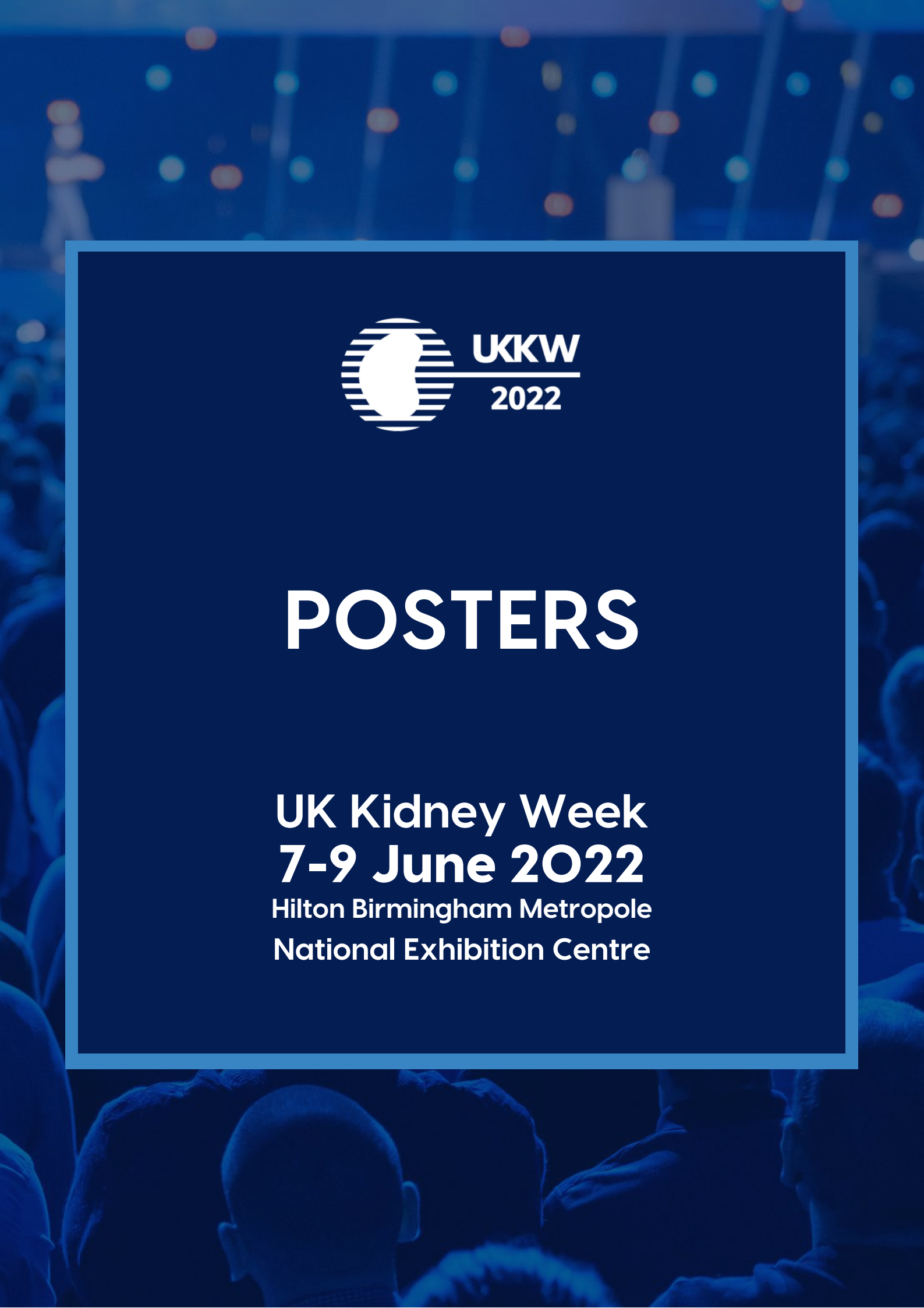

POSTERS

UK Kidney Week
7-9 June 2022
Hilton Birmingham Metropole
National Exhibition Centre

Contents

Wednesday 8th June, 12:00-13:00

Track A - AKI 1

1

A Rare Presentation of AKI due to retroperitoneal fibrosis as a result of Gastric Linitis Plastica: a case-based review

AKI

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Introduction: Retroperitoneal fibrosis (RPF), reviewed herein, is a rare fibro-inflammatory disease that develops around the abdominal aorta and the iliac arteries, and spreads into the adjacent retroperitoneum, where it frequently causes ureteral obstruction and renal failure. Obstructive uropathy is the most common complication, although other types of renal involvement may occur. RPF can extend to the renal vascular peduncle; this may cause compression of renal veins and renal arteries.

Gastric linitis plastica is a diffuse type of cancer prone to the development of a unique clinical course, including the occurrence of RPF, with rapid progression. Delayed systemic treatment results in a poor outcome, and thus an appropriate and prompt clinical diagnosis is important.

We present a rare case of gastric linitis masquerading as retroperitoneal fibrosis, with AKI resulting from both obstruction and compression of the urinary system.

Case report: A 52-year-old Dutch man with no significant past medical history was admitted with acute renal failure, after a 4-months period of early satiety, epigastric pain and weight loss. He was prescribed Omeprazole and underwent an upper endoscopy which revealed thickened and oedematous gastric folds. Biopsies were not diagnostic. However, the pain became worst, spreading to the lumbar regions with no urinary symptoms. A blood test revealed impairment of the kidney function and a CT scan showed bilateral hydronephrosis with hydroureters and ascites. Bilateral JJ ureteral stents were placed. However, the kidney function continued to worsen, with a serum creatinine of 236 µmol/L on admission (from 89 µmol/L, 2 months earlier) to 855 µmol/L 3 days later. The patient was becoming increasingly oliguric and was referred to the renal service.

Initial examination was unremarkable apart from bilateral costovertebral angle (CVA) tenderness. Urine dipstick was unremarkable.

A repeated scan was performed and revealed both stents in place with no evidence of hydronephrosis.

Positron emission tomography (PET) did not indicate abnormal accumulation of 18F-fluorodeoxyglucose apart for a moderate gastric fixation. 50 ml of yellow fluid was retrieved by abdominal paracentesis; this revealed an exudate with negative cytology.

CT scan showing Stents in place with no evidence of hydronephrosis Presence of ascites

At this point, it was decided to initiate glucocorticoid therapy intravenously. Within less than 24h, the patient' urine output started to increase and by the next day, the serum creatinine was already falling, to 277 micromoles/L 5 days later. The patient was discharged a week later on 60 mg of prednisolone per day.

A month later, an ultrasound-guided upper endoscopy with biopsy was performed; this had revealed a poorly differentiated adenocarcinoma cells consistent with linitis plastica. Abnormal cells were also found in the ascitic fluid when a second tap was performed.

Discussion: Our patient had a rare presentation of gastric cancer in the form of both ureteral obstruction and compression of the kidneys due to inflammatory disease spreading into the adjacent retroperitoneum. The insertion of stents was not enough to improve the renal function despite alleviating the ureteral obstruction. In the present case, we could not determine a definitive diagnosis prior to initiating steroid treatment. We had considered malignant lymphoma or metastasis of malignant cancer as a differential diagnosis, but the images did not reveal any retroperitoneal nodular tumours. The presence of ascites could have suggested peritoneal carcinomatosis. We therapeutically diagnosed this case as primary retroperitoneal fibrosis. Since we could rapidly initiate treatment with steroid therapy, we were able to avoid dialysis.

In conclusion, one of the most important diagnostic challenges in RPF is the differentiation between primary and secondary diseases. As noted in this case, some forms of secondary RPF may be radiographically and histologically indistinguishable from idiopathic RPF.

A dilemma in the diagnosis and management of this disease may arise because even when negative biopsies are obtained, some cases of gastric cancer with RPF do not show masses on imaging.

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Track A - AKI 1

2

Evolution of an AKI Service in a district general hospital

AKI

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Background: Acute Kidney Injury (AKI) is one of the major complications of the acutely ill, posing significant rates of mortality and morbidity, including the development of chronic kidney disease and associated complications. Across the Black Country there is a large non-white and socioeconomically deprived population, with a high burden of chronic diseases, meaning that their risk of developing AKI is high. In response to a GIRFT review of renal services in Wolverhampton, a multi-disciplinary AKI service has been developed. This service aims to reduce the rate and length of AKI through early intervention, implementation of AKI care standards in management, and follow-up for these cohort of patients, as per NICE AKI guidelines (2019).

Results: Since its inception in April 2021, 1258 AKI stage 2&3 in-patients have been reviewed within 24 hours of AKI e-alert (100%) and appropriate AKI management plan initiated, Targets of 100% for initial fluid balance review and medication review were achieved in all of these patients. To improve post AKI care and reduce length of stay, an AKI follow-up clinic was established and 165 patients with unresolved AKI have been followed up so far. Our median length of stay for AKI patients is 11 days compared to a national average of 12 days. The AKI service also audits and coordinates all transfers from non-renal centres, for patients requiring urgent haemodialysis or other renal interventions, such as renal biopsy. Since the audit began in September 2021, 35 patients have been transferred, and timelines measured from referral to transfer to intervention, identifying the reasons behind any delays and consequences thereof. As a result of the information gathered in this audit, two dedicated AKI beds have been ring-fenced for transfers, leading to a marked reduction in transfer times.

Methods: Our AKI Service consists of a Lead AKI Consultant (renal nephrologist), Lead AKI Clinical Nurse Specialist (CNS) and three further AKI Clinical Nurse Specialists, as well as a weekly on-call renal consultant and renal registrar.

The journey of an AKI patient is illustrated in figure 1:

In addition, the AKI service offers:

1) Delivery of targeted educational sessions to relevant staff involved in the care of patients with AKI.

2) Participation in Cardiorenal meetings monthly, in liaison with Heart Failure and Chronic Kidney Disease teams which facilitates shared learning as well as optimising management of this complex group of patients.

3) Collaboration with colorectal, gastroenterology and dietetic teams in the development of guidelines to prevent and manage AKI in patients with high output ileostomies and short gut syndrome.

5) Regular HES coding review to improve accuracy of AKI coding of Hospital AKI episode.

Conclusion: The implementation of our multidisciplinary AKI team has been instrumental in improving standards of AKI care in patients with AKI stage 2 & 3 as per national recommendations. Through our AKI follow-up service we have achieved follow-up of all patients with unresolved AKI and optimised the recovery of AKI following discharge. Further development work is in progress to increase the number of AKI CNSs which will enable us to see all appropriate AKI stage 1 patients in hospital and strengthen our education programme for patients with high risk of acquiring AKI in the community. Through closer collaboration with primary care we aim to reduce the incidence of community acquired AKI and readmission rates to hospital. Our service strives to manage the whole spectrum of AKI; from prevention, early recognition and treatment through to detailed and comprehensive follow-up, in order to ensure that these patients are given the very best care and high standards are maintained.

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Track A - AKI 1

3

Feasibility study: Exploring the potential recruitment of patients with acute kidney injury

AKI

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Introduction: Accurate and systemic fluid assessment in patients with acute kidney injury [AKI] is required to enable appropriate and timely management and is a fundamental requirement when looking after a deteriorating patient (1). There is evidence to suggest that physical fluid assessment is varied and is not undertaken well in practice (2). Therefore, this study was designed to gather data to support the development of an enhanced fluid assessment tool for nurses. The aim of this initial feasibility work was to identify if it was possible to identify patients that could be recruited presenting with community acquired AKI. This would inform the main prospective cohort study which aims to examine fluid assessment.

Methods: Adult patients admitted to a UK District General Hospital [DGH] with an e-alert for AKI from 4/10/21-17/10/21 were identified as eligible for recruitment with data being collected on two separate days per week. All patients, whose lab results generated an e-alert, were reviewed to identify if there was a rise in creatinine >1.5x baseline within the last 3 months. Patient data was collected relating to the stage of AKI, cause, comorbidities, mental capacity, willingness to participate in theory, inclusion criteria (adult, capacity and within 72 hours of admission) and fluid assessment.

Results: An average of 143 e-alerts were received per day. Of these, there were approximately 43 new alerts/day; a total of 21 patients had a physical review (including urine output, JVP, oedema, NEWS2) over the 2 weeks of data collection (a total of 4 days). 13 patients were seen within 72 hours of admission and were deemed to have a community acquired AKI. Four patients were deemed not to have capacity, this was identified from their notes, NEWS2 and discussion with the clinical team. Three patients had communication barriers. Therefore, of the 21 patients who were physically reviewed, 4 would have been eligible for recruitment to the main study and been able to consent – indicating that 2 patients a week can reasonably be expected to be recruited to the planned research.

Discussion: The importance of feasibility work should not be under-estimated in terms of the value and insight that it adds to research design and planning. There are many reasons patients develop AKI, however it is known that certain patient groups are at increased risk; these include older age,

sepsis, cognitive impairment and elevated NEWS2 scores (3), all of which could influence capacity and the ability to give informed consent. This work highlighted the potential challenges of recruiting patients that fulfil the research inclusion criteria for studies that examine fluid assessment in patients with community acquired AKI, especially within the context of a DGH.

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Track A - AKI 1

4

Retrospective review of AKI and renal outcomes in critically ill COVID-19 patients admitted to 2 sister centres of Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust over a 12-month period

AKI

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2020 has been a year marked by COVID-19 pandemic. Across the world, AKI (acute kidney injury) incidence in COVID-19 patients has been variable ranging from 2%-17%. ICNAR (Intensive care National Audit and Research data) suggests in UK, 23% critical care cohort with COVID pneumonia needed CVVH (Continuous Veno-Venous Haemofiltration) compared to 17% in other pneumonias.

We are still trying to understand this condition and how it affects patients. We know that AKI is associated with higher mortality in hospitalised patients. However, there is limited data on characteristics of critical care COVID-19 admissions with AKI and its long-term outcomes.

Our objective is to look at baseline characteristics of critical care COVID-19 admissions and the characteristics of patients who developed AKI, length of critical care stay, survival rate and renal recovery at 3-6months post discharge.

This is a retrospective observational study of patients with COVID-19 who needed critical care admission at DRI (Doncaster Royal Infirmary) or Bassetlaw hospital between 1st April 2020 to 31st March 2021. Data was gathered from Critical care admission records and Trust electronic system.

288 patients with COVID-19 (69% Male, Median Age 62yrs, Mean Charlson Comorbidity Index (CCI) 2.6, Hypertension 52%, Diabetes 36%, Chronic Kidney Disease (CKD) 22%) were admitted to critical care during this 12 month period. Of these, 107 (37%) patients developed AKI (28% CVVH, 24% AKI stage1, 25% AKI stage 2 and 22% AKI stage 3). Among patients with AKI, 71% needed respiratory support (Non-invasive and/or invasive ventilation). Length of stay was longer (Mean 14 days vs 10 days) and associated with high mortality (71% vs 28%; p value <0.001) compared to patients who did not develop AKI.

Majority of patients who developed AKI were males, with background history of hypertension, CKD and mean CCI of 3. In our cohort, none of the AKI survivors were dependent on renal replacement therapy post discharge and majority of them recovered to their baseline renal function. However, at 6 months 10 (6%) of AKI survivors had chronic kidney disease.

AKI in critically ill COVID 19 patients seems to be part of multiorgan failure as evidenced by majority of AKI patients needing further organ support such as non-invasive and/or invasive ventilation. Mortality was significantly higher in patients who developed AKI, with COVID pneumonitis and multi organ failure as the commonest cause of death.

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Track B - AKI 2

5

Acetaminophen Induced Acute Kidney Injury

AKI, Case reports

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Introduction: Acetaminophen is one of the most common analgesic medications available over the counter. Acetaminophen overdose can cause both hepatic and renal injuries. The literature suggests the incidence of acute kidney injury is around 2% - 10% in those with acetaminophen overdose. Acetaminophen-induced liver necrosis has been studied extensively, but the extrahepatic manifestations of acetaminophen toxicity are currently not described well in the literature. The pathophysiology of renal toxicity in acetaminophen poisoning has been attributed to cytochrome P-450 mixed function oxidase isoenzymes present in the kidney, although other mechanisms have been elucidated, including the role of prostaglandin synthetase and N-deacetylase enzymes. We report a case of acute kidney injury from acetaminophen overdose.

Case Description: A 17 year old boy presented to emergency department with intentional overdose of paracetamol (500 mg x 47 Tables) (23500 mg) few hours after ingestion. Patient had no history of alcohol abuse or renal insufficiency. It was a staggered overdose hence NAC infusion was started in Emergency unit. Patient received total 4 bags of NAC infusion. His paracetamol level was 42, salicylate level less than 50 and rest of the toxicology screening was negative. On first day of admission, creatinine level was normal, 50, on day 2 slightly increased to 65, and since day 3 creatinine increased to 128 and drastically shot up to 254 on day 4 and peaked at day 5 to 260. Mean whilst, his liver functions including ALT and ALP remained within normal range. Clotting profile also remains within normal range with no deterioration. Creatinine kinase was 35. Urine dip showed red cells with no macroscopic haematuria. Urine PCR was negative.

Discussion: Urgent consultation was made with renal team. USG urinary tract was sought urgently which revealed normal size kidneys with no evidence of obstructive pathology. Patient denied taking any nephrotoxic drugs or other herbal medicines. There was no history of previous overdose or substance misuse. Patient was monitored closely in acute medical unit. Intravenous normal saline 0.9% was prescribed 6 hourly and electrolytes were checked twice daily. Urine output was adequate throughout the admission. On day 6 of admission, creatinine level improved to 93 and patient was discharged with renal clinic follow up. Patient's vital signs were stable throughout.

Conclusion: As no obvious cause of renal failure was sought, we believe this acute kidney injury was related to acetaminophen overdose. It is stated that NAC has a clear role in preventing acetaminophen-induced liver necrosis, but it has not demonstrated any benefit in preventing nephropathy. Treatment with NAC did not worsen nephropathy in a small series of patients who have been studied. In summary although paracetamol overdose related nephrotoxicity is rarely seen

it should be kept in mind that it can occur even without hepatotoxicity and these patients should be closely monitored.

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Track B - AKI 2

6

Improving time to dialysis initiation for AKI in patients admitted to non-renal hubs through the introduction of a Renal AKI in-reach service

AKI, Haemodialysis - service delivery

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Introduction: Acute kidney injury (AKI) 30-day adjusted mortality can be as high as 30.5% . The Northeast and Cumbria (NENC) region as one of the highest AKI rates according to UKKA AKI Dashboard (2022). Those with long-duration AKI (lasting seven or more days) have the highest mortality risk (relative risk 2.28), compared to patients experiencing AKI for two or fewer days (relative risk 1.42). The Renal Medicine Get It Right First Time (GIRFT) report reported longer dialysis initiation times for those admitted but needing renal replacement therapy (RRT) in non-renal hub; following initiation of an AKI in-reach programme to our non-renal hub In September 2020, we looked into our own performance.

Methods: An inter-trust Nephrology in-reach service was already in place to identify patients. We looked at patients transferred from non-renal hubs, and specific timings such as between acceptance and transfer, arrival and dialysis start time, and overall acceptance to start time. 36 patients were transferred between August 2020 and July 2021. Bidirectional electronic records were interrogated using the time that temporary venous line insertion as a surrogate for RRT initiation.

Results: 19/36 (53%) were transferred to a renal hub due to AKI and considered eligible for transfer for renal replacement therapy (RRT). Seven out of 19 (37%) went on to have RRT; the remaining 12 either recovered function or were thought to be inappropriate for RRT. The difference between accepting the patient and time to first dialysis ranged between just over one day to under nine days (24.45 - 215.25 hours; median = 24.52 hours, mean = 54.48 hours).

Discussion: The upper limit of start times was skewed by one outlier; in this patient intravenous diuretics were used before progressing to RRT eight days later. We compared our mean time to dialysis with published data from Renal GIRFT between renal versus non-renal centres, which showed start times of just over four days and over 9 days respectively. Figure 1 compares published mean times with our own; the average start time was almost 48 hours less than the published time for patients admitted straight to a renal centre for AKI RRT. Following the initiation of the AKI service, we site the reasons as: strengthened communication between hubs, swift decision-making by visiting consultant presence; and early prioritisation of beds through team working. These findings are impressive as infection prevention control (IPC) require source isolation of transfers to side rooms from our non-renal hub. Additionally patient flow has been challenged by Covid-19 IPC policies with differ between the centres and the ambulance service providing the transfers. Our

acclaimed interventional nephrology service too, has undoubtedly contributed to these swift times impact on mortality due to reduction in duration of AKI.

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Track B - AKI 2

7

Setting up Out of Hours Acute Kidney Injury service at large teaching hospital

AKI

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Background and Aim: Acute kidney injury (AKI) is a widely recognised serious health care issue. Up to 25% of hospital patients can develop it, with poor outcomes. The trust set up the AKI Team in 2014 to improve AKI detection, care, and outcomes after local audit in 2014 showed poor AKI care management. Successful implementation of a Multifaceted Quality Improvement (QI) Programme for AKI across the main hospital campus since 2015 saw significant improvement in AKI care and outcomes; recognition within 24hrs improved from 52% to 95% since 2016; 34% reduction in AKI incidence, 26% in length of stay (LoS), 42% in AKI days (time to recovery) and 10% less AKI associated mortality.

AKI service consists of two AKI Clinical nurse specialist covering 5-7 days service from 07:30 am to 15:30pm, during the Out of Hours (OOH ,i.e., 15.30pm to 7.30 am) the service is supported by ward medical team. There is a potential delay in detecting and managing AKI during out of hours due to the current working hours of the AKI team.

Aim: The primary aim of this project is to establish a nurse-led 24-hour Acute Kidney Injury (AKI) service

Methods: A retro respective data was collected for one month to establish AKI Stage 2/3 alerts occurring outside the working hours of AKI team at one site of the hospital. The OOH team was trained to access to AKI e-alert system. The OOH team runs the system once at midnight and identify all stage 2/3 AKI patients for review. Learning sessions were organised to train all OOH Acute Care Practitioners. The OOH team members spent a day with the AKI team, to ensure consistent care. The trust standard care bundle was used to deliver the AKI care. Develop and test changes was aimed at making improvements using Plan Do Study Act Cycles.

Results: Retro respective data analysis of one month showed 24 AKI Stage 2/3 cases were alerted on the clinical system between 15:00 and 24:00 outside the working time of AKI team. Over a period of two months, due to competing pressures and sickness, the list was run for 38 days out of 60 days. 36 patients(20 AKI stage 2 patients and 12 AKI stage 3 patients) were reviewed by OOH teams. 48% (n=13) AKI cases were not recognised, and the OOH were the first to see the patients for AKI review. 52%(n=19) cases of AKI were already recognised by the parent team before review by OOH team.

Fluids were prescribed for 55% of patients and 21% of medications reviewed within 6 hours of AKI alert.

Conclusion: By expanding the AKI service in collaboration with OOH team we hope to recognise AKI in first 6-12 hours. This project will commence OOH nurse led intervention in the expectation that early identification will enable rapid treatment and thereby improve patient outcome. We also anticipate this will lead to the development of streamlined patient pathways which will be equally applicable to our other hospital sites

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Track B - AKI 2

8

Risk factors for acute kidney injury and outcomes among sepsis admissions in Malawi.

AKI

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Introduction: Acute kidney injury (AKI) is a common and severe complication of sepsis, but data on impact in sub-Saharan Africa (SSA) are lacking. We determined AKI prevalence, risk factors and outcomes in adults with sepsis in Malawi.

Methods: We conducted a prospective cohort study of sepsis-related AKI among acute admissions of Zomba Central Hospital between 3rd February 2021 and 19th July 2021. Adult patients with suspected infection and a decision to admit to hospital were recruited. We assessed the demographic, clinical, laboratory and ultrasonography characteristics of 101 sepsis patients. We compared AKI versus no AKI using either $\chi 2$ or Fisher's exact test for categorical variables and two-sample t-test for continuous variables. Baseline creatinine was back calculated using the Modification of Diet in Renal Disease equation, without race correction, with an assumed GFR of 100 mL/min/1.73m2. AKI stages were defined according to Kidney Disease Improving Global Outcomes (KDIGO) guidelines. Chronic kidney disease (CKD) was defined as an eGFR < 60 mL/min/1.73m2 at 3 months using a modified Modification of Diet in Renal Disease (MDRD) equation. Risk factors were identified using logistic regression and mortality outcomes were assessed using survival curves with a Cox proportional hazard regression model to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

Results: The median (IQR) age was 38 (29-48), 88 had known HIV status of which 53/88 (60%) were people living with HIV, and 42/53 (79%) were receiving antiretroviral therapy. At presentation, 33/101 (33%) had AKI; 18/33 (55%) had stage 3 AKI. Survival at 3 months was 66/101 (65%). Prevalence of CKD in survivors with available samples at 3 months was 12/61 (20%); 7/19 (37%) had presented with AKI whereas 5/42 (12%) had not (p = 0.06). AKI was independently associated with qSOFA score (OR 3.10, 95% CI 1.09-8.84), older age (age 60 versus 40: OR 4.53, 95% CI 2.24-14.66), and HIV positivity (OR 4.87, 95% CI 1.38-17.13). After adjustment for age and qSOFA, living with HIV was independently associated with death (HR 3.91, 95% CI 1.06-14.48).

Conclusion: AKI is common among sepsis admissions in Malawi and associated with sepsis severity, older age, living with HIV and hypertension. A fifth of sepsis admissions have evidence of CKD at 3 month follow up, rising to nearly 40% if AKI was present on admission. This study provides support

for the implementation of AKI screening among sepsis admissions for targeted preventive measures and community follow up to reduce mortality and incidence of CKD.

Figure 1: Kaplan-Meier estimate of survival function following sepsis admission.

A: HR hazard ratio of death from Cox proportional hazards model stratified by AKI status with 95% confidence intervals

B: HR not reported as stratified by AKI status (proportional hazard assumption for AKI does not hold).

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Track B - AKI 2

9

Setting up a novel AKI service in a trust without on-site renal services: early experience and impact

AKI, Patient outcome and experience

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Introduction: An acute kidney injury (AKI) service was introduced to a hospital without on-site renal services in September 2020, with tertiary renal care provided by two neighbouring trusts. The main aims of the service comprised improving the recognition, treatment, follow up and prevention of harm for patients with incident and prevalent AKI and CKD (chronic kidney disease). The service encountered over seven hundred patients seen within the first twelve months of operation. Two Band 7 nurses were recruited to provide continuous 52-week cover between 08:30 and 17:00 Monday-Friday, and 4 hours/week of nephrologist input, with out of hours support provided by the on-call consultant teams and Acute Intervention Team based at the hospital. Data was collected over the first 12 months of operation to quality assure and inform future regional service development.

Method: Patient notes of those with an AKI code (N17) were examined pre- and post-AKI service introduction. Metrics examined included length of stay, admission to intensive care, hospital standardised mortality ratio (HSMR), summary hospital-level mortality indicator (SHMI) and CR-AI (C2-AI.com (Copeland Clinical Ai, formerly Crab Clinical Informatics)).

Results: Length of stay (LOS) reduced for those with AKI within the first 12 months of the service being introduced (see figure 1). This is compared with the median length of stay for the UK of 12 days (UK Renal Registry July 2020). The trend in admissions to critical care from the emergency department and wards for patients with AKI has reduced (see figures 2 and 3).

HSMR, SHMI and CR-AI have all reduced in the first quarter of 2021. Using CR-AI data, prospective estimated cost-savings are projected to be at least £2 million.

Data collection regarding the transfer times of those requiring an inpatient renal bed and/or renal replacement therapy is ongoing to guide coordination of the referral process regionally.

Discussion: The above metrics highlight the positive impact since the introduction of the AKI specialist nurse and in-reach service, and highlight the wider scope for development e.g. expansion to 7-day nursing presence. These findings are impressive as the service was launched during a worldwide Covid-19 pandemic for all clinicians. Additionally, the gains seen in LOS are striking as careful selection and counselling of patients resulted in cases of conservative management of both AKI and AKI-on-CKD, avoiding further transit and expediting palliative discharge in some cases.

Quality improvement projects are ongoing, including the integration of an AKI risk app within the electronic patient record to help reduce hospital-acquired AKI, which has yielded early positive results. Furthermore, we are developing a pathway for patients requiring follow-up, as well as a shared referral portal to tertiary renal services at the neighbouring trusts.

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Track B - AKI 2

10

The importance of early recovery of renal function after AKI on long term outcomes

AKI

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Introduction: Acute kidney injury (AKI) is increasing among hospitalised populations and is associated with long-term adverse outcomes, including the development or progression of CKD, heart failure and mortality. Further detail is needed about the time course of injury and recovery following AKI to target future research and identify potential therapeutic targets to improve long term outcomes. We have previously reported the rates of kidney disease progression following AKI. In this analysis, we sought to determine the interaction between the non-recovery of kidney function at 90 days after an episode of AKI, and subsequent risk of mortality and heart failure.

Methods: We recruited two matched cohorts of hospitalised individuals who had survived to at least 90 days after hospital discharge. The cohorts consisted of people who had sustained AKI during hospital admission (exposed group), and those who had not (non-exposed group), and were matched 1:1 for age, baseline eGFR stage and presence of diabetes. Renal function and albuminuria were measured at 3 months, one, three and five years after index hospitalisation. Mortality and episodes of hospitalisation for heart failure were recorded. Univariable time to survival analyses were conducted with the Kaplan Meir method and comparisons were performed with the log rank test, and a fully adjusted multivariable analysis performed with Cox proportional hazards model.

Results: 866 exposed and non-exposed participants were recruited and successfully matched. Over the 5 year follow up period, 112 (26%) of the AKI group and 82 (19%) of the non-exposed group died, p=0.014. Survival time was shorter in the AKI group, Log rank 6.42 p= 0.01. 90 (21%) of the AKI group and 67 (16%) of the non-exposed group had at least 1 episode of heart failure 0=0.042. Time to heart failure event was shorter in the AKI group than the non-exposed group, Log rank 4.87 p=0.027.
The increased hazard ratio in the AKI group for both mortality and heart failure events was independent when corrected for age, diabetes, CKD at baseline and smoking history. However, the hazard ratios of AKI on both mortality and heart failure events were reduced and no longer statistically significant when adjusted for albuminuria and change in eGFR measured 3 months after hospitalisation.

Conclusions: In a general hospitalised population, mortality and heart failure events were more common after hospitalisation with AKI. The increased hazard of AKI on these endpoints was accounted for by early non-recovery of renal function, emphasising the critical role of renal recovery in patients who have sustained AKI. Strategies for minimising long-term outcomes should focus on

the early recovery period after AKI. Persistent abnormalities at 90 days may help to risk stratify individuals and allow prioritisation of those at greatest risk.

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Track B - AKI 2

11

Variation within UK laboratories in the handling of Paediatric AKI requests and alerts as evidenced by External Quality Assessment data

AKI

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Introduction: One of the functions of the UK NEQAS for Acute and Chronic Kidney Disease External Quality Assessment (EQA) Scheme is to look at the impact of Creatinine results on the Acute Kidney Injury (AKI) algorithm that laboratories use. In December 2021, specimens designed to probe the current laboratory practice of handling paediatric creatinine requests and detection of Acute Kidney Injury (AKI), were sent to over 200 clinical laboratories.

Method: Three different serum specimens were prepared and distributed to 407 individual analysers for AKI within the scheme (Distribution 182). The hypothetical patient was Boris, a 10 year old male, whose specimens were collected 6 days previously (182A), 2 days previously (182B) and today (182C), the day of receipt. Laboratories analysed the specimens for Creatinine and reported an AKI alert based on the AKI algorithm used within their laboratory information management system (LIMS). An online questionnaire was also provided at data entry point where laboratories reported their EQA results.

Results: Creatinine results were reported by 363 laboratory registrations (some laboratories have multiple registrations corresponding to multiple analysers). 234 (~65%) of laboratory registrations use an enzymatic creatinine assay, with the remainder using a compensated kinetic jaffe assay. Within both method principles laboratories may use one of a number of different manufacturer platforms for their creatinine assay. As expected, variation is observed for the creatinine result, both within and between methods. Table 1 shows the enzymatic creatinine mean and the expected AKI stage for the specimens distributed. The AKI Stage 3 alert is based on the creatinine result being greater than 3 times the upper limit of normal for a creatinine for a 10 year old male. This is highly dependent on the reference range that the laboratory uses. The associated questionnaire showed at least 50 different reference ranges are currently in use, by laboratories, for creatinine in paediatrics, and there are differences between laboratories on what age they would report an AKI from (ranging from 2 days to 18 years). For a 10 year old male there is wide variation both at the lower and upper limits (Figure 1). Figure 2 shows a plot of each laboratory's response by method (x-axis) against their creatinine result (y-axis), shaded based on the AKI result. Of the 352 laboratories that reported an AKI alert for Specimen 182C, 45% identified an AKI Stage 3 and 39% an AKI Stage 2.

Discussion: It is clear from the responses to the EQA and the associated questionnaire that there is variation in the handling of creatinine results in paediatrics and the reporting of AKI. The main focus at present is the education of laboratories to analyse and report AKI results in all children over 30 days; however, there does need to be some guidance about the reference ranges that laboratories should be using as this will impact any algorithm which is based on them.

Wednesday 8th June, 12:00-13:00

Track C - Anaemia

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Reducing the harm associated in treating hyperkalaemia with insulin and dextrose

Pharmacology, medicines management including anaemia and MBD

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Introduction: Inpatient treatment of hyperkalaemia with insulin and dextrose can be complicated by iatrogenic hypoglycaemia. Individuals with renal impairment are at an increased risk of both hyperkalaemia as well as insulin-induced hypoglycaemia. The aim of this project was two-fold. Firstly, to assess the incidence of hypoglycaemia in hospitalised patients with renal disease following acute treatment of hyperkalaemia with insulin and dextrose. Secondly, to assess the impact of the subsequent introduction of a local guideline incorporating the use of sodium zirconium cyclosilicate (SZC) for patients with moderate hyperkalaemia.

Methods: As part of a quality improvement project, baseline data was obtained by a retrospective search of electronic prescribing records from January to June 2019 to identify all patients, within our large urban renal centre, admitted under the care of a renal physician who received the co-administration of insulin and dextrose. Pertinent audit data was obtained retrospectively from the electronic patient record; all patients with renal disease regardless of modality of treatment were included. In October 2019, SZC became available and was included within the Trust guidelines for the management of moderate hyperkalaemia. After, establishing a significant burden of hypoglycaemia in the initial observation period, a requirement for hourly-capillary blood glucose monitoring (for up to 6 hours) following the administration of insulin for hyperkalaemia was incorporated into the guidelines. A re-audit was undertaken between January and June 2021 using identical criteria but included all patients in whom SZC was initiated for hyperkalaemia.

Results: Insulin and dextrose was administered for hyperkalemia on 126 occasions in 2019 (75 patients, aged 57 ± 15 years (mean ± SD) years [total of 843 admissions between this period], compared with 21 occasions in 2021 (21 patients, 55 ± 16 years) [total of 780 admissions]. Pre-intervention, 34% (42/124) of treatments resulted in hypoglycaemia (glucose ≤ 4mmol/L), in whom 17/42 developed severe hypoglycaemia (≤ 2.8 mmol/L). In those who experienced hypoglycaemia, 48% (15/31) of patients were diabetic, 49% (15/31) were treated with dialysis. Time to lowest glucose level, amongst those experiencing hypoglycaemia, was 6.1 ± 6.7 hours (mean +/- SD). Following the new guidelines hypoglycaemia occurred in 9.5% (2/21) episodes, of which one was severe.

In 2019, insulin was frequently being administered inappropriately, 58% (73/124) of patients had a potassium ≤ 6.4 mmol/L; only 38% (28/73) of these had an ECG of which 25% (7/28) were abnormal. In contrast, the majority of patients treated in 2021, 90% (19/21), had a potassium >6.5mmol/L. The reduction in insulin use in 2021 was associated with a rise in the use of SZC for which there were 295 administrations in 75 patients for the acute treatment of hyperkalaemia.

Discussion: Significant harm arises from the use of insulin and dextrose for the management of hyperkalaemia in patients with renal disease. The two-fold introduction of SZC alongside changes in patient care after the administration of insulin, resulted in more appropriate use of insulin and dextrose as well as a significant reduction in the iatrogenic burden of hypoglycaemia.

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Track C - Anaemia

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Safe Opiate Analgesia Prescribing in Renal Disease - Assessment of Current Knowledge and Practice Among the Medical Workforce

Pharmacology, medicines management including anaemia and MBD

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Introduction: Opiates are known for both their potent analgesic and potential psychoactive effects. Their narrow therapeutic index, protein/lipid binding, multiple derivatives and hepatic/renal metabolism/excretion can cause significant morbidity and mortality if inappropriately prescribed. As effective analgesia, they should be offered to those with renal impairment when required, however need to be used with caution and appropriate modifications. Guidelines for use in renal impairment exist from renal, pharmacological and palliative bodies however none are universally accepted. Furthermore, there is a lack of consensus regarding the degree of renal impairment below which modifications should be made or clear instructions specifying these modifications.

Aim: Assessment of understanding of prescribing amongst junior doctors and actual prescribing practices at a large teaching hospital.

Methods: A 7 question electronic survey was distributed to all junior doctors in the London training programmes regarding knowledge about and current practice of prescribing opiates in renal impairment. Responses were collected over one month. Additionally, an audit of opiate prescribing at a 1300 bed hospital was undertaken in patients with eGFR <60 between 01/01/2021 and 01/02/2021.

Results: The survey distributed via Health Education England (HEE) was answered by 258 junior doctors, 62% were foundation year 1/2. The majority (97%) reported altering their prescription depending on renal function: 95% change the drug prescribed, 73% the dose and 42% the dosing interval. The majority (65%) would alter the prescription below an eGFR 30ml/min/1.73m2, while 5% stated altering prescriptions if below 60ml/min/1.73m2. Age (84%), BMI (61%) and concurrent prescriptions (79%) were the three main other patient factors considered when prescribing opiates. Albumin was only considered by 3% as a key factor. Most (73%) would prescribe either a mid-level or strong opiate rather than both simultaneously and the vast majority (98%) would choose oxycodone for a haemodialysis patient rather than morphine.

The prescribing practices in the questionnaire were reflected in the audit of actual prescriptions. The audit did however reveal confusion in prescribing practice with often multiple opiate prescriptions written within minutes of one another. While most were cancelled preventing multiple simultaneous prescriptions, some overlapped, allowing potential for inadvertent administration of large doses of opiates. There was evidence of pharmacist, pain team and palliative care team involvement in the prescriptions. A key difference between reported and actual practice, was the eGFR below which changes were made. Changes to the opiate prescription including from morphine to oxycodone and dose reduction tended to occur below an eGFR 60.

Discussion: Opiate overdoses can be life-threatening and can occur at lower doses in renal impairment compared to the general population. The survey and audit have identified areas to target for improvement of safe prescribing. Targeted approaches could include the auto-population of dose of oxycodone when prescribing oxycodone online and a renal impairment order set for anticipatory medications for end of life. Errors in prescribing as well as the multiple prescriptions when initiating analgesia in patients with renal impairment revealed a need for easily accessible guidelines for opiate prescribing in renal failure as well as an education programme amongst prescribers.

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Track C - Anaemia

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Understanding and Attitudes Towards Pharmacogenomics in Practice Among Members of the Renal Medicine Community in the United Kingdom

Pharmacology, medicines management including anaemia and MBD, Staff education

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INTRODUCTION: Pharmacogenomics refers to the use of an individual's genetic variation in predicting their response to medications. It is a form of precision medicine with the goal of tailoring drugs and dosing based on an individual's genetic makeup. The advent of pharmacogenomics has been hypothesised to provide a potential window to patient tailored therapy as opposed to the approach of one size fits all. An increasing number of pharmacogenomic markers have been identified for a variety of medication in the past decade. Their use in clinical practice however is not prevalent and varies considerably across different specialties and in different countries.

OBJECTIVES: The aim of this survey was to assess perceived interest and knowledge of pharmacogenomics as well as to identify its current and proposed applications by renal healthcare professionals in the United Kingdom.

METHODS: The survey comprised of 8 questions and was distributed to members of the UK Kidney Association (UKKA) as an electronic survey through the society. All registered members of the society were given equal opportunity to respond regardless of discipline and length of practise. The survey was circulated by UKKA in 2021 and ran over 30 days.

RESULTS: There were 75 respondents, majority (72%) doctors, others included pharmacy, nursing and non-clinical staff. Approximately half (54.4%) rated their knowledge of pharmacogenomics as little or none at all despite 88.9% of the respondents being in clinical practice for over 10 years. However, almost all respondents (95.5%) felt pharmacogenomics would have a positive impact on improving patient outcomes and most (74.2%) felt that it should be implemented if testing became widely available. Amongst surveyed participants, the most common pharmacogenomic testing in use was measurement of thiopurine S-methyltransferase (TPMT) activity levels. An area which respondents felt would be a beneficial to implement pharmacogenomics was drug metabolism and Cytochrome P450 polymorphisms with a particular interest in immunosuppression including calcineurin inhibitors. Criticisms raised included limited validation data and potential high implementation costs involved in pharmacogenomic testing for a yet unproven benefit on patient outcomes in some areas.

CONCLUSION: The Royal College of Physicians (RCP) and Royal Pharmacological Society are exploring implementation of Pharmacogenomics in clinical practice. Though the response to this survey was <10% of the UKKA membership, this may reflect in part the lack of awareness around the subject

area. This survey has highlighted the need for more education for renal healthcare professionals in the area of pharmacogenomics, especially as it is a growing field in the wake of more accessible genomic testing. Many are in agreement about the potential benefits of pharmacogenomics, such as in the dosing of immunosuppression and avoiding potential adverse events. However, it is true that further research maybe required to validate the utility of these tests in widespread clinical practice.

Acknowledgement: Prof Claire Shovlin for permitting use of adapted forms of questionnaire among specialties in Working Group and the late Prof Donal O'Donoghue OBE a lead on the Working Group

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Track D - Children and young adults

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Identifying phenotypic features to inform genetic screening in children with persistent haematuria

Genetic and rare diseases, Paediatrics

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Background: Persistent incidentally detected haematuria is prevalent in paediatrics and is commonly referred to paediatric nephrologists. It is important to identify which children are at higher probability of having an underlying genetic diagnosis. Mutations in COL4A3, COL4A4 and COL4A5 that make up the glomerular basement membrane results in a clinical spectrum of disease including Alport syndrome and thin basement membrane disease with widely differing prognoses. Progression to chronic kidney disease can occur during childhood making early interventions important. The benefits of genetic diagnosis are many, including determining carrier status, understanding disease phenotype and prognosis, early implementation of ACEI therapy as well as avoiding invasive renal biopsies. However, genetic testing is costly and it would be helpful to identify features that make testing more likely to be positive.

Methods: We analysed a group of children referred to our tertiary paediatric nephrology unit, for persistent microscopic haematuria between 2014-2018 and who had had genetic panels assessing for variants in COL4A3,4,5 and 6 and NPHS2 by next generation sequencing. The purpose of this retrospective cohort review was to assess the clinical features of those tested, and to investigate if any of those features corresponded with a greater likelihood of predicting a genetic diagnosis. Information was obtained by accessing electronic clinical records. Of the 99 children who had genetic testing, 5 children were excluded due to insufficient available information. The characteristics that were assessed in the 94 remaining children included: hearing loss or visual problems either in the proband or in first degree relatives, proteinuria at the time of referral, family history of renal disease, abnormal renal function, hypertension and proteinuria, and a history of previous urinary tract infections. The probability of certain characteristics being associated with an underlying genetic diagnosis was evaluated by calculating likelihood ratios.

Results: Of the 94 children, 65% were male. Median age was 9 years (range 9 months-16 years). Median time from haematuria onset to referral to the tertiary nephrology centre was 7 months (range 1-108 months) and median time from referral to genetic testing was 8 months (range 1-86 months). 28% of the children were found to have an underlying genetic cause of their haematuria or had genetic variants of yet unknown clinical significance (VUS). In the children who had VUS, 38% of mutations were in COL4A3, 31% in COL4A4, 15% in COL4A5, 8% in COL4A6 and 8% in NPHS2. Of the characteristics analysed, co-existing visual problems demonstrated a notable increased likelihood of

a genetic diagnosis (likelihood ratio=25). Co-existing family history of renal disease only led to a marginal increased likelihood of a genetic diagnosis (likelihood ratio=1.87).

Conclusion. This is the largest single centre review to date correlating clinical phenotype in children with persistent haematuria with COL4 genetic testing. From this we can infer that children who present with haematuria should have an early ophthalmological assessment and those who also have visual impairment should be prioritised for genetic testing to assess for variations in the COL4A genes as this increases the pre-test probability of a positive genetic result.

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Track D - Children and young adults

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Costs of hospital outpatient medicines for patients pre and post renal transplant for 2006-2018

Paediatrics, Transplantation - quality improvement

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Background: The NICE Health Technology Asssessment 'Immunosuppressive therapy for kidney transplantation in children and adolescents:systematic review and economic evaluation' published in 2016 found limited data for costs of medicines used to treat paediatric renal transplant patients. Electronic systems allow this data to be extracted relatively easily and on a regular basis.

Method: Patients were identified who received a renal transplant between 2005 and 2019 at a children's hospital. Data for outpatient medicine costs, pre and post transplant, and tacrolimus levels were extracted from the hospital's electronic health records and uploaded into the hospital's digital research environment for manipulation.

Results: 370 patients (220(59%) male) were identified. The number of patients per year are shown (Figure 1). Costs include both pre and post transplant costs for all patients. The tacrolimus levels included those taken in all settings (including as an inpatient).

Tacrolimus preparations accounted for the highest cost during this period (Figure 2). It was matched by the combined costs of home haemodialysis and peritoneal dialysis (the majority pre transplant costs).

Since 2014 the amount of tacrolimus prescribed as granules or as liquid (unlicensed) has varied between 32% and 45% (Figure 3). The average cost/mg tacrolimus per year was £2.04 (range £1.70 - £2.40) between 2006-2018 (Figure 3). Tacrolimus levels measured were below 5nanogram/ml on 37% of occasions over the 13 year period (Figure 4).

Discussion: NHS Clinical Commissioning repatriated tacrolimus prescribing to hospitals in 2015 and thus hospital costs increased. Some of the variation on cost can be attributed to the proportion of different formulations used in any year. With the increasing competition in the market the cost/mg should decrease. This does rely on a willingness to 'switch' which requires effort by the clinical team to achieve it safely. Whilst there are many reasons why a patient's tacrolimus level may be outside the 'therapeutic range', embedding research findings about the pharmacokinetics/dynamics and genetics of tacrolimus into clinical practice may change this.

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Track D - Children and young adults

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Developing Young Adult Peer Support Training

Transitional and young adult care

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Introduction: Young adults have been identified as an 'at risk' group for poor psychosocial outcomes. Peer support involves people with chronic kidney disease using their shared personal experience to provide short term, practical, emotional and social support to people, their families and carers. Previous work has shown that peer support can be successfully delivered within renal units. Our aim was to develop a peer support programme which trained young adults to support younger people transitioning from paediatrics (16-18 year olds) and those who enter adult services during their young adult years (18-30 year olds).

Method: Developing the Training. We developed a three session 'Young Adult Peer Support Course'. This was adapted from previous work from both Guy's and St Thomas' Hospital and the West Midlands Renal Network. The focus of session one was on understanding the boundaries of the role. Session two involved developing practical skills and managing difficult situations. Session 3 looked at the practicalities of offering peer support. The training was delivered by the Renal Young Adult Worker and the Renal Psychologist. The volunteers also had to undertake NHS Voluntary Services Training and complete the appropriate recruitment and DBS checks for a NHS volunteer role.

The first course trained six peer supporters. Course ratings were collected from 5 participants who completed the course (unfortunately 1 participant died following the training; their qualitative comments were available to be included).

Results: Participants rated their knowledge of renal peer support on a scale of 1 to 10 (from no prior knowledge to extremely knowledgeable). Peer supporters reported having significantly more knowledge of renal peer support after training (M = 9.4, SD = .55) than before training (M = 5, SD = 1.22), t(4) = -6.49, p = .003.

All five respondents rated the training length as 'just right', as opposed to 'too long' or 'too short'. For the ratings on how clear and easy to understand training was out of 5, the mean was 4.8 (range 1). Participants rated how useful training was out of 5. The mean was 4.6 (range 1).

Participants' qualitative responses were also analysed and highlighted the social benefit of training as a group of young adults, the impact of covid on the training structure and the usefulness of a formal recruitment process, albeit recognising this was a slow formal process.

Discussion: The course was highly valued by the participants. The recruitment processes although time-consuming enabled young people to experience a recruitment process which for some young people was their first experience of applying for a job. Covid has brought additional challenges such as having to undertake the training virtually and the peer supporters have not be allowed to attend face to face transition clinics due to Covid rules. Some of the young adult peer supporters have commenced targeted virtual peer support.

Conclusion: Young adults are very enthusiastic about peer support and highly rated the programme. While Covid presented a number of additional challenges, we look forward to implementing face-to-face support on site in the near future.

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Track D - Children and young adults

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Exploring patient, family and clinician perspectives about the psychosocial factors influencing access to kidney transplantation and transplant outcomes for children

Behavioural, psychological and quality of life, Paediatrics

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Introduction: Kidney transplantation is often seen as the optimal form of kidney replacement therapy for children and young people (CYP) with stage 5 Chronic Kidney Disease (CKD5). Psychosocial factors have been cited to delay their access to a kidney transplant, however it is unclear what these factors are.

We undertook a multi-centre qualitative study that explored the range of psychological and social factors that CYP, their carers and their paediatric nephrology multi-disciplinary team (MDT) perceived to influence how soon a CYP with CKD5 accesses a kidney transplant. This included factors that were perceived to influence kidney transplantation outcomes or deemed important to patients and their families in terms of their quality of life (QoL).

Material and methods: Semi-structured interviews were conducted with CYP, their carers and their paediatric nephrology MDT across 7 tertiary paediatric nephrology units in the United Kingdom. These interviews were reviewed for pertinent themes using thematic Analysis following the approach of Braun and Clarke.

Results: A total of 36 interviews were conducted with 13 families and 16 members of the paediatric nephrology MDT. The majority of participating families identified as White (57%), followed by Black (22%) or Asian (21%). The following themes were deemed important to accessing kidney transplantation and post-transplant outcomes: health beliefs; relationship with and trust in healthcare; support networks; family relationships; socioeconomic circumstances; culture and race; and mental health and coping strategies. Specific challenges from living with CKD5 and living through the COVID-19 pandemic were also discussed due to their impact on QoL and accessing a kidney transplant.

Conclusions: There are a wide range of psychosocial factors that are perceived to influence a CYP's access to kidney transplantation. Longitudinal and prospective studies are needed to fully assess the relationship between these psychosocial factors and a CYP's access to, and outcomes of, kidney transplantation.

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Track D - Children and young adults

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Unfractionated versus low molecular weight heparin for paediatric haemodialysis anticoagulation: A single centre experience

Paediatrics

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During haemodialysis, anticoagulation of the circuit is required to prevent intra-circuit thrombus reducing dialysis efficacy, and potentially obstructing flow, with subsequent blood loss. The risk of intra-circuit thrombus occurs partly due to activation of platelets and coagulation factors when contacting foreign surfaces. In children, this risk is amplified due to the relative reduced blood volume in comparison to the machine's surface area compared with adults, with lower flow rates further increasing risk. Traditional anticoagulation with unfractionated heparin (UFH) was standard practice in most adult and paediatric haemodialysis units[1]. European guidance in 2002 promoted use of low molecular weight heparins (LMWH) in preference to UFH due to improved anticoagulation predictability, an increased half-life, lower thrombus risk, and cost efficacy[2-3]. Many paediatric units have continued to use UFH. Our unit introduced tinzaparin use in January 2020. This retrospective study aimed to determine whether this anticoagulant change has led to fewer line-related complications.

Data was retrospectively collected from all paediatric patients aged 0-18 years receiving haemodialysis between 01/07/2017 and 30/06/2020 at our centre, from electronic patient record, SERPR. Data collected included patient age, number of haemodialysis central venous catheters (CVC) per patient requiring replacement during haemodialysis, reasons for CVC removal, anticoagulant at time of CVC removal, number of CVC infections, number of shortened haemodialysis sessions due to CVC issues, and subsequent number of additional haemodialysis sessions scheduled.

Fifteen patients (eleven male, age range: three-seventeen years) who received haemodialysis between 1/7/17 and 30/6/20 were identified. Nine only received heparin, four received only tinzaparin and two received a combination of both. Thirty-five CVC were inserted across all fifteen patients with twenty-one CVC changes. Heparin was in use for nineteen (90.4%) CVC changes, tinzaparin was in use for one (4.8%) CVC change and a combination of heparin and tinzaparin was in use for one (4.8%) CVC change. The most common reason for a CVC change was infection (6), "not working" (5) and "replaced" (3). Eighty-six (5.7%) of haemodialysis sessions were terminated early due to CVC issues using heparin, compared to twelve (2%) haemodialysis sessions using tinzaparin. Across the whole, 'alarms' were noted as a reason for stopping a haemodialysis session early 112 times, followed by clots (18) and loss of/poor flow (15). Seventy-one additional haemodialysis

sessions were scheduled. Fifty-three (2.5%) of total haemodialysis sessions in patients receiving heparin and eighteen (2%) of total haemodialysis sessions in patients receiving tinzaparin.

In this single retrospective review of a practice change in a single paediatric centre, no new safety issues arose due to use of LMW heparin for HD anticoagulation. Fewer HD sessions had issues requiring early termination of HD. Far fewer CVC changes have been required since we changed practice to use of LMW heparin, though key limitations include other practice changes occurring simultaneously within our haemodialysis unit, and a change in patients receiving HD due to transplantation. The early data from this study suggests use of LMWH in paediatric HD patients is equally justified, with similar benefits to those seen in adult practice.

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Track E - Epidemiology, public health, health inequalities

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The effect of patient and practice factors on peritoneal dialysis technique survival

Epidemiology, public health and prevention, Home therapies - research

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Introduction: Peritoneal dialysis (PD)is a renal replacement therapy option that proved to be comparable to haemodialysis with good outcomes.PD Outcomes have improved at a much faster rate than those for haemodialysis (HD) over the past twenty years, particularly in young non-diabetic patients. PD has several advantages over unit HD; preservation of the residual renal function, higher quality of life, and hemodynamic stability. Furthermore, PD costs almost 60-70 % less than unit-based HD. Several studies demonstrated that centers with a higher number of PD patients or with a higher percentage of patients on PD had better technique survival which reflects that more experience with PD may lead to better technique survival. This study seeks to describe the technique survival rates of PD in the UK and to examine which patient and practice factors are associated with technique survival.

Methods: All adult patients treated with an episode of PD between 1.1.07 and 31.12.2012 in the UK were included in this retrospective cohort study. Age, biological sex, primary renal disease, socio-economic status, ethnic origin, renal centre where patient received treatment, treatment type, dates of treatment start and stop, outcomes following episode of PD and the number of patients receiving HD and PD in each centre on 31.12.2012 were collected from the UK Renal Registry database. Practice patterns were obtained from the 2010 UK Renal Registry Survey. Shared frailty Cox regression analysis was used to examine associations between patient and renal centre factors and PD technique survival using the renal centre as the shared frailty term and efron tied failure estimation.

Results: There were 10,267 patients who started PD between 2008 and 2012. The median time on PD (median technique survival) for all patients was 1 year and 4 months. There was significant variation between renal centres in the median time their patients spent on PD, ranging between 9 months and 2 years 9 months. Overall 13% of first PD episodes lasted for less than 90 days, 9% between 3-6 months, 23% between 1-2 years, 15% between 2-3 years, 9% between 3-4 years, 6% between 4-5 years and 7% over 5 years.There was significantly better PD technique survival in larger PD centres (HR 0.89 95%CI 0.85-0.94). There was no difference in PD technique survival between patients from different races or deprivation quintiles. Patients with diabetes and ‘other’ causes of ESRD had shorter PD technique survival compared with patients with polycystic kidney disease (1.12 (95%CI (1.04-1.20)). PD technique survival was significantly better in older compared with younger age groups, even in patients who switched to HD following their episode of PD (HR 0.70 95%CI 0.66-

0.74). Technique survival was worse in centres where it was harder to obtain a timely catheter insertion (HR 1.04 (1.02-1.07)). More education nurses per 100 RRT patients but not renal centre RRT population size was associated with greater PD technique survival. There was also no association with more home dialysis nurses. There was no association between physician enthusiasm for PD and technique survival.

Conclusion: Renal centres with larger PD patient populations also had longer median technique survival times as has been shown in previous studies. Although physician enthusiasm (as measured here) was not associated with longer treatment times with PD the centres with longest PD treatment times were Dudley, Kilmarnock, Derby, Antrim and Birmingham QEH and further work to examine and share good practices associated with improved technique survival could improve quality of care for all PD patients.

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Track E - Epidemiology, public health, health inequalities

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Addressing health inequalities – still urgent, more relevant!

Epidemiology, public health and prevention, Patient outcome and experience, Other

Jain Neerja[1], Ferguson Jackie[1]

[1]*Kidney Research UK*

Introduction: Improving prevention and early detection and ensuring that everyone in the UK has access to the right treatment for them is key to improving kidney health for everyone. Yet, not everyone is equal when it comes to kidney disease. Some groups are particularly disadvantaged. For instance, people from South Asian and Black backgrounds are three to five times more likely to require dialysis treatment and typically wait longer than people from Caucasian backgrounds to receive a kidney transplant. Reducing inequalities will bring benefits to individuals and their families, the healthcare system and wider society.

We wanted to find answers to fundamental questions about why certain groups face higher risks of kidney disease, why they can have worse outcomes and how can research be used to reduce them?

As an organisation with long standing experience in driving interventional projects to address health inequalities, this is a strategic priority and cross cutting theme.

Methods: We commissioned an expert review of the existing evidence of health inequalities in kidney disease, to better understand this, and to develop an agenda to address the underlying causes. It sets out an overview of what we know so far and crucially, provides recommendations for key research areas to improve our understanding of these inequalities and how to tackle them. This report will support the kidney community to effectively reduce health inequalities.

As an organisation, we proactively addressed health inequalities through our work and any funded by ourselves. This includes through building on our legacy of community outreach awareness campaigns and bespoke research studies to address inequalities for example increasing engagement of the “poorly reached” in renal research.

Results: Our commissioned review identified 27 recommendations for the renal community. These research recommendations mainly focus on inequalities experienced by ethnic minority groups and socially deprived people, as prioritised in the full report. However, other disadvantaged groups must not be forgotten, and we will need to progress research as the extent of these inequalities is defined. These fall into three main categories: 1. Predicting or preventing kidney disease. This includes identifying if there is sufficient evidence to test ways to target early life risk factors for CKD. 2. Protecting patients from progression of kidney disease and further harm: e.g., gather all the evidence in respect of age, socioeconomic deprivation, and ethnicity, about access to care and poor

outcomes following cases of AKI. 3. Delivering treatment: e.g., develop an intervention to increase the use of home therapies in groups that are traditionally low users of the service. This latter recommendation was the subject of a very successful pilot project that we undertook, which we are now planning to scale up.

Discussion: To address the 27 recommendations, there is much to do and it is the responsibility of everyone in the renal community. We need to identify and implement best practice tailored to the communities served. Ongoing research is needed to better understand the causes and solutions. Funding and commitment from multiple agencies are required to fully address health inequalities.

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Track E - Epidemiology, public health, health inequalities

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Associations between frailty trajectories and cardiovascular, renal, and mortality outcomes in chronic kidney disease

Epidemiology, public health and prevention

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Background: Frailty is characterized by the loss of biological reserves and vulnerability to adverse outcomes. In individuals with chronic kidney disease (CKD), numerous pathophysiological factors may be responsible for frailty development including inflammation, physical inactivity, reduced energy intake, and metabolic acidosis. Given that both CKD and frailty incur a significant healthcare burden, it is important to understand the relationship of CKD and frailty in real-world routine clinical practice, and how simple frailty assessment methods (e.g., frailty indexes) may be useful. We investigated the risk of frailty development in CKD and the impact of frailty status on mortality and end stage kidney disease (ESKD).

Methods: A retrospective cohort study using primary care records from the Clinical Practice Research Datalink (CPRD) linked to Hospital Episode Statistics (HES) and the United Kingdom Office for National Statistics (ONS) was undertaken in 819,893 participants aged ≥40 years, of which 140,674 had CKD. Frailty was defined using an electronic frailty index (eFI), generated electronically from primary care records. Cox proportional hazard and flexible parametric survival models were used to investigate the risk of developing frailty and the effect of frailty on risk of all-cause and cardiovascular mortality, and ESKD.

Results: The majority of those with CKD (75.3%) were frail (versus 45.4% in those without CKD (no-CKD)). Over 3 years (median), 69.5% of those with CKD developed frailty. Compared to no-CKD, those with CKD had increased rates of developing mild (hazard ratio (HR): 1.02; 95%CI: 1.01-1.04), moderate (1.30; 1.26-1.34), and severe (1.50; 1.37-1.65) frailty. Mild (1.22; 1.19-1.24), moderate (1.60; 1.56-1.63), and severe (2.16; 2.11-2.22) frailty was associated with increased rates of all-cause and cardiovascular-related mortality (mild 1.35; 1.31-1.39; moderate 1.96; 1.90-2.02; severe 2.91; 2.81-3.02). 10-year survival probability in CKD and no-CKD groups stratified by frailty at baseline is shown in Figure 1. Compared to being non-frail, all stages of frailty significantly increased ESKD rates.

Figure 1. 10-year survival probability in CKD and no-CKD groups stratified by frailty at baseline

Discussion: Frailty is highly prevalent and associated with adverse outcomes in people with CKD, including mortality and risk of ESKD. Preventative interventions should be initiated to mitigate the development of frailty. The use of a simple frailty index, generated electronically from health records, can predict outcomes, and may aid prioritization for management of people with frailty.

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Track E - Epidemiology, public health, health inequalities

23

Can primary care consultation patterns identify children who go on to develop severe chronic kidney disease?

Epidemiology, public health and prevention

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Background: When chronic kidney disease (CKD) advances, complications relating to kidney function decline occur. These may cause symptoms which in turn prompt medical review. Understanding whether symptoms associated with CKD development in children and young people (CYP) are reported to primary care may provide an opportunity for earlier detection of CKD through targeted screening. The aim of this study was to test the hypothesis that CYP who go on to develop severe CKD (stages 4, 5 or kidney replacement therapy requirement) could be identified from children in the general population based on their prior symptom reporting and consultation frequency.

Methods: A nested case-control study using Clinical Practice Research Datalink was performed. Cases were CYP aged under 21 years with an incident code for severe CKD during the study period (2000-2018); the date of coding was considered the index date. Controls were children without severe CKD matched on age (+/-3 years), sex and a practice-level variable. Conditional logistic regression modelling was used to examine the association between possible CKD symptoms and consultation frequency with subsequent case status in the 6 and 24 months prior to the index date. An exploratory multivariable logistic regression analysis was also performed to determine whether symptoms and consultation frequency could be used to derive a clinical prediction model for severe CKD.

Results: Several symptoms were predictive of severe CKD in the 24 months before the index date, including growth concerns (Odds Ratio, OR 7.35, 95% confidence interval, CI 3.52, 15.36), change in urine colour (OR 6.52, 95% CI 2.03, 20.97), oedema (OR 5.72, 95% CI 2.92, 11.23), urinary tract infection (OR 3.32, 95% CI 2.05, 5.38) and vomiting (OR 2.95, 95% CI 1.96, 4.43). However, due to the low CKD incidence, the positive predictive value of symptoms was low. Cases consulted more frequently than controls before the index date in both timeframes. Findings were similar when CYP with known kidney disease were excluded. In a multivariable model, several symptoms along with consultation frequency demonstrated modest discrimination for severe CKD (bootstrapped concordance statistic 0.70, 95% CI 0.66, 0.73), with acceptable calibration.

Conclusion: Key symptoms and primary care consultation frequency are associated with subsequent coding for severe CKD in the 24 months prior to diagnosis. Individual symptoms, however, have a low positive predictive value. Clinical symptoms together with consultation frequency may be used

to develop a pragmatic clinical prediction model which has modest discrimination for severe CKD in children and young people.

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Track E - Epidemiology, public health, health inequalities

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Clusters of conditions in chronic kidney disease: A Welsh population study

CKD, Epidemiology, public health and prevention

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Introduction: People with two or more chronic conditions (multimorbidity) suffer from high treatment burden as they have to cope with numerous medications and attend multiple specialists. Multimorbidity is common in people with chronic kidney disease (CKD) and is associated with adverse outcomes. We aimed to explore: 1) what different clusters of conditions are associated with CKD and how these change as kidney function declines; and 2) associations between clusters of conditions and adverse outcomes.

Methods: We studied the Secure Anonymised Information Linkage Databank (SAIL) between 2006 and 2021: an electronic health records repository for 79% of the population of Wales (UK). We estimated the date at which patients crossed estimated glomerular filtration rate (eGFR) thresholds: 90, 75, 60, 45, 30 and 15mL/min/1.73m2. We identified 27 chronic conditions using ICD-10 codes and prescription data. We applied a k-modes clustering algorithm within each eGFR category, at the dates patients crossed eGFR thresholds. To help describe each cluster, we identified “key conditions” which were common in the cluster and more common than in the overall eGFR category (prevalence greater than 20% and more than double the prevalence in the overall eGFR category). To help determine whether these clusters were clinically meaningful, we studied the association between clusters and adverse outcomes risk using Cox proportional hazards models (all-cause mortality and major adverse cardiovascular events: MACE), with clusters having no key conditions as the reference group.

Results: Overall, 533,362 patients were included in the analysis. Median age was lowest in the eGFR 90 category (56 years, IQI: 47-64) and highest in the eGFR 30 category (81 years, IQI: 73-87). Patients in the low eGFR categories had the highest number of conditions. The most frequently recorded condition was hypertension, which ranged from 34.4% for eGFR 90 to 86.1% for eGFR 15. Diabetes ranged from 17.5% for eGFR 90 to 53.4% for eGFR 15. Chronic pain ranged from 21.5% for eGFR 90 to 38.4% for eGFR 15. In most eGFR categories, the majority of patients were included in one cluster with no key conditions (Figure 1). Various conditions clustered together, with cardiovascular conditions and diabetes often co-existing at low eGFR. Chronic pain and depression featured prominently, often in combination with physical conditions. The relative rates of each outcome were highest in the clusters with cardiovascular key conditions: for example, at eGFR 15, the hazard ratio for MACE in the “Pulmonary disease, asthma & heart failure” cluster was 2.3 (95% confidence interval 1.9-2.9; adjusted for age and sex).

Discussion: We have described the prevalence of chronic conditions at different levels of kidney function and we have identified clusters of conditions. Multimorbidity became extremely common at lower eGFR, clustering in unexpected ways: at lower eGFR, combinations of cardiovascular diseases and depression became prominent, as well as chronic pain. Patients in clusters with cardiovascular key conditions were at greatest risk of adverse outcomes. Identification of disease clusters with refinement by eGFR may allow targeted approaches to therapy.

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Track E - Epidemiology, public health, health inequalities

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Diagnosis of advanced cancer and subsequent outcome in people with CKD: an analysis of a national population cohort

CKD

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Introduction: Chronic kidney disease (CKD) is associated with increased risk of incidence and death from some cancers. We sought to determine whether patients with CKD were more likely to present with advanced cancer (stage 3 or 4), and whether this explained reduced cancer survival in people with CKD.

Methods: Data were from Secure Anonymised Information Linkage Databank (SAIL): a Welsh primary care cohort with linkage to cancer and death registries. Participants were included if they had a new diagnosis of cancer between 01/01/2009 and 01/10/2020 and if they had kidney function tested in advance of and within two years of cancer diagnosis. Estimated glomerular filtration rate was calculated from serum creatinine (eGFRcr; CKD-EPI 2009 equation). CKD stage was determined if there were two concordant eGFRcr measures at least 3 months apart: no CKD (eGFRcr >60mL/min/1.73m2: reference group), CKD G3 (eGFRcr 30-59 mL/min/1.73m2) or CKD G4-5 (eGFRcr <30 mL/min/1.73m2). Albuminuria was not consistently available for CKD staging. Logistic regression models (adjusted for age, sex, smoking status and number of comorbidities) were used to determine odds of presenting with advanced cancer (stage 3/4) according to CKD stage. The cumulative incidence function was used to estimate probabilities of cancer death by CKD stage (i.e., where cancer was the primary cause of death and risk was assessed from the date of cancer diagnosis). Cox proportional hazards models (adjusted for variables as above plus cancer stage at diagnosis) tested association between CKD stage and hazards of cancer death.

Results: There were 111,081 participants: at time of cancer diagnosis, 85,582 had no CKD (22,591 cancer deaths; median follow-up 4.0, IQR 1.4-6.2 years), 22,076 had CKD G3 (7,187 cancer deaths, median follow-up 2.4 IQR 0.4-4.6 years) and 3,423 had CKD G4-5 (1,175 cancer deaths, median follow-up 1.0, IQR 0.1-3.4 years). Compared to those with no CKD, participants with CKD were at lower risk of presenting with advanced cancer: G3 aOR 0.84 (95% CI 0.80-0.87, p<0.001) and G4-5 aOR 0.76 (95% CI 0.70-0.84, p<0.001). The odds of presenting with advanced cancer decreased by 3% for each 10 mL/min/1.73m2 reduction in eGFRcr below 60 mL/min/1.73m2 (aOR 0.97, 95% CI 0.95-0.99, p=0.038). The risk of cancer death 3 months after cancer diagnosis was more than twice as high in people with CKD G4-5 (17.9%, 95% CI 16.5-19.2%) compared to those with no CKD (7.9%, 95% CI 7.7-8.1%; see Figure). Compared to those with no CKD, CKD G3 (aHR 1.05, 95% CI 1.01-1.10,

p=0.007) and CKD G4-5 (aHR 1.25, 95% CI 1.15-1.36, p<0.001) were associated with increased hazards of cancer death.

Discussion: Patients with CKD are at lower risk of presenting with advanced cancer than those without CKD. Reduced cancer survival in patients with CKD may not be attributable to cancer diagnosis delays, but may instead be due to differences in choice, dose, duration or efficacy of cancer treatment. The evidence base for cancer treatment is limited by the exclusion of patients with CKD from clinical cancer trials. Scrutiny of cancer treatment choices in CKD is required.

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Track E - Epidemiology, public health, health inequalities

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What is the nature of the cardiovascular risk associated with kidney stone formation? A systematic review and meta-analysis

Cardiovascular disease and diabetes, Epidemiology, public health and prevention

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Introduction. Previous epidemiological studies have shown that kidney stone formers are at greater risk of developing forms of cardiovascular disease (CVD), but the exact types have not been clarified and the mechanisms linking these conditions have not been explored. Understanding these could inform future preventative strategies.

Methods. We performed a systematic review of the epidemiology of kidney stone formation (KSF) and CVD. The epidemiological search generated 669 papers, which after applying criteria (study design type; cardiovascular outcomes provided; non-kidney stone former control group present; relative risk stated with 95% confidence intervals (CI)) resulted in 13 papers. These studies consisted of 15 different cohorts with a total of 4,212,103 individuals. Of these, 226,466 were kidney stone formers. The mechanistic search generated 180 papers, which after applying inclusion criteria (provide evidence for a pathophysiological mechanism; address both CVD and KSF) resulted in 13 papers that were reviewed. The large reduction from searched to reviewed papers was due to our strict inclusion criteria.

Results. We found that kidney stone formers are more likely than non-kidney stone formers to develop CVD, with a 24% higher risk (95% CI: 20-28%) of coronary artery disease, a 16% higher risk (95% CI: 14-19%) of stroke/transient ischaemic attacks (TIAs) and a 35% higher risk (95% CI: 14-61%) of developing peripheral arterial disease. Four mechanisms that could contribute to both KSF and CVD were identified, including, intimal/medial vascular calcification, oxidative stress via osteopontin effects, cholesterol-induced pathology, and endothelial dysfunction.

Discussion. Although the epidemiological link between KSF and CVD has previously been reported, this is the largest systematic review to be performed, and the first to specify cardiovascular outcomes in this manner. Vascular calcification via inflammatory mechanisms may represent a common pathway for both KSF and CVD. Future mechanistic studies should stratify kidney stones by chemical type and determine the extent of calcium deposits in intimal and medial vascular tissue in

stone formers. Our findings may justify earlier clinical intervention to address the higher cardiovascular risk in kidney stone formers.

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Track E - Epidemiology, public health, health inequalities

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Taking action on Health Inequalities: a strategy

Patient outcome and experience, Other

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Introduction: Improving prevention and early detection and ensuring that everyone has access to the right treatment for them, is key to improving kidney health. Yet not everyone is equal. Some groups are particularly disadvantaged. Reducing inequalities will bring benefits to individuals, their families, the NHS, and wider society.

As an organisation, we started addressing renal health inequalities over 20 years ago. We have had the subject as a strategic aim for several years and embedded it as a cross cutting strategic theme.

Methods: Over 2 decades, we proactively, in partnership with “at risk” groups, consolidated a trusted outreach programme. Central to this, we have developed an initiative called Peer Educators (PEs) to engender trust, educate and empower these communities.

We have undertaken a range of research, QI, and awareness projects across the kidney disease spectrum. We realise the importance and huge effectiveness of collaboration. So, local project advisory groups are convened which include local stakeholders from faith, community, and health organisations. The contribution of patients with “rarely heard” voices cannot be overestimated.

Currently, three bespoke studies address aspects of health inequality utilising our engagement initiative.

Results: Mindful of the ever- increasing burden that inequalities places upon kidney patients and “at risk” communities, particularly during a pandemic, we are proactive. We commissioned a CRT study to support home albuminuria testing in patients with hypertension, using smart phone technology. One arm involves trained PEs supporting patients to manage testing and education/ self- care. Another study addresses under representation of minority groups in research (recommended by the Renal Research Strategy). PEs will test whether trusted peers can support and increase interest in research participation, given unethical historical (Tuskegee), and present, mistrust in medical research. The PhD initiated a UK wide survey of renal health care professionals and researchers to elicit barriers to and facilitators of research among patients. A similar patient survey is planned as is co-production with patients of a novel research aid/guide to facilitate research.

Our community engagement and trust initiative has trained >160 Peer Educators from a cross section of ages, ethnicities, religions & socio-economic status; we have engagement with tens of thousands of people ‘at risk’ in cities including, Leicester, Bradford, Glasgow, & London. Events occur at places of worship, & community events with numerous media profiling achieved. Thousands of

people have signed onto the NHS ODR. The initiative is multi award winning & evidence based, gaining repeat funding including from NHS England and Scottish Government.

Strategically, our research grants process prompts applicants to consider and address inequalities. Our PPIE groups that help us determine & deliver research and raise awareness are now more diverse and we remain vigilant to ensure due representation.

Discussion: Despite our proactive approach, we recognise the continued need to addressing health inequalities in their widest form. Our experience, track record and partnership approach has proved fruitful, and we will build on this learning. We have evolved our Peer Educator initiative which is now being used to drive innovations in renal care.

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Track F - Genetics and Rare Diseases

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DNAJB11-related PKD: a local case series

Genetic and rare diseases

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Background: Autosomal Dominant Polycystic Kidney Disease (ADPKD) due to variants in PKD1 or PKD2 genes is characterised by the formation of multiple renal cysts and is a well-recognised cause of end stage renal failure. Heterozygous pathogenic variants in DNAJB11 have been demonstrated to cause an intermediate phenotype between ADPKD and autosomal dominant tubulointerstitial kidney disease (ADTKD), with multiple cysts, non-enlarged kidneys, and interstitial fibrosis with limited renal functional impairment(1). Biallelic variants cause multiorgan malformations and may be prenatally lethal (2)(3).

Case description: We describe three cases of DNAJB11-related PKD. Details of the patients' laboratory tests, imaging and variants are shown in the Table.

Patient 1 presented aged 79 years. Her medical background was hypothyroidism (on levothyroxine treatment). Her family history was negative for renal pathologies, but she reported a sister with liver cysts. Renal ultrasound identified multiple renal cysts during investigation of poor appetite, itching and recurrent urinary tract infections in primary care. ADPKD was suspected however, since family history and imaging were not diagnostic, genetic testing was arranged. A gene panel test identified a likely pathogenic frameshift variant in DNAJB11.

Patient 2 (Patient 1's daughter) presented aged 58. Her medical background included fibromatosis aged 33, mild hypertension and progressive non-proteinuric CKD with estimated GFR 48ml/min. Her father had renal amyloidosis, a brother had diabetic nephropathy and another brother was reported to have "inflamed kidneys" not otherwise specified. Renal imaging did not identify any cysts. Targeted testing for the familial DNAJB11 variant was requested after confirmation of her mother's results and the same likely pathogenic variant was confirmed.

Patient 3 presented aged 68. His medical background included gout, benign prostate hypertrophy and hypertension. His mother was reported to have "weak kidneys" but never required dialysis. No other family members were known to have kidney disease. During assessment of abdominal pain, CT scanning revealed an incidental finding of multiple renal cysts. Progressive non-proteinuric CKD was identified with estimated GFR 39ml/min. Cystic renal disease panel analysis identified a pathogenic truncating variant in DNAJB11.

Discussion: There are limited published case series of DNAJB11-related PKD (also called polycystic kidney disease type 6) with only 77 cases reported by 2020(1). Our cohort concurs with previous

reports that renal cysts may develop later in life, as compared to PKD1/PKD2-related ADPKD, and progression to ESRF is slower. Genome database GnomAD data indicates the minimum prevalence of DNAJB11-related ADPKD to be 0.85/10,000, hence the condition is almost certainly underdiagnosed and underreported. Our cohort adds further details to the patients described in the literature. Confirming a diagnosis of DNAJB11-related PKD in patients with cystic kidney disease and their relatives assists in prognostic counselling and in live donor kidney transplant assessment. There are no published data on the utility of treatment options including tolvaptan. Analysis of DNAJB11 is available through the NHS National Genomic Test Directory R193 Cystic Renal Diseases panel.

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Track F - Genetics and Rare Diseases

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Evaluating Ravulizumab in Thrombotic Microangiopathy Associated With a Trigger: Rationale and Design of a Global Phase 3 Randomized, Double-blind, Placebo-Controlled Study

Genetic and rare diseases

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Ravulizumab, a monoclonal antibody specific for C5, is approved in the US for treatment of atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).

Pivotal phase 3 trials in aHUS included patients with primary disease and TMAs following renal transplant and pregnancy, yet excluded TMA caused by other triggers. Complement involvement in pathophysiology of TMA associated with one or more triggers (secondary TMA) is not fully understood and benefit of terminal complement blockade in these cases requires further evidence.

This Phase 3 randomized, placebo-controlled, global trial (NCT04743804) investigates efficacy and safety of ravulizumab in patients with TMA associated with a trigger (Figure). Randomization will be stratified by dialysis status and primary trigger type. Adults with severe acute kidney injury and a diagnosis of TMA (based on protocol-defined criteria: thrombocytopenia, microangiopathic hemolytic anemia, elevated lactate dehydrogenase) associated with at least one trigger (autoimmune disease [lupus nephritis, systemic sclerosis-associated TMA], infection, solid organ transplant, drugs, or malignant hypertension) will be included. Exclusion criteria include postpartum aHUS, aHUS-associated mutations, TMA due to hematopoietic stem cell transplantation, chronic kidney disease with eGFR ≤45 mL/min/1.73 m2, primary or secondary glomerular diseases (other than lupus), familial or acquired ADAMTS13 deficiency (activity <5%), or a positive direct Coombs' test.

The primary outcome is complete TMA response during the 26-week treatment period. Additional outcomes include time to complete TMA response, TMA response duration, hematologic response, and renal response assessed by change in eGFR and by dialysis requirement. Safety will be assessed through Week 26 and Week 52.

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Track G - Haemodialysis Quality Improvement and Implementation

30

A review of amputation data for diabetic in-centre haemodialysis patients undergoing diabetic foot screening.

Cardiovascular disease and diabetes

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Introduction: The prevalence of diabetes is increasing worldwide. Microvascular complications including diabetic foot ulceration are common and can lead to significant morbidity including the need for amputation. End-stage renal disease requiring dialysis is an independent risk factor for foot ulceration and major amputation, with the incidence of amputation 10 times higher than in the general diabetic population [1,2]. Mortality is also significantly higher in patients with renal impairment [1].

Early recognition and treatment of patients with diabetes and feet at risk of ulcers and amputations is therefore vital to delay or prevent adverse outcomes. KDIGO, ADA and IWDGF guidelines recommend routine preventive foot care to reduce risk of foot complications, with foot inspection recommended every 1-3 months [3,4,5].

Our centre previously developed an initiative (DDIP – Diabetes and Dialysis Improvement Project) to promote foot screening. This involved distribution of education to both patients and staff, a training package, bi-monthly basic foot inspections on the haemodialysis unit and recording of the above data on our local renal database. Early referral to the local podiatry service was promoted, with the assistance of Trust and community Podiatry teams. We now review amputation data over the last 5 years to assess any benefit from the DDIP intervention.

Methods: Data on all diabetes related amputations (toe, foot, leg) in haemodialysis patients from January 2017 – September 2021 was analysed. We reviewed the local renal database for information on patient demographics, haemodialysis centre and mortality. Two satellite haemodialysis units associated with our centre incorporated DDIP foot screening into their routine practise. Roughly 176 patients dialyse between these centres each year, and the rate of diabetes in this cohort is approximately 37%.

Results: There were 48 amputation procedures in total in the time period involving 35 haemodialysis patients across 7 satellite units (6 women, 29 men). There were 13 toe amputations, 13 foot amputations and 22 leg amputations. Ten patients underwent more than one amputation procedure. Patients undergoing more than one amputation surgery in one admission (such as below knee amputation followed by above knee amputation) were counted as one incident. Of the 35

patients undergoing amputation, 8 (23%) were still alive at the time of data collection. 10 patients (29%) had died within 120 days of amputation surgery.

Figure 1 demonstrates the incidence of amputation in this patient cohort over the five year period. There was a reduction from 5.1% patients undergoing amputation surgery at the start of the DDIP programme, to 0.6% patients undergoing surgery in the last two years. This equates to a change from 138.21 amputations per 1000 dialysis patients with diabetes, to 15.36 amputations per 1000 dialysis patients with diabetes per year.

Discussion: The incidence of diabetes-related amputations has reduced in haemodialysis patients partaking in the DDIP programme. This suggests that basic foot screening on the haemodialysis unit may have a role to play in identifying diabetic foot complications early, allowing timely referral and management with an aim to reduce morbidity and mortality. We aim to introduce DDIP to other haemodialysis units associated with our centre.

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Track G - Haemodialysis Quality Improvement and Implementation

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Heparin versus TaurolockTM-HEP500 lock solution: Infection, occlusion and survival of tunnelled haemodialysis catheters in clinical practice

Haemodialysis - quality improvement, Vascular access

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Background: The UK Kidney Association (UKKA) recommend an antimicrobial or antibiotic lock solution to reduce haemodialysis (HD) catheter related bacteraemia and other infections. In 2019 our renal region converted from using heparin (1,000 I.U. /ml) to TaurolockTM-HEP500 to 'lock' tunnelled HD central venous catheters (T-CVC).

We present efficacy outcomes including T-CVC survival, the need for catheter thrombolysis and infection rates in people receiving in-centre HD (ICHD) before and after this change in policy.

Methods: The date of T-CVC insertion and removal, the reason for T-CVC removal, positive blood culture and causative organisms, and lock solution and thrombolytic (alteplase - Actilyse Cathflo® 2mg) administration data were extracted from our integrated renal database and Electronic Prescribing and Medicines Administration (EPMA) system using SQL coding for all T-CVC inserted for ICHD between 08/2018 and 08/2021.

Results: 362 T-CVCs were inserted between 08/2018 and 08/2021. Data pertaining to 237 T-CVC are included for analysis. 45 T-CVC were excluded from analysis due to incomplete data. A subgroup of 80 T-CVC initially locked with heparin were changed to TaurolockTM-HEP500. These data are not presented.

Heparin (1,000 I.U. /ml) was the initial lock solution for 98 T-CVC (total 23,644 catheter days). TaurolockTM-HEP500 was the initial lock solution for 139 T-CVC (total 38,054 catheter days).

The median time in situ ('survival') for T-CVC locked with TaurolockTM-HEP500 was 229 days, versus 168 days for heparin-locked T-CVC (Table 1).

There were significantly fewer positive blood cultures ($p<0.0007$) and significantly fewer S. aureus infections ($p<0.0001$) per 1000 catheter days in patients with T-CVC locked with TaurolockTM-HEP500 (Table 1). No MRSA bacteraemia was noted in patients with T-CVC locked with TaurolockTM-HEP500, compared to 4 MRSA infections in patients with T-CVC locked with heparin (Table 1).

Catheters were significantly less likely to be removed due to infection with TaurolockTM-HEP500-locked T-CVC (p=0.03), and less likely to be removed due to poor blood flow with heparin-locked T-CVC (Table 1).

The median time to first alteplase (T-CVC 'dwell') therapy for T-CVC locked with TaurolockTM-HEP500 was 137 days and 88 days for heparin-locked T-CVC (Table 1).

Overall, more alteplase was instilled into T-CVC locked with TaurolockTM-HEP500 (Table 1).

Discussion: Positive blood culture rates were lower in patients with T-CVC locked with TaurolockTM-HEP500 compared to heparin (1,000 I.U. /ml), including S. aureus and MRSA. Catheter survival, removal due to infection and 'time to first alteplase' rates also improved with TaurolockTM-HEP500.

Overall, more alteplase was instilled into T-CVC locked with TaurolockTM-HEP500 and more T-CVC locked with TaurolockTM-HEP500 were removed due to poor blood flow.

We will review 'line insertion' and 'definitive access' availability along with catheter 'problem solving' practices in our department in an attempt to explain the increased use of expensive thrombolytic treatments in T-CVC locked with TaurolockTM-HEP500.

We will elucidate from subgroup data (n=80 T-CVC, data not presented) whether converting from heparin to TaurolockTM-HEP500 in the same catheter improves T-CVC infection, occlusion and survival.

We will establish the cost-effectiveness of our current practice using the present efficacy data, and locking solution and thrombolytic cost data.

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Track G - Haemodialysis Quality Improvement and Implementation

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Hypersensitivity Reactions During Haemodialysis: A Proposed Management Algorithm

Haemodialysis - quality improvement

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Introduction/Background: Haemodialysis hypersensitivity, anaphylaxis and anaphylactoid reactions are well described in clinical practice and relatively common. During haemodialysis, the patient is exposed to a number of components including the dialyser, haemodialysis lines and vascular access catheters amongst others. Despite advances in the aforementioned components, life-threatening reactions still occur. It is therefore imperative to recognize those potential reactions when assessing adverse dialysis events as re-exposure to dialytic treatments could be life threatening. These episodes often result in decreased treatment efficiency and compliance as well as poor quality of life of haemodialysis patients. It is equally important to identify the possible allergens involved and formulate management guidelines, which currently aren't available.

Methods: This is a retrospective analysis of 28 prevalent HD patients identified as having allergic reaction presumably to dialysis catheter from July 2008 to January 2019. An allergic reaction was defined as a combination of clinical symptoms (rash, hypotension, desaturation, shortness of breath, dizziness) and rise in eosinophils. Clinical data was retrospectively collected from the medical/nursing notes with haematological and biochemical variables from the patients' electronic notes (PROTON Information System V2.82a) and DatixWeb(v14.0.30,Datix Ltd.,London UK).

Results: 28 patients with symptoms suggesting allergic reaction were identified in total (female =12, male =16). 2 patients experienced loss of consciousness/cardiac arrest at the start of the dialysis. Eosinophilia was confirmed in 24 patients.10 patients had their access or modality of RRT changed with subsequent resolution of symptoms, 6 patients received premedication with chlorpheniramine and/or hydrocortisone. In the remaining 12 patients no documentation was found on the treatment/intervention received. On a further data analysis it became apparent that a number of patients who had their dialysis access changed continued to have allergic reactions during the treatment and several suspected allergens have been postulated including sterilisation methods particularly ethylenoxide, dialyser membranes (synthetic and cellulose), dialysis tubing, and medications administered.

Discussion: Although allergic reactions during haemodialysis remain quite common, however robust algorithm and systematic management guidelines are lacking. We therefore designed an algorithm to manage allergic reactions on haemodialysis (flow chart attached). We suggest dividing the reactions into 3 groups: Type A allergic reaction (Anaphylaxis), type B (Anaphylactoid) and haemodynamic reactions (unexplained hypotension in the first 30 min of dialysis). In suspected type

A reaction: stop dialysis immediately, do not wash back and treat as per anaphylaxis protocol, send serum hypersensitivity markers and admit patient for further investigations. In suspected type B reactions, treat patient with antihistamines/hydrocortisone, stop the dialysis if symptoms ongoing/worsening and start systematic work up over the next dialysis sessions to identify likely allergen. In patients with unexplained hypotension and in the first 30 min of HD cardiac causes need to be ruled out and relevant cardiac work up arranged.

Conclusion: Timely recognition and treatment of allergic reactions during haemodialysis are crucial to maintain this life saving treatment. Our proposed management algorithm will increase awareness and provide a pragmatic approach of these potential life-threatening complications of dialysis treatment.

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Track G - Haemodialysis Quality Improvement and Implementation

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Management of adults with diabetes mellitus on the haemodialysis unit: an audit.

Haemodialysis - quality improvement

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Introduction: Diabetes Mellitus (DM) is the leading cause of endstage kidney disease in the UK. Altered glucose homeostasis or pharmacokinetics of hypoglycaemic medications and regular hospital attendances all result in specific challenges in the management of DM patients on haemodialysis (HD).

These challenges were highlighted in the Joint Diabetes Society guideline "Management of adults with diabetes on the haemodialysis unit" (2016). We carried out an audit against these guidelines in a teritiary renal unit, focusing on organisation of care and glycaemic control, with the aim of improving quality of DM care among our patients.

Methods: The audit data covered 12 months for all patients with diabetes across our four haemodialysis units. Data of interest were collected from the electronic patient record on specialist reviews, monitoring of glycaemic control and diabetes medications prescribed. A patient questionnaire was used as a complementary tool.

Results: 153 patients were identified with DM among a population of 335 haemodialysis patients. 12 (8%) had type 1 diabetes. Review of diabetes care was documented at least once in 12 months by a renal consultant in 100%, renal dietician in 100%, diabetes consultant or diabetes specialist nurse (DSN) in 40%, and diabetic foot specialist in 14% of patients. Documented retinal screen report was only available for one patient. 10% of patients had at least one recorded value of HbA1C above 80 mmol/mol, while 61% of the 93 patients on hypoglycaemic agents (insulin or sulfonylurea) had at least one value below 58 mmol/mol.

Patients who exceeded the HBA1C "ceiling" of 80 mmol/mol were more likely to be reviewed by a diabetes specialist than those who did not ($p < 0.001$ by Fisher's Exact) but in those at risk of hypoglycaemia with HBA1C below the "floor" value of 58, specialist review was no more likely than in the population as a whole ($p = 0.21$ by Fisher's Exact).

64 participants completed the questionnaire. 80% reported diabetes care was reviewed at least once (34% by diabetes team, 38% by renal team, 48% by primary care). 92% of respondents on treatment associated with a risk of hypoglycaemia reported they monitored their glucose and 30 of the 35 (86%) patients on insulin were confident in adjusting the dose independently.

Discussion: Less than half of diabetes patients in our centre had specialist diabetes input during a 12-month period. Low HBA1C was seen in a majority of patients at risk of hypoglycaemia and our data

suggests it was not routinely recognized as an indication to refer for specialist input. HBA1C above target was much less common but did appear to trigger specialist review.

The findings of this audit are being used to support the case for a dedicated renal DSN, to provide in-reach and identify dialysis patients at risk. Our questionnaire responses suggest many patients are having key diabetes interventions in primary care and therefore an additional role for a renal DSN could be to provide support to help community services provide safe diabetes care in the haemodialysis population.

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Retrospective Audit of Pre- and Post-Dialysis Serum Potassium and Bicarbonate Levels in Haemodialysis Patients: Working Towards an Individualised and Protocolised Dialysate Prescription

Haemodialysis - quality improvement

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The UK haemodialysis population continues to expand, now encompassing over 25,000 individuals(1). A vital function of dialysis is serum potassium regulation, since extreme levels of which may precipitate potentially lethal cardiovascular events such as ventricular arrhythmias. During dialysis, significant shifts in potassium occur. Additional to absolute potassium level, rapid fluctuations caused by greater differences between dialysate and serum concentrations increase cardiac instability. Those with a serum potassium of above 5mmol/L dialysed with a low (1mmol/L) dialysate experienced increased mortality(2). The use of a high bicarbonate dialysate solution is associated with a higher frequency of hypotensive symptoms(3) and may precipitate a rapid shift of potassium from the extra- to the intra-cellular compartment, potentially leading to sudden hypokalaemic dysrhythmias or cardiac arrest(4). Furthermore, mild metabolic alkalosis is associated with more frequent hypotensive episodes(5), and similarly to potassium, increased serum concentrations are correlated with greater mortality(6). To minimise cardiovascular sequelae, the Renal Association advises optimal pre-dialysis serum concentrations of both potassium (4-6mmol/L) and bicarbonate (18-26mmol/L). Despite these standards, adherence is historically sub-optimal at our centre, with only 86% and 59% of patients achieving these targets respectively(7). To understand why, an audit of current pre- and post-dialysis levels was required alongside an analysis of current dialysis prescribing practice.

This retrospective audit was performed during August 2021. It included all 317 in-centre haemodialysis patients across four sites where monthly quality assurance blood tests were available; the trust's main renal hub (RH) and three satellite units (S1, S2 and S3) were included in analysis. Pre- and post-dialysis serum concentrations were obtained via a database query of IT software linked to all units.

We observed 263 (83%) of the 317 patients had a pre-dialysis potassium within target: specifically, 55 (75%, median 4.5mmol/L) at RH (n=73), 64 (86%, median 4.9mmol/L) at S1 (n=74), 70 (77%, median 4.7mmol/L) at S2 (n=91), and 74 (94%, median 4.6mmol/L) at S3 (n=79). Those with a pre-dialysis potassium <4mmo/L were prescribed either 2mmol/L (n=35) or 3mmol/L (n=7) dialysate, and all (n=13) with >6mmol/L were dialysed against a 2mmol/L solution. Pre-dialysis bicarbonate levels were available for 316 patients, of which 171 (54%) were within range: specifically, 23 (32%, median 28mmol/L) at RH (n=73), 44 (59%, median 26mmol/L) at S1 (n=74), 51 (57%, median 26mmol/L) at

S2 (n=90), and 53 (67%, median 26mmol/L) at S3 (n=79). Patients at S1 and S3, uniformly dialysed using a 35mmol/L solution, demonstrated lower post-dialysis bicarbonate levels (median 30 at both sites) and a reduced shift in serum concentration, than those patients dialysed at RH and S2, uniformly dialysed using a 38mmol/L solution (median 34 and 32mmol/L respectively).

This audit highlighted deficiencies in local dialysis prescribing practice. Pre-dialysis serum potassium and bicarbonate levels can be positively influenced by corresponding dialysate changes(8,9). Consequently, following local clinical governance approval, plans to make 1mmol/L potassium dialysate unavailable for routine use, protocolise the adoption of 3mmol/L potassium dialysate, and routinely dialyse all patients with a 35mmol/L bicarbonate solution across the four sites have been ratified. Re-audit of the effects of these interventions will follow.

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Root Cause Analysis of tunnelled dialysis central venous catheter Sepsis– repetitive chore or worthwhile assessment?

Vascular access

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Introduction: Root-cause analysis (RCA) is a structured process to analyse a serious incident, and should involve the multi-disciplinary team. We have looked at our tunnelled dialysis catheter (TDC) bacteraemias 2020-2021 to assess the value of such activity.

Method: RCA was used to scrutinise TDC bacteraemia data and clinical history prior to positive blood cultures by Dialysis Unit Managers, Vascular Access Nurse, Speciality dialysis doctor, Consultant Nephrologist and Consultant Microbiologist.

Results: Over two years, there were 32 bacteraemia episodes in 28 patients; 4 patients each had two episodes.

In 12/32 cases Staphylococcus aureus was the causative organism. One patient had a chronic MRSA hip infection.

The outcomes of the RCAs were grouped by the reason for the sepsis, where determined:

41% attributed to patient issues, either poor personal hygiene, or interference with CVC dressings. 19% were due to patients being severely immune-compromised.

22% were determined to have no obvious cause on analysis.

9% were attributed to nursing staff error, where the CVC was left in situ, after no longer being used and neither regularly flushed or redressed during that time.

One patient, who was MSSA screen positive, was not decolonised prior to CVC insertion.

Of note we have had only one temporary vascular access catheter related bacteraemia in over 10 years.

Discussion: RCA has proved invaluable in highlighting important information, generating changes in our protocols as follows:-

•Endeavour to remove all plastic at the earliest opportunity, whether it be Tenckhoff or a TDC. We now remove TDCs within 10 days of being notified as no longer in use.

•Three monthly decolonisation for all positive patients and three monthly swabbing for negative patients. However, decolonisation may not always be effective with some patients failing to complete this. Decolonisation failure helps to identify patients who may be chronic Staphylococcus aureus carriers.

•Although we routinely swab nose and throat, some patients were found to be colonised at other sites. Therefore a change to our protocol is to swab all pertinent patients three monthly for nose, throat, TDC exit site, PD catheter exit sites and any other wound sites e.g. diabetic foot ulcers

•Diabetic foot ulcers are a recurring problem and treatment with antibiotics may not be sufficient to eradicate the infection. Debridement of the ulcer may need to be considered. However, creating new or larger wounds may not always be advisable, but early referrals should be made as appropriate to the Podiatric , Orthopaedic and Vascular teams

•High Risk or immune compromised patients should be highlighted to the team to ensure particular care of their vascular access

•Personal hygiene for all is of the utmost importance. Connection/disconnection to the dialysis machine and CVC dressing technique should be scrupulously maintained and surgical ANTT adhered to at all times

Conclusion: We have a below average infection rate (0.38 per 1000 catheter days) when benchmarked against national figures. However, we cannot afford to be relaxed with these numbers and RCA continues to be our most valuable tool in the continuous fight against preventing CVC infection.

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Post Tunneled Haemodialysis Line Insertion Chest Imaging – What To Look For?

Vascular access

Adwaney Anamika[1], Corbett Richard[1], Ashby Damien[1]

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Background: Central venous catheters have traditionally provided haemodialysis access when a fistula is declined or not achieved. These are often done as day case procedures by transplant surgeons and nephrologists in addition to interventional radiologists. Nephrology trainees are often asked to comment on the position of tunneled lines intended to be used as access for haemodialysis. However, unlike Nasogastric Tube placement, there are no guidelines to support trainees in evaluating tunneled line position when reviewing a chest radiograph. We conducted a quality improvement project to evaluate the safe positioning of a tunneled haemodialysis line and if it is safe for use.

Methods: All patients undergoing tunneled line insertion in a single urban renal unit between January 2018 and December 2018 were retrospectively analysed. We excluded all patients who have had a previous right internal jugular tunneled line, a left sided line or were found to have a malpositioned line. A total of 5 observers then reviewed a small subset of chest imaging performed immediately after line insertion. Each observer measured from the highest point of the tunneled line to various key landmarks including the carina, aortic arch and line tips. Once an acceptable inter-observer coefficient was achieved, each post line insertion chest radiograph was reviewed independently by one of the observers.

Results: Out of 167 patients, 162 (aged 25 – 90, mean 63.3 years, 66.7% male) were included in our analysis. Each tunneled line was determined to be within the right superior vena cava, without any kinks and with appropriate tip separation of both tesio lines.

The mean height of our patients was 1.66m (95% CI 1.65–1.69) with a median of 5.69. The highest point (HP) of the tunneled dialysis line to the aortic arch was 5.81cm (95% CI 5.55 – 6.09, median 5.69), to the carina was 9.75cm (95% CI 9.44-10.06, median 9.9), to the highest line tip 12.12cm (95%CI 11.56-12.92, Median 11.7) and the lowest line tip 15.25cm (95%CI 14.81-15.69, Median 15.29). Line tip spacing is 3.07cm (95% CI 2.82-3.32, Median 2.94).

The ratio of patient height to distance between the HP and carina is 6.37 (95% CI 5.46-7.27, Median 7.56).

Conclusions: When asked to review a chest radiograph post tunneled line insertion we recommend confirming the tunneled dialysis line is in the correct vessel, lies straight within the superior vena

cava (SVC) and the line tips (if two separate tunneled lines) are appropriately separated to allow adequate dialysis.

We then suggest the highest line point is identified first alongside key landmarks such as the carina and line tips. We found the measurement between the highest point of the tunneled line and the carina is the most reproducible measurement and should be performed (mean 9.75cm, 95% CI 9.44-10.06, median 9.9)

We believe this quality improvement project is needed to form the basis of a training module directed towards renal trainees to help guide the safe assessment of chest imaging post tunneled line insertion.

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Ultrafiltration volume determines subsequent inter-dialytic weight gain in people on haemodialysis.

Haemodialysis - research

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INTRODUCTION: Excessive ultrafiltration, either by volume or rate of removal, is increasingly recognised as harmful in haemodialysis patients, contributing to intra-dialytic hypotension and loss of residual kidney function [1]. Greater fluid intake clearly leads to greater fluid removal, since dialysis protocols aim to return the patient to a consistent weight by the end of the session. But reverse causality is also possible: greater fluid removal could lead to increased thirst, thus causing greater fluid intake [2].

A between-patient analysis cannot determine the direction of this causality, since temporal relationships are lost when average values are used for each patient [3]. Instead this study uses a within-patient analysis, to examine the relationship between ultrafiltration during dialysis sessions, and weight gained during the subsequent inter-dialytic interval.

METHOD: In a large urban dialysis centre, a random sample of patients was selected from four satellite dialysis units, stratified by unit, gender and access type (arteriovenous or catheter). Patients were eligible for inclusion if they had been receiving thrice-weekly dialysis in the same unit for at least a year, and were clinically stable during this period, with no more than 14 days' cumulative hospitalisation. Electronic records were obtained for 12 months of outpatient dialysis for each patient, along with background clinical information. Target weights were calculated as a rounded median of the last six post-dialysis weights.

Data were analysed within patients over the observation period, as well as between patient averages. Correlations were sought between variables within patients: the number of patients with a significant within-patient linear association ($p<0.05$) is reported, as well as the significance of this number, as an observation from a binomial distribution with N=100, p=0.05. Microsoft Excel v16 was used for data analysis.

RESULTS: From 100 patients, median(IQR) age 67(53-75) years, observed over a year, complete records were available for 15 263 (98%) dialysis sessions with the subsequent inter-dialytic interval. Mean(±within-patient sd) pre-dialysis weight was 2.71(±1.15)% above target weight. Larger ultrafiltration volume was associated with greater subsequent inter-dialytic weight gain in 87/100 patients ($p<0.001$), and 15% of the within-patient variation in inter-dialytic weight gain was explained by variation in ultrafiltration volume at the previous dialysis session. Lower post-dialysis weight (relative to target weight) was also associated with greater subsequent inter-dialytic weight

gain in 77/100 patients ($p<0.001$). In addition, the rate of weight gain was dependent on the duration of the inter-dialytic interval, being 1.21(±0.53)%/day during 2-day gaps, and 1.11(±0.38)%/day during 3-day gaps ($p<0.001$), suggesting a non-linear pattern of fluid intake, greatest immediately after dialysis and diminishing over the course of the inter-dialytic interval.

DISCUSSION: Fluid intake in haemodialysis patients is determined by the ultrafiltration volume and end-weight of the most recent dialysis session, and diminishes during the inter-dialytic interval. Greater fluid intake is therefore a consequence, as well as a cause, of larger ultrafiltration volumes [4]. This bidirectional relationship between dialysis fluid parameters suggests the need to re-examine protocols for fluid removal in haemodialysis patients.

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A Study of Body Composition in Haemodialysis patients, The Correlation between Clinical Frailty Scores and Muscle Mass

Haemodialysis - research

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Introduction: It is well recognised that haemodialysis patients are more susceptible to becoming frail. An increased level of frailty in this patient group is also associated with increased mortality. Furthermore, there has been recent interest in applying frailty scores in clinical practice in order to quantify changes in functional status. We aim to investigate the relationship between body composition and frailty, examining the risk factors for frailty in HD patients.

Methods: A cohort of 30 haemodialysis were included in the study. Rockwood frailty score was used to score patients by two independent investigators. Body Composition by bioimpedance was assessed using the InBody 770 body composition analyser, which gives a detailed assessment of segmental distribution of muscle, fat and fluids. Basic patient demographics, co-morbidities, past medical history, biochemical indices and inflammatory markers were also collected.

Results: The mean age of the patients in the study was 63.3±12.4 years and the mean body mass index was 24.7± 3.7kg/m2. The mean frailty score was 4.1±1.2 (maximum frailty = 9) and mean skeletal muscle mass was 25.2±6.5kg. Whole phase angle was 4.1±3.2. There was no correlation between frailty scores and body fat mass (r=0.246, P= 0.198), BMI (r=-0.031, P= 0.874), CRP (r=-0.079, P=0.677) and Kt/V (r=0.303, P=0.104). In a univariate analysis age (R2=0.2, Beta = 0.045, P = 0.015), serum albumin (R2=0.217, Beta = -0.124, P = 0.009) and skeletal muscle mass (R2=0.282, Beta = -0.1.1, P = 0.003) predicted frailty score in haemodialysis patients. In multivariable linear regression analysis age, serum albumin level and skeletal muscle mass continued to independently predict frailty scores (adjusted R2 for the whole model = 0.503, table 1).

PredictorsBetaB (95%CI)Standard ErrorP

Age0.3170.032 (0.004-0.059)0.0140.029

Albumin-0.387-0.104 (-0.179- -0.028)0.0370.009

Skeletal muscle Mass-0.401-0.076 (-0.140 - -0.023)0.0260.007

Discussion: Lower muscle mass and serum albumin are potentially reversible risk factors for frailty in HD patients. Further work should focus the relationship between measures of frailty and outcomes as well as on interventions to maintain nutrition and muscle mass in this vulnerable population.

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Living haemodialysis: a photovoice exploration of the lived experience of usual care from the NightLife study.

Haemodialysis - research

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Background: For people with end-stage kidney disease thrice weekly, in-centre, daytime, haemodialysis is a standard, life-giving treatment option. The NightLife study (ISRCTN87042063) seeks to explore the outcomes of in-centre, nocturnal haemodialysis compared with daytime/usual care. Workstream two of this study involves a qualitative process evaluation, using photovoice and interviews with patients, to build an in-depth understanding of the experience of daytime dialysis to be compared against a similar and forthcoming exploration of night-time experience. The findings of the first stages of the process evaluation are presented and discussed here to raise awareness of the complexity and diversity of the lived experience of in-centre, daytime, haemodialysis and the variety of impacts this experience can have.

Methods: Photovoice (a visual method using participant-driven photography and discussion) and interviews were carried out with 30 patients experiencing in-centre, daytime, haemodialysis, across three renal units in England. The findings have been analysed using interpretive engagement and four linked themes are identified: relationality, disruption, continuity/endurance, and temporality.

Findings: In-centre, day time haemodialysis was found to be outwardly homogenous, patients all have relatively similar clinical care/treatment routines, yet the experience of this varies between patients owing to the variety and diversity of factors that interact to produce individual experience. Each of the four themes found across the participant photographs and talk show the complexity of lived experience and builds an in-depth appreciation of in-centre, daytime haemodialysis.

Relationality shows how human, material, sensory and environmental factors exist in a fluid and mutliplicitous relationship with each other to create experience. ‘Being on dialysis, I’ve got no hair left in the front. I’ve been trying to, no shampoo or nothing. I feel a bit down so I don’t buy any nice clothes or jewellery anymore’.

Disruption focuses on the struggle unanimously shown and discussed by patients. ‘So I’ve missed school, I dropped out from college, I didn’t go to uni, my work is like on and off. It’s not good… I’ve managed to overcome the anxiety, but you know, at back of my head I’ve still got that thing where if I don’t find a transplant, what am I going to do? I can’t be here the rest of my life’.

Continuity/endurance highlights the continuous and essential nature of the experience. 'You think to yourself, here I am again'

Temporality shows the ebs and flows of in-centre, daytime dialysis with regard to everyday practicality, emotions and care.

'Come here, go home, eat, sleep, that's it. And then the next day is like I can do whatever I want, because I don't have to come here'

Conclusion: In the main, the experience of daytime care was not positive, although it was generally accepted and endured. It is likely that the themes common to the in-centre, daytime, haemodialysis experience will be different for those experiencing night-time care.

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Middle molecules as predictors of residual renal function: data from the Incremental HD feasibility trial

Haemodialysis - research

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Introduction: Middle molecules blood concentrations in haemodialysis (HD) relate to residual kidney function (RKF) as their clearance is dependent on renal clearance. Several of these have been proposed as potentially useful indicators of RKF in patients on HD which can be measured using a blood level and might avoid the need for inter-dialytic urine collection. Such molecules may also be useful as outcome measures in future dialysis trials where estimates of RKF are required.

Methods: The multi-centre Incremental HD feasibility trial randomised 55 incident HDs patients with urea clearance ≥3ml/min/1.73m2 across 4 UK centres to standard or incremental schedules for 12 months. Incremental HD involved 2x weekly sessions, upwardly adjusting HD dose as RKF was lost. Standard HD was 3x weekly for 3.5-4 hours. Primary outcome data already published has shown progressive loss of RKF in both arms during the study with a trend towards lower rate of loss of RKF in the incremental HD arm but not reaching statistical significance.

We analysed pre-dialysis middle molecule blood levels for beta-2 microglobulin and beta trace protein measured monthly during the trial to determine if there were between-group differences in rate of loss of RKF differed between study arms. Change in middle molecule blood levels was analysed using mixed effects models. RKF was measured as urea clearance by monthly inter-dialytic urine collection.

Results: Beta-2 microglobulin showed overall slightly better correlation with RKF than beta-trace protein (r=0.56 v 0.52). Beta-2 microglobulin levels were similar at baseline between study arms. In both arms, there was a progressive rise in beta-2 microglobulin level during the 12 months after randomisation as residual renal function was progressively lost. Although after 3 months beta-2 microglobulin levels were lower in the incremental HD arm compared to the standard care arm, groups were not significantly different at any time point. In a mixed effects model in which study arm and time (and their interaction) were included as fixed effects with a random intercept, although there was a significant relationship of beta-2 microglobulin level with time ($p<0.001$), study

arm and the interaction of study arm with time did not predict trajectory of beta-2 microglobulin level (p 0.28 and 0.69 respectively).

Discussion: There was a moderate relationship of beta-2 microglobulin concentration with RKF as measured by urea clearance. Similar to published primary outcome data not demonstrating a significant relationship of RKF with study arm, we found that randomisation to incremental HD compared to standard HD did not predict a slower rise in beta-2 microglobulin blood level trajectory. The relationship of middle molecule levels to RKF and their simplicity of measurement pre-dialysis makes them useful outcome measures in HD clinical trials where RKF is an outcome of interest.

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Predicting Residual Kidney Function in patients on haemodialysis: Role of Protein-Bound Uremic Toxins

Haemodialysis - research

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Introduction: Residual kidney function (RKF) is a strong predictor of outcomes in patients receiving haemodialysis. Its estimation requires interdialytic urine collections which are cumbersome. The capacity to estimate RKF from plasma levels of solutes would increase convenience and facilitate the clinical use of estimated RKF in procedures such as incremental haemodialysis. Middle molecules such as Beta-2-microglobulin (B2M) and Beta trace protein (BTP) have been used in prediction models. We sought to explore whether plasma levels of Protein-Bound Uremic Toxins (PBUTs), many of which are known to correlate with RKF could improve current models.

Methods: This was a multi-centre study involving three UK renal centres. Interdialytic urine collection was carried out in 157 patients receiving haemodialysis (HD) or haemodiafiltration (HDF). Predialysis samples for urea, creatinine, B2M, BTP, and PBUTs were also obtained, along with demographic details. Measured glomerular filtration rate (mGFR) was calculated as the mean of urea and creatinine clearances. The relationships between mGFR and plasma solute levels were explored by calculating correlation coefficients. Models were constructed using multi-variable linear regression, initially based on plasma levels of B2M and BTP. Plasma levels of PBUTs were then included sequentially in the best model.

Results: Correlations between pre-dialysis solute levels and mGFR are shown in Figure 1. The best correlations were obtained with BTP, B2M, creatinine, HA-tot, IS-tot, HA-free, and IAA-free in that order.

The best multivariable model based on B2M, BTP, and creatinine is shown in box 1. The model explained 61% of the variation of mGFR.

Adding plasma levels of PBUTs sequentially to this model produced little improvement. The best model included the addition of log (IAA-free) and explained 0.64 of the variance of mGFR.

Conclusion: Plasma levels of PBUTs especially Hippuric Acid (Total and Free), Indoxyl Sulphate (total), and Indoleacetic Acid (Free), correlate strongly with mGFR. However, they add little predictive power to GFR models based on Beta-2-microglobulin and Beta trace protein and add complexity and expense. Hence, they are unlikely to find a clinical application for this purpose.

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Variation in unit-level clinical practices for volume management in the BISTRO trial: different practices were observed but these were largely stable from 2017-2021

Haemodialysis - research

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Introduction: Variation in clinical practice related to volume management has been reported previously and this may influence patient outcomes. BISTRO, (Bioelectrical Impedance Spectroscopy to preserve renal output), a trial in which such practice variation might confound the intervention, provided an opportunity to interrogate this in the participating centres in more detail than previously reported.

Methods: A unit-level questionnaire was constructed to interrogate the following domains: sodium dialysate concentration, nutrition and salt intake, residual kidney function (RKF), diuretics, incremental dialysis, fluid assessment, fluid management, dialysate temperature (see table for detail). The clinician in charge of the unit was asked to complete in the early stages of the trial (2017-18) and at the end (2020-21).

Results: Of 34 centres enrolled across the 4 UK nations, 32 contributed clinical data to the trial. 26 completed the first survey (with 5 entering the trial after the window for completion of the first survey), and 31 competed the second survey. In 10 cases it was completed by the same person. In the majority of units practices did not change between the two surveys, and where they appeared to from the summary data (see table), this was either due to the additional 5 centres in the second survey (e.g. centres routinely measuring RFK) or tended to favour a reduction in blanket policies (e.g. fluid restriction). Generally, protocols and policies for fluid management were lacking. Consistency of reporting between the surveys was excellent where this could be tested (e.g. numeric values for dialysate [Na+] or sub-questions).

Discussion: Significant variation between units in their approach to fluid management was seen in the BISTRO centres which was stable for the course of the study. This justifies stratification for centre in the trial randomisation design and provides further evidence for the need to test important differences in practice in randomised trials.

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A CLOSED LOOP AUDIT OF CKD-MBD PARAMETERS IN PATIENTS RECEIVING HOME HAEMODIALYSIS IN NORTH WEST LONDON CENTRE

Home therapies - quality improvement

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Method: We conducted a retrospective review of the 6 most recent monthly biochemistry results for serum phosphate, corrected calcium and PTH levels of all patients actively receiving HHD under the care of Hammersmith Hospital (n=33) between January and September 2020. Subsequently, a monthly multidisciplinary review of blood tests (with nephrologists, specialist nurses and dietitians) focusing on CKD-MBD parameters was implemented to facilitate timely prescription changes. Additionally, two questionnaires were conducted; 1) an adapted Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS) questionnaire assessed adherence with phosphate binders and 2) a diet questionnaire assessed dietary phosphate knowledge. At the end of twelve months, a re-audit was conducted in the patients from the original cohort (n= 23; following 4 transplants, 3 incentre transitions and 3 deaths).

Results: The initial audit revealed that of the 33 included patients, 14(42%) recorded all bone parameters within target range. Examining CKD-MBD parameters individually, 27(82%) had adjusted calcium within target range [4(12%) < 2.2 mmol/L and 1(3%) > 2.6mmol/L], 22(66%) had a serum PTH in target range [9(27%) > 9 times ULN and 2 (8%) < 2 times ULN, excluding those with parathyroidectomies] and 17(51%) recorded a median serum phosphate within target [11(33%) > 1.7 mmol/L and 5(15%) <1.1mmol/L].

Table 1 summarises baseline demographics of the final audit group (n=23). Re-audit after twelve months revealed 10(43%) recorded all bone parameters within target range. Examining CKD-MBD parameters individually, PTH targets had improved (from 66% to 83%). This was associated with increased use of calcimimetics, with 3(17%) recording PTH > 9 times ULN (from 9(27%) at baseline). However, there was no significant change in phosphate (12(54%) within target range, 7(29%) above range) and calcium (18(78%) within target range).

Of the 23 patients included for final analysis, 15(65%) were actively prescribed phosphate binders. BAASIS questionnaire revealed notable non-adherence with 8(53%) admitting to having missed doses in the last month, 5(33%) consistently missing more than 4 doses, and 6(40%) not consuming alongside meals. Additionally, the dietary questionnaire revealed a lack of knowledge of hidden sources of dietary phosphate in all surveyed patients (n=11 responses).

Conclusions: Based upon UK Renal Association 2015 standards for CKD-MBD, in patients undergoing HHD:

1.Over half are failing to maintain all serum bone parameters within target range.

2.Approximately one third have hyperphosphataemia.

3.Despite high prescription of phosphate binders (65%), compliance and understanding of dietary phosphate sources is suboptimal and likely contributory to sub-standard CKD-MBD targets.

4.Therapeutic measures should support patient self-management strategies through facilitating medication compliance and dietary awareness.

5.Increased dialysis time to enhance phosphate clearance remains an option based on individual patient preference.

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A new suite of patient education and training resources to promote and improve access to home haemodialysis (HHD), and bolster our HHD training programme

Home therapies - quality improvement, Patient education

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Background: In-centre haemodialysis (ICHD) remains the norm in Wales despite home dialysis therapies offering advantages in terms of quality of life, survival, convenience and cost-effectiveness. The Welsh Renal Clinical Network (WRCN) has set a target for at least 15% of dialysis patients to undertake HD at home. The Getting it Right First Time (GIRFT) report recommends that renal centres in England expand access to home dialysis.

With Welsh Government (WG) funds, a core team of renal clinicians and multimedia developers have created a suite of education resources to promote the benefits of home haemodialysis (HHD) to people with kidney disease. HHD patient training material will be available on our new e-learning platform.

Our long-term goal is to increase and sustain the number of people that receive HD at home.

Methods: A suite of information resources has been developed with patients, clinical collaborators, our charity partner and WRCN colleagues. We have created a series of animations, 'Meet the Expert' videos and patient stories. We have developed an augmented reality (AR) app and 360° virtual tour videos to help people visualise HD at home.

Our material will soon be available on a new public NHS Wales website. Much of our content will also be available on paper and 'off-line' to minimise digital exclusion.

Our new e-learning platform will include 'how to' videos, technical tutorials and interactive problem solving videos for people in training for- and established on HHD. This platform will allow patients to track progress towards curriculum completion and provide an additional method of communication with the HHD team.

Results: Table 1 contains a small selection of material and associated web links. At the time of writing the content is unfinished. It will be available on our public NHS Wales website in due course. Most content has been developed for HHD, but we have also created material with more general renal topics (Table 1).

Conclusion: We continue to create and refine our work. A robust strategy for content implementation and service evaluation is being developed.

We intend to use our new skills and experience to create similar educational content across other areas of kidney disease.

We hope our work will improve understanding and access to home HD, and ultimately increase and sustain the number of people that receive HD at home.

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Track I - Peritoneal dialysis and home haemodialysis

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Are trainees receiving sufficient peritoneal dialysis training?

Home therapies - research

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Background: The 2022 Joint Royal Colleges Training Board renal medicine curriculum lists management of a peritoneal dialysis (PD) program as one of the essential learning outcomes for renal trainees. Moreover, greater numbers of patients are choosing peritoneal dialysis, a growth that may be expected to continue given GIRFT recommendations that a minimum of 20% of prevalent dialysis patients should be receiving a home therapy. This will require a medical workforce confident in the delivery of care for the person doing PD. This study sought to explore the exposure and perception of training in PD amongst nephrology trainees in London.

Methods: A cross-sectional, online, anonymised survey, was circulated to all renal trainees in London in January 2022. The survey included Likert scales in relation to questions relating to experience, as well as open free text responses.

Results: There were 38 responses covering trainees between ST3 and ST7. Approximately half of trainees were in the final two years of the training program. Most trainees reported limited experience of managing PD patients in the outpatient setting. Of the respondents, 24% had an opportunity to review PD patients in the outpatient clinic once every 3 months whilst 16% reviewed patients every 4-6 months and 18% reviewed patients less than once every 6 months. With respect to PD multidisciplinary team meetings, 24% of respondents attended a meeting every 2-3 months whilst 21% attended every 4-6 months and 47% attended less than six-monthly.

Most respondents reported prescribing PD as their major knowledge gap. Only 5% of trainees were confident with regards to adjusting APD prescriptions in the outpatient setting; 26% were somewhat confident and 34% were not at all confident. Similarly, only 8% of trainees were confident about altering outpatient CAPD prescriptions; 37% were somewhat confident and 18% were not at all confident.

In contrast, most trainees were confident (58%) or very confident (11%) about management of peritonitis. In terms of managing fluid overload in the emergent setting, 34 % were confident and 45% were somewhat confident. Overall, 16% were confident or very confident that they would be able to manage a peritoneal dialysis program by the end of training; 45% were not so confident and 13% were not at all confident. No respondents were able to insert PD catheters independently; 21% were able to insert PD catheters under supervision, while the remainder were not able to insert PD catheters at all.

Finally, only 29% trainees had attended a PD course. Two common themes in free text responses were that clinical experience was principally limited to troubleshooting acute events and the need for formalised teaching on prescribing PD.

Conclusions: Within a single large deanery, renal trainees have considerable experience and confidence in the management of managing emergent complications of PD. However, they report limited experience of managing PD patients in the outpatient setting and lack of confidence in prescribing PD. Alongside strategies to promote PD as part of the growth in people dialysing at home, training institutions need to ensure trainees have the opportunity to gain outpatient experience and to develop competency in prescribing PD.

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Comparison of outcomes between peritoneal dialysis catheter insertion techniques: a single centre study

Home therapies - quality improvement, Other

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Introduction: Peritoneal dialysis (PD) is a home-based dialysis therapy which confers a multitude of potential benefits for patients with kidney failure compared to hospital-based haemodialysis. Inserting PD catheter percutaneously under local anaesthesia provides an easier and quicker pathway for dialysis initiation compared to performing it under general anaesthesia (open or laparoscopic). In this study, we compared outcomes in our centre between percutaneous (PCI) and surgical PD catheter insertions (SCI) over a period of 2 years.

Methods: This was a retrospective analysis performed on all PD catheters inserted from January 2019 to December 2020. Demographic information and data on catheter related complications were collected from medical records. Statistical analysis was carried out using R statistical software.

Results: A total of 78 procedures were included in the study, of which 45 were percutaneous insertions. 48 patients (61.5%) were males. Median BMI at insertion was 26.8 kg/m2. Median age was 70 years. We analysed several way comparisons between the percutaneous and surgical (open or laparoscopic) insertion groups. There were no complications from percutaneous insertion which necessitated hospitalisation post-procedure. Of the 28 episodes of exit site infection during the follow-up period, those with PCI had a higher proportion of infections compared to SCI (33% vs. 21%). The overall peritonitis rate was below the recommended threshold of 0.5 episodes/patient-year throughout the study period, usually remaining around 0.3 – 0.4 episodes/patient-year. There were no significant differences in either the peritonitis rates or the rates of catheter removal secondary to peritonitis between the two groups. It was also seen that 42% patients with PCI had technical problems such as poor drainage in the first month compared to 12% with SCI. There was no significant difference in the overall rates of PD technique failure between the two groups. We also analysed microbial spectrum for positive cultures of peritonitis cases which showed a slight gram-negative dominance in SCI compared to gram positive in MCI though with a small sample size.

Conclusion: Our results indicate percutaneous PD catheter insertion under local anaesthesia is a safe procedure and has comparable outcomes to surgical insertions under general anaesthesia. However, the percutaneous insertion has an added advantage of it being a daycase procedure and avoids potential complications from general anaesthesia in high-risk patients, thereby enabling better

access to PD. Further measures to enhance training in PCI as part of higher training curriculum should be considered.

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Extending scope and promoting service continuity to deliver safe care and additional support to the assisted automated peritoneal dialysis community

Home therapies - quality improvement, Home therapies - service delivery

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Historically, the organisation sub-contracted the Assisted APD service (aAPD) via industry partners, this proved to be extremely costly and recurrent problems with workforce shortfalls were becoming more prevalent. The organisation carried overall responsibility for service delivery, patient safety and care so, elected to provide its own aAPD service.

This presentation observes challenges encountered in introducing new practice and changing culture.

Challenges:

· Promotion

· Momentum

· Resources

· Changing attitudes and practice.

· Team support

· Skilled workforce

Methods: The team was briefed. An interim plan was suggested to mitigate further immediate risk. The interim plan was to migrate staffing resources from dialysis units with reduced capacity into the aAPD service. A select group of staff were educated and supported as designated aAPD service providers, a sub team of NHSP workers were recruited and trained, the organisation agreed to fund up to 2 WTE NHSP workers

APD training for permanent staff and NHSP workers was supported by industry partners.

Nursing, medical and directorate teams collaborated to produce a business case to future-proof the aAPD service.

Successful service change led to the development of a new service, the existing team developed new skills, and the aAPD staff were able to support other aspects of home dialysis by learning all modalities of RRT. The organisation was able to use some existing resources to improve service delivery, expand service options and extend the skill set within the team

Results: Finances were redirected through business case approval. Home dialysis service quality improved. Staff developed new skills, patients gained more treatment options and a better quality of life. No further patients missed aAPD treatments. The service was able to demonstrate reduced hospital admissions as some treatments could be prescribed at home. Consistent communication and continuity of care has improved the service

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Healthcare professionals' perceptions and understanding of Assisted Peritoneal Dialysis Service (asPD)

Home therapies - service delivery, Other

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Background / Introduction: Assisted peritoneal dialysis (asPD) offers an opportunity to provide a home-dialysis modality for the increasingly older and frailer population with established kidney failure. At our centre with a high use of asPD the majority of older, frail people still commence in-centre haemodialysis. We therefore sought the perceptions of healthcare workers from across renal services to determine their perceptions of the advantages, disadvantages and challenges associated with asPD.

Methods: A 13-item questionnaire (with combined multiple choice, ranking and summative questions) was distributed across healthcare professionals within the department. These included a series of short patient vignettes with a request to rank the most appropriate dialysis modality. Whilst anonymised, individuals were asked to identify their role.

Results: Within a total response of 37, there was a broad range of doctors (n=11) and nurses (n=19) including both those involved and not involved with the routine care of people undertaking PD.

The 3 main advantages identified were: reduction in hospital and transport time (n=29), treatment done at home (n=25), reassurance to patients and families as a medical intervention (n=20). The 3 main disadvantages identified are: use of external contractor providers of asPD service where family becomes reluctant to engage in assistance (n=21); patients waiting at home for technicians to arrive (n=17); increased costs compared to standard PD care (n=16).

Several challenges were highlighted: PD staff - insufficient technician's number, workload with associated phone calls; non-PD staff - need clarity on asPD patient criteria and service expectations; all staff – risk of increased dependence by patient and family

Conclusions: Variations between staff groups in recommending asPD as a treatment of choice to their patients identifies a need for education and open communication between teams about asPD. Setting expectations of the asPD service with appropriate resources identified could support patients' choice of dialysis treatment at home.

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Incidence of hernias post-Laparoscopic Peritoneal Catheter insertion

Home therapies - service delivery, Vascular access

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Introduction: There are multiple techniques for peritoneal dialysis catheter insertion. Our centre switched practice from mini-laparotomy implantation to laparoscopic catheter insertion. Since the implementation of the new technique, there were reports of an increase in the incidence of hernia complications.

We reviewed the outcomes of our centre and compared the results to other published centres reviewing the incidence of hernia complications.

Methodology: A retrospective analysis of PD catheter insertion was conducted for the period 2015-2021. Data from the surgical theatre database was interrogated and cross referenced to renal database to review the incidence of umbilical hernia and port related hernia. In addition, the length of time for appearance of the hernia, and as well as the length of time to surgical repair were assessed.

Results: Ninety-seven patients underwent laparoscopic PD catheter insertion during the study time period. There were 12 (12.4%) patients that underwent hernia repairs - 5 umbilical hernias; 1 port related hernia and 6 inguinal hernias. The primary cause of end stage renal disease was Polycystic Kidney Disease (3 patients) and diabetes (3 patients).

The average interval between PD initiation and umbilical hernia repair was 19 months and 15 months for inguinal hernia repair. Overall the average time between PD initiation and hernia repair was 14 months.

Discussion/ Conclusion:

In our centre, laparoscopic insertion of PD catheters does not appear to increase the risk of hernias when compared to other published results. The most common hernias after PD catheter insertion are umbilical and inguinal.

As we have a single surgeon doing laparoscopic insertion of our PD catheters has led to similar outcomes of hernia complications when compared to national and international incidence.

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Introducing medical insertion of peritoneal dialysis (PD) catheter increases the total number of patients commencing PD without increased risk of peritonitis or malposition.

Home therapies - quality improvement, Home therapies - service delivery

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Introduction: Compared with haemodialysis (HD), peritoneal dialysis (PD) potentially offers improved quality of life, greater preservation of residual renal function, preserved vascular access and reduced incidence of viral hepatitis. The healthcare system also benefits through reduced costs but access to PD can be limited by the availability of appropriate catheter insertion facilities. A PD catheter can be inserted by surgical (laparoscopic or open, both typically under general anaesthesia) or medical (percutaneous, under local anaesthesia) techniques.

We examined the benefits of introducing a service for PD catheter insertion via medical technique in a tertiary renal unit. Following training of two nephrologists via an accredited national course, this service was offered in addition to surgical insertions that had previously been available. This study seeks to determine whether introducing medical insertion safely increased the number of patients commenced on PD.

Methods: Data were collected retrospectively using electronic health records (EHR). EHR were reviewed over two time periods: July 2017 to June 2019 (surgical insertions alone) and July 2019 to June 2021 (medical and surgical insertions). Data were collected on the incidence of peritonitis within 90 days and malposition (defined as the requirement for catheter repositioning). Incidence of complications between the medical and surgical groups was compared using Fisher's exact test.

Results: From June 2017 to July 2019 there were 44 PD catheter insertions (all surgical), compared to a total of 63 insertions (33 medical, 30 surgical) between July 2019 and June 2021, demonstrating a 43% increase in the number of patients commenced on PD. We compared complications between the 74 surgical insertions and 33 medical insertions across the full 4-year period. There was no significant difference in incidence of peritonitis within 90 days between the surgical insertions (14%) and medical insertions (15%), p=0.77, or in incidence of malposition: 7% in surgical versus 9% in medical, p=0.70.

Discussion: In our study population, introduction of percutaneous local anaesthetic PD catheter insertion by nephrologists was associated with a large increase in the number of patients starting PD and no increase in early peritonitis or the need for catheter repositioning.

Not all patients are suitable for medical insertion—contraindications include significant obesity or previous major abdominal surgery—but a hybrid medical/surgical service has allowed PD to be offered to patients in whom general anasthaesia is medically contraindicated and to reduce pressure on operating theatre space.

A limitation of our assessment of safety and efficacy in these two groups is that the patients are likely to be unmatched in terms of risk. In a hybrid service, technically more challenging patients will tend to be offered surgical insertion. Future studies in a larger population could compare these patient groups using propensity matching.

Notwithstanding these limitations, we demonstrated that introduction of medical insertion of peritoneal dialysis catheters may increase the total number of patients initiated on PD without any increased risk of major complications.

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Microbial Spectrum, Relevance of Empirical Antibiotics and Antifungals for PD Peritonitis – a Single Centre Study

Home therapies - quality improvement

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Introduction: Peritonitis is a common complication of peritoneal dialysis (PD) and is a direct cause of death in around 16% of PD patients. It is also the most common cause of technique failure. Prompt treatment of peritonitis in PD is therefore imperative. ISPD guidelines recommend the antibiotic choice to be tailored depending on local microbial spectrum related to PD peritonitis. The guideline also recommends prophylactic antifungal treatment for secondary prevention in conjunction with the antibiotic treatment.

Our centre protocol for treatment of PD peritonitis recommends empirical vancomycin and ciprofloxacin intraperitoneally at the time of diagnosis until the culture results are available. This review was conducted with a view to evaluate the appropriateness of this antibiotic regimen and to explore the necessity of using antifungals for secondary prevention as per the ISPD guidelines.

Methods: Data on all PD peritonitis episodes from January 2018 – December 2021 were retrieved using electronic patient records. Specific culture results along with microbial antibiotic sensitivities were reviewed and analysed for appropriateness of antibiotic selection and the need for antifungal therapy.

Results: Over the four year period, all of the 43 peritonitis episodes recorded were included in the analysis. Nine of these cultures did not have any growth and 5 cultures showed mixed growth including both Gram positive and Gram negative organisms. Out of a total of 25 Gram positive peritoneal culture results, only one Gram-positive peritoneal culture organism (Lactobacillus Paracasei) was resistant to Vancomycin. Of the 13 Gram-negative cultures, only 4 were resistant to Ciprofloxacin (Pseudomonas Luteola, Roseomonas mucosa, E.coli and Pseudomonas aeruginosa). There was only 1 case of fungal peritonitis (Candida albicans) during this period. There were no cases of relapsing or recurrent peritonitis leading to PD technique failure.

Discussion: The empirical initial treatment of PD peritonitis with vancomycin and ciprofloxacin is an appropriate initial management for majority of the PD peritonitis infections. In addition, it is easier to train patients to administer ciprofloxacin intraperitoneally at home, thereby avoiding hospital admissions for initial treatment. With no cases of relapsing or recurrent peritonitis during this review period, our protocol treatment successfully clears the infection in every episode. Apart from one confirmed case, there had been no increased incidence of fungal peritonitis in our centre over a

period of 4 years. Hence, the argument for using antifungal therapy routinely in our centre is weak and a review is being conducted in detail about the utility of the current ISPD guidelines for our unit.

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Digital Based Education promoting patient understanding and acceptance of Home-Based Dialysis

Home therapies - quality improvement, Patient education

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Background: The role of a 'Home Therapies - Pre-Dialysis Link Nurse' is to support patients who have decided they would prefer to do their dialysis at home. They need to be guided through the mass of relevant information to help them understand what they can expect along the way. Prior to the pandemic, an in-person information/education event was delivered thrice yearly, for patients and family to facilitate treatment decision making. People could see dialysis equipment, hear from peers and get to grips with all the different options available. Covid 19 made treatment choice education more challenging, with the limitations on face-to-face events. To maintain effective engagement, discussions were moved to video and telephone calls. However, for individuals with cultural, cognitive or language challenges this was less than ideal.

Method: Alongside the move to virtual consultations, individuals and their family were signposted to the 'My Kidney Journey' website and talked through how to utilise it. This enabled them to access information about the different modalities, including animation clips, video films and testimonies, at the right time for them, to help them understand how dialysis works and provide answers to their questions. Once home visits were reinstated, individuals and their relatives were guided through the website as part of their home visit and encouraged to look at it in their own time.

Case Study 1

•Mrs A an elderly female from Pakistan with limited English.

•Disengaged from education and treatment decision making.

•Daughter in law introduced to My Kidney Journey.

•Daughter in law able to engage mother-in-law and family.

•Mrs A agreed to PD

Case Study 2

•Mr B limited knowledge and interest in treatment decision making.

•Wife exhausted trying to explain dialysis related information.

•My Kidney Journey introduced to wife who was able to engage her husband so they both understood the implications of dialysis for their future.

•Ability to visualise treatment and answer questions that arose.

Discussion: Pre pandemic, a big part of treatment decision making guidance was discussing what they had learnt at the thrice yearly open day. During the pandemic the website became the basis for these discussions. The 'My Kidney Journey' website has proven to be a good digital resource, supporting and supplementing the information discussed on home visits.

Conclusion: My Kidney Journey relays information about dialysis treatments in an easy-to-understand manner, is suitable for use with people with various learning styles and is accessible at any time – to fit in with patient/carer/family needs. Since using this extra tool with individuals making treatment decisions, several have embarked on home therapies and report the website useful, especially at the beginning of their journey.

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Reducing culture negative rates and improving time to diagnosis in PD peritonitis

Home therapies - quality improvement, Home therapies - service delivery

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Introduction: Effective treatment of PD peritonitis is enhanced by the identification of the causative organism, enabling targeted antibiotics and identification of potential sources of infection. ISPD guidelines recommend that less than 15% of all peritonitis episodes should be culture-negative. Given local historic culture-negative rates in excess of 20% a collaborative quality-improvement project (QIP) was instituted to address culture-negative peritonitis rates.

Methods: As part of a multi-disciplinary QIP, two innovations were introduced in July 2019. Firstly, peritoneal fluid was inoculated into blood culture bottles for all patients presenting in-hours, alongside standard collection within universal containers. Secondly, peritoneal fluid in universal containers was processed using the water lysis method to liberate any intracellular organisms prior to culture.

A retrospective assessment was made of all episodes of peritonitis in patients presenting between July 2019 and July 2021. Culture results for universal containers and blood culture bottles were obtained from electronic patient health records and laboratory reporting systems.

Results: During the 24 months, 95 patients experienced 136 episodes of peritonitis, with a centre peritonitis rate of 0.31 events/ patient years. Overall culture negative rates during this period was 35%, compared with a culture negative rate of 34% in the preceding 18 months to July 2019.

PD fluid was sent in paired universal containers and blood culture bottles for 57 distinct episodes of peritonitis. The culture negative rates were 26% and 39% for blood culture bottles and universal containers respectively. The sensitivity for fluid in blood culture bottles was 100% and specificity 71%. Use of blood culture bottles increased the microbiology processing costs by 34%. In the 36 episodes in which both blood culture bottles and universal containers returned a positive result, a positive culture was reported 21.9 (11.2-32.6) [mean (95%CI)] hr earlier from blood culture bottles compared to universal containers.

Discussion: Inoculation of PD fluid in blood culture bottles results in both lower culture-negative rates and a clinically relevant improvement in the time until positive culture compared to the use of universal containers. Use of blood culture bottles only marginally increases the cost of

microbiological analysis but offers the opportunity to offer earlier intervention with targeted antibiotics.

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Patient Reported Outcomes Following Renal Transplantation: The Future Of Holistic Post-transplant Care

Patient outcome and experience, Transplantation - research

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Introduction: Patients with renal disease prioritise symptoms and functionality over the biochemistry and clinical guidelines, which clinicians traditionally rely on. Whilst kidney transplantation is expected to offer better survival and quality of life than dialysis, many recipients suffer limitations in their daily lives, due to factors associated with transplantation, such as immunosuppression side effects and infection. This study aimed to assess patient reported outcomes after kidney transplantation, to improve understanding and facilitate enhanced holistic post-transplant care.

Methods: A retrospective analysis of a prospectively maintained database of patients completing PHQ-9 and GAD-7 questionnaires, each consecutive year following renal transplantation, was conducted between 2013 and 2020 at a single institution.

Results: 698 patients returned PHQ-9 and GAD-7 questionnaires during the time period. After excluding incomplete records, 599 patients were included in the final analysis. There was a male preponderance (81.0%), and median age of 54 (range 19-84). The median number of consecutive completed annual questionnaires per patient was 3 (range 1-8). The majority of patients (70.1%) scored no depression on PHQ-9, followed by 18.5% reporting mild depression, with 11.3% falling into moderate to severe categories. Mean score at last assessment was worse than at first assessment (4.0 vs 2.6, $p<0.001$), but remained within the 'no depression' category. With GAD-7, 83.1% of patients scored minimal anxiety, followed by 9.6% reporting mild anxiety, with the remaining 7.1% scoring moderate or severe anxiety. Mean score at last assessment was worse than at first assessment (2.9 vs 1.9, $p<0.001$), but remained within the 'minimal anxiety' range.

Conclusion: Most patients undergoing renal transplantation do not suffer from depression or anxiety post-operatively, however, a significant proportion experience moderate to severe depression and anxiety. Prospective studies understanding the causes, and links with routinely collected biochemical data, will enable clinicians to identify and support at risk patients, delivering holistic evidenced based care.

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Track J - Quality Improvement, patient reported outcomes and experience

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A collaborative model of home monitoring of meningococcal vaccine titres improves compliance

Home therapies - quality improvement

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Introduction: The C5 inhibitors Eculizumab and Ravulizumab have revolutionised the management of atypical haemolytic uraemic syndrome (aHUS), however, a direct consequence of this complement blockade is a >600 fold increased risk of meningococcal disease. This is mitigated by vaccination and antibiotic prophylaxis. In England, annual measurement of meningococcal ACWY titres is therefore undertaken for the duration of treatment. aHUS management is coordinated through a single highly specialised service in England through a shared care protocol with most patients receiving Eculizumab by homecare services. Given this model and the geographically disparate patient group, we audited performance of annual titre measurement.

Methods: An initial audit of meningococcal vaccination titres measurement was performed for a twelve-month period (2017-2018) at a time when monitoring was predominately performed through local primary care. This was verified by comparing our own records with those of the Meningococcal Reference Unit (MRU), UK Health Security Agency (formerly PHE). Following discussions with key stakeholders, The National Renal Complement Therapeutics Centre specialist nurses, (NRCTC SpNs) instigated a pilot scheme with the aim of improving vaccination monitoring and reducing patients' risk of meningococcal sepsis. A repeat audit was performed over twelve months, (2021-2022) to assess the introduction of a central monitoring strategy.

Results: The NRCTC SpNs initial audit from 2017/18 identified that only 31% of our patient cohort had had a meningococcal ACWY titre taken during this period.

An agreement between the NRCTC, homecare and pharmaceutical companies resulted in vaccine titres being requested directly by NRCTC SpNs and taken by homecare nurses when patients are being cannulated at home to receive Eculizumab. Samples go straight to a central lab (MRU) and the results go directly to the NRCTC SpNs for interpretation, and clinical recommendations. This avoided a separate visit to a healthcare professional to have a blood test; prevented an additional invasive procedure and crucially, ensures titres are taken at the appropriate time to enhance patient safety by reducing risk of meningococcal sepsis.

A repeat audit of meningococcal monitoring following the introduction of the NRCTC SpNs' surveillance system has demonstrably improved compliance with 95% of patients within our cohort having titres measured during this period. All patients with titres below threshold went on to receive

a booster vaccination. No cases of meningococcal disease have occurred since implementation – additional interventions include NRCTC SpNs virtual consultations reinforcing antibiotic prophylaxis.

Conclusions: This collaborative surveillance system with homecare companies, the MRU, overseen by NRCTC SpNs has resulted in improved patient care. 95% of patients now have annual measurement of vaccine titres and receive boosters as required. The results were shared with patients directly and the relevant clinicians involved in their care, to ensure robust communication between primary, secondary and tertiary care. This transformative approach has led to a new model for remote NRCTC monitoring and is yielding similar benefits across other diagnostic and safety parameters at the NRCTC

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Advanced Kidney Care - Education Service Redesign

CKD

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Background, Problem Statement and Pandemic State: We have a multi-disciplinary Advanced Kidney Care team that consists of five nurses with allocated roles for patient pathway management, including education. Expertise for supporting decision making for modality choice varies between team members and the focus is on supporting generalisation and standardisation of education delivery so that all nurses feel confident to present home therapies, with a focus on peritoneal dialysis (PD) as first choice home therapy.

When the COVID-19 Pandemic began, we adapted the way we were working and moved from face-to-face education delivery to delivering most of the patient education virtually, via Vidyo initially but that proved challenging, so we converted to WhatsApp video which has been great albeit a bit small on our phones. Awaiting 'Doctor Doctor' video system now to enable virtual communication. This change led to a systematic focus on optimising the pathway for patients choosing PD, including through effective use of digital education tools.

Method and Key Actions and Goal Statement: During the pandemic we realised new ways of working that could add value to the patient experience and service delivery. With that in mind we collaborated with our regional Baxter team, who have expertise in LEAN methodology and service pathway mapping. Initially we mapped the current pathway which gave us the clarity to identify focus areas that needed to be improved. Multi-disciplinary focus groups centred their approach on developing a robust patient pathway for the future, utilising virtual and digital technologies to support the patient decision making process. The goal was to deliver innovative, effective high quality patient information, whilst reducing the risks to individuals' associated with the COVID-19 Pandemic.

Results: Between April & September 2021, critical changes were made to the AKC PD education pathway, using QI techniques. These changes included:

•Service redesign

•Implementation of virtual clinics

•Virtual education packs with multiple tools and visual resources

During the 12 months prior to the QI project PD numbers remained virtually static with a 1.6% increase and a shift towards greater APD numbers (85% APD v 15% CAPD). The post QI 12 months saw a 10.2% growth in PD numbers (APD 83% v CAPD 17%).

The education tools were discussed and reviewed on an individual basis with patients to ensure the appropriate resource were tailored to individual needs. Resources were made easy for patients to access via e-links or a QR code.

Over 500 virtual education sessions per year have been delivered since the new pathway was introduced, vastly reducing the number of patients needing to be seen on the ward reduced need for home visits and the associated risks this brings.

Shorter education sessions facilitate better retention of information and avoid information overload. With greater access to translation support from patient's family and friends, in combination with visualisation of non-verbal communication, that would be lost in telephone follow-up, staff are better able to gauge patient reactions and carry out home assessments virtually.

Despite Covid pandemic related restrictions, the collaborative team were able to initiate and maintain involvement in the implementation of a robust QI programme, that has seen a growth in PD numbers and continues to evolve.

Conclusion: Key to our success was pathway standardisation across the advanced kidney care nursing team: removal of variation; optimisation of digital educational tools for example Baxter's My Kidney Journey and Patient Charity websites. However, virtual interactions with the patients and their families remain critical for consolidation of their learning, addressing misconceptions and supporting shared decision making. Going forward most patients manage to access the information they need more rapidly, and staff address questions as they arise in order to support an informed and shared treatment option decision. Timely, treatment decision-making has facilitated smoother organisation of necessary interventions and PD access creation.

Future Considerations: As an Advanced Kidney Care service, referrals are received from multiple sites, covering a wide geography and this can be challenging, in terms of point of referral and equity of patient experience. A focus moving forward is to embed these quality improvements beyond our own Advanced Kidney Care nursing team to improve education for those outreach services.

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Diabetes care in people with diabetes on peritoneal dialysis: An audit at three large university hospital foundation trusts

Cardiovascular disease and diabetes, Home therapies - quality improvement

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Introduction: The percentage of people on renal replacement therapy with a diagnosis of diabetes is increasing annually. People with diabetes (PwD) on dialysis are often at risk of fragmented diabetes care and management of their diabetes can be complex and challenging with predisposition to glycaemic variability and hypoglycaemia.

The Joint British Diabetes Societies (JBDS) guideline 'Management of adults with diabetes on the haemodialysis unit' in 2016 established the Diabetes in Haemodialysis programme. The aim of this programme was to improve the organisation of care for PwD on haemodialysis.

In contrast there is little known about the standards of diabetes care received by PwD on peritoneal dialysis (PD).

Methods: We audited the care of all PwD on PD at 3 large university hospital foundation trusts between December 2021-January 2022 against the standards set in the JBDS 2016 Diabetes in Haemodialysis guidance shown below:

•100% of PwD should have

odocumented annual review of glycaemic control by a diabetes specialist

odocumented annual eye screening.

odocumented annual foot risk assessment

•Target HbA1c 58-68mmol/mol, >80mmol/mol represents poor glycaemic control, if <58mmol/mol reduction in treatment should be considered as increased risk of hypoglycaemia

Results: 65 participant records were examined, and demographics were broadly similar across the sites except for ethnicity (see Table1). All participants except one were on glucose containing dialysis regimes.

The frequency with which patients were seen by a hospital based diabetes specialist team varied between centres. The percentage seen at least annually at site1, 2 and 3 was 94%, 65% and 63% respectively. Of those people seen less than annually 58% were on insulin.

Of the cohort 92% were in a retinal screening program with at least annual review, 77% had at least an annual foot review, which were broadly similar across the three sites.

Most recent HbA1c results were in the clinically acceptable range of 58-80mmol/mol in 32% of people and 9% had poor control (>80mmol/mol). Of the 58% of people who had HbA1c <58mmol/mol, 66% were on a treatment that could be associated with hypoglycaemia (sulphonylurea or insulin). Self-reported hypoglycaemic events (at least 1 event per month) were reported by 21% of this subgroup. Of the 65 people 2 had a diabetes related admission in the preceding 12 months.

Discussion: We observed that frequency with which PwD on PD were seen by a diabetes specialist team varied both within and between centres. Overall adherence to the retinal screening aims was good but the frequency of foot review was sub-optimal. We observed that 58% of the cohort had an HbA1c <58mmol/mol and of this group two thirds were on treatments that could cause hypoglycaemia. In this group 1 in 5 people reported hypoglycaemic events and would benefit from diabetes specialist input to review and reduce insulin or sulphonulurea doses. We aim to extend this audit to other sites and use the information collected to inform future quality improvement work aimed at improving and standardising the care of PwD on PD.

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Effectiveness of telephone consultation of nephrology clinic from patients' perspective

Patient outcome and experience, Other

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Telephone consultation as part of the healthcare system initiative remains a contemporary approach which minimizes disease transmission between patients and healthcare professionals, also allowing better allocation of healthcare resources. With the ongoing COVID-19 pandemic, telemedicine proves its value for the follow-up of patients with chronic conditions, with many clinicians highly emphasizing such clinical approach. However, little is known in the aspect of patient's feedback and their opinion on such changes.

From the timeframe of June 2020 – January 2021, the survey consisting of questions based on experience of telephone consultation with grading of 1 – 5 (1 = completely agree, 2=agree, 3= Neither, 4= Disagree, 5= Completely disagree) were sent to 178 patients who were part of General Nephrology/Low Clearance/Transplant follow up in West Suffolk Hospital Nephrology led by consultants. The survey covered the overall telephone clinic experience, communication barriers and the overall satisfaction why telephone clinic suited the patient. Results are then analyzed using R studio statistical software, with comparisons between groups were made using x^2/Fisher exact test for categorical data.

178 survey sent, 88 responses (49.4%) were received, with majority of patients aged >60 years old (89.8%). These include 32 males (36.6%), Female 25 (28.4%) and anonymous 31 (35.2%). 77 (87.5%) of these responders have both blood pressures & weighing scales facilities in their home, and 70 (79.5%) had less than 20miles to travel to the nephrology clinic.

For questions focusing on the overall experience of telephone clinic, 'Agree' responses ranged from 65 (73.9%) to 76 (86.4%), claiming that quality of the call was good where they could hear the clinician well, and queries were being taken care of with reassurance. Telephone clinic communication barriers were also identified, 55 (62.5%) 'Disagree' that it was difficult to form a connection with the doctor or ask questions, and 59 (67.1%) 'Disagree' that clinician spent too much time on small talk. With potential factors to why telephone clinic is better for patients, most commonly 29 (33%) responders claimed being clinically vulnerable, followed by 24 (27.3%) having mobility issues.

Our study showed no statistically significant difference in telephone clinic experience based on gender, clinic type (General Nephrology, Transplant, Low Clearance) or age cohort among the patients. Majority of patients surveyed had a positive experience with telephone consultation, with the commonest barrier identified was the inability to ask questions during consultation. Limitations include a small sample size, with less than half response rate from the total survey sent. Of the responses received, very limited data was taken from patients attending low clearance clinic. Overall, the study showed positive patients' feedback on telephone consultation during the height of COVID-19 pandemic period.

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Track J - Quality Improvement, patient reported outcomes and experience

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Improving access to renal transplantation in Shropshire

Transplantation - service delivery, Transplantation - quality improvement

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Introduction: The last GIRFT report helped highlight the lack of access to renal transplantation in Shropshire. This helped support the major changes that were required to improve access.

Method: We qualitatively describe the quality improvement interventions that were used to improve our access to renal transplantation. The improved outcomes are described using mainly retrospective data. Prospective rolling pre-emptive listing data is also presented.

Results (See PDF for sample charts)

Quality improvement interventions are described including what occurred to change the culture behind transplantation including survival, hospital admissions and financial aspects to our CKD, dialysis and business teams. Early transplant discussions with patients during CKD/RRT educational opportunities were incorporated. Regular transplant listing decisions were reviewed either during clinic, but also via MDT meetings to highlight any barriers to listing that needed to be addressed (before advanced kidney clinic entry). The use of Clinical Vision live reports and West Midlands Transplant First data tool were made available to all members of the team of where the patients were in the transplant workup pathway under a specified consultant name so issues could be addressed promptly. With limited specialised nursing numbers (one in CKD, and one renal transplant coordinator) as the CKD team numbers increased in the last 2 years, review of the advanced kidney care patient MDT included transplant plans to increase pre-emptive rates. Consultant SPA time identified for transplantation. The pre-transplant nurse led education clinic has been highlighted as exemplar from GIRFT.

Data to increase access to renal transplantation improvements include:

1) Listing by 2 years for incident RRT patients from 20.8% to 100% since 2019.

2) Time taken from transplantation education to pre-emptive listing has fallen from median 10 months to 6 months with the aim for a 18 week pathway

3) Identification and transplant referrals have increased from 18 patients in 2016, to approximately 50/yr for the last 2 years.

4) Earlier patient identification/workup has meant the median eGFR is now 16 at referral if the patient is listed as pre-emptive. This has meant >80% of patients remain pre-emptive at listing for the last 2 years, as compare to 50% in 2016. The living donor transplant rates is now 48% of the transplanted patients this year.

5) The incident transplantation rate per million population has increased to within 95% confidence limits from being below 99% confidence limits previously.

Conclusion: With the multi-faceted approach we have improved our patient access to transplantation. Although there was 48% living donor transplants so far this tax year, it is hoped with increasing the WTE transplant nurse from one to three over the year, there will be more pre-emptive living transplantation. This year alternate month Teams MDT meetings with our consultant colleagues at the tertiary transplant centre has recommenced.

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Measurement of patient satisfaction with Vascular Access

Vascular access

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Introduction: Fistulas are the gold standard type of access for haemodialysis patients. Based on All Wales vascular access audit data for 2020/21,on average,73% of prevalent HD patients were dialysing via an AVF. For patients on haemodialysis, multiple aspects of care can impact on their quality of life. All types of vascular access are associated with complications and require maintenance. The patients experience with different types of access play an important role in their choices. Defining a better understanding of patients views and experiences is fundamental to tailoring individualised care, addressing concerns to improve AVF uptake. The aim of this study is to measure the overall satisfaction of haemodialysis patients with their vascular access with the aim of defining areas for quality improvement.

Method: Short form vascular access questionnaire (SF-VAQ) is a short and simple questionnaire with robust psychometric properties,developed by Kosa et al, which is tested to measure the satisfaction of haemodialysis patients with their vascular access.

SF-VAQ was administered in 7 dialysis units, obtaining 200 prevalent patients who completed the questionnaire. This process was carried out by 3 Vascular Access Clinical Nurse Specialists between July 2021 and September 2021 to patients willing to participate in the survey. The questionnaire took approximately 5 mins to complete. This was divided into 4 domains: Overall satisfaction, Physical symptoms, Social functioning and Complications. A 7 point scale was used to measure level of agreement. Low scores indicate satisfaction, high scores indicate dissatisfaction, the exception being the domain of overall satisfaction where the opposite scoring is true.

Results: 200 patients completed the SF-VAQ, 125 had AVF as primary access,56 had tunneled lines (TL), 6 patients had grafts (AVG)and 13 had AVF and TL simultaneously. Average satisfaction rate values were 5.57. This shows that overall patients were satisfied with their vascular access. The average for AVF,TL and AVG were 5.96,5.411 and 5.833 respectively. For patients with AVF and TL the mean was 5.071. Patients were more satisfied with AVF than TL or AVG.

In the social domain which includes daily activities, sleep, appearance and bathing, the mean was 2.11 for AVF, 3.013 for TL and 1.625 for AVG. The highest level of dissatisfaction was bathing with the value of 3.839 for TL. Patients showed more dissatisfaction on appearance with TL than AVF or AVG.

In the physical domain which assesses pain, bleeding, swelling and bruising, the mean was 2.54 for AVF,1.527 for TL and 2.75 for AVG. Highest dissatisfaction was recorded for bruising and pain with AVG followed by bruising for AVF and TL simultaneously and pain for AVF.

In complications domain which includes problems on dialysis, hospitalization and access longevity concerns, the mean was 2.081 for AVF, 2.580 for TL and 3 for AVG. Patients with AVG showing highest dissatisfaction.

The mean across all the domains were 2.244 for AVF, 2.373 for TL and 2.458 for AVG. This indicates patients with AVG reported the highest levels of dissatisfaction with AVF patients reporting the lowest.

Discussion: We found that different types of access were associated with different levels of satisfaction. Overall, patients with AVF reported the highest satisfaction followed by AVG and TL.

However, each domain demonstrated different access types with highest levels of dissatisfaction.

AVG were highest for physical, with pain reported higher than AVF or TL. This could be due to more diligent adherence to rope ladder cannulation to avoid graft damage, where AVF may have higher area puncture technique resulting in loss of sensitivity, causing less pain. (Parisotto et al 2014). Buttonhole technique is also only used in AVF and is demonstrated to produce less pain (Castro et al 2010). The questionnaires did not capture the use of topical anaesthetics which could impact on their perception of pain. (Fujimoto et al 2020).Patients with simultaneous AVF and TL showed dissatisfaction in all domains. This could be attributed to first cannulations, multiple infiltrations leading to TL insertion. This could explain patients concerns regarding longevity and hospitalisations.

The SF-VAQ could be complemented with additional data collection such as demographics including age, gender, and ethnicity, comorbidities, vascular access interventions and cannulation techniques.

This could increase our understanding of patients views and experiences with vascular access which is fundamental to tailoring individualised care and improving AVF uptake.

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The elusive search for a prospective method of monitoring renal biopsy complications; a single centre's experience with SPC charting

Diagnostics, Other

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Introduction: Renal biopsy is an essential part of diagnosis and monitoring response to treatment of renal patients. In a modest sized renal unit in the UK we perform 50 to 70 biopsies a year, with a changing field of practitioners, mostly renal registrars, assistants, and equipment changes including ultrasound equipment and needle types.

It is challenging to monitor complications, and usually complication rates are monitored on a yearly basis and compared to local standards and to national guidance. Local standards suggested a haematuria rate of 10%, CT or blood transfusion 1 in 50-100, embolisation 1 in 1500 and nephrectomy 1 in 3000.

Several times during the year we noticed an apparent increase in complications and considered to possibility of a real time way of monitoring these complications to indicate if they were out of expected frequency.

Method: After discussion with the Quality Improvement team in our hospital, we trialled the use of Statistical Process Control (SPC) charts to monitor the biopsy complications in real time.

The registrar designated responsible for biopsy complications auditing was trained in use of SPC charts, and began prospective collection of data.

To provide run-in and context, 3 years of retrospective patient notes were analysed for complications.

Complications were detected by analysing the discharge summaries, length of stay and imaging done in the time encompassing the biopsy event. These were categorised and added to a run-time chart.

Outcome: Due to the rarity of renal biopsies (2-12 a month) in our unit, and the additional rarity of complications as above, the data was analysed monthly, and included summation of any complications regardless of severity.

The SPC chart shows the data over a 5 year period of follow-up – 3 retrospective and 2 prospective.

Significant events during this period are marked on the chart for context of changes to equipment and practitioners.

Discussion: Due to the rarity of events overall, the presence of any events at all create a variance from baseline, and hence can create the appearance of a significant concern. The SPC chart enables an ongoing surveillance on this rate of complications and will reveal any ongoing deviation from baseline with sustained complications.

Due to the small numbers involved there was no possible statistical analysis beyond a visual check according to Nelson Rules for SPC charting, and ideally there would be a more robust or automated way of monitoring for complications.

However I believe ongoing monitoring for complications in some format provides a higher level of confidence in the procedure, and in any changes made to the equipment or technique rather than reliance on gut feeling or delayed data. This method is therefore submitted for discussion in the wider UK nephrology field.

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Track J - Quality Improvement, patient reported outcomes and experience

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The North West Operational Delivery Network (ODN) with Kidney Quality Improvement Partnership (KQuIP) approach to build Quality Improvement capability and leadership in preparation for the Renal Service Transformation Programme.

Patient outcome and experience, Staff education, Other

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Introduction: The North West (NW) Renal Operation Delivery Network (ODN), made up of six trusts, has been running as an emergency network since the outbreak of COVID-19 in March 2020. With the Renal Service Transformation Programme (RSTP) and Renal Getting It Right First Time (GIRFT) Report, there is a regional drive for change and improvement within the NW kidney community. The NW ODN agreed that the Kidney Quality Improvement Partnership (KQuIP) will deliver these national drivers through the KQuIP programme.

What did NW KQuIP do? The ODN appointed medical leads for each workstream. Each lead developed an aim, driver diagram, and measurement strategy. Equipped with these, the KQuIP programme manager and regional QI (Quality Improvement) clinical lead, held a virtual QI SWOT analysis meeting with each renal unit in the region. After completing all 6 analyses, 2 regional quality improvement priorities emerged: Pre-emptive Kidney Transplant and Home Therapies. Each unit found and mobilised a medical and AHP (Allied Health Professionals) project lead per project. The (Virtual) KQuIP Essential QI Training Programme (4 QI workshops) was delivered to project leads and patients over 5 months (July – Dec 2021). Each workshop consisted of a formal QI presentation followed by breakout rooms for each project. Each breakout room was facilitated by a member of the KQuIP Faculty.

What are the results? Each workshop was attended by healthcare professionals and patients and supported by the KQuIP faculty from around the region.

At the end of each workshop, attendees were asked to complete a simple 3 question survey monkey. The results helped to improve the later workshops.

In December's QI Workshop (5 months after the first workshop) each project lead presented their project aim, driver diagram and measurement to the other project leads.

Feedback: “Each workshop was well delivered, well-structured and some good engagement... I enjoyed being involved, thank you for inviting me. It is an exciting time. Such a good idea to involve patients as they really challenged the HCPs on their aims, actions and pathways.” (Healthcare Professional)

“I learnt a lot today which I will apply to a current … project we are running in collaboration with some community stakeholders who will be engaging with their immediate community. Thank you. Really informative.” (Patient)

What is NW KQuIP’s next steps: Having completed the (virtual) Essential QI Training Programme, the ODN have asked for ongoing KQuIP Support in the region which will include:

Monthly QI Drop-In sessions with alternating monthly project peer assist meetings

Quarterly Workshops to share evidence of improving

Annual QI Conference in November

Conclusion: With the emerging NW ODN, RSTP and Renal GIRFT Report, 2021 saw the building of QI capability and leadership in the region. KQuIP delivered the virtual Essential QI Training Programme to healthcare professionals and patients over a 5-month period. From July to September 2021, QI concepts, tools and techniques were introduced to project leads. To have projects leads apply these in brief time has given the ODN and KQuIP in the NW confidence that the coming years will be full of collaboration and improvements for people living with kidney disease in the region.

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Understanding constructs of kidney function and kidney failure amongst older patients with advanced kidney disease and those close to them: results from a secondary qualitative analysis of patient and carer interviews

CKD, Patient education

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Background: Each year over 3800 UK older adults commence kidney replacement therapy, predominantly haemodialysis1, despite the survival benefit of dialysis over conservative care remaining uncertain for older, comorbid people2. Older patients face difficulty when choosing between treatment options for kidney failure and need help navigating this process. Challenges include low health literacy3-5, variable communication practices between renal units6-9, and regional variation in treatment rates10-12. Relatives often play an important role in supporting patients with these decisions 13. We aimed to explore understanding of kidney function and failure amongst older patients with advanced kidney disease, and their loved ones.

Methods: A secondary qualitative analysis was conducted of 25 transcripts of face-to-face, semi-structured interviews from the UNPACK study (15 with older patients and 10 with close persons). Figure 1. outlines the UNPACK study aims and eligibility criteria.

Data were analysed using inductive thematic analysis, including constant comparative approaches derived from grounded theory. Using a team approach, transcripts were coded until thematic saturation, a novel coding framework was derived and themes identified.

Results: The median patient age was 81. Gender and prior treatment decision were balanced. All participants were of white ethnicity. Comorbidity burden was high. Median duration of full-time education equivalent was 11 years.

Three themes were identified.

a.Vital blood cleaning organs

Participants generally understood the kidneys to be critical organs for survival. Many described their role as ‘blood cleaning’ organs using mechanistic constructs. There was less certainty about underlying diagnoses and about symptoms of kidney failure. The ‘unwitnessed’ nature of critical kidney functions in both health and disease contributed to feelings of detachment, uncertainty and reliance upon information from clinicians.

b.Dominance of numbers

Participants were almost unanimous in their attention to numerical measures of kidney function. Numbers appeared to provide something concrete set against the silent, intangible disease process. This appeared to heavily influence views on thresholds for treatment initiation and kidney failure, which was often conflated as death.

c.Controlling and predicting the future

Most participants regarded kidney failure as inevitable. This view appeared to be supported by use of graphs in clinical consultations, which were considered to predict the future. Despite this, participants remained uncertain about their prognosis. Some interviewees appeared to view their involvement in treatment decision making as an opportunity to exert control over their future.

Discussion: Older patients with advanced kidney disease and their loved ones were uncertain regarding many aspects of kidney disease and its treatments. This seemed to allow concrete numerical measures to dominate constructs of kidney failure, contributing to treatment decisions. The influence of clinicians on this requires exploration, but these findings suggest that reliance upon eGFR and plotting trends in kidney function may have unforeseen consequences upon communication.

Clinicians should take concerted steps to optimise patient understanding of kidney function and failure, given the impact on shared decision making. This is of particular relevance as the kidney community transitions to use of risk equations in clinical practice. Further research is required to inform the most effective methods of individualised communication.

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Track K - Case Reports 1

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A case series of experience of using tolvaptan in autosomal dominant polycystic kidney disease (ADPKD) in adults with Chronic Kidney Disease (CKD) Stage 5

Case reports, Patient outcome and experience

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Introduction: According to the Summary of Product Characteristics (SPC) the risk of hepatic damage in patients taking tolvaptan with severely reduced renal function (i.e. estimated glomerular filtration rate (eGFR) < 20 mL/min/1.73 m2) may be increased; these patients should be carefully monitored for hepatic toxicity. In addition tolvaptan should be discontinued if CKD progresses to stage 5 (eGFR < 15 mL/min/1.73 m2) as there is no safety and efficacy data available in these patients.1,2 Despite these concerns we decided to continue tolvaptan treatment into CKD stage 5 to ascertain if there was possible benefit to continuing treatment with appropriate monitoring in place.

Here we present a limited case series:

Case 1:

Ethnicity: White British

Sex: Female

This patient's renal function dropped to CKD stage 5 in September 2019. Blood testing for renal function, hepatic transaminases and bilirubin was continued at regular 6-weekly intervals thereafter. Concurrent monitoring for symptoms that may indicate liver injury (such as fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, dark urine or jaundice) were also conducted in clinic and patients were advised to promptly report these symptoms should they arise.

The patient continued with their tolvaptan treatment until April 2020 at which point their treatment was stopped. The patient did not experience any adverse effects or derangement in their liver function whilst taking tolvaptan. At the time treatment was stopped in accordance with treatment guidelines and our lack of experience using tolvaptan in patients with CKD stage 5.

Case 2:

Ethnicity: Black

Sex: Male

This patient's renal function dropped to CKD stage 5 in June 2020. The patient did not experience any adverse effects or derangement in their liver function whilst taking tolvaptan. The patient continued on with their tolvaptan treatment until November 2021 at which point they started haemodialysis.

Case 3:

Ethnicity: White British

Sex: Female

Case 3 entered CKD stage 5 in August 2019. They still remain on tolvaptan and have experienced no problems or any adverse effects for the last 2.5 years. Her liver function has remained stable and she has displayed no signs or symptoms of liver injury. The current plan is to continue tolvaptan under surveillance and the patient will stop treatment when they start renal replacement therapy or if they do not fulfil the treatment safety monitoring guidelines.

Discussion: From our limited experience we have not experienced any adverse effects when continuing the tolvaptan in patients with CKD stage 5. We will continue to assess each patient on a case by case basis and determine whether it would be beneficial continuing tolvaptan into CKD stage 5. One must carefully asses each patient's fluid balance and the risk of developing an acute kidney injury (AKI) should patients be unable to cope with the aquatic demands of treatment thus predisposing them to the renal toxic effects of tolvaptan when dehydrated. In addition one must consider if stopping a patient established on tolvaptan will lead to a faster decline in renal function and hasten their need to start renal replacement therapy due to progression of their ADPKD in the absence of tolvaptan. Due to the experience we have thus far gained we aim to continue tolvaptan if it is deemed to be safe and of clinical benefit. Blood testing for renal function, hepatic transaminases and bilirubin will continue for CKD stage 5 patients at regular 6-8 weekly intervals. Concurrent monitoring for symptoms that may indicate liver injury (such as fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, dark urine or jaundice) will also conducted in clinic and patients will be advised to promptly report these symptoms should they arise.

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Calciphylaxis: A case series report - is prevalence increasing?

Case reports, Genetic and rare diseases

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Introduction: Calciphylaxis is a rare, severe complication of chronic kidney disease mineral bone disorder. It is characterized by arteriolar calcification of the subcutaneous fat and dermis, and has been associated with mortality rates of approximately 50% within a year of diagnosis. Between March 2012 and March 2020 the UK calciphylaxis study (UKCS) recruited 139 patients from 36 enrolled renal centres; an average of 1 case every 2.6 years per centre. Annual incidence of calciphylaxis amongst dialysis patients at Royal Devon and Exeter NHS Foundation Trust (RD&E) was 0.17% in 2019 (1 case), 0.34% in 2020 (2 cases) and 0.52% in 2021 (3 cases) plus 1 case in a transplant patient; a further 2 have been identified in 2022. The case series presented here aims to raise awareness of i) calciphylaxis risk factors ii) the need for early specialist assessment iii) the registry of rare kidney diseases (RaDaR).

Methods: Patients were included if they had a diagnosis of calciphylaxis between 01.02.2020 and 01.02.2022. Data regarding demographics, dialysis modality, BMI, medications, and mineral bone parameters were collected from RD&E clinical databases. Data were recorded from initiation of dialysis through to calciphylaxis diagnosis. Data regarding calciphylaxis lesions, treatments and current vital status are summarised.

Results: 8 patients with clinical features of calciphylaxis were included; 5 of whom had skin biopsy confirmation. Median age was 63 years (IQR: 53-73), BMI 28.5kg/m2 (IQR: 22.5-34), 100% were white, 75% females, and median time from onset of kidney failure was 4 years (IQR: 2-10). 75% of patients had history of recurrent hypercalcaemia (corrected calcium >2.55mmol/L) and 88% recurrent hyperphosphatemia (phosphate >1.5mmol/L). 63% (5 of 8) had refractory secondary hyperparathyroidism; 2 of whom underwent parathyroidectomy and 3 received calcimimetic treatment. Warfarin therapy exposure was recorded in 75% (6 of 8) patients; a finding consistent with the literature. 75% (6 of 8) were prescribed active vitamin D and 88% (7 of 8) a calcium based binder. 88% (7 of 8) patients had lower leg lesions; 2 of whom also had upper leg lesions. 1 patient had an abdominal wound. Median follow up time was 6 months (range 1-24); 6 of the 8 patients remain alive although 1 of these has withdrawn from dialysis. Lesions have completely healed in 4 patients; 3 of these received daily dialysis and sodium thiosulphate and 1 (transplant patient) received hypobaric oxygen therapy and sodium thiosulphate. 3 patients had their skin lesions for at least 2 months, being managed by primary care, before calciphylaxis was suspected; 1 has died and 1 remains acutely unwell. Only 1 patient has been enrolled into RaDaR.

Summary: RD&E have seen a rise in calciphylaxis incidence. Recurrent hypercalcaemia and hyperphosphataemia, refractory SHPT, hypotension and warfarin use were the most common risk factors. Lesions were not always identified promptly (as possible calciphylaxis) delaying diagnosis and management. More awareness of calciphylaxis is required; submitting data to RaDaR is vital to help determine the UK calciphylaxis incidence and inform possible prevention and treatment strategies.

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Dialysis induced intermittent SVC obstruction

Case reports, Vascular access

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Introduction: A 71 year old woman attended for outpatient haemodialysis in July of 2020 in her usual state, having recovered from Covid pneumonia 2 months previously.

She had a background of crohns disease, ileostomy, parastomal hernia with chronic fistulation, and previous DVT. She started haemodialysis for ESRF of unknown cause 7 years previously, initially on a right forearm fistula which failed in the first year. She dialysed for 4 years on Right internal jugular (RIJ) tunnelled lines, and 3 years on fistulae. Current access was a RIJ line inserted 8 months previously. Since her covid pneumonia her 'lumens were reversed' on dialysis due to poor aspiration from the proximal lumen.

10 minutes into dialysis she became extremely short of breath and the dialysis nursing team called the oncall renal registrar describing that she was purple in colour and complaining of severe headache. He asked for them to stop dialysis and attended immediately. On arrival to the unit he found her colour to be improving, but noted marked distension of the veins across her head, neck and chest, and soft tissue swelling to both supraclavicular fossae. She was transferred to the emergency department on high flow oxygen, and after 30 minutes of waiting in the department she had normal observations and the above findings had completely resolved.

Methods: Due to a strong suspicion of SVC obstruction a CT venogram of the major vessels was performed which revealed non-occlusive thrombus around the distal tip of the dialysis catheter Figure 1. Pemberton's test did not reveal any changes clinically.

A repeat attempt at haemodialysis was attempted with medical staff standing by. 10 minutes into dialysis with a flow of 200ml/min she had recurrent shortness of breath, severe headache and her upper body changed to a marked dusky colour with visible distension of the veins on face and neck.

A diagnosis of intermittent SVC obstruction was made, and close examination of the showed that the proximal and distal lumens of the line were positioned on either side of the thrombus in such a way that when dialysis was commenced with the lines reversed from their standard use, the effect was an accelerated SVC obstruction with immediate effect on the patient. When the line was not in use there was no obstruction of the vein.Figure 2

Results: A temporary femoral line was inserted for dialysis. Removal of the RIJ line was discussed with the interventional radiology and cardiothoracic surgery team. She was deemed too high risk for

general anaesthetic or aggressive intervention, and alternative access (tunnelled femoral line) was inserted while she was anticoagulated with initially with LMWH then with apixaban 2.5mg BD.

Repeat interval CT after 3 months showed reduction in size of the thrombus. At this time the patient's femoral line was removed due to infection, and she was unwilling for other attempts at access. She recommenced dialysis via her RIJ tunnelled line (with lumens used in 'normal' orientation) with no further symptoms. After 3 months she withdrew from dialysis and passed away.

Discussion: The Renal Association guidelines (2015) advise that >60% of patients initating planned haemodialysis should be on either AVF or AVG. In UK registry data (in 2019) 54.4% started with definitive access, and 29.4% initiated with a tunnelled line, 16.2% with a non-tunnelled line1

The thrombotic complications of tunnelled lines are well documented2, and along with an increased infection risk are one of the reasons for the guidelines above. Indeed, SVC obstruction secondary to dialysis catheters has been previously reported 3 4.

In the case discussed above she had a major thrombotic risk in a previous unprovoked DVT, followed by recent infection with SARS-COV2 which induces a prothrombotic inflammatory state and is strongly associated with DVT and PE, which may explain her reason for developing a significant thrombus in a relatively new line.

The initial CT report was reassuring to the clinical team, and while there is record of intermittent SVC obstruction due to a line5, in this case the rapid onset of symptoms (minutes) and resultion in minutes falsely reassured the team.

I believe this is the first presentation of a case of dialysis associated intermitted SVC obstruction in the literature, and knowledge of this possibility may help colleagues diagnose and manage cases in the future.

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IgA vasculitis following COVID-19 vaccination: a review of the literature

Case reports, COVID-19 including vaccination

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Introduction: There have been sporadic but increasing reports of IgA vasculitis following vaccination against COVID-19. This mirrors previous reports of IgA vasculitis following vaccination against influenza, suggesting a possible common mechanism where immune activation in response to vaccination activates or exacerbates vasculitis. IgA vasculitis and IgA nephropathy are commonly associated with bacterial and viral infections of the upper respiratory tract, and cases have been reported following COVID-19 infection. We review the literature regarding IgA vasculitis following COVID-19 vaccination reported thus far.

Methods: A literature search was conducted using the PubMed database on 8th of February 2022, searching for the terms IgA vasculitis or IgA nephropathy and COVID-19 vaccine or COVID-19 vaccination (or related terms). Duplicates were removed, then each paper's title, abstract, and full text was assessed for relevance and validity. All English-language papers which described at least one case of IgA vasculitis or nephropathy following COVID-19 vaccination were included in the analysis.

Results: The search found 37 papers. Nine papers were excluded due to irrelevance, while one case was excluded for not being available in English. Across the included 27 papers (listed in References), a total of 42 cases of IgA vasculitis or nephropathy following COVID-19 vaccination were described. 26 of these cases (62%) were new diagnoses. 21 cases (50%) occurred following the BNT162b2 (Pfizer) vaccine, with 19 (45%) following mRNA-1273 (Moderna) and 2 (5%) following AZD1222 (AstraZeneca) vaccines. Symptom onset occurred within 2 days post-vaccination in 57% of patients. The majority of patients had a relatively benign disease course, with haematuria and proteinuria resolving on subsequent follow up. 25 patients (59%) received no or supportive treatment only, while 14 (33%) received glucocorticoid therapy. There was one reported case of rapidly progressive glomerulonephritis requiring five days of haemodialysis. In this case, renal function slowly improved following three subsequent days of treatment with intravenous methylprednisolone, returning to near baseline by day 30. 27 (64%) patients presented with symptoms after the second dose of COVID-19 vaccine, with 4 reported cases of patients with symptoms following both first and second vaccine doses.

Discussion: IgA vasculitis following COVID-19 vaccination is an increasingly reported phenomenon. The rapid global rollout of COVID-19 vaccines means that both extremely rare complications will be reported with some frequency, and that the onset of unrelated disease can coincide with vaccination by chance. It is estimated that over 10 billion doses have been administered globally at the time of writing. This makes interpretation of causality challenging in this case. The majority of patients described have had relatively mild disease courses, requiring either supportive treatment only or short courses of glucocorticoid therapy. The majority of patients presented with macroscopic haematuria, which correlates with a better prognosis in IgA nephropathy. There is no suggestion that the risks of IgA vasculitis following COVID-19 vaccination outweigh the vaccine's benefits. As the majority of cases were new diagnoses, acute episodes of IgA vasculitis following vaccination represent a novel differential for patients presenting with haematuria and proteinuria.

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Renal infarction following SARS-CoV-2 infection

Case reports, COVID-19 including vaccination

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Background: SARS-CoV-2 has been shown to affect patients in a variety of ways with disease severity reflected by multiple organ involvement (1). Hypercoagulability is a well-recognised extra-pulmonary complication of SARS-CoV-2, predisposing patients to thrombotic events (2). Recent studies have shown that despite Venous thromboembolism (VTE) prophylaxis, patients, in particular those requiring hospitalisation and critical care admission are at increased risk of thromboembolism. To a lesser extent arterial manifestations such as renal or limb ischemia have been reported(3). We report the case of a previously fit and well 34-year-old female diagnosed with renal infarction and abdominal aortic mural thrombus, following mild SARS-CoV-2 infection.

Case presentation: A 34 years-old female presented with acute onset right flank pain, rigors, nausea, and vomiting. She had no previous medical history but was a smoker and took the combined oral contraceptive pill. She was a mother of two and had not experienced any previous miscarriages or pregnancy related complications. Two weeks prior to admission, she reported anosmia and pharyngitis lasting a few days. Initial examination and observations were unremarkable with blood tests showing leucocytosis and mildly elevated C-reactive protein with preserved renal function. Due to hospitalisation, she underwent both PCR and SARS-CoV-2 antibody testing. Whilst her PCR was negative for acute infection she had positive SARS-CoV-2 nucleocapsid antibodies indicating previous infection. Her presentation was preceded the rollout of vaccination.

A contrast enhanced CT scan of the abdomen and pelvis demonstrated multiple ischaemic lesions within the right kidney together with a mural thrombus of the supra-renal abdominal aorta. Considering the atypical nature and extent of this thrombus, she underwent further extensive assessment. She was found to be tall and of thin built with features of joint hyper-mobility. She did not meet the diagnostic criteria for Marfan's nor Ehlers-Danlos syndrome. Her mutation screen for Marfan's and the rest of her connective tissue disease screen were negative. An echocardiogram did not identify any thrombus and Holter monitor was normal. Her thrombophilia screen was largely negative except for a positive lupus anticoagulant which when repeated six months later had become negative.

Discussion: Although the exact process remains unclear, several mechanisms have been postulated to explain the link between SARS-CoV-2 and pro-thrombotic states(4). These include endothelial dysfunction causing microvascular thrombosis, as well as sepsis induced coagulopathy. Renal

infarction has been reported in some case studies (5,6)but remains a rare complication despite this patient's individual risk factors.

Renal hypoperfusion and cytopathic effects on the kidney tubular cells are thought to contribute to renal impairment in SARS-CoV-2 (5). In this case, the patient had preserved renal function, likely as a result of only one kidney being affected. It was suggested that a viral induced secondary antiphospholipid syndrome (APS) was the cause of her extensive thrombotic event. Transiently positive cardiolipin antibody and lupus anticoagulant have been seen in patients with HIV, EBV and SARS-CoV-2 infection (7,8). It is recognised that infection can cause an increase in lupus anticoagulant, which can then predispose patients to a clinical manifestation of APS(9).

This case highlights the risks associated in otherwise young and healthy individuals, who acquire mild SARS-CoV-2 infection and reinforces the benefits of vaccination. Renal infarction whilst rare, is a recognised complication of SARS-CoV-2 and in the context of extensive thrombotic disease other causes such as a secondary APS should be considered.

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Track L - Case Reports 2

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A rare case of Monoclonal gammopathy of undetermined significance causing large vessel vasculitis

Case reports

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Introduction: Our case is of interesting, rare, and serious complication of MGUS (Monoclonal Gammopathy of Undetermined Significance) of which there are minimal other case reports in published literature.

Case Report: A 59-year-old man presented with unilateral pain and discolouration of his 4th and 5th toes suggestive of digital ischaemia (Figure 1). This was accompanied by a history of general malaise, loss of appetite and weight loss. He had a past medical history of two unprovoked venous thromboembolisms (VTE) in the preceding 18 months and a history of MGUS with monoclonal IgG lambda paraprotein band. Initial investigations included a raised C Reactive Protein and Erythrocyte Sedimentation Rate alongside leucocytosis, thrombocytosis and normocytic anaemia A computerized tomography (CT) scan showed evidence of significant distal abdominal aortic wall thickness and proximal peroneal and anterior tibial arteries stenosis on the left, in keeping with inflammatory vasculitis. A full immunology screen was completed which included, connective tissue screen, complements, ANCA and lupus serology, which were all negative. Biopsy of the toes showed evidence of light chain and immunoglobulin deposition on immunofluorescence suggesting vasculitis secondary to his haematological diagnosis of MGUS. The patient was treated initially with high dose glucocorticoids with rapid improvement in his inflammatory markers. Further remission induction treatment consisted of Cyclophosphamide given as the CYCLOPS (1) regime and then later maintenance azathioprine. Treatment resulted in a significant improvement in his symptoms and features of digital ischaemia.

Discussion: MGUS is a preneoplastic plasma cell disorder. It exists on a spectrum of monoclonal plasma cell disorder along with smouldering multiple myeloma and multiple myeloma. The disorder is characterised by a serum monoclonal (M) protein of less than 3g/dL, bone marrow clonal plasma cells less than 10 % and an absence of plasma cell dyscrasia related end organ damage; hypercalcemia, renal failure, anaemia or lytic lesions. Vasculitis is a disease process characterised by inflammation and necrosis of vessel walls (2,3)). There are several types of vasculitidies which are classified by the size of vessel affected (4). There have been several case reports of MGUS causing small vessel vasculitis but case reports looking at MGUS in the context of large vessel vasculitis are seldom. There has been one case report of MGUS presenting at the same time as a giant cell arteritis in which it was hypothesised that the vasculitis was a result of an immune mediated response to cytokine production and amyloid deposits. In our case the biopsy showed deposition of kappa and

lambda light chains in the vessel wall despite only IgG lambda paraprotein being identified serologically.

Conclusion: Our case highlights a rare but potentially serious complication of monoclonal gammopathy of unknown significance. Using radiological imaging, and histopathology we have demonstrated a causative relationship between MGUS and large vessel vasculitis.

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Track L - Case Reports 2

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An unusual presentation of IgG4 related disease following SARS-COVID-19 infection in a patient who had previously been diagnosed with focal segmental glomerulosclerosis.

Case reports

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This case reports details a patient presentation who initially was diagnosed with focal segmental glomerulosclerosis (FSGS) and following relapse during SARS-COV-19 infection was diagnosed with IgG4 related disease, during which time he developed a paraprotein.

The patient initially presented at the age of twenty-four, with a medical history significant only for ulcerative colitis. He had typical symptoms of nephrotic syndrome and was diagnosed with minimal change disease following a kidney biopsy. A relapse of nephrotic syndrome led to a second kidney biopsy being undertaken, with findings consistent with FSGS. During this time, the patient did not respond to steroids but was responsive to ciclosporin and mycophenolate mofetil. However, following a further relapse after COVID-19 infection, immunological testing revealed a biclonal paraprotein, and both bone barrow biopsy and kidney biopsy showed IgG4 positive plasma cells and he was diagnosed with likely IgG4-related disease. Clinicians should be aware of evolving pathophysiology as well as relapses of nephrotic syndrome following COVID-19.

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Famciclovir as an alternative treatment in patients with aciclovir induced crystal nephropathy. A case report.

Case reports

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Background: Acute kidney injury is a well documented complication of aciclovir treatment. Medications that are insoluble in urine can precipitate within the renal tubules, leading to the formation of crystals within the kidneys causing crystal nephropathy. The risk of crystal formation increases with the presence of dehydration, underlying renal disease and alterations in urine pH that predispose to crystal precipitation 1 .These crystals can cause acute kidney injury (AKI) due to intratubular obstruction. Aciclovir is an antiviral medication is an insoluble medication that has been shown to cause crystal nephropathy. This process usually develops 24-48 hours post administration2.

Case Report: A 28 year old Caucasian female with a past medical history of primary ovarian failure, eczema and asthma presented to the emergency department with a 5 day history of progressively worsening facial blistering vesicles around her eyes and mouth which were confirmed as Herpes Simplex Virus (HSV1). She had been started on oral flucloxacillin and acyclovir in the community while swabs were pending without significant improvement. Baseline blood tests confirmed normal renal function (creatinine 42umol/l and eGFR >90) and on examination she was felt to be well hydrated. She was commenced on Intravenous aciclovir and flucloxacillin in the ED department.

1 hour into the IV aciclovir infusion, she developed severe, cramping abdominal and loin pain. A CT abdomen and pelvis was performed which showed bright bilateral swelling and oedema of the kidneys which involved the perirenal fat. No ureteric obstruction was identified and the renal veins were patient. Within 4 hours of the acyclovir infusion she had a stage 3 AKI (creatinine 172umol/l). Urine dip was positive for blood and protein.

A provisional diagnosis of crystal nephropathy from IV aciclovir was made. She continued to have a good urine output and she was commenced rapid fluid replacement with diuretics in order force a high volume diuresis. This was targeted to maintain a urine output of approximately 100-150mls/hour.

Outcome: 12 hours after the forced high volume diuresis, her creatinine continued to climb however at a slower rate (see Graph 1). Her renal function was monitored daily and rapidly improved over the next 72 hours. 96 hours after starting high volume diuresis, her renal function recovered to near baseline.

Aciclovir had been suspended at the time she developed AKI and abdominal pain, however her facial HSV infection continued to worsen without treatment. Given the proximity to her eyes a decision was made to start famciclovir. Her renal function remained stable and there was a gradual improvement in her HSV infection.

Conclusion: Early forced, high volume diuresis was invaluable in the management of this patient. The rapid onset of acute kidney injury and severe abdominal secondary to aciclovir related crystal nephropathy is rare, particularly in a well hydrated young patient with no pre-existing renal impairment. In this situation, oral famciclovir was tolerated as an alternative option to treat the patients' HSV in patients with recent crystal nephropathy.

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Track L - Case Reports 2

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A case of a bad hair day: tubulointerstitial nephritis following hair supplement use

Case reports

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A 65-year-old woman presented with a 10-week history of feeling generally unwell with persistent nausea, reduced appetite and reported weight loss of 15 kilograms. She described thinning hair for one year, but no other systemic symptoms. Her past medical history included type 2 diabetes mellitus, non-alcoholic fatty liver disease, hypertension and ductal carcinoma in situ in remission following radiotherapy and Letrozole. Her longstanding prescribed medications included metformin, ramipril, calcium carbonate and ergocalciferol, letrozole and rosuvastatin. On detailed questioning, she reported taking an over-the-counter hair supplement twice a day for the preceding few months.

Clinical examination showed her to be normotensive and euvolaemic. She had an active urinary sediment with 2+ blood and protein on dipstick analysis (uPCR of 96), no casts were seen on urine microscopy. Serum creatinine was 413 umol/L from a baseline of 77 umol/L five months previously. Aside from a new normocytic anaemia Hb 103 g/L, non-invasive autoimmune and myeloma screens were unremarkable. Renal tract imaging demonstrated no anatomical abnormalities nor obstruction.

We proceeded to native kidney biopsy which revealed an active tubulointerstitial nephritis (TIN) with well-preserved background parenchyma. She commenced a tapering course of oral prednisolone with a resultant improvement in serum creatinine to 161 umol/L over initial four weeks of treatment.

Her drug history was reviewed with her GP and confirmed no interim new/antibiotic prescriptions. It was felt the most likely culprit of her TIN was the hair supplement. Whilst the supplement itself has not been linked to TIN in the published literature, it contains several ingredients including horsetail extract (Equisetum arvense), cherry concentrate and vitamin C that have been associated with various renal pathologies.

The use of horsetail extract is not recommended in chronic kidney disease (CKD) due to the risk of hypoglycaemia. However, its use as a treatment for kidney disease has been supported in alternative medicine. Excess vitamin C intake has been associated with hyperoxaluria and TIN in numerous case reports, with some showing chronic use to cause an irreversible nephropathy. There are several case reports linking cherry concentrate to acute kidney injury (AKI) in patients with known CKD. TIN was reported in a patient with previous normal renal function due to use of supplements containing cherry extract, requiring a protracted course of steroid treatment. The postulated mechanism for this is by COX inhibition by anthocyanins from the extract.

In conclusion, this case of TIN is likely related to the use of a freely available hair supplement. Though we cannot be certain of the causative agent, the cherry extract contained therein is a probable culprit. This case also emphasises the importance of a detailed history in patients presenting with AKI including any illicit, herbal or over the counter remedies.

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Track L - Case Reports 2

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Spontaneous remission of Pure Red Cell Aplasia (PRCA) associated with Anti EPO antibodies in a patient receiving regular Haemodiafiltration

Case reports

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Diagnosis: A seventy-five year old man, who had been receiving Haemodiafiltration in a satellite dialysis unit for 2 years and 5 months, became symptomatically anaemic in November 2020, despite previously stable and effective ESA therapy for Renal Anaemia (RA). He was admitted to hospital for blood transfusion, and initial investigations demonstrated a severe reduction in reticulocyte count (consistently < 10x10^9/L). Cell counts were otherwise normal, Parvovirus B19 infection was excluded serologically, and no other known causes of isolated failure of erythropoiesis, haemolysis or blood loss were apparent. PRCA due to the presence of anti-Erythropoietin antibodies (anti-EPO abs) was confirmed serologically on 2nd February 2021(titre: 31.6 mcg/ml). ESA therapy was stopped.

Management: The diagnosis and potential further treatment options, including immunosuppression, were discussed with the patient. In the context of the ongoing COVID-19 pandemic, the patient was extremely reluctant to consider any immunosuppressive therapy, but preferred to have support for his haemoglobin with blood transfusions on dialysis, with an agreed threshold for treatment of Hb < 80 g/dl with symptoms of breathlessness or angina, based on symptoms he'd previously experienced at this level of anaemia.

Progress: Between the beginning of December 2020 and the end of July 2021 he received 16 whole blood transfusions of 2 units each. He experienced no new symptoms and received no other new therapies. In August 2021 he noticed he had become less symptomatic, and monthly blood tests showed a rise in reticulocytes to 34x10^9/L, the first time this parameter had been measure at a level greater than 20x10^9/l in 10 months. A progressive increase in reticulocytes has been observed, and in December 2021, his Hb reached the target range for therapy of Renal anaemia with ESA despite not receiving this therapy. He remains well and has not received a transfusion for 6 months

Comment: PRCA is a rare but well recognised complication of ESA therapy 1, mediated by Anti-EPO Abs, which necessitates discontinuation of this therapy. All commercially available ESAs have been associated with this phenomenon, and cross-reactivity of the Anti-EPO abs mitigates against switching to an alternative product due to likely clinical ineffectiveness and risk of anaphylaxis. In addition, Anti Epo Abs neutralise any residual native circulating erythropoietin, potentially rendering patients profoundly anaemic. Long-term transfusion requirements may lead to iron overload.

Several immunosuppressive regimes have been advocated, intending to suppress the anti EPO abs such that endogenous erythropoietin may become sufficiently abundant to reduce transfusion requirements, but reports are anecdotal and risk/benefit considerations are difficult to quantify. Reports of spontaneous recovery of PRCA to the extent described are extremely rare2, but this possibility should be taken in to account when evaluating treatment options.

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Track L - Case Reports 2

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Unmasking of Tangier disease in a patient with nephrotic syndrome

Case reports

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Nephrotic syndrome is associated with injury to podocytes and glomeruli and is associated with complications such as infection, thromboembolism and dyslipidaemia. Rarely, disorders of lipid metabolism, such as Familial lecithin-cholesterol acyl transferase (LCAT) and Apolipoprotein E (APOE) deficiencies, cause nephrotic syndrome with progressive kidney disease. Tangier disease - a rare condition belonging to the same family of lipid disorders - is not however associated with kidney disease. We report on a patient presenting with nephrotic syndrome, leading to the unmasking of Tangier disease.

A 34-year old man of Turkish origin presented with ankle swelling, fatigue and decreased exercise tolerance. He had no past medical history and a family history of unexplained splenomegaly. Examination revealed bilateral ankle oedema and splenomegaly. Urine dipstick was positive for blood and nephrotic-range protein. Blood results revealed hypoalbuminaemia (21 g/L), serum creatinine (61 µmol/L), hypertriglyceridaemia (13.0 mmol/L), undetectable high density lipoprotein cholesterol (<0.1 mmol/L) and normal cholesterol (4.1 mmol/L).

Kidney ultrasound was unremarkable. Acute serological screen was negative. Kidney biopsy showed membranous nephropathy with full house positive immunofluorescence. Investigations for secondary causes with computed tomography and nuclear medicine positron emission tomography imaging demonstrated enlarged retroperitoneal and mesenteric lymph nodes and splenomegaly suggestive of a lymphoproliferative disorder. Lymph node and bone marrow biopsies showed a "sea blue histiocytosis" with almost identical appearances of vacuolated histiocytes on both samples, suggestive of a storage or metabolic disorder. Whole genome sequencing revealed a pathological homozygous variant for ATP binding cassette subfamily A member 1 (ABCA1) c.1510-1G>A, consistent with a diagnosis of Tangier disease.

Further review of kidney biopsy did not show evidence of lipid deposits. The patient's renal function gradually declined (serum creatinine 133 umol/L) therefore he was started on rituximab.

Tangier disease (TD) is an extremely rare autosomal recessive disorder of lipid metabolism, with an estimated prevalence of less than 1 in 1,000,000 people. Typical presentation includes lymphadenopathy, hepatosplenomegaly, enlarged yellow-orange tonsils and peripheral neuropathy. Biochemical changes include thrombocytopenia, hypoalphalipoproteinaemia and hypertriglyceridaemia. Unlike in nephrotic syndrome, however, cholesterol remains normal.

The diagnosis of underlying or associated metabolic lipoprotein disorders remains challenging as they can be masked by similar lipid abnormalities characteristic of nephrotic syndrome. TD is not typically associated with renal disease apart from mild proteinuria. In this case it is, therefore, unclear whether the membranous GN is directly or indirectly related to Tangier disease or just two coincidental rare conditions. There has been progressive decline in renal function, and to reverse or prevent this, the patient has begun a trial of immunosuppressive treatment (rituximab).

In conclusion, this case highlights the importance of a logical stepwise clinical and biochemical assessment of patients with unexplained nephrotic disease. Metabolic disorders causing nephrotic syndrome are rare but should be considered in those with unexplained persistent nephrotic syndrome especially with progressive kidney disease and lipid deposition on renal biopsy. Tangier disease, unlike nephrotic syndrome, is associated with low or normal total serum cholesterol and the absence of hypercholesterolaemia in nephrotic syndrome should alert to the possibility of an underlying lipid metabolic disorder.

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Track M - Chronic kidney disease

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Chronic Kidney Disease optimisation in primary care.

CKD

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Introduction:Patients with Chronic Kidney Disease (CKD) have an increased mortality and morbidity.1 The literature states that the prevalence of CKD (G3a – G5) is between 11.4% and 13.6%. UK Nephrologists review patients with CKD G4 – G5, hence many patients with CKD are managed in primary care.

Objectives: To ascertain if CKD optimisation in primary care is beneficial for patients. CKD optimisation is a term coined by the authors; however, it links to principals within national and international guidelines which recommend that CKD patients have immunisations, BP controlled, secondary cardiovascular measures implemented, lifestyle enhanced and medication managed.

Methods: The project was conducted in a suburban GP practice. Adult patients, who were less than 70 years, with CKD (G3a – G3b) were identified (i.e. those patients managed by primary care with the lowest renal function). The project ran from 7th October 2019 to 14th August 2020. During this time, the project was designed, baseline audits completed, clinics created and conducted, patient care plans developed and utilised, audits re-run, results analysed, and the project collated. As the project was a service development it did not require ethics approval.

To assess CKD optimisation, eight parameters (CKD coding, influenza and pneumococcal vaccination, eGFR and ACR monitoring, statin prescribed, recent BP check and BP controlled) that were measured in the baseline audit were compared to results from the repeat audit. These parameters were assessed as being either optimised, needs improvement or suboptimal.

Results: A modified Emis search identified 23 CKD G3a – G3b patients who were less than 70 years old. All the patients were invited to attend a 30 minute kidney clinic appointment. 14 patients, i.e. 61% of patients, attended the clinic and were entered into the repeat audit. 8 CKD optimisation parameters were assessed per patient; therefore, there were a total of 112 parameters analysed. For these patients at baseline 25% (28/112) parameters were optimised, 4% (4/112) needed improvement and 71% (71/112) were suboptimal. Whereas the repeat audit established that 83% (93/112) parameters were optimised, 8% (9/112) needed improvement and 9% (10/112) were suboptimal.

Discussion: The project met its objective of demonstrating that CKD optimisation in primary care is beneficial for patients.

The limitations of the project were: 1) patients who were less than 70 years of age were included to ensure the project was completed in the necessary timescales 2) the clinic was stopped on 18th March 2020 due to the coronavirus pandemic and restrictions imposed on GP services2, thus affecting the number of patients included.

If the project is accepted for publication, it is hoped that it will be utilised by other GP practices to optimise CKD patients. If this occurred further research could be conducted assessing whether mortality and morbidity decreases with CKD optimisation.

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Track M - Chronic kidney disease

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Clinical utility of the Kidney Failure Risk Equation in advanced kidney care

CKD

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Introduction: The 4-variable Kidney Failure Risk Equation (KFRE) has been validated in multi-national populations(1), including the UK(2), to differentiate between patients with chronic kidney disease at risk of progression to end stage and those that are not. Whilst it is now incorporated into national guidance to assist referral from primary to secondary care(3), some authors have suggested KFRE could also aid in prompting earlier referral for dialysis access or transplant assessment in patients with advanced kidney disease(4,5). This study aims to quantify what benefit, in terms of time gains, could be achieved if KFRE criteria were adopted to help guide these referrals in addition to current practice.

Methods: All patients starting dialysis at a single nephrology unit from the 1st of January 2017 until the 30th September 2021, known for >90 days and who had suitable data-sets available for KFRE calculation, were identified using electronic records. One hundred of these patients were included in this study. KFRE scores were calculated based on the latest and, if possible, earliest assessments of proteinuria prior to dialysis initiation. Where unavailable, albumin:creatinine ratio values were calculated using an accepted protein:creatinine ratio conversion formula(6). Tests of discrimination (receiver-operator curve creation) and calibration (regression analysis) were performed. Patient clinical course was examined to extract dates and context around referrals for dialysis access, transplant assessment and outcomes. Patients who started dialysis via an unplanned access (n=19), or were referred for transplant assessment (n=49) had further KFRE scores calculated based on proteinuria assessments along their clinical time course. Using a suggested KFRE referral point, defined as a 2 year risk score of ≥40%, patients in these sub-groups were analysed to see if they met KFRE criteria for referrals earlier than actual referral dates.

Results: The 4-variable KFRE 2 and 5 year risk scores displayed strong discrimination in the sample (C-statistic = 0.837 & 0.851) and KFRE 2 year risk scores were acceptably calibrated to allow further analysis (R-squared = 0.931, β = 0.965). Proteinuria assessment and frequency varied greatly within the sample. Of 19 patients starting dialysis on an unplanned access, only 2 met KFRE referral criteria earlier than actual referral date by 29 and 112 days respectively. Lower KFRE cut offs would not have referred notably more patients. Of 49 patients to be referred for transplant assessment, 10 (20.4%) clinically appropriate patients would have met KFRE referral criteria earlier than actual referral date, with a median gain of 70 days (IQR 33.5 to 138.5) and this KFRE referral point would have been a median of 208 days prior to dialysis initiation (IQR 158 to 326).

Discussion: The results suggest that using KFRE based referral criteria alongside current practice may offer only modest advantages with regard to dialysis access referral but may have more of a role in referral for timely transplant assessment in advanced kidney care. KFRE criteria should not be used to guide referral in isolation however. Practices regarding proteinuria assessment and frequency would likely have to change in order for any gains to be maximised.

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Track M - Chronic kidney disease

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Inconsistency of CKD definition in pregnancy limits accurate assessment of pregnancy related outcomes in a systematic review.

CKD

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Introduction: Chronic Kidney Disease (CKD) is associated with adverse pregnancy-related outcomes. This systematic review and meta-analysis aimed to estimate the magnitude of the association between falling eGFR and rising proteinuria as defined by different CKD stages and maternal and foetal outcomes.

Methods: A literature search was performed using specific search terms, identifying studies where foetal and/or maternal outcomes in a group defined as CKD were compared with the general population. Studies were screened and data collection was performed independently by two separate authors. A meta-analysis of studies where the CKD population could be defined were performed for maternal and foetal adverse outcome. The definitions used were defined post hoc due to study reporting limitations. The definitions are ICD codes/medical records, biopsy proven, proteinuria, CKD 3-5 (equivalent) and CKD 1-2. All ratios are presented as odds ratios (OR).

Results: A total of 19 studies were included for analysis. The primary CKD categories used CKD 1-2 or 3-5 grouped populations were mostly .or entirely, these CKD stages. However, Incomplete reporting or heterogeneity in CKD definition between studies limited the ability to estimate the association between CKD stage and maternal and foetal outcomes precisely.

Populations with CKD 3-5 had a large increase in perinatal mortality (OR 12.68 [1.69, 95.13]) compared to CKD 1-2 studies (OR 2.22 [0.5, 9.97]) or CKD defined by proteinuria (OR 2.45 [1.05, 5.72]). There was substantial imprecision in the estimate for the association between CKD 3-5 and Preterm births <37 weeks (OR 20.97 [0.80, 547.80]), whilst the estimate for CKD 1-2 had a smaller magnitude but a tighter confidence interval (OR 5.35 [1.80, 15.94]). Similar results were also obtained for pre-eclampsia where CKD 3-5 equivalent population had wide confidence intervals compared to other groups. Furthermore, the confidence intervals of outcomes from CKD 3-5 predominant studies compared to CKD 1-2 studies overlap in outcomes such as perinatal mortality, preterm birth and pre-eclampsia.

Discussion: Recently published systematic reviews combined studies irrespective of CKD definition without accounting for CKD definition heterogeneity. Firstly, 6 studies used proteinuria in their CKD definition in ranges which can be physiological in pregnancy. The majority of these paticipants had diabetes which could also be a confounder. Secondly, many studies till date have included predominantly CKD 1-2 population which can cause inaccuracy in clinically significant estimation.

Finally, we identify that CKD 3-5 category might overlap with CKD 1-2 category for outcomes as above and have large confidence intervals. Hence, they may not be significantly different in comparison to each other. As it contradicts the expectation of worse outcomes for lower eGFR, it raises the possibility of an underlying process requiring investigation.

Conclusion: There is significant heterogeneity in CKD definition in pregnancy which limits the ability to draw meaningful results from existing data, emphasising the need for further, high methodological quality studies. The similarity of the association with maternal/foetal outcomes and CKD1-2 and 3-5 raises the possibility that a lot of the association described for CKD 3-5 may reflect confounding rather than a direct impact of lower GFR.

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Measurement of urine ACR for risk stratification of chronic kidney disease in primary care

CKD

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Introduction: Chronic kidney disease (CKD) is estimated to affect 10% of adults in England, and is predominately managed in primary care. Urine ACR (uACR) testing is recommended in current guidelines, to stratify risk and guide management.

Our group demonstrated in a 2007-13 cohort that uACR measurement in patients with biochemically-defined CKD was performed in just 35% of patients. ACR was more likely to be performed in younger patients, those with diabetes, and those registered as having CKD.

Historically, the CKD Quality Outcomes Framework (QoF) incentivised that all patients with CKD should be registered, have a uACR measured, and their BP treated to <140/90. However in 2015-16 the latter requirements were removed, with the QoF asking GP practices to simply register patients with CKD.

Updated NICE CKD 2020 guidelines stipulate that adults with, or at risk of, CKD should be risk stratified with a 4-variable (age, sex, eGFR and uACR) kidney failure risk equation. In order to allow such risk stratification, uACR is required.

We aimed to determine what proportion of patients coded with CKD in a large 2017-19 primary care cohort had had an ACR measured within a year.

Methods: A retrospective cohort of people over 18 who had been coded as CKD (CKD stage 3-5 using CKD-EPI eGFR) from routine clinical biochemistry data, was identified using The Care and Health Information Analytics (CHIA) database, a shared clinical record containing anonymised individual linked extracts of clinical records from 85 GP practices in Hampshire and laboratory data from 2 large hospitals, with a total registered population of approximately 700,000 people.

Descriptive statistics were used to analyse characteristics of individuals who had uACR within one year of the study start date (October 2017).

Results: 35,958 patients (5.1%) were registered as having CKD.

In patients who were registered as having CKD, 30.4% overall had an ACR within one year of the baseline. 59.2% of people with type 1 and 61.4% of people with type 2 diabetes had an ACR within the year, compared to 16.6% for people without diabetes.

Discussion: Identifying patients at risk of CKD progression is vitally important in primary care. Our analysis of this cohort demonstrated that CKD was likely to be under-detected. uACR, an essential component of risk stratification, remains poorly performed in primary care settings, especially in people with CKD who are not diabetic.

Greater understanding of the barriers to uACR measurement in primary care is essential to improve risk stratification, allowing targeted early intervention and patient education to slow progression of CKD and improve long term clinical outcomes.

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Primary care and CKD – what are the common questions? An analysis of GP referrals to the North West London 'Virtual' Kidney Care Clinic

CKD

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Introduction: The Renal Directorate at Imperial College Healthcare NHS Trust provides kidney care to approximately 2.4 million people in North West London. GPs can refer for specialist renal input via the electronic referral system. Most referrals do not require review in a specialist renal clinic and the consultant nephrologist can provide a consultation directly into the primary care electronic record (SystmOne and EMIS) within 48 hours of referral. An analysis of the referrals to the 'virtual' kidney care clinic was undertaken to understand the most common areas that GPs requested advice and guidance on.

Methods: 75 consecutive referrals in July-August 2021 were analysed. The analysis consisted of categorising what specific question the GP asked in their referral and what the consultant nephrologist reviewing the patient's GP record deemed to be the referral theme, and what advice was given.

Results: 75 referrals were analysed, and over half (40/75) of those patients were referred by the GP due to a decline in eGFR. Of those 40 patients, 15 had diabetes mellitus, and 9 had heart failure. The second most common reason individuals were referred (7/75) was due to US kidney abnormalities, including renal cysts, renal cortical thinning and loss of corticomedullary differentiation. Other common questions included asking for management advice for: acute kidney injury (5/75), increase in proteinuria in people with diabetes mellitus (4/75), advanced CKD in older adults (4/75), recurrent hyperkalaemia (3/75) and stable chronic kidney disease (3/75).

The most common nephrologist referral themes were as follows: optimising management of diabetic nephropathy (15/75), management of stable CKD (13/75), management of advanced CKD in older adults (11/75), change in eGFR associated with drug treatment in heart failure (8/75), AKI management (8/75) and US kidney abnormalities (3/75).

Discussion: The most common reason GPs referred patients to the kidney care team was due to concern over a decline in eGFR. The kidney care team assessed that these individuals most commonly had progressive diabetic nephropathy, stable chronic kidney disease, change in eGFR associated with drug treatment in heart failure or age-related decline in eGFR.

Following on from this analysis, an educational initiative is being developed in conjunction with primary care to provide the referrer with brief standardised advice, termed ‘educational cookies’, relevant to the question they are asking. This will be in addition to the patient specific consultation advice. These ‘educational cookies’ will be included in the advice given in the electronic patient record, with the intention of addressing educational needs in managing CKD in primary care in North West London.

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The Impact of UK Intra-laboratory Variation in Serum Creatinine and Urine ACR Assays on Kidney Failure Risk Equation Result

CKD

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Introduction: The updated NICE chronic kidney disease (CKD) guidelines have recommended the use of the 4-variable Kidney Failure Risk Equation (KFRE). The guidelines have also re-stated the recommendation that laboratories should use the CKD-EPI estimated glomerular filtration rate (eGFR) formula based on an enzymatic creatinine assay and laboratories should participate in a national External Quality Assessment (EQA) programme.

We aimed to study the impact of UK-wide intra-laboratory variation in serum creatinine and urine albumin-creatinine ratio results and the impact on KFRE results.

Methods: Data from two UK NEQAS schemes was used to model the impact of real world systems across three different analytical measurements, on seven different analytical platforms. The additive effect of each analytical measurement bias, imprecision and uncertainty was investigated when combined to give an approximate spread of data.

Results from two cases (April and August 2021) using serum creatinine and urine albumin creatinine ratio (ACR) from EQA specimens distributed through ISO17043:2010 accredited UK NEQAS schemes were used to calculate five year KFRE results. The specimens were chosen at concentrations that would calculate a KFRE close to the new 5% threshold for referral to secondary care.

Results: 157 and 159 matched data sets from the same laboratories participated in Case 1 and Case 2 respectively. Approximately 60% of UK laboratories use an enzymatic creatinine assay with the remaining 40% using compensated kinetic Jaffe. Table 1 shows a description of the cases and a summary of the results. The absolute range for eGFR was 10 mL/min/1.73 m2 in both cases.

Data by manufacturer and method (Figure 1) showed clustering of results, a common finding in EQA data due to the relative method biases. There is a big overlap between the enzymatic and compensated kinetic Jaffe data, indicating that it is not just the poorer, compensated kinetic Jaffe assay, that is causing the wide spread.

At a median 5 year KFRE of 5.8%, 5.1% of laboratories calculated a KFRE which is more than 1 percentage point below the threshold of 5% for referral, which is a potential clinical risk.

Though there is unwarranted variation in the creatinine results, the spread of the data is sufficiently tight to allow the output of the KFRE to remain a good predictive value in a broad range of healthcare environments

Conclusions: The vast majority of UK laboratories participate in the UK NEQAS scheme for serum creatinine. However, many laboratories continue to use the compensated kinetic Jaffe method despite UK NEQAS and NICE recommending that specific assays such as enzymatic assays are used. Variation in results also occurs between manufacturers leading to variation in KFRE results. National implementation of KFRE requires a consistent and coordinated approach. Laboratories should complete the transition to enzymatic creatinine assays.

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Update on the AFiRM study (Application of Functional Renal MRI to improve assessment of chronic kidney disease)

CKD, Diagnostics

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Background: The global burden of chronic kidney disease (CKD) is significant, affecting as many as 10% of the world's population. CKD can progress to kidney failure, increases cardiovascular risk and costs the NHS >£1.4billion annually. Better imaging methods to determine cause and prognosis of kidney diseases are required for improved patient stratification and targeting of current treatments, and to underpin new drug development to identify those most likely to respond to candidate therapeutics.

Current imaging techniques for the kidney are limited and cannot determine type or extent of renal injury. Renal Magnetic Resonance Imaging (MRI) has emerged as a versatile technique in which whole kidney structural and functional MRI measurements can be performed in a single multiparametric scan. This allows multiple aspects of the pathology that contribute to CKD progression to be assessed, including altered tissue microstructure (inflammation/fibrosis), oxygenation and perfusion.

The AFiRM study is funded by the NIHR Efficacy and Mechanism Evaluation (EME) Programme (project NIHR128494). It is a UK-wide multi-centre study to determine if multiparametric renal MRI can provide structural and functional assessments of the kidneys that deliver prognostic information and ultimately help guide treatment decisions. This abstract describes the study design and current progress since recruitment commenced in June 2021.

Methods: The AFiRM study has three stages.

Stage 1: A pilot phase to test patient tolerance, data completeness and central data collection processes. Stop-go criteria will be assessed in February 2022.

Stage 2: A multicentre, prospective cohort study of 450 people with CKD from 10 UK centres, with renal multiparametric MRI collected at baseline and Year 2. Annual follow-up visits will collect eGFR, albuminuria and change in clinical status until Year 4. Long-term outcomes will be determined with individual patient tracking of kidney failure events via the UK Renal Registry at Year 5 and 10. Cause

and effect between the renal MRI measures (alone and in combination) and the progression of CKD will be determined.

Stage 3: A mechanistic sub-study of 45 patients (from Stage 2) who have had a routine renal biopsy. Detailed comparisons will be made between multiparametric MRI and histopathological changes. Tissue blocks will undergo quantitative analysis of fibrosis, capillary density and inflammation using immunohistochemistry techniques.

Results: As of January 2022, 58 participants have been recruited from six UK centres. Mean age is 57 years, 34 (59%) are male and 9 (16%) have had a renal biopsy within six months prior to recruitment. Distribution across CKD stages is: stage G1/2 20%; stage G3A 26%; stage 3B 31%; and stage G4 23%. The most common identified causes of CKD are diabetic kidney disease (21%), IgA nephropathy (15%), and tubulointerstitial disease (12%).

Conclusions: The AFiRM study is a large-scale multicentre clinical study of renal multiparametric MRI in people with CKD, building on the UKRIN-MAPS MRC Partnership grant (MR/R02264X/1) to develop UK-wide, harmonised renal MRI capability with centralised image upload and storage, analysis and quality assurance. Recruitment to AFiRM is scheduled to complete in August 2023, after which results of the baseline measures are expected.

Links:

AFiRM study website: https://www.uhdb.nhs.uk/afirm-study/

UKRIN-MAPS website: https://www.nottingham.ac.uk/research/groups/spmic/research/uk-renal-imaging-network/ukrin-maps.aspx

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Using routine primary care data to explore renal function trajectories in chronic kidney disease

CKD

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Background: There has been relatively little exploration of renal function trajectories in early-stage chronic kidney disease (CKD) to date. Whilst progression of CKD to end stage renal disease is well recognised, some cohorts have shown that the renal function may remain constant or even improve over time. Quantifying long term renal function is challenging due to the natural variation in eGFR, which can make it difficult for clinicians to classify CKD stage. Understanding this variation in renal function may help to inform clinical decision making and early-stage CKD management.

Methods: A retrospective cohort of adults coded with CKD in primary care was identified from a Hampshire-based pseudonymised electronic primary care database containing clinical information and primary/hospital biochemistry data. Baseline was defined from October 1st 2017 to March 31st 2018, and follow-up from April 1st 2018 to October 1st 2019. Individuals were characterised into KDIGO CKD stage using the CKD-EPI formula by their first eGFR measurement in the baseline period, and throughout follow-up until their final eGFR measurement. Due to limited availability, urinary ACR measurements were not used to classify CKD stage. Descriptive statistics were used to analyse change in CKD stage during follow-up.

Results: 35,958 individuals were identified with CKD from which 773 individuals on renal replacement therapy, 13,586 individuals missing baseline and 2,161 individuals missing follow-up renal function were excluded leaving 20,211 people in the analysis. At baseline, 691 (3.4%) individuals were in CKD stage 1, 5,791 (28.7%) in CKD stage 2, 6,680 (33.1%) in stage 3a, 4,855 (24.0%) in stage 3b, 1,860 (9.2%) in stage 4 and 334 (1.7%) in stage 5. Over two-thirds of participants in baseline stage 3a (n=4,661, 69.8%), stage 3b (n=3,439, 70.8%) and stage 4 (n=1,291, 69.4%,) changed CKD stage at least once during follow-up, with a minority (n=4,004) remaining exclusively in their baseline stage. Notably 3,792 (18.5%) individuals' last follow-up CKD stage was higher than their baseline stage, and 3,983 lower (19.7%).

Conclusion: In CKD, transition of CKD stage is common and thus a single blood test should not be used to classify CKD stage. An agreed definition of stable or rising eGFR is required, in addition to exploration of factors associated with this period. A key limitation was the use of a single eGFR measurement to classify baseline stage with guidelines recommending two measurements spaced in time for CKD diagnosis. Secondly, there was potential selection bias introduced with the exclusion of those without renal function measures.

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COVID-19 treatments in non-hospitalised patients: A South West Wales Renal Service experience on identifying, triaging, treating and outcomes.

COVID-19 including vaccination

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COVID-19 presents a significant risk of complications, hospitalisation and death in people with renal conditions. A Renal Pharmacist led COVID-19 service was established in December 2021 to identify, triage and treat people with CKD in the community for COVID-19. People on unit haemodialysis present a logistical challenge for treatment; offering treatment on routine dialysis session was established. The public and clinician awareness and access to these new treatments was limited at this time. A patient education animation was created to raise awareness and to enable informed consent. Treatment options included a neutralising monoclonal antibodies (nMAb) infusion or oral antivirals. This review evaluates the responsiveness of this service, measured against; i) time to treatment from symptoms onset ii) time to treatment from PCR and iii) 14 day outcomes for patients treated.

During the first month of establishing the service (January 2022), 463 patients with CKD known to the renal service were identified as having COVID-19 by way of PCR, using a daily data extraction from the renal electronic patient record database. 35 patients thought to be eligible for treatment were then contacted by a Pharmacist to establish if they were symptomatic and the date of onset. Patients were offered treatment if they met treatment criteria. Patients triaged for treatment included 17 unit haemodialysis (HD), 11 transplant recipients, 1 peritoneal dialysis and 6 patient with CKD on an immunosuppressant. A further 42 identified were inpatients and not part of the treatment criteria.

Following triage, 18 patients received sotrovimab (nMAb), 5 of which were on unit haemodialysis. 3 patients received molnupiravir (antiviral), 1 of which was on unit haemodialysis. 10 patients did not receive treatment as they did not meet treatment criteria, asymptomatic (n=6) or beyond treatment window (n=4). 3 patients declined treatment and 1 patient died prior to triage of a non-COVID cause.

The mean time to treatment from onset of symptoms was 3.1 days for the population and 3.1 days for the HD cohort. The mean time to treatment from PCR was 1.6 days for population and 2 days for HD cohort. Outcome at day 14 was assessed, 20 patients (95%) recovered without further clinical intervention and 1 patient who received nMAb on dialysis required radiological imaging due to ongoing shortness of breath then subsequently recovered.

This method allows for rapid identification of patients with COVID-19 under the care of the renal service. Being able to treat people whilst they receive their routine unit haemodialysis ensures

access equitability compared to the CKD population. This review has shown patients who received treatment on haemodialysis do not appear to be significantly disadvantaged in time to treatment metrics and prevented further clinical deterioration. An animation of treatment options and accessing services, which was given to patients ahead of triage, is an effective tool in allowing patients to make an informed decision for treatment whilst improving efficiency of clinician time. This resulted in a treatment acceptance rate of 87.5% of patients eligible.

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HLA Alleles Associated with COVID-19 Susceptibility and Severity

COVID-19 including vaccination

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The COVID-19 pandemic has caused a significant loss of life globally. Chronic kidney disease patients have been identified as particularly susceptible to both infection and mortality, with the highest risk in dialysis patients who additionally were unable to shield. The burden of disease has not been uniformly distributed, and as a result there has been considerable interest in genetic factors which may influence susceptibility to and severity of COVID-19 infection.

The human leucocyte antigen (HLA) transmembrane proteins present pathogen derived peptides to T-cells. They are highly polymorphic resulting from adaptation to environmental pathogens. HLA genes have previously been associated with a number of other infectious diseases. This study aimed to identify any HLA alleles associated with susceptibility to or severity of COVID-19 disease in our dialysis patients.

All prevalent dialysis patients on March 1st 2020 who had previously had HLA typing performed by either Sequence Specific Oligonucleotides (SSO) or Next Generation Sequencing (NGS) were included in the study (n=327). The COVID-19 cases were identified by either polymerase chain reaction (PCR) or positive anti-nucleocaspid protein (anti-NP) serology. Clinical data related to their infection was collected from the electronic patient record system, and cases were classified as either mild (outpatient management) or severe (inpatient management). For each patient the number of copies of an HLA allele was counted as a dose, and this was used as the predictor variable for logistic regression analysis carried out using R (version 4.1.2). Odds were adjusted for age, gender, ethnicity and waitlist status (used as a surrogate for fitness).

After adjustment 6 HLA alleles were associated with an increased risk of infection: HLA-A*02:06 (OR 10.98, p=0.02), HLA-B*15:02 (OR 6.78, p=0.016), HLA-B*40:06 (OR 2.26, p=0.039), HLA-C*08:01 (OR 4.57, p=0.08), HLA-C*17:01 (OR 4.34, p=0.028), and HLA-DRB1*14:04 (OR 3.21, p=0.028). 4 HLA alleles were associated with a decreased risk of infection: HLA-A*26:01 (OR 0.173, p=0.002), HLA-B*08:01 (OR 0.54, p=0.049), HLA-C*07:01 (OR 0.58, p= 0.047), and HLA-C*12:03 (OR 0.37, p=0.037). 2 HLA alleles were associated with an increased risk of severe infection: HLA-A*01:01 (OR 2.31, p=0.041) and HLA-DRB1*11:04 (OR 6.89, p=0.038).

Our study has shown a potential role for patient HLA affecting the likelihood of being infected with SARS-CoV-2 and the severity of the infection. The higher number of associations of HLA Class I alleles is consistent with data showing the importance of CD8+ T cells in COVID-19 infection.

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Evaluating the long-term effects of COVID-19 vs the presence of uraemic symptoms for patients with end stage renal disease receiving haemodialysis

COVID-19 including vaccination

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Introduction:Uraemia is a clinical condition associated with decline in renal function. It is characterised by dysfunction in acid-base homeostasis, fluid and electrolyte regulation, hormone production and waste elimination. Uraemic symptoms most commonly occur in patients with chronic kidney disease and end-stage kidney disease (ESKD). Uraemic symptoms tend to arise at a creatinine clearance of less than 10ml/min. COVID-19 infection has been associated with the development of a syndrome of persistent signs and symptoms. NICE have defined post-COVID-19 syndrome as “signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis”. This syndrome is often called “long COVID”. A lot of the symptoms that patients with ESKD have can overlap with those of long COVID. NICE have recommend the use of a screening questionnaire to help identify all of a patient’s symptoms. Many of the symptoms listed in these questionnaires overlap with those that an ESKD patient would experience due to uraemia. The aim of this study was to see if a validated questionnaire used to identify post-COVID-19 syndrome in the general population can differentiate whether haemodialysis patients were experiencing post-COVID symptoms or uraemic symptoms.

Methods: Patients undergoing chronic haemodialysis were given the COVID-19 Yorkshire Rehabilitation Scale questionnaire to complete. This questionnaire has been validated as a clinically useful measure of post-COVID symptoms in a general population. It consists of 14 questions that identify and evaluate current and pre-COVID symptoms. Responses were obtained from two patient groups – those with a history of prior COVID-19 infection more than 12 weeks ago (confirmed by PCR), and those with no history of infection. The prevalence of symptoms such as anorexia, nausea, pruritus, breathlessness, fatigue and muscle pain was evaluated in both patient groups.

Results: 10 patients were identified to be included in this study. 6 patients had a history of COVID-19 infection with a confirmed positive PCR result. 4 patients who had never contracted COVID-19 were included as a control group. In the covid and non-covid populations respectively, the median age of participants was ¬¬59 and 54 years. The data collected from the study is included in the tables attached. The data highlights the similarities of symptoms experienced by both groups. Information on primary renal diagnosis and dialysis access of patients in each group is also included.

Conclusion: The burden of uraemic symptoms among patients on dialysis is substantial and may have been impacted by covid-19 infection. Uraemic symptoms are a major contributor to the poor health-related quality of life experienced by patients on dialysis. This study has two principal findings: for haemodialysis patients the symptoms of long COVID and uraemia overlap, and the screening tests used to identify long COVID symptoms are not specific for this population. Identification of the post-covid-19 syndrome can enable a multi-disciplinary team approach towards management and rehabilitation in terms of the physical, psychological and psychiatric aspects of the condition. New tools to identify long COVID in patients on haemodialysis are needed.

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Omicron is far less of a problem in vaccinated dialysis patients compared to previous COVID strains

COVID-19 including vaccination

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Introduction: In 2021 we reported the mortality of the first waves of COVID19 in ~1300 prevalent dialysis patients, and on the antibody efficiency of the SinoPharm vaccine in this patient group. Whilst spike antibody levels were induced in ~50% of patients after a primary course we saw an increment in antibody levels in most patients and we subsequently ensured that all dialysis patients were offered a booster dose The efficacy of the SinoPharm vaccination was well demonstrated in a normal population in previous waves, but it is unclear how protective vaccination was against serious disease and death with subsequent waves.

Methods: We looked at the mortality in dialysis patients with and without vaccination during the various waves of COVID19. More recently we noted a further large wave of cases infected largely with the Omicron (B1.1.529) variant of COVID-19, despite vaccination and booster doses. Whilst the scale of this infection exceeded previous waves in terms of numbers and rapidity of infection, and this stretched our isolation capacity, it was not clear how mortality would change.

Results: Compared with previous waves, most dialysis patients experienced mild disease. To date, no dialysis patient has died from COVID or its complications in the recent wave (fig 1).

Conclusion: Given the previous waves were associated with appreciable hospitalisation and deaths, the Omicron variant was associated with increased infectivity but did appear far less dangerous in Sinopharm vaccinated dialysis patients. There is little data available on the efficacy of this vaccine on this variant in preventing severe disease.

Explanations for this phenomenon include an almost 100% vaccinated dialysis population, survivor effects or a viral strain that produced considerably attenuated disease. Given the 36 mutations in the spike protein in the Omicron variant, monoclonal antibody responses to mRNA vaccines may have been suboptimal, whilst polyclonal antibodies may have been induced by killed virus and adjuvant.. Whilst vaccination did not have any clear effect upon acquisition of the virus, mortality and morbidity were strikingly attenuated. We speculate that the SinoPharm may have induced a robust T-cell response to variants with spike protein mutations, like Omicron, to prevent severe complications in vulnerable groups.

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Breakthrough SARS-CoV-2 infection after second COVID-19 vaccination in populations with chronic kidney disease in England: a cohort study from OpenSAFELY

COVID-19 including vaccination, Epidemiology, public health and prevention

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Background: As non-pharmaceutical public health interventions in England are being phased out, there is an imperative to better understand risks of breakthrough infection, hospitalisation and death in patients with chronic kidney disease (CKD) after COVID-19 vaccination. We used a primary care database with coverage of approximately 40% of the population of England to describe the incidence rates of outcomes in CKD patients.

Methods: The OpenSAFELY-TPP primary care data was linked to secondary care, SARS-CoV-2 testing, and death registration data. We included individuals who had received two doses of a COVID-19 vaccine and remained alive and without evidence of SARS-CoV-2 infection within two weeks of vaccination, with follow-up up to 1 November 2021.

To measure public health burden, we summarised rates of outcomes (SARS-CoV-2 infection, COVID-19 hospitalisation and COVID-19-related death). We obtained age-adjusted hazard ratios for each outcome by CKD stage using a Cox regression model for those not on dialysis or with kidney transplant.

Results: Results are summarised in Table 1. Of approximately 24 million people, over 15 million had received two COVID-19 vaccine doses. The incidence of SARS-CoV-2 infection was higher in dialysis and transplant patients compared to those not on renal replacement therapy, with the highest rate per 1000 person-years found in transplant recipients who had previously been on dialysis at 142.9 (95% CI 137.9-111.9).

COVID-19 hospitalisation increased by CKD stage. Rates per 1000 person-years remained high in patients on dialysis or with kidney transplant, highest in dialysis patients who had previously had a kidney transplant at 39.2 (95% CI 33.8-45.5), compared to 2.2 (95% CI 2.1-2.2) in those without CKD.

COVID-19 death rates also increased by CKD stage, with similar rates in people with kidney transplant as those at CKD stage 5. The highest rate of death per 1000 person-years was in dialysis patients with a previous kidney transplant at 14.7 (95% CI 11.5-18.7).

Among people not on dialysis or with kidney transplant, age-adjusted hazard ratios for SARS-CoV-2 infection were lower in people with CKD stages 3A, 3B and 4 compared to people without CKD, but

increased at CKD stage 5 (figure 1). The age-adjusted hazard ratios for hospitalisation and death, both increased by CKD stage to almost 4 times in people with CKD stage 4 and over 8 times in people with CKD stage 5.

Discussion: After two doses of a COVID-19 vaccine. people with CKD had higher rates of COVID-19 hospitalisation and death compared to those without CKD. Rates of hospitalisation and death were highest amongst people with CKD stage 5, dialysis patients and kidney transplant recipients.

National level electronic health record data can be rapidly described to inform policy making with respect to clinically vulnerable groups. We are currently evaluating the impact of additional primary and booster vaccine doses, and comparing vaccine types.

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Breakthrough SARS-CoV-2 infections in fully vaccinated kidney transplant recipients

COVID-19 including vaccination, Transplantation - research

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Introduction: Data from the first wave of the SARS-CoV-2 pandemic showed that kidney transplant recipients (KTRs) had relatively low infection rates (likely due to measures such as shielding and mask wearing) but high mortality when infected. A massive vaccination effort ensured rapid vaccine roll out; unfortunately, approximately 50% of transplant recipients do not mount an antibody response. What is unknown is whether vaccines still have some effect at preventing severe infections or deaths despite an unmeasurable antibody titre.

Methods: Prospective data was kept on all KTRs with SARS-CoV-2 infection and vaccination. Baseline and post vaccine serology was collected. Further information was gathered from the electronic health record.

Results: Of 2100 kidney transplant recipients in follow up, 32 have been admitted to hospital with SARS-CoV-2 following vaccination (14 days post second dose). 66% were male, the mean age was 56. The majority of these (23, 71.8%) were maintained on tacrolimus and an anti-proliferative ± steroids. Only 7 (21%) had detectable antibodies following vaccination. 84% had severe infection requiring oxygen or ITU admission. 12(37.5%) died.

Those who died were older (63 v 52 years, p 0.008) and less likely to be white (table 1). Maintenance immunosuppression, vaccine type and time since transplant were not significantly different between the groups.

During the first wave we had a 42.5% mortality rate from COVID, post vaccination our mortality rate remains high at 37.5% (figure 1).

Discussion: Severe COVID remains a threat in our immunosuppressed population with a mortality rate similar to that seen pre vaccination. Only 21% of these patients with breakthrough infection have detectable antibodies compared to 55% in our overall KTR population; this suggests patients with negative serology are at high risk of breakthrough infection. This high risk group should be prioritised for prophylaxis

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Changes to the incident and prevalent kidney replacement therapy populations during the first year of the COVID-19 pandemic.

COVID-19 including vaccination, Epidemiology, public health and prevention

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Introduction: The last two years have seen abrupt and unprecedented changes to the population reaching and living with kidney failure, and to the health services available to them. The first UK COVID-19 case was confirmed on 29th January 2020, and the first deaths in March. It rapidly became evident that people with kidney disease were at elevated risk. Older people and those with chronic kidney disease, diabetes, and hypertension are more likely to die following infection. COVID-19 causes acute kidney injury associated with poor outcomes. Those receiving in-centre haemodialysis (ICHD) are 45 times more likely to die from COVID-19 than the general population. Once baseline health is considered, those with kidney transplants are at even higher risk. Those with kidney failure were deemed Clinically Extremely Vulnerable and advised to shield. Kidney units endeavoured to provide safe care despite overburdened services and incomplete evidence as to which policy provides best protection against nosocomial transmission. Transplantation was interrupted unevenly across the country and in mid-April 2020, just three UK transplant centres were active. Since surveillance began, 16,146 people with chronic kidney disease and kidney failure have been reported to the UK Renal Registry as having had COVID-19, of whom 2,661 (16.5%) died. This analysis charts the shifts in dialysis and transplant provision between 2019 and 2020.

Methods: The UK incident (first transplanted or starting dialysis) and prevalent (already transplanted or receiving dialysis) kidney replacement therapy (KRT) populations were compared between 2019 and 2020. Individuals were stratified by the modality of kidney replacement therapy: ICHD; home haemodialysis (HHD); peritoneal dialysis (PD); and transplant (Xp). Changes to treatment modality pre- and mid-pandemic were compared by tabulating modality transitions over the subsequent six months for individuals receiving KRT in June 2019, and in December 2019.

Results: The total population incident to KRT fell from 8,070 in 2019 to 7,373 in 2020. There was a drop in incidence to ICHD from 5,682 to 5,244. Pre-emptive transplant fell from 675 to 438. PD incidence appeared stable (1,634 vs 1,629). Contrasting with the typical annual rise, the prevalent population was essentially stable (68,146 to 68,249), explained by a decline in the ICHD population (24,372 to 24,155) and a rise in the population receiving PD (3,636 to 3,822). The transplanted population rose marginally from 38,742 to 38,895. Analysis of modality changes showed the documented increase in mortality amongst those receiving ICHD (9.0 - 11.9%) and the transplanted

(1.7 – 2.1%). There was also a sharp drop in transplantation of individuals undertaking all dialysis modalities (ICHD 3.9 – 2.3%; HHD 6.0 – 3.4%; PD 7.8 – 4.9%).

Conclusion: In the first year of the UK COVID-19 pandemic there were changes in the makeup of the incident and prevalent KRT populations, reflecting the high mortality amongst the clinically vulnerable – both those already receiving KRT, and those who may have reached kidney failure had they survived. The sharp drop in transplantation and maintenance of home dialysis rates likely reflect service changes adaptive to novel demands and attempts to protect individuals from COVID19.

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Evaluating optimal time interval of SARS-CoV-2 vaccine doses post-transplant

COVID-19 including vaccination, Transplantation - research

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Introduction: In general pre-transplant immunisation results in more robust immune responses which continues to provide protection in the post-transplant setting. For vaccinations which require repeat administration, there is lack of evidence for the optimal timing of inoculation.

We present our preliminary analysis of the dynamics of SARS-CoV-2 serological responses post-transplant and following administration of 3rd primary doses in newly immunosuppressed patients.

Methods: All patients had received 2-doses of a SARS-CoV-2 vaccine pre-transplant. Patients had serological testing pre-transplant, and again at a median time of 48 (32-67) days post-transplant and/or 22 days (14-30) following 3rd-dose vaccine. Spike protein antibodies (anti-S) were detected using the Abbott assay (positive cut-off 7.1 BAU/ml).

Results: In 46 patients (13 with prior exposure), median anti-S concentrations waned post-transplant; 1154(215-4274) and 459(75-2794) BAU/ml, p=0.0002, in the exposed group; and 87(30-938) and 30(9-251) BAU/ml, p<0.001, in the non-exposed groups at baseline and follow-up respectively (Figure 1). 6/46 (13.0%) were anti-S negative at follow up, with 3 patients being non-responders pre-transplant. 22/46(47.8%) had anti-S >234 BAU/ml (surrogate level for protection) pre-transplant, with only 4/22(18.2%) falling <234 at follow up. Of 40 patients receiving 3rd-vaccine doses post-transplant, 15/40 (37.5%) became 'boosted' (had increased anti-S). Variables associated with boosting included time to 3rd-vaccine, no-prior COVID-19, ChAdOx1 priming and immunosuppression minimisation. ChAdOx1 priming independently associated with 'boosting', OR 7.35 (1.4-54.0), p=0.03.

In patients who received a 3rd-dose vaccine within the first 3-months, anti-S remained significantly lower compared with pre-transplant, median 530(63-2458) and 308(37-1394) BAU/ml respectively, p=0.02.

Conclusion: Preliminary results of this ongoing study suggest that anti-S wanes post-transplant. 'Boosting' pre-transplant may be beneficial in providing protection for the early post-transplant period where responses to 3rd-doses are weak. The study also highlights the benefit of mixing of vaccines to maximise immune responses in transplant recipients.

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Impact of COVID-19 on patient reported experience of kidney care in 2020: a qualitative analysis

COVID-19 including vaccination, Patient outcome and experience

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Introduction: In 2020 COVID-19 overwhelmed healthcare settings, changing how healthcare was delivered and consequently patient experience of kidney care. Since 2016, kidney patients could report their experience in the annual Kidney Patient Reported Experience Measure (Kidney PREM), facilitated by the UK Kidney Association (UKKA) and Kidney Care UK (KCUK). Kidney PREM is a 39-item survey, covering 13 themes of care. Due to the pandemic, Kidney PREM was online only in 2020. In addition to the usual free-text question about other comments regarding their kidney care, four questions exploring the impact of COVID-19 were introduced.

Methods: Of the new questions, one was scalar asking participants to rate their experience of care during COVID-19 from -3 (much worse) to +3 (much better). The remaining three were free-text: 'What was good about your experience of kidney care during COVID-19?', 'What was bad about your experience of kidney care during COVID-19?', and 'What could have been done, if anything, to make your experience of kidney care better during COVID-19?'. Using computer-assisted coding software, QDA Miner, comments were filtered, clustered, and coded under the 13 Kidney PREM themes or emergent themes as appropriate. To better understand how COVID-19 had impacted patient experience of kidney care, codes were analysed by treatment type.

Results The scalar question elicited 7,071 responses. Most reported that their care had remained the same (Figure 1), but 28.5% of CKD patients reported a worse experience of care compared to just 7.1% of satellite and 10.3% of hospital haemodialysis. 'What was good about your experience of kidney care during COVID-19?' elicited positive comments and examples about how well staff had cared for them during COVID-19. 'What was bad about your experience of kidney care during COVID-19?' revealed concerns about long waiting times within units, the dearth of face-to-face appointments, difficulties contacting the renal team and lack of mental health support. Areas suggested for improvement included the need to ensure that unit staffing matched the needs of patients – though such comments were often linked to positive comments about staff and the need to improve communication with staff. There were differences by treatment modality. Patients living with CKD and transplanted patients, were most concerned about lack of opportunity for face-to-face

appointments and about difficulties contacting the renal team. This also concerned patients on home therapies, though most were appreciative of being able to continue their treatment at home. Patients receiving hospital and satellite haemodialysis were generally grateful for the care and support received, though lack of discussion about changes to service provision and lack of consultant presence during dialysis sessions, were raised as concerns.

Discussion: Perhaps the most notable aspect of the findings is that in spite of the major disruption caused by the pandemic, the majority of patients reported that there had been no change in their kidney care experience. There were some overall differences in relation to treatment modality, likely relating to differences in direct access to care. Learning from this could be important in shaping future responses to service disruptions.

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Use of intravenous Sotrovimab in non-hospitalised in-centre haemodialysis patients with COVID-19 – a single centre experience.

COVID-19 including vaccination

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Introduction: COVID-19 disproportionately causes hospitalisation and severe disease in those with underlying health conditions, including patients with chronic kidney disease (CKD)1. Neutralising monoclonal antibodies (nMABs) are synthetic monoclonal antibodies that bind to the spike protein of SARS-CoV-2, preventing entry of the virus into the host cell and its replication2. The nMAB, sotrovimab has recently been shown in an interim analysis of a multicentre, double-blind, phase 3 trial to effectively reduced the risk of hospitalisation or death by 85% in high-risk individuals (≥55 years; diabetes requiring medical intervention; body mass index >30; CKD (Glomerular filtration rate <60mls/min/m2); congestive heart failure or obstructive airway disease)3. From December 2021 sotrovimab was available for use as a first line treatment in the UK for non-hospitalised COVID-19 positive patient considered high risk for severe disease and where contraindicated molnupiravir, an antiviral could also be offered as an alternative. We retrospectively examined our use of these medications in a cohort of haemodialysis patients with COVID-19.

Methods: In this retrospective study we reviewed all in-centre haemodialysis patients with a positive SARS-CoV-2 PCR between 16th December 2021 and 18th January 2022 who were eligible for administration of nMAB therapy. Patients receiving immunosuppression for autoimmune disease or renal transplantation were excluded, as well as those who received in-hospital nMAB. Peritoneal dialysis patients were excluded due to low infection rate (2.5%). Data collection included patient demographic, receipt of sotrovimab or molnupiravir, quantified spike antibody, SARS-CoV-2 genotype and admission to hospital in subsequent 28 days following COVID-19 symptoms. The local covid medicines delivery unit (CMDU) were involved with providing the medications. Sotrovimab was administered as an infusion in 100mls 0.9% normal saline in the last 60 minutes of dialysis.

Results: 71 (14%) in-centre haemodialysis patients tested positive for COVID-19 from a cohort of 507 between 16th December 2021 and 18th January 2022. 63 (88%) of eligible patients received treatment; 59 patients (93.7%) received sotrovimab and 4 patients (6.3%) received molnupiravir. Mean age was 61.8 years (15.8). 68% (n=42) affected were male and 32% (n=20) female. Six patients (12.7%) were admitted in the 28 days following treatment and included chest pain (n=1); increasing falls (n=1); acute stroke (n=1); bacteraemia (n=1) and complications of dialysis (n=1). No patients required oxygen therapy or admission to intensive care. 51 (80.9%) patients had spike antibody results available all of which were positive with mean titres of 1859.3 (919.9). 71.4% of

positive SARS-CoV-2 PCR were confirmed to be Omicron variant on genotyping. 1.6% were confirmed Delta variant. Sotrovimab was well tolerated with no reported side-effects. One patient who received molnupiravir reported dry throat and nausea and did not complete the course.

Discussion: In our experience sotrovimab was well tolerated in our haemodialysis population. 12.7% of patients were admitted to hospital for any cause within 28 days of receiving sotrovimab or molnupiravir, of which none required oxygen therapy or admission to ITU. The primary reason for the five admissions were not consistent with progression of COVID-19 indicating that sotrovimab is effective in reducing risk of severe disease.

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Changes in health and lifestyle behaviours of people living with kidney disease as a result of the COVID-19 pandemic

Patient outcome and experience, Rehabilitation, exercise and lifestyle

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Introduction: During the COVID-19 pandemic, the UK implemented lockdown measures to minimise the spread of the virus by limiting travel, socialising, and physical activity. For people considered 'extremely vulnerable', such as those with chronic kidney disease (CKD), a shielding programme was implemented. These measures impacted people's daily lives and disrupted their ability to maintain positive lifestyle behaviours such as being active and eating healthily. Patient activation is the term used to describe the knowledge, skills, and confidence to engage in health-promoting behaviours. Patients with higher activation levels may be expected to manage their health better during stressful times, but there is limited evidence on the impact of COVID-19 on the lifestyles of those with CKD. As such, this analysis explores changes in lifestyle behaviours during the pandemic across different levels of patient activation in people with non-dialysis CKD (ND-CKD) and kidney transplant recipients (KTR).

Methods: 234 participants (mean age 63.2 (±11.2) years, 55% male, 51% KTRs) completed a bespoke online survey, between May and June 2021, about changes to their health and lifestyle behaviours during the pandemic. Patient activation was assessed using the Patient Activation Measure (PAM). Respondents' agreement to statement of PAM questions 10 (ability to maintain lifestyle) and 13 (confidence to maintain lifestyle) were classed as binary (I.e., 'disagree' and 'agree'). Chi-squared analysis was conducted to compare changes in health and lifestyle behaviours (i.e., alcohol consumption, physical activity, and diet) between those who agreed and disagreed with PAM questions 10 and 13.

Results: A total of 67/234 (29%) participants reported self-isolating during the pandemic; 28 (42%) of these reported shielding with others in their household. 182/234 (77%) participants reported feeling able to maintain lifestyle behaviours and 175/234 (75%) reported feeling confident about maintaining lifestyle behaviours during stressful times.

General health and physical activities were more frequently reported to decline during the pandemic than kidney health and other lifestyle behaviours by all groups.

A greater proportion of those who felt they were able to maintain lifestyle behaviours (on the PAM) reported improvements in eating habits ($P<0.001$), physical activity levels ($P<0.001$), and general

health (P<0.001). Individuals who were confident in maintaining lifestyle behaviours also reported improvements in eating habits (P<0.001) and physical activity levels (P=0.001). Those unable to maintain lifestyle behaviours reported declines in their general health (P=0.041) and kidney health (P=0.023).

Conclusion: The findings highlight that although most participants reported feeling confident and able to maintain lifestyle behaviours, some participants' lifestyle behaviours got worse during the pandemic. Regardless of activation, general health and exercise behaviours were the most frequently reported to decline. Our findings are similar to those reported in the general population, older people, and other long-term conditions, including diabetes. Identifying people with lower levels of activation, or who score low on questions 10 and 13 of the PAM, can indicate those who need additional support to prevent deterioration in lifestyle behaviours in difficult and challenging circumstances. Interventions to improve activation and self-management may assist with increases in confidence and ability to maintain healthy lifestyle behaviours.

Keywords: Kidney disease, Patient activation measures, self-management, lifestyle changes, COVID.

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Differences in the validity of 'remote' versus 'in-person' physical function testing in people living with non-dialysis CKD

Behavioural, psychological and quality of life, Rehabilitation, exercise and lifestyle

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Introduction: People living with non-dialysis chronic kidney disease (CKD) often display reduced physical function, which may contribute to poor quality of life (QoL). The sit to stand 60 (STS-60) is a simple, equipment-free, objective test to assess functional status. The increased requirement for remote patient management introduces the need for valid methods to measure functional status remotely. However, there is limited empirical evidence on the validity of remotely assessed physical function. The 12-Item Short-Form Health Survey (SF-12) is a commonly used QoL measure, and it also assesses functional status through its physical function (PF) domain. In the present analysis, we compared the validity of a 'remote' non-supervised and 'in-person' supervised STS-60 test in two cohorts of non-dialysis CKD patients against the SF-12 PF domain.

Methods: Data from two independent studies were used in the analysis. In study 1, 48 patients (age: 66.8±11.4 years, 22 (45.8%) males, eGFR: 40.9±20.6ml/min/1.73m2) completed an 'in-person' supervised STS-60 test. In study 2, 51 patients (age: 64.4±13.6 years, 33 (64.7%) males, eGFR: 31.3±12.8ml/min/1.73m2) completed a 'remote' STS-60 test at home, without direct supervision or any 'live' guidance. Partial correlations adjusted for age, sex, and eGFR were used to investigate the association between STS-60 and SF-12 PF in both studies. Correlation coefficients were compared by using the Fisher z transformation. Differences between the two studies' correlation coefficients were assessed by z statistic.

Results: In study 1, the mean repetitions completed during the 'in-person' STS-60 was 24.7±8.9. In study 2, the mean repetitions completed during the 'remote' STS-60 was 22.5±9.7. Both the 'in-person' (r=.654, p<.001) and 'remote' STS-60 were associated with the SF-12 PF (r=.852, p<.001). No significant differences were seen between the two coefficients (difference = -0.198 (95% confidence interval: -0.198- 0.216), z statistic= -1.345, 512, p=.178).

Discussion: The present data suggest that both the 'in person' and 'remote' STS-60 performance are valid markers of perceived physical function status (as defined using the SF-12 PF domain). In the 'remote' group, a stronger correlation was observed than in the 'in-person' group. Still, there was no statistical difference between the two coefficients. Thus researchers wishing to measure functional status remotely may consider using a remote STS-60 test. Also, in the 'remote' group, patients were given minimal guidance via an instruction sheet, but no other instructions (i.e. monitoring via a video

call) were utilised. Our findings suggest that simple online instructions to ensure accurate STS-60 completion can be adequate to produce a measurement, and provide an image of one's functional status.

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Feasibility of conducting a remote randomised controlled trial of 'My Kidneys & Me': an online self-management programme for people living with kidney disease

Behavioural, psychological and quality of life, Patient education

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Background: For people living with long-term conditions, taking an active role in the management of their own health is desirable. Self-management requires the individual to have appropriate knowledge, skills, and confidence (termed patient activation) to be effective. Currently, there is a lack of resources available for people with non-dialysis chronic kidney disease (ND-CKD) to improve self-management behaviours and to support active involvement in one's healthcare. We developed 'My Kidneys & Me' (MK&M), a 10-week online self-management programme for people with ND-CKD, which aims to improve knowledge, promote self-care skills, increase self-efficacy, and enhance wellbeing. Currently, MK&M is undergoing evaluation in the 'SMILE-K' multi-centre randomised control trial (RCT), which is conducted entirely online (remotely). The primary outcome of 'SMILE-K' is patient activation. To ensure that the full-scale trial protocol was feasible, and to minimise methodological weaknesses, we conducted a nested single-blind feasibility pilot. Here we report the results of this nested study and preliminary usage data for 'MK&M'.

Methods: The 'SMILE-K' trial employs an entirely remote recruitment and outcome assessment methods. Participants are allocated into intervention and control arms using a 2:1 randomisation. The first 60 participants were included in the nested pilot and followed up for 10-weeks. Assessment surveys, including the Patient Activation Measure (PAM), were collected electronically at baseline (pre-randomisation), and 10 weeks later. Progression criteria were set a-priori, using the 'red' (stop), 'amber' (make changes), and 'green' (go) system to specify targets for progression, based on recruitment rates, acceptability of recruitment and randomisation methods, the feasibility and acceptability of outcome assessments, and engagement with and usage of 'MK&M'.

Results: Of the first 128 people who expressed interest in the study, 77/128 (60%) consented to participate. Of these, 60/77 (78%) completed the baseline assessment survey and were subsequently randomised and included in the pilot. The participants had a mean age of 63 (range: 20-88) years and 63% (n=38) were male. Sending study invitations via post was the most commonly used method of recruitment across different sites. However, additionally discussing the study with potential participants (either face-to-face or via telephone) was found to increase recruitment rate. All the pre-specified 'stop' progression criteria thresholds were exceeded, indicating that the full planned RCT is feasible. Access to and engagement with 'MK&M' were high with 36/41 (88%) participants activating their account and logging in. Participants logged into 'MK&M' a mean of 35 times during the 10-week follow-up period and spent a mean of 14 minutes per login.

Discussion: This nested pilot study provides evidence for the feasibility of the full-scale 'SMILE-K' trial. Numerous lessons were learnt from conducting this entirely remote trial design. From the pilot findings, we identified areas for improvement and have made subsequent small amendments to the protocol to improve delivery of 'MK&M' and 'SMILE-K'. The 'SMILE-K' trial is currently ongoing and we anticipate that the results will be available in 2023.

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Track P - Living with kidney disease

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Predictors of quality of life from analysis of the baseline data of CKD patients with and without iron deficiency without anaemia from the Iron and Heart study.

Behavioural, psychological and quality of life, Pharmacology, medicines management including anaemia and MBD

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Introduction: The prevalence of chronic kidney disease (CKD) is increasing worldwide. CKD is associated with an increased morbidity and mortality whilst negatively impacting quality of life (QOL). QOL represents the functional impact of disease on the subjective feeling of affected individuals about their physical, mental, spiritual, emotional and social wellbeing. Both physical inactivity and impaired physical function are strongly associated with increased morbidity, mortality and reduced QOL. Intravenous iron administration may improve physical functioning in patients with CKD, and therefore potentially improve their QOL. In the Iron and Heart trial randomised controlled trial, a pre-specified secondary outcome was change in quality-of-life measures using the KDQOL-SF questionnaire.

Methods: Adult patients with established non dialysis dependent CKD stages G3b-5 with a serum ferritin (SF) of less than 100mcg/L and/or a transferrin saturation (TSAT) of less than 20% without anemia (haemoglobin (Hb) 110-150g/L for males and females) were eligible to participate. A second control group of patients with CKD and without anaemia or iron deficiency allowed for baseline comparisons. Patients were randomized to intravenous (IV) iron (1000 mg iron Isomaltoside, single dose) or placebo IV saline. QOL measurements were collected using KDQOL-SF at baseline, 1 and 3 months. The KDQOL-SF is a reliable and valid measure of generic health related QOL scoring system. This data represents the non-disease specific SF36 information separated into 2 component summary measures (physical and mental health) with eight concept scales: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role emotional and mental health (MH); with higher scores correlating to better QOL.

Results: 74 Patients were included in this study; 26 IV iron, 28 placebo, 10 CKD control and 10 healthy control. Comparative statistical analysis using one-way ANOVA tests of the 8 KDQOL-SF score domains in IV iron, placebo IV saline and CKD control demonstrated no significant difference at baseline, 1 month or 3 month (table 1). Comparison of MH scores at baseline and 3 months in the placebo and treatment groups showed a decline in average MH score for patient's receiving placebo IV saline (baseline 45.0; 3 month 42.2; 95% CI: -6.09-10.9) whilst patient's receiving IV iron had a modest increase (baseline 46.5; 3 month 49.9; 95% CI: -8.25-1.59).

Discussion: Administration of IV iron to CKD patients with iron deficiency without anaemia appears to halt the decline in MH score seen in patients receiving placebo IV saline. Whilst the increased mental health score at 3 months was modest it was not statistically significant, a longer follow-up or larger study population may be required to demonstrate a significant increase in MH score. Our study may not have been sufficiently powered to detect differences between groups in other domains of the KDQOL-SF.

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Self-help intervention preferences among informal caregivers of adults with kidney conditions: an online cross-sectional survey

Behavioural, psychological and quality of life

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Introduction: Informal caregivers provide important help and support to people with kidney conditions. However, informal caregivers often experience common mental health difficulties, such as depression and anxiety, while in the caregiving role. Informal caregiver's mental health negatively impacts their own wellbeing, and can also impact the wellbeing of the person they care for. One potential solution to address informal caregivers' need for psychological support is the development of cognitive behavioural therapy self-help (CBT-SH) interventions. CBT-SH interventions can increase access to psychological support as they are less reliant on extensive involvement of healthcare professionals, and can be delivered in a variety of formats. However, there is a lack of research exploring CBT-SH intervention preferences among informal caregivers of adults with kidney conditions. Following the development phrase of the Medical Research Council framework for developing and evaluating complex interventions, we aim to explore CBT-SH intervention preferences among informal caregivers of adults with kidney conditions to inform the development of an intervention that is acceptable to users and optimised for implementation into routine practice.

Methods: Informal caregivers' self-help intervention preferences were explored using an online cross-sectional survey. Adults living in the UK who were providing unpaid care to an adult with a kidney condition were eligible to participate. Participants were recruited via social media, websites, newsletters, and/or magazines of non-profit organisations for people with kidney conditions and/or informal caregivers. The survey contained questions related to (1) characteristics of the informal caregiver; (2) characteristics of the person with a kidney condition; (3) self-help intervention preferences (e.g. content, delivery format); and (4) informal caregