Dietitian at Barts Health NHS Trust for the past 17 years. During this time, I have led the renal dietetic renal team and have worked in all areas of renal dietetics, currently specializing in dietetic management of those on peritoneal dialysis. I hold the position of guidelines lead on the Renal Nutrition Group of the British Dietetic Association. I was part of the dietetic group who updated UKKA Multi-professional Renal Workforce Plan for Adults and Children with Kidney Disease and am currently part of the multi-professional group writing the UKKA Hypertension in Dialysis guideline. For the past 3 years I have been working part time with the London Kidney Network as one of the multi-professional leads. This has been a fantastic opportunity to work across London to support the implementation of the RSTP and GIRTH and improve the outcomes for those with CKD. I have been working the home therapies workstream leading on workforce and training and leading the wider nursing group whilst a nursing lead is appointed.

Abstract

Introduction: The importance of supporting sustainable growth in home dialysis, including peritoneal dialysis (PD) has recently come to the fore. A skilled and adequately resourced workforce is central to high quality care; nurses, in particular play a key role in the delivery of PD with wide ranging and varied roles depending on the service model. However, there is limited guidance as to what good staffing ratios look like; in an effort to identify good practices, we investigated the variation in PD nursing numbers across a regional network.

Methods: The PD teams across all the renal units in our region were contacted. We identified the skill mix and whole time equivalent (WTE) of nursing staff along with nursing roles including patient training. Where home haemodialysis and peritoneal dialysis nursing teams were combined, the lead nurse was asked to estimate the time spent on each modality. Nursing workforce size was compared by unit with the prevalent PD population as well as peritonitis rates, as a marker of quality of care.

Results: Across the seven renal units, two units provided an in-house assisted PD service, the nursing team delivering these services were excluded from the analysis. There was a wide variation in nursing workforce skill mix, three units were led by a Band 8a nurse, while registered nurses (Band 5 and greater) formed between 60-100% of the workforce.

The key workforce descriptors are included in Table 1. Prevalent PD nursing staff to patient ratios ranged from 15 to 22. In general, units with larger PD programs had higher staff ratios. Peritonitis rates were weakly positively correlated with nursing workforce ratios ($r=0.33$, $p=0.48$). The unit with the highest patient to staff ratio, along with the lowest proportion of registered nurses had the highest peritonitis rate.

Unit	PD numbers Dec 2022	Registered Nurses (WTE)	Non-registered nurses (WTE)	Total nursing workforce (WTE)	% of registered nurses	Number of patients per nursing staff	Peritonitis rate (per 1 PD patient year) Dec 2022
A	237	6.47	4.4	10.87	60	22	0.455
B	199	10.5	0.8	11.3	93	18	0.249
C	150	8.8	1.4	10.2	86	15	0.336
D	129	6	2	8	75	16	0.365
E	106	7	0	7	100	15	0.272
F	71	4	0	4	100	18	0.320
G	46	4	0.5	4.5	89	10	0.348

Discussion: There are great variations at regional level between units in both workforce numbers but also skill mix along with the tasks undertaken by PD nursing teams. The use of nursing workforce ratios is further confounded by the effect of small changes in patient or staff numbers. The use of prevalent PD population alone is also limited as an indicator of workforce demands given that the greatest care needs arise at the start, and to a lesser extent at the end, of dialysis, particularly around patient training. It is unsurprising that there was an, albeit non-significant, correlation between workforce size and peritonitis rates.

The delivery of high-quality and safe PD services require an appropriately resourced and skilled nursing workforce, to ensure sustainable growth in home dialysis, the use of staffing ratios alone are unlikely to define what good care looks like.

428: An intervention bundle to improve home dialysis uptake: results of the 'Intervening to eliminate the centre effect variation in home dialysis use' ('Inter-CEPt') study

Professor Simon Davies[1], Professor Iestyn Williams[2], Dr Mark Lambie[1], Ms Louise Weight[1], Mr David Coyle[3], Dr Sarah Damery[2], Dr James Fotheringham[4], Dr Kerry Allen[2], Dr Ivonne Solis-Trapala[1], Dr Jessica Potts[1]

[1]Keele University, Newcastle-under-Lyme. [2]University of Birmingham, Birmingham. [3]Devices for Dignity MIC, Birmingham. [4]University of Sheffield, Sheffield

Biography - Professor Iestyn Williams

Iestyn is a Professor of Health Policy and Management and Director of Research for the School of Social Policy. He is involved in a range of research, teaching and knowledge transfer work and has a broad methodological experience and expertise. He specialises in social science approaches to Health Services Research, employing mixed methods study designs. He has specific expertise in: priority setting, decision making and decommissioning in health care; strategic planning and decision making; implementation studies, and intervention development.

Abstract

Introduction: In England there is inequity of access to home dialysis, especially among ethnic minorities and socially deprived patients. The Inter-CEPt study employed mixed multi-disciplinary research methods to investigate the determinants of home therapies usage. Centre-level factors influencing uptake were identified from ethnographies of four renal centres in the English NHS and graphical Markov modelling incorporating results from a national survey with patient-level data from the UK renal registry.

Methods: Drawing on principles of user-centred design and theories of behaviour change, results were used to inform the development of an intervention 'bundle', in which the COM-B framework was used to identify potential behaviour change strategies targeting the modifiable factors identified in the study. These were discussed in two deliberative stakeholder workshops and subject to rapid evidence review and contemporary cost effectiveness analysis.

Results: The 'Location of Care in Kidney Life' (LOCAL) intervention bundle is designed to support kidney centres and their patients in making decisions over location and modality of dialysis treatment, recognising that kidney teams and services have different resources to draw on and can face a variety of challenges when considering how to improve use of home dialysis. The study found that services optimise use when they have the time, resources, expertise and inclination to take a flexible 'learning' approach. This suggests that centre culture is perhaps the single most important factor. In recognition of this, the LOCAL bundle is designed to help create the conditions for more effective consideration of location of care, and to knit together the elements required to achieve this.

The two main components of the bundle are recommendations for a) service improvement cycles to identify and overcome impediments to optimal use of home dialysis, and b) adoption of dedicated 'location of care' roles within multi-disciplinary teams (see figure). The bundle also recommends making Assisted Peritoneal Dialysis universally available and investing in home dialysis roadshows. For most kidney services in England, implementation of the bundle will require some allocation or reallocation of resources that the economic evaluation shows would likely be cost effective.

Success will therefore depend on local ownership, willingness to innovate and, where necessary, change behaviour. It is also clear that the bundle will require the dedication of some resources – especially human – in order to have a significant impact.

Discussion: The 'Location of Care in Kidney Life' (LOCAL) intervention bundle is an evidence-based, coproduced service intervention designed to improve uptake of home dialysis. The next phase of this work will involve evaluation of its implementation and outcomes, drawing on multiple quantitative and qualitative measures.

Study Registration Number
Award ID: NIHR128364

Preventing kidney complications associated with diabetes: the hot potato!

272: New clinical pathways to transform identification and management of early stage chronic kidney disease in people with and without Type 2 diabetes across London

Ms Linda Tarm[1,2], Dr Catriona Shaw[3,1], Dr Neel Basudev[1,4,5], Dr Kieran McCafferty[6,1]

[1]London Kidney Network, London. [2]Guy's & St Thomas' NHS Foundation Trust, London. [3]King's College Hospital NHS Foundation Trust, London. [4]London Diabetes Clinical Network, London. [5]Health Innovation Network (South London Academic Health Science Network), London. [6]Barts Health NHS Trust, London

Biography - Ms Linda Tarm

Linda Tarm is the Clinical Co-Chair of the Chronic Kidney Disease (CKD) Prevention Workstream within the London Kidney Network. She provides strategic oversight and leadership to ensure the workstream is on track to achieve its aims, which includes supporting primary care to optimise early identification, coding and management of CKD. Linda's role has a strong focus on collaboration and cross-partnership working with primary and secondary care, both at local and national level. Linda qualified as a Dietitian in New Zealand and was awarded a National Institute for Health & Research Bursary to complete a Masters in Clinical Research in London. Prior to joining the London Kidney Network, Linda led the Guy's & St Thomas' Renal Dietetic Service. She has extensive clinical and renal experience and is particularly interested in preventative care and improving patient outcomes. Linda has established effective partnerships across networks, organisations, teams and at an individual level.

Abstract

Introduction: Chronic kidney disease (CKD) affects 1 in 10 people in the UK, costs the NHS at least £1.95 billion each year and is predicted to become the fifth leading cause of premature death by 2040.[1] To improve outcomes in people with or at risk of CKD, urgent action is needed to identify CKD early, prevent its progression and optimise management.

Several landmark trials[2,3] have transformed the evidence base for Sodium-glucose co-transporter-2 inhibitors (SGLT2i) in CKD.

Our aim was to use this new evidence to develop pathways to support primary care to identify and optimise CKD management early in people with or at risk of CKD using crude SGLT2i use as an indicator of progress.

Methods: The London Kidney Network (LKN) brought together clinicians (including nephrologists, diabetologists, GPs, AHPs) to produce three pathways, i.e.:

1. CKD Early Identification Pathway
2. CKD Optimisation Pathway for adults with Type 2 diabetes (T2DM) and CKD
3. CKD Optimisation Pathway for adults with albuminuria, but without T2DM

Our pathways align with relevant NICE,[4-6] UKKA[7,8] and ABCD[8] recommendations on CKD assessment, management and treatment. We also examined data sources to explore SGLT2i use in London over time.

Results:

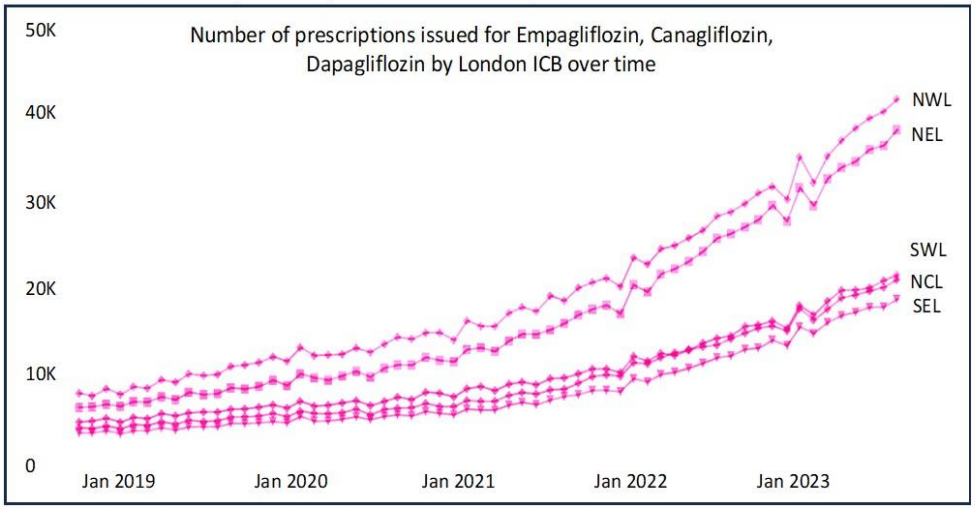
Pathway 1: CKD Early Identification Pathway

This pathway is a kidney health check for adults at risk of CKD including those with T2DM or hypertension. It includes both the uACR and eGFR test, and emphasises the importance of regular uACR testing along with coding, patient education and lifestyle advice for those diagnosed with CKD.

Pathways 2 & 3: CKD Optimisation Pathways for adults with T2DM and CKD and for those with albuminuria but without T2DM

These pathways focus on '3 key actions within 3 months' to save lives in those with and without T2DM. They are based on optimising ACEi/ARB dose in month 1, starting SGLT2i according to licence/indication in month 2 and BP optimisation in month 3.

Figure 1: Using open prescribing data, SGLT2i use in London Integrated Care Boards (ICBs) has risen by over 50% since the LKN pathways launched in September 2022



Key:
NWL = Northwest London
NEL = Northeast London
SWL = Southwest London
NCL = Northcentral London
SEL = Southeast London

Discussion: These pathways were launched in September 2022 and are now integrated into official CKD guidelines across London Integrated Care Systems. Our pathways may have helped to account for the rise in crude SGLT2i use across London. However, it is likely that other initiatives (e.g. as part of extending licences for SGLT2i in heart failure, along with increasing familiarity with this class in T2DM) will have contributed to this rise. In addition, this data does not describe the prevalence of SGLT2i use compared to the population who could benefit. Despite this overall increase, significant variation exists within London ICBs in crude SGLT2i usage. Tackling this inequality will be a future focus of work.

Supporting implementation of our pathways has provided valuable insight into the barriers and enablers to better CKD care across London. We will be updating our pathways as new medical therapies become available/are approved by NICE, e.g. Finerenone and the expansion of SGLT2i use in CKD with Empagliflozin.

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566: Serum miRNAs as novel biomarkers and modulators of rapidly progressing Chronic Kidney Disease in patients with Diabetes

Mr Callum McDowall[1], Dr Liliana Shalamanova[1], Dr Fiona Wilkinson[1], Dr James Pritchett[1], Dr Stephen White[2], Professor Philip Kalra[3]

[1]Manchester Metropolitan University, Manchester. [2]Newcastle University, Newcastle. [3]Salford Royal Hospital, Salford

Biography - Mr Callum McDowall

Callum McDowall is a 2nd year PhD student at Manchester Metropolitan University investigating miRNAs as potential biomarkers for the detection of Chronic Kidney Disease progression speed. Following the completion of a BSc Biomedical Science at the Manchester Metropolitan University, Callum obtained an MRes degree from the Manchester Metropolitan University on a project investigating in vitro the mechanisms of tubulointerstitial fibrosis triggered by diabetes. Prior to undertaking his PhD studentship, Callum worked for several years at Lonza and AstraZeneca as a scientist where he gained experience of vector construction and protein purification for both industry and research.

Abstract

Background and Aims: Chronic kidney disease (CKD) is very common in diabetes, occurring in around 40% of patients. Without treatment, CKD can lead to end stage renal disease (ESRD), which requires costly dialysis and transplantation. Current treatments aim to prevent CKD or slow down its progression to ESRD. The speed of CKD progression is patient-specific, and at present there are no biomarkers which can predict which patient with diabetes will develop CKD; level of albuminuria is an important but variably reliable biomarker of speed of CKD progression.

The current methods for rapid identification of patients prone to accelerated CKD progression are limited, as they are based on measuring estimated glomerular filtration rate (eGFR) over prolonged periods of time, as well as albuminuria. Therefore, there is a clinical need for novel biomarkers that can predict early potential rapid CKD progression in patients.

The aim of this project is to determine whether serum microRNAs (miRs) can be used as biomarkers to predict the speed of CKD progression in diabetes patients, and to identify potential treatment targets associated with such dysregulated miRs.

Methods: miRs were isolated from sera of 34 patients with type 2 diabetes classed with either slow or fast progressing CKD by their eGFR (n=17; obtained from the Salford Kidney Study sample collection). Several miRs were found to be significantly dysregulated in fast progressing patients by using Next Generation Sequencing (NGS) of miRs in individual serum samples. An additional 49 diabetic CKD patient serum samples (slow (n=29) or fast progressors (n=20)) were used to validate the potential miR biomarker panel by qPCR.

Results: The NGS miR analysis of the initial 34 CKD patient sera produced a panel of 16 miRs that were either significantly upregulated or downregulated in the fast-progressing patients compared to slow progressors. The qPCR validation of this initial panel in 49 additional CKD patient serum samples demonstrated that 6 miRs were significantly upregulated in the fast-progressing patients. The levels of these miRs correlated with demographic and clinical parameters. ROC curve analysis revealed that the individual predictive power of each of those 6 miRs to define either a slow or fast progressing CKD patient was between 63-75%. Determination of a miR combination the strongest predictive power is ongoing.

Conclusions: A potential biomarker panel of 6 miRs has been identified and validated by qPCR, with each miR having a predictive power of between 63-75% for fast progression of CKD. A panel of miRs that could accurately predict progression speed of CKD patients could lead to faster and earlier diagnosis of patients to enable better treatment.

Work is ongoing to explore the predictive power of this miR biomarker panel, and potential novel therapeutic targets to prevent CKD or delay its progression to ESRD.

Interventional nephrology should exist in every renal unit

372: The impact of software-assisted remote vascular access surveillance on detecting stenosis and thrombotic complications

Dr. Alshymaa Eltahan[1,2], Zulfikar Pondor[1], Dr. Rosemary Donne[1,3], Dr. David Lewis[1], Dr. Maharajan Raman[1], Paul Hinchliffe[1], Jan Cowperthwaite[1], Paula Gleave[1], Dr. Dimitrios Poulikakos[1,3]

[1]Salford Renal Department, Northern Care Alliance NHS Foundation Trust, Manchester, United Kingdom. [2]Faculty of medicine, Helwan university, Cairo, Egypt. [3]University of Manchester, Manchester, United Kingdom

Biography - Dr. Dimitrios Poulikakos

Dr. Dimitrios Poulikakos is the Clinical Director for Renal Services in Northern Care Alliance NHS Foundation Trust and was appointed as a Consultant Nephrologist in August 2015. He graduated from the University of Athens, completed his MD (Res) at St George's University of London in cardiac risk stratification in Chronic Kidney Disease. He currently holds a senior honorary senior lecturer post at the University of Manchester.

Abstract

Background: Optimal arteriovenous access monitoring and surveillance aims for early detection of dysfunctional access, enabling pre-emptive referral for angioplasty or surgery to prevent access loss or thrombosis. Here we compared the addition of remote software surveillance to standard clinical care in our units.

Method: From January – December 2023 we conducted a 12-month prospective study of maintenance hemodialysis (HD) patients. We used Vasc-Alert software technology to assist clinical decision making for vascular access (VA) surveillance in 2 out of 5 HD units. In these units, vascular access risk score was calculated using Vasc-Alert software platform from routinely collected data from the dialysis procedure as previously described **[1]**. Patients with high Vasc-Alert access risk score (≥7) underwent clinical assessment and were referred for fistulogram if they met the relevant KDOQI criteria **[2]**. The following variables were collected from all 5 HD units: baseline permanent VA prevalence, subsequent VA events (stenosis or thrombosis), access abandonment (i.e unsalvageable access loss), complication free days (CFD)-extended over one year (defined as days without serious vascular access events, radiological or surgical intervention, VA infection, hospitalisation or use of central venous catheter). Data was collected on patients who were pre-emptively referred for diagnostic fistulogram +/- angioplasty but thrombosed while awaiting intervention. Median time interval from the date of fistulogram request till the date of confirmed thrombosed access was calculated. Comparison between HD units with Vasc-Alert use (Group 1) or without (Group 2) was performed using appropriate statistical tests depending on the type and distribution of the data. Survival analysis of post-intervention primary patency rate was conducted at 3 and 6 months defined as the time from the index procedure until the next access thrombosis or reintervention **[3]**.

Results: There were 81 (53.6%) patients with permanent VA in group 1and 201 (59.3%) patients in group 2at the start of the study. We recorded 23 (28.4%) episodes of stenosis and 6 (7.4%) episodes of thrombosis in Group 1 and 40 (19.9%) episodes of stenosis and 21 (10.4%) episodes of thrombosis in Group 2 (p value 0.121 and 0.432, respectively). In Group 2, 11 patients (5.5%) developed repeated stenosis and 2 patients (1%) repeated thrombosis. In Group 1, 5 /6 (83%) cases preemptively referred for diagnostic fistulogram +/- angioplasty developed thrombosis whilst awaiting elective intervention, compared with 4/21 (19%) in group 2 (p value = 0.008) **(Fig. 1)**. The median time interval from the date of fistulogram request till date of thrombosed VA was 26 days with Interquartile range (IQR 25-75%) of 21-34 days. Group 1 had better post-intervention primary patency

rate of VA **(Fig.2)** and longer CFD-extended compared to group 2 (p values < 0.001 and 0.002 respectively) **(Table 1)**.

Discussion: Our study shows that integrating Vasc-Alert technology into the VA surveillance program was associated with improved early detection of high-risk access, higher primary patency rates and CFD-extended. Additionally, our data emphasizes the need to enhance interventional radiology capacity for timely access intervention, to realise the true potential of Vasc-Alert technology in prevent access thrombosis.

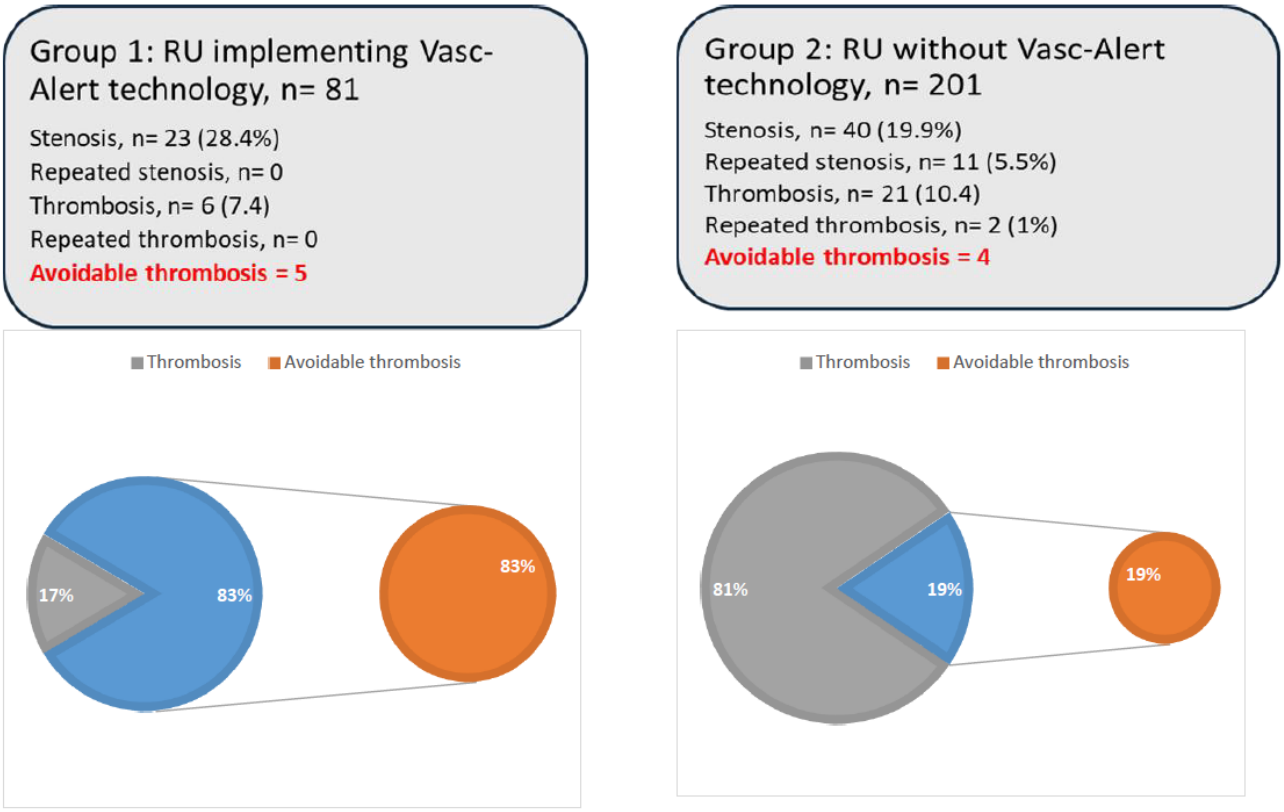

Figure (1): Pre-emptive referral for angioplasty, with thrombosis occurrence whilst waiting. Test statistics,FE: Fisher's exact test; p value = 0.008*, significant at p<0.05.

Table (1): Comparison between eventful cases in the study groups:

		Total (n = 80)	Group 1 (n = 29)	Group 2 (n = 51)	Test statistic	p-value
VA VINTAGE	Median [IQR]	3.00 [2.00 - 6.00]	3.00 [2.00 - 5.00]	3.00 [2.00 - 6.00]	Z = 0.406	0.684
	Min - Max	0.00 - 19.00	0.00 - 16.00	0.00 - 19.00		
CFD-extended	Median [IQR]	363.00 [356.00 - 364.00]	364.00 [363.00 - 364.00]	362.00 [354.00 - 363.00]	Z =3.047	**0.002***
	Min - Max	314.00 - 365.00	314.00 - 365.00	316.00 - 364.00		
Access Abandonment	Yes	10 (12.5%)	3 (10.3%)	7 (13.7%)	FE	0.740

Group 1 with Vasc-Alert, group 2 without Vasc-Alert, CFD: Complication free days, Z: Mann-Whitney test; FE: Fisher's exact test; significant at p<0.05.

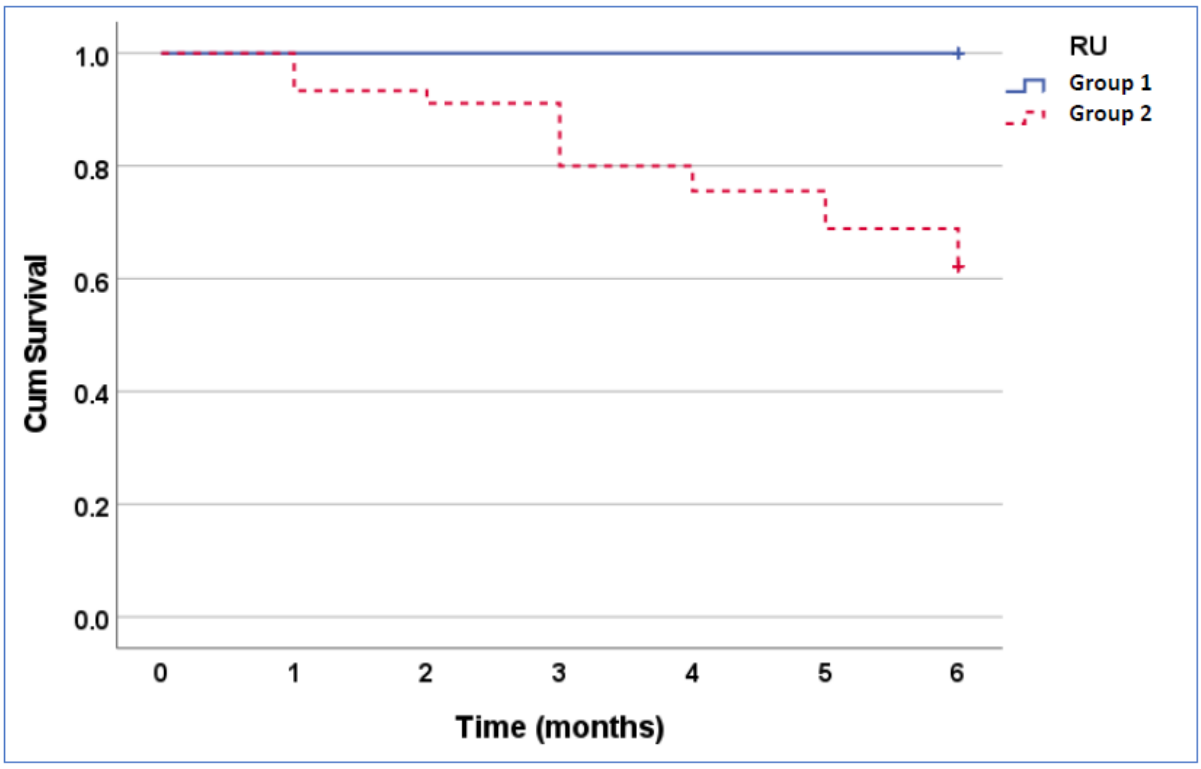

Figure (2): Kaplan-Meier curve of post-intervention primary patency rate, group 1 with Vasc-Alert, group 2 without Vasc-Alert, p value < 0.001.

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325: Assessing the efficacy of a nephrologist-led pathway in identifying stenosis of arteriovenous fistulae (AVF).

Dr Daniel Arenstein[1], Dr Shalabh Srivastava[2], Dr Rauri Clark[2], Dr James Andrews[2], Dr Saeed Ahmed[2]

[1]South Tyneside District Hospital, South Shields. [2]Sunderland Royal Hospital, Sunderland

Biography - Dr Daniel Arenstein

My name is Dr Daniel Arenstein, from South Tyneside and Sunderland Foundation Trust in the North East of England. At the time of undertaking my quality improvement project, I was employed as an SHO on the newly-created renal ward at South Tyneside District Hospital. My interest in radiology led to me to investigate the role of diagnostic and interventional imaging within the specialty of nephrology.

Abstract

Introduction: AVFs are a very common means of ascertaining long-term venous access through which to deliver haemodialysis. As such, their preservation is essential to mitigating the risk of significantly increased morbidity and mortality posed by their loss. Stenosis, the most common complication of AVFs, increases the risk of thrombus formation and thus can ultimately lead to loss of venous access. The traditional pathway for investigating clinically suspected AVF stenosis via radiology referral was recently replaced by an interventional nephrologist-led model in the trust, utilizing point-of-care ultrasound (POCUS). A previous study demonstrated that this new pathway led to earlier radiological diagnosis and subsequent intervention following clinical identification. However, the accuracy with which stenosis is identified by nephrologists via this pathway is yet to be evaluated, which is what this study aims to do.

Methodology: A list was generated of all the patients between January and September 2023 to have been investigated with a fistulogram following referral via the new pathway due to a POCUS finding of stenosis. Of these, it was recorded in how many cases angioplasty was subsequently performed. The measured outcome, angioplasty, was selected for its capacity to act as a surrogate marker for clinical significance, given that angioplasty is assumed to only be performed in cases where stenosis is clinically significant. Fistulogram was chosen as the mode of investigation for the measured outcome as it is the gold-standard test for measuring venous patency.

Results: 35 patients met the inclusion criteria and, of these, 33 received angioplasty following fistulogram. Thus, there were 33 true positive and 2 false positive findings respectively. The positive predictive value can therefore be calculated as 94%.

Discussion: The results demonstrate that interventional nephrologists achieve a high degree of accuracy in identifying clinically significant stenosis via the new pathway. As such, it is demonstrated that the new pathway does not sacrifice efficacy for expedience and thus has an overall beneficial effect on patient outcomes. It may be appropriate to consider emulating this pathway model in other trusts where possible in order to achieve similar outcomes. The study was limited by a lack of published standard to compare the findings with and did not include data on the accuracy of the old pathway for comparison – this should be considered for inclusion in future investigations. It was rendered unnecessary to record stenosis location with relation to AVF as its only relevance would be in affecting clinical significance, the impact of which has already been accounted for by the measured outcome. Due to the data collection methodology used, negative POCUS findings were not included, resulting in sensitivity and specificity being beyond the scope of this study.

Optimising nutrition in advanced kidney care - an update for all

525: A Combined Home-based ExERcISe and Nutritional ApproacH to Improve Frailty Status in Kidney Transplant Recipients (The CHERISH Study): A Randomised Controlled Study

Dr Winnie Chan[1,2], Mr James Donnelly[1], Professor Carolyn Greig[1], Dr Richard Borrows[2]

[1]School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham. [2]Department of Nephrology, University Hospitals Birmingham NHS Foundation Trust

Biography - Dr Winnie Chan

Dr Chan is a Postdoctoral Research Fellow at University of Birmingham, funded by a Joint Kidney Research UK and Daphne Jackson Fellowship. She has over 10 years of experience as a clinical dietitian specializing in renal nutrition. She is currently an Education Committee Member of the ISRNM. Dr. Chan received her Bachelor's Degree in Nutrition and Postgraduate Diploma in Dietetics from King's College, University of London. She obtained her PhD from the University of Birmingham, co-funded by an NHS West Midlands Strategic Health Authority PhD Research Training Fellowship, and a British Renal Society Research Grant. Her current research work focuses on nutrition and exercise interventions in CKD. In addition to consistent publications in well-respected journals, Dr. Chan has authored book chapters and PEN Knowledge Pathway in the field of renal nutrition. She co-authored the KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update. She serves on the editorial board of Journal of Renal Nutrition. She is a multi-award-winning researcher, having delivered numerous presentations and invited lectures in her areas of academic and clinical expertise at national and international conferences. To date, she continues her pivotal role as an Expert Adviser for the NICE Centre for Guidelines in Renal Disease.

Abstract

Introduction: Post-transplantation frailty is common, with a prevalence of up to 52% in kidney transplant recipients (KTRs), and is associated with increased mortality, recurrent hospitalisation and inferior quality of life (QoL). Resistance exercise training (RET) was found to improve frailty in this patient group. Both high and low protein intakes were associated with potential risk of graft failure. To date, no studies have evaluated the safety and efficacy of RET combined with protein supplementation (RETPS) in KTRs. The objectives of this study were to investigate the effect of RETPS on kidney function and frailty status in KTRs, and assess its impact on QoL.

Methods: Forty clinically stable KTRs ≥1 year post-transplantation [mean age=54±14 years; 50% male, median time post-transplantation=7 years] were enrolled and randomised to either RET (n=20) or RETPS (n=20). All participants completed a 30-minute home-based progressive RET regimen 2-3 times weekly for 12 weeks, guided by an exercise worksheet and a study-specific video link. Participants received weekly telephone call to ensure safety and compliance of the interventions. The RETPS group received additional body-weight-adjusted whey protein supplementation 1-hour post exercise. Total daily dietary protein intake did not exceed 1.40 g/kg/day to confine to a safe level of protein consumption in KTRs. Kidney function was measured by estimated glomerular filtration rate (eGFR), creatinine, and albumin-creatinine ratio (ACR). Frailty was evaluated using Fried Frailty Phenotype (FFP), Short Performance Physical Battery (SPPB), 60-second Sit-to-Stand test (60s-STST), handgrip- (HG) and back-leg-chest- (BLC) derived muscle strength, bioimpedance-derived lean tissue index (LTI), and ultrasound-derived thigh muscle thickness (TMT). QoL was assessed using Short Form (SF)-36 questionnaire. All measurements were performed at baseline and at week 12.

Results: Kidney function did not differ significantly between baseline and week 12 in both RET [eGFR: 62.1 vs 59.7 ml/min; creatinine: 107.3 vs 111.5 mmol/L; ACR: 12.8 vs 10.4 mg/mmol] and RETPS [eGFR: 61.2 vs 60.7 ml/min; creatinine: 101.1 vs 102.2 mmol/L; ACR: 17.6 vs 20.9 mg/mmol] groups. Frailty status assessed by FFP and SPPB improved in both RET [FFP: 2.5 vs 1.3, $p<0.001$; SPPB: 7.2 vs 11.6, $p<0.001$] and RETPS [FFP: 2.8 vs 1.1, $p<0.001$; SPPB: 6.4 vs 10.9, $p<0.001$] groups, but the improvements did not differ significantly between groups ($p>0.23$). Improvements in 60s-STST, HG-derived muscle strength, BLC-derived muscle strength, and ultrasound-derived TMT were observed in both RET [60s-STST: 23 vs 27, $p<0.001$; HG-derived muscle strength: 24 vs 30 kg, $p<0.001$; BLC-derived muscle strength: 62 vs 71 kg, $p<0.001$; ultrasound-derived TMT: 15 vs 19 mm, $p<0.001$] and RETPS [60s-STST: 20 vs 29, $p<0.001$; HG-derived muscle strength: 24 vs 32 kg, $p<0.001$; BLC-derived muscle strength: 57 vs 80 kg, $p<0.001$; ultrasound-derived TMT: 14 vs 21 mm, $p<0.001$] groups, with greater improvements in RETPS group for 60s-STST ($p<0.01$), HG-derived muscle strength ($p<0.05$), BLC-derived muscle strength ($p<0.05$), and ultrasound-derived TMT ($p<0.001$). For bioimpedance-derived LTI, improvement was observed only in RETPS group [12.8 vs 14.8 kg/m^2, $p<0.05$]. SF-36-derived overall-, physical- and mental- related QoL improved in both groups ($p<0.05$ for all), with RETPS group reporting a greater improvement in physical-related QoL ($p<0.05$).

Conclusion: This represents the first study demonstrating RET combined with protein supplementation is safe and effective in improving frailty and QoL in KTRs. Protein supplementation augments increased muscle mass and strength beyond RET effect, further enhancing improvement in physical-related QoL.

180: Plant-based diets and CKD – development of 3 plant-based factsheets; a collaboration with the Renal Nutrition Group (RNG) and the Plant Based Health Professionals (PBHP).

Mrs Angeline Taylor

Renal Nutrition Group (RNG) Chair, Kidney Care UK Kidney Kitchen Lead Dietitian. UKKA sustainability committee member, UKKA and Kidney Care UK Patient Information Committee member

Biography - Mrs Angeline Taylor

Angeline Taylor has been a registered dietitian for 15 years and worked within the kidney specialty for the past 12 years. Currently, Angeline holds the position of Renal Dietitian Team Lead in the NHS, Chair of the British Dietetic Association Renal Nutrition Group (RNG), and Renal Dietitian for Kidney Care UK's Kidney Kitchen. She also sits on the UK Kidney Association Sustainability committee and the UKKA and Kidney Care UK Information committee. She is extremely passionate and committed to supporting those with kidney conditions to live a healthy lifestyle, and advocates a plant-based approach to managing kidney disease. Angeline see patients with a variety of kidney conditions and at various stages of the disease, from early to advanced stages of chronic kidney disease, dialysis, kidney transplantation, as well as acute illness on a busy NHS ward.

Abstract

Introduction: Plant-based diets (PBD), rich in nutrients, confer diverse health benefits; this includes reducing the risk of developing heart disease, diabetes, and certain cancers while also supporting cardiovascular health and weight management. In Chronic Kidney Disease (CKD), PBD can lower potential renal acid load (PRAL), foster a healthier gut microbiome, reduce uremic toxins and slow CKD progression.

Such diets can also help to mitigate CKD complications including hyperkalaemia and hyperphosphatemia. In addition, PBD align with sustainable choices, benefiting the environment as well as individual health. Patient education factsheets produced in collaboration with the Renal Nutrition Group (RNG) and Plant-Based Health Professionals UK (PBHP), were created to support and empower CKD patients to safely embrace PBD.

Methods: The demand for patient information on PBD tailored for CKD patients in stages 1-5 without dialysis, those undergoing dialysis, and transplant recipients arose. In response, three separate factsheets were created with a focus on guiding patients interested in adopting a PBD. To ensure patient comprehension, a readability app was used during the writing process. Graphic design support from PBHP was enlisted for the inclusion of visually supportive images. The factsheets underwent two rounds of review including feedback from the RNG committee before receiving final approval.

Results: Three unique factsheets are now available elucidating the advantages of adopting a plant-based diet in the distinct stages of CKD: stages 1-5 (non-dialysis), during dialysis, and post-transplantation. Each factsheet comprehensively covers optimal food groups and recommended quantities for regular inclusion. Beyond dietary guidance, these resources also incorporate additional lifestyle advice. Accessible freely on the PBHP website, RNG members can also find them in the dedicated resources section of the RNG webpages. These factsheets serve as valuable tools, offering clear information to a wide audience, contributing to informed decision-making regarding plant-based dietary choices at various stages of CKD.

Discussion: Recent years have seen an increased interest in PBD for both sustainability and health reasons. PBD, rich in nutrients, offer diverse health advantages, including lower risks of heart disease, diabetes, and certain cancers. Their reduced saturated fat content supports cardiovascular health, and they show promise in weight management and preventing obesity-related conditions. In CKD, PBD exhibit a low PRAL, slowing CKD

progression by mitigating metabolic acidosis. They also promote a healthier gut microbiome, which in turn reduces inflammation, supports immune function, and decreases uremic toxin production.

Furthermore, PBD may address CKD complications such as hyperkalaemia and hyperphosphatemia, with foods that offer a lower bioavailability compared to animal products and processed foods.

People with CKD, particularly late stage, can feel uncertain on what foods they are able to safely consume. PBHP have responded to a previously unmet need developing factsheets aimed to empower patients. These resources offer clear guidance on the range of foods that support overall health and CKD. Educating patients through factsheets aligns with a proactive approach to healthcare, empowering individuals to actively participate in their treatment and promoting a better quality of life in the context of CKD.

All three factsheets can be found under the condition section of the factsheet page.

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Inflammation as a key driver of kidney dysfunction

448: GATA3 haploinsufficiency in renal stromal cells results in dysregulated immune responses in the kidney following ischemic injury

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Division of Infection and immunity, School of Medicine, Cardiff University, Cardiff, UK

Biography - Dr Irina Grigorieva
Biography: I am a Research Associate at the Wales Kidney Research Unit (WKRU) in Cardiff University. I have established an independent research niche within WKRU following my Marie Curie Fellowship at the Medical University in Vienna. My research focuses on molecular mechanisms underlying kidney development, repair and regeneration. I study transcription factors, long non-coding RNAs and matrix proteins that regulate renal stromal cell differentiation, heterogeneity and repose to injury using a variety of cutting-edge techniques including genetic models and lineage labelling, single-cell transcriptomics and multiplexed immunofluorescence imaging.

Abstract
Background: Stromal mesenchymal cells are critical regulators of immune cell responses in the kidney. Our recent single-nucleus snRNA-seq analysis provided high-resolution insights into kidney stromal cell heterogeneity revealing discrete cell types that are associated with different disease outcomes. We have identified a unique stromal cell type marked by expression of the transcription factor GATA3 that confers renal protection and limits fibrosis progression in rodent models of kidney injury. Stromal-specific deficiency of *Gata3* in knockout mice resulted in exacerbated kidney injury, fibrosis progression and enhanced inflammation compared to wild-type mice following ischaemia-reperfusion-injury (IRI). To identify the transcriptomic changes conferred by *Gata3* deficiency we have performed bulk RNA sequence analysis specifically in stromal cells and uncovered dysregulated stromal-immune cell crosstalk.

Methods: Foxd1-Cre line was used to lineage-label renal stromal cells in *Rosa26*^{tdTomato} reporter mice. *Gata3* was selectively inactivated in the renal stroma by crossing reporter and floxed *Gata3* mice (*Gata3-Het*$^{Foxd1\text{-}tdTom}$). Bilateral 20-min IRI was induced in *Gata3-Het*$^{Foxd1\text{-}tdTom}$ (n=3) and *WT*$^{Foxd1\text{-}tdTom}$ (n=3) mice and kidneys were retrieved at 7-days post injury. Sham animals underwent laparotomy only (n=3 per genotype). Reporter tdTom+ stromal cells (≥100,000 cells) were isolated by FACS for bulk RNA sequencing (n=12). Expression of candidate genes was validated by qRT-PCR and immunofluorescence staining in kidney sections.

Results: RNA-seq differential gene expression analysis confirmed deficiency of *Gata3* in kidney stromal cells of *Gata3-Het*$^{Foxd1\text{-}tdTom}$ mice and was validated by qRT-PCR. Compensatory expression of other GATA factors in stromal cells was not detected. Transcriptomic changes in *WT*$^{Foxd1\text{-}tdTom}$ stromal cells at 7-days post IRI compared to sham included 138 differentially expressed genes (DEGs) of which 40% were long non-coding RNAs; >80% of DEGS were downregulated (log2fold-change<-0.5, adjusted p<0.05). Conversely, >10,000 DEGs (adjusted p<0.05) were identified in stromal cells of *Gata3-Het*$^{Foxd1\text{-}tdTom}$ compared to *WT*$^{Foxd1\text{-}tdTom}$ mice at 7-days post IRI revealing that GATA3 is critical for regulation of stromal cell responses post IRI. Gene set enrichment (GSEA) and pathway analysis (IPA) of 2,595 up-regulated and 1,029 downregulated DEGs (log2fold-change >2) identified innate immune response pathways such as "cytokine storm", "Toll-like receptor signalling" and “macrophage activation signalling” as most significant. Proinflammatory cytokines included TNF-α, INF-γ and IL6 signalling pathway genes, as well as complement genes. Negatively enriched genes were metabolic genes including oxidative

phosphorylation and fatty-acid metabolism suggesting that deficiency of GATA3 alters metabolism of stromal cells. Ongoing work focuses on deconvolution of bulk RNA-seq data with snRNA-seq data to identify DEGs in GATA3+ stromal clusters.

Conclusion: Our novel data shows that GATA3+ stromal cells are critical in mediating immune responses in the kidney post injury. Further studies to identify GATA3 regulated genes associated with the reno-protective stromal cell responses will inform potential stroma-targeted therapeutic interventions to modulate inflammatory responses in the kidney.

183: Macrophages may aggravate kidney injury in absence of lymphoid cells, in immunodeficient mouse model of adenine induced CKD.

PhD Federica Petrillo[1], Lorraine Miller[2], Matthew Dearman[2], Lucy Flint[3], MD Söderberg Magnus[4], Tajana Tesan Tomic[5], Aurélie Thomas[2], Stephanie Ling[3], PhD Shrikant Mulay[1], PhD Pernille BL Hansen[1], PhD Kevin Woollard[1]

[1]Early CVRM, Bioscience Renal, Research and Early Development. [2]CPSS, Animal Sciences & Technologies. [3]IDA, Discovery Imaging. [4]CVRM Pathology, Pathology, Clinical Pharmacology and Safety Sciences. [5]eCVRM, Cell/Mol Pharmacology

Biography - PhD Federica Petrillo

Federica completed her PhD in translational Nephrology, and first postdoc in Italy in Naples where she mainly focused chronic kidney diseases and the role of microRNAs Nephrogenic Diabetes Insipidus disease. She moved to Aarhus University in Denmark at Department of Biomedicine for her postdoc where she spent 4 years working on molecular mechanisms underlying CKD progression in combination with RNA sequencing data to explore and identify new pathophysiological pathways. Federica published in high impact factor journals. In her spare time, she likes to cook, listen to jazz music, and theatre.

Abstract

Introduction: Myeloid and lymphoid subpopulations have shown to be both protective and mediators of kidney injury in models of CKD. Mechanisms of cross talk between pro- and anti-inflammatory actions of these effector cells is unclear.

Methods: NSG mice (NOD.Cg-PrkdcscidIl2rgtm1Wjl/SzJ) are deficient in mature lymphocytes, in natural killer (NK) cell cytotoxic activity and in cytokine signalling. In the current study we established a novel NSG mouse model of kidney injury by inducing renal failure through dietary delivery of 0.15% adenine for 7 days and compared to C57BL/6N mice. We used Image Mass Cytometry (IMC) to label 34 markers of immune cell kidney network and kidney injury pattern in adenine versus controls in NSG mice.

Results: NSG mice showed 12% weight-loss already after 3 days of treatment, after 6 days of adenine they lost 17% of weight, while C57BL/6N mice after 7 days of treatment showed 10% weight-loss. Renal dysfunction was more severe in NSG mice with 2x fold increase in Blood Urea Nitrogen (BUN), plasma Creatinine and significant increase in urinary excreted kidney injury markers, KIM-1 and NGAL. NSG mice showed downregulation of multiple epithelial markers (Megalin, SGLT2, GLUT-1, NKCC2, E-Cadherin) and upregulated markers of fibrosis (αSMA, Collagen I, Vimentin) not seen in C57BL/6N mice. Immune profile of NSG mice treated with 0.15% adenine revealed an increased macrophage-based inflammation profile with upregulated F4/80, CD45, CD11b, CD206, and a loss of innate and adaptive lymphocytes immune response markers, CD4 and MHC II. Lack of lymphoid cell populations in NSG mice may lead to a perpetual recruitment of activated macrophages and worsening kidney damage.

Summary: This data demonstrated the use of humanized NSG mice in CKD pre-clinical models and highlights the need to understand the anti-inflammatory actions of lymphoid subpopulations, such as T-regulatory cells in renal diseases.

How can the kidney community help make CKD a higher priority for governments and the NHS?

276: Validation of the Kidney Failure Risk Equation (KFRE) in individuals with chronic kidney disease and multimorbidity

Dr Heather Walker[1], Professor Jaun-Jesus Carrero[2], Dr Anne-Laure Faucon[2], Dr Bhautesh Jani[3], Dr Katie Gallacher[3], Professor Patrick Mark[1,4], Dr Michael Sullivan[1,4]

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Biography - Dr Heather Walker

Heather Walker is a renal and general medicine clinical trainee in NHS Tayside, having undertaken her undergraduate training at the University of Dundee and obtaining a Bachelor of Medical Sciences (BMSc) in Forensic Medicine alongside her medical degree (MBChB). Within her postgraduate training she has undertaken an Academic Foundation post and secured a SCREDS clinical lectureship post in Renal Medicine at the University of Dundee. She is currently Out of Programme completing a Clinical Research Fellowship with the University of Glasgow, as part of the Multimorbidity PhD programme for Health Professionals. Research interests include the use of routinely collected data to study the epidemiology of kidney disease and improve patient outcomes and renal healthcare at a population level.

Abstract

Background and aims: Increasing numbers of individuals with chronic kidney disease (CKD) experience multiple long-term conditions (multimorbidity). Clinical guidance recommends the use of validated risk prediction equations, such as the kidney failure risk equation (KFRE), to guide referral to specialist kidney care services. However, multimorbidity may impact the accuracy of creatinine-based eGFR and bias the prognostic utility of KFRE. Equations with alternative filtration markers, such as Cystatin C eGFR (eGFRcys) or the combined creatinine and Cystatin C eGFR (eGFRcrcys), may improve KFRE's risk stratification and discrimination of future kidney failure risks.

This study aimed to validate the four-variable KFRE in individuals with CKD, with and without multimorbidity in a research-based cohort (UK Biobank) and a population-based cohort (Stockholm Creatinine Measurements project (SCREAM)). The study also assessed the performance of KFRE when using eGFRcr, eGFRcys and eGFRcrcys.

Methods: Individuals from both cohorts were included if they had CKD, defined as eGFR<60mL/min/1.73m^2 by any of the three eGFR equations (eGFRcr, eGFRcys and eGFRcrcys), and had available proteinuria measurement at time of testing or within the previous 12 months. Multimorbidity was defined as the presence of two or more long-term conditions in addition to CKD and was grouped into multimorbidity clusters based on previous research. The outcome was kidney failure, defined as the need for long-term dialysis or kidney transplantation. KFRE performance at 2- and 5-years was assessed using the area under the receiver operating characteristic curve and c-index for discrimination and calibration curves for calibration.

Results: We included 24,489 individuals from UK Biobank and 42,902 individuals from SCREAM (mean age 62.8 (SD 5.6) and 70.1 (SD14.1), 54% and 66% female, respectively). In UK biobank, 14,998 individuals had

multimorbidity, of which 5,375 had cardiometabolic multimorbidity. In SCREAM, 30,147 had multimorbidity and 17,854 cardiometabolic multimorbidity.

Overall, there were 252 and 312 kidney failure events and 1,108 and 1,471 death events in UK Biobank and 918 and 1,098 kidney failure events and 8,785 and 10,152 death events in SCREAM within 2- and 5-years respectively.

Model performance was consistent across both cohorts. Discrimination power of KFRE was good in individuals with and without multimorbidity and across the 2-year and 5-year models (Table 1). Calibration plots revealed over-estimation of risk at 2-years in both cohorts and under-estimation of risk at 5-years in patients with multimorbidity in UK Biobank. There was no improvement in model performance when using eGFRcys or eGFRcrcys compared to eGFRCr.

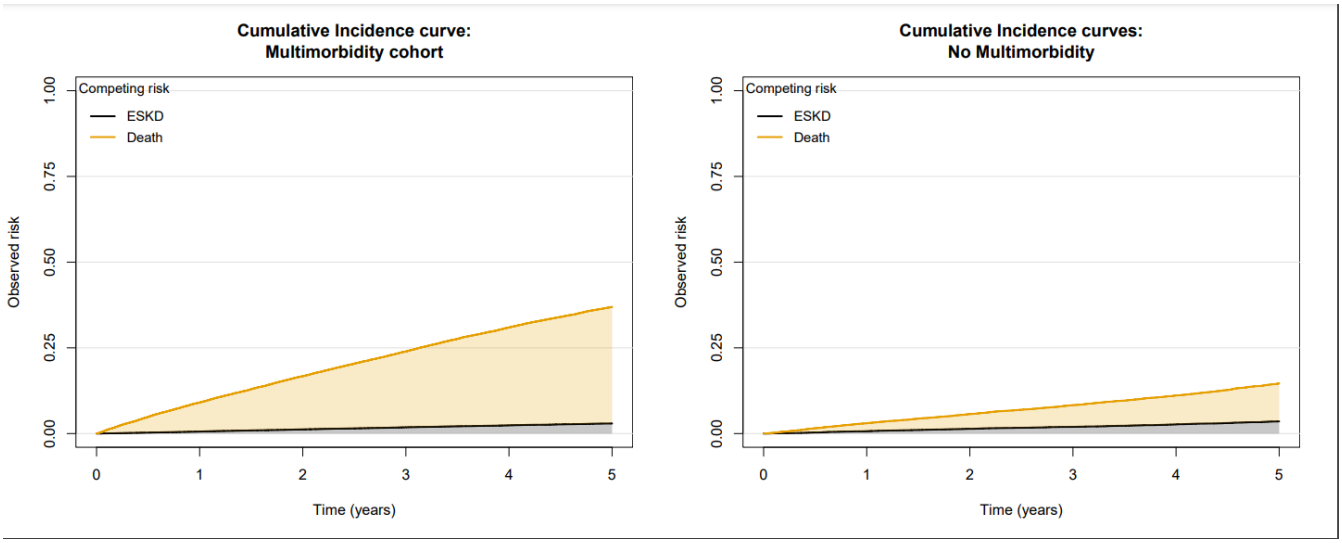
There was a higher cumulative incidence of both kidney failure and death in the multimorbidity group, with a prominent increase in risk of death over time compared to the no multimorbidity group. This was most evident in the SCREAM cohort (Figure 1).

Conclusions: KFRE adequately predicts kidney failure in individuals with multimorbidity and either creatinine or cystatin C can be used. Given the high rates of mortality amongst people with multimorbidity, exploration of models that account for the competing risk of death is warranted.

Table 1. Discrimination power of KFRE

eGFR equation used in KFRE		AUC (95% CI)			
		UK Biobank		SCREAM	
		2-year KFRE	5-year KFRE	2-year KFRE	5-year KFRE
eGFRcr	Multimorbidity	0.89 (0.86-0.92)	0.90 (0.87-0.93)	0.89 (0.87-0.91)	0.88 (0.86-0.90)
	No-multimorbidity	0.89 (0.83-0.95)	0.89 (0.83-0.94)	0.90 (0.88-0.93)	0.89 (0.86-0.91)
eGFRcys	Multimorbidity	0.91 (0.88-0.93)	0.91 (0.88-0.94)	0.89 (0.87-0.91)	0.88 (0.86-0.89)
	No-multimorbidity	0.90 (0.84-0.96)	0.89 (0.84-0.95)	0.91 (0.89-0.94)	0.90 (0.87-0.92)
eGFRcrcys	Multimorbidity	0.91 (0.88-0.94)	0.91 (0.88-094)	0.89 (0.88-0.91)	0.88 (0.87-0.90)
	No-multimorbidity	0.90 (0.84-0.96)	0.90 (0.84-0.95)	0.91 (0.89-0.94)	0.90 (0.87-0.92)

Figure 1. Cumulative incidence of kidney failure and death in SCREAM: multimorbidity compared to no multimorbidity cohort


Cumulative Incidence curve:
Multimorbidity cohort
Competing risk
ESKD
Death
Observed risk
0.00
0.25
0.50
0.75
1.00
0
1
2
3
4
5
Time (years)
Cumulative Incidence curves:
No Multimorbidity
Competing risk
ESKD
Death
Observed risk
0.00
0.25
0.50
0.75
1.00
0
1
2
3
4
5
Time (years)

188: Let's Talk Kidneys: early intervention in chronic kidney disease – the patient view

Mrs Samantha Sharp, Mrs Fiona Loud

Kidney Care UK, Alton, Hampshire, UK

Biography - Mrs Samantha Sharp
Samantha Sharp is senior policy officer at Kidney Care UK, where she has worked since 2019 on various public policy issues including early intervention and detection of CKD and support during the Covid pandemic. A key focus of her work is capturing the views and experience of people affected by kidney disease and seeking to use ensure public policy is informed by it. She holds a MA in public policy from King's College London. Prior to working for Kidney Care UK, Samantha worked in research management at the Institute of Psychiatry, Psychology and Neuroscience and, before that, in the policy team at Alzheimer's Society, where she worked to campaign for better support for people with dementia and their carers.

Biography - Mrs Fiona Loud
Fiona Loud is Policy Director of Kidney Care UK. She led the charity's work on Covid-19, the organ donation opt-out law and continuation of dialysis provision in the EU post Brexit. She is involved with numerous other groups, working to improve standards of care for kidney patients. She set up and chaired the UK Renal Registry patient council and has contributed as a lay representative to many of the kidney guidelines produced by NICE. She is chair of the Organ Donation committee at West Herts hospital, and vice chair of the Lister Area Kidney Patients Association. Fiona spent 5 years on dialysis (PD and HD) after her kidneys failed as a consequence of the rare disease tuberous sclerosis and also kidney cancer, before receiving a transplant from her husband in late 2006. She was voted a HSJ top 50 patient leader. She is an Honorary member of the UKKA in recognition for outstanding contribution to the UK kidney community. She is co-chair of the stakeholder forum of the DHSC Organ Utilisation Group.

Abstract
Introduction: Around 1 in 10 of the global population have chronic kidney disease (CKD) (1) and an estimated half of those are undiagnosed. (2,3) All CKD stages are associated with increased risk of mortality, cardiovascular disease (CVD) and the need for kidney replacement therapy – dialysis or kidney transplantation.(1) Yet CKD suffers from a lack of prominence in health policy, screening and monitoring rates require improvement, and 1 in 6 people start kidney replacement therapy within 90 days of first seeing a kidney specialist.(4) Understanding the views and experience of people affected by CKD highlights key opportunities for improvement.

Methods: A patient survey ran between 24 May and 17 June 2023. 569 responses were received – approximately 2 in 3 responses from people with kidneys close to failure or already failed and 1 in 3 from people in the earlier stages of CKD. We commissioned medeConnect to conduct an online interview of 1,003 GPs between 5 and 26 October 2023.

Results: 65% of people with diabetes and 65% of people with high blood pressure said they were not told they were at increased risk of CKD, prior to CKD diagnosis. There was inconsistency in whether GPs would tell their patients with high blood pressure or diabetes about their increased CKD risk. In patients with diabetes 1% of GPs never, 9% rarely, 35% sometimes, 43% often and 13% always shared CKD risk. In patients with high blood pressure 1% of GPs never, 9% rarely, 34% sometimes, 43% often and 43% always shared CKD risk.

GPs varied in confidence in talking to people with CKD about the likely progression of their CKD. On a scale of 1-5, where 1 was not at all confident and 5 extremely confident, 1% gave a score of 1, 11% a score of 2, 44% a score of 3, 38% a score of 4 and 6% a score of 5.

In terms of information provision, the top three areas people wished to receive information on were; more specific advice on diet and fluid intake; having the likely progression of their kidney disease explained to them; more advice about how to maintain health and wellbeing. Only 3 in 10 survey respondents said they were told how to contact kidney patient charities for further support.

Discussion: Our research and nationally collected data highlight major opportunities for improvements in identification and early intervention in CKD. Central to this is making people partners in their own care by sharing information and decision making and enabling people to take control of their own health. Sharing information about kidney risk with people with diabetes and high blood pressure can encourage monitoring and increase the potential for early intervention.

Inconsistency in GPs' confidence in sharing information on likely progression of CKD highlights the need for support for primary care to offer tailored information about kidney function and likely progression in a way that does not create anxiety and provides reassurance for people less likely to progress. Tools such as Kidney Failure Risk Equation should be used.(5)

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Quality of life as the focus of management of anaemia in CKD

317: Pioneering 2024 guidelines - revolutionising anaemia of CKD management with HIF-PHi agents

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Biography - Dr Sebastian Spencer

Sebastian is an early career researcher with an academic interest in anaemia, peritoneal dialysis and earlier detection of CKD. He is currently an academic clinical fellow in renal medicine sponsored by the NIHR scheme and is based in Hull University Teaching Hospitals Trust.

Abstract

Background: This 2024 draft clinical practice guideline redefines the landscape of anaemia of Chronic Kidney Disease (CKD), building on the foundation of previously published UK guidelines. The robust recommendations are graded using the modified GRADE system, reflecting both strength (strong or weak) and evidence level (A-D). Endorsed by the UK Kidney Association, who will provide the platform for wider consultation before publication, it aligns with the NICE Guideline for anaemia management in CKD 2021.

Methods: Extensive evidence review from July 2016 to May 2023, encompassing systematic literature searches across MEDLINE, PUBMED, Embase, and Cochrane Library. The guideline committee curated evidence from prospective trials, controlled trials, meta-analyses, and Cochrane reviews, ensuring a comprehensive evidence base for the guidelines.

Results: This poster integrates novel guidelines for the treatment of anaemia with Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors (HIF-PHi). Recommendations cover initiation of HIF-PHi therapy to dose adjustments and safety considerations. The guidelines encompass diverse CKD populations, including non-dialysis dependent CKD (NDD-CKD), dialysis-dependent CKD (DD-CKD), and those intolerant to Erythropoiesis Stimulating Agent (ESA) therapy.

Discussion: Guideline 4.1 advocates the initiation of HIF-PHi agents post-iron repletion for symptomatic anaemia, particularly in those suitable for transplantation. Guideline 4.1.1 extends this recommendation to DD-CKD, emphasizing the quality of life and avoiding transfusions. Guideline 4.1.2 introduces HIF-PHi therapy for individuals intolerant to ESA, offering a new avenue for effective anaemia management.

Guideline 4.3 emphasizes target Hb levels with HIF-PHi therapy, considering age groups and parity with ESA therapy. Safety recommendations (Guideline 4.8) highlight considerations for specific subgroups, reinforcing the need for cautious use in individuals with known CVD or thrombotic events. Guideline 4.9 underscores the importance of vigilant monitoring to achieve and stabilize the desired Hb target range.

This poster amalgamates the novel guidelines with the overarching background, providing a visual narrative that encapsulates the role of HIF-PHi agents in an evolving landscape of anaemia of CKD management.

546: A retrospective multi-centre audit on safety related outcomes of roxadustat

Miss Kathrine Parker[1,2], Matthew Holloway[3], Carol Anderson[3], Cathy Pogson[4], Clare Morlidge[5], Robert Brown[6], Sara Perkins[6], Sharon Benton[7], Gareth Bryant[8], Natasha Moore[9], Christina Mensah[9], Jaskiran Sanghera[9]

[1]Manchester University NHS Foundation Trust, Manchester. [2]University of Manchester, Manchester. [3]East Kent Hospitals University NHS Foundation Trust, Kent. [4]Portsmouth Hospitals University NHS Trust, Portsmouth. [5]East and North Hertfordshire NHS Trust, Stevenage. [6]Richard Bright Renal Service, Bristol. [7]Royal Cornwall NHS Hospital Trust, Cornwall. [8]Cardiff and Vale University Health Board, Cardiff. [9]Guy's and St Thomas' NHS Foundation Trust, London

Biography - Miss Kathrine Parker

Kathrine has worked as a specialist renal pharmacist at Manchester University NHS Foundation trust since 2010. In 2016 she completed her Masters in clinical pharmacy exploring immunosuppression in elderly transplant recipients. In 2019 she received a personal funding award from the NIHR to investigate anticoagulant use in advanced kidney disease as part of a clinical academic doctoral fellowship. Her other interests include drug dosing in dialysis, symptom management in advanced kidney disease, kidney transplantation immunosuppression in the elderly and PD peritonitis. Kathrine prescribes for patients on dialysis unit and in the kidney transplant clinic. Kathrine is the current co-lead for the renal pharmacy group research group, co-chairs the UKKA symptom workstream within the supportive care SIG and sits on the clinical practice guideline committee. She is the current UK Kidney Association Academic Vice President representing the multi-professional team.

Abstract

Introduction: Roxadustat is the first in class oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), licensed in Europe for treatment of anaemia in chronic kidney disease (CKD). In July 2022 National Institute for Health and Care Excellence (NICE) recommended roxadustat for treating anaemia in CKD for patients not on dialysis to maintain a haemoglobin of 100-120g/L. With roxadustat being more widely used in practice anecdotal reports suggest that some patients may experience a rapid rise in haemoglobin, which may predispose patients to adverse effects. Some of the most serious reported side effects from the clinical studies of Roxadustat included thromboembolic events, seizures and infections. The aim of this audit was to look at real-world data from CKD patients prescribed roxadustat from eight UK renal centres, to assess safety related outcomes which is an area of current interest to clinicians.

Methods: The UK Renal Pharmacy Group (RPG) research group and Association of Nephrology Nurses UK (ANNUK) anaemia group collaboratively developed a data collection tool which included details of roxadustat dosing, weight, anaemia bloods and adverse effects. Each renal centre undertook a local audit of current practice and anonymised data was inputted into the tool. Data was pooled for analysis. Roxadustat prescription did not have to be current, to capture those who had ceased therapy.

Results: One hundred and forty patients from eight UK renal centres were included with a median follow up of 18 weeks. The median haemoglobin at Roxadustat initiation was 93g/L. Four out of six patients that started dialysis switched to erythropoietin. Thirty-two percent of patients (n=36) achieved a haemoglobin over target with eight patients stopping therapy completely and a further five having therapy suspended before a dose reduction, table 1. For the majority of patients who experienced a haemoglobin above 120g/L this occurred within eight weeks of starting roxadustat, table 1. When the dose was reduced this was either a reduction in frequency of administration (once-twice weekly) or a reduction in thrice weekly dose. Twelve patients were initiated on a lower than licensed dose and these patients all had haemoglobin within target. The most common

adverse effect resulting in treatment cessation was venous thromboembolism in five patients, with three of these having supratherapeutic haemoglobin at 4-8 weeks and the other two having a rapid rise in haemoglobin of >20g/L in this timeframe. Other adverse effects are reported in Table 1.

Conclusion: Roxadustat was effective and well tolerated with adverse effect rates similar or lower than those published in the manufacturers licensing datasheet. Due to the high number of patients requiring dose reduction renal units were using unlicensed dosing of roxadustat, administering it once-twice weekly to use up patients medication supply whilst still maintaining haemoglobin. Further to this some units decided to initiate roxadustat at lower than licensed doses. Initiating at a dose band lower than the licensed dose may be a reasonable approach to avoid rapid rises in haemoglobin which may contribute to adverse effects and avoid additional requirement for monitoring.

Bloods at initiation, median (Interquartile range 25th-75th)	
eGFR, ml/min/1.73m^2	15 (10-21)
Iron saturation, %	25 (20-31)
Serum ferritin, microg/L	304 (164-180)
Haemoglobin, g/L	93 (85-98)
Iron administration during roxadustat, n	18 (12.9%)
Dose adjustments, n (%)	
Held and then reduced	5 (3.5%)
Reduced	31 (22%)
Same dose	48 (34%)
Increased	10 (7%)
Initiated on lower dose- no dose adjustment	12 (8.6%)
Time after treatment initiation to first high haemoglobin (>120g/L), n	
4 weeks	8 (5.7%)
8 weeks	22 (15.7%)
12 weeks	13 (9.3%)
26 weeks	1 (0.7%)
Reasons for stopping therapy, n (%)	
Stopped due to adverse effect	13 (9.3%)
Stopped due to high Hb	8 (5.7%)
Stopped due to dialysis initiation	4 (2.8%)
Stopped - other	10 (7.1%)
Adverse effect, n (%)	
Venous thromboembolism	5 (3.5%)
Stroke	1 (0.7%)
Hypertension	6 (4.3%)
Hyperkalaemia	1 (0.7%)
Seizures	2 (1.4%)
Serious Infection	1 (0.7%)
Gastrointestinal	5 (3.5%)
Headaches	2 (1.4%)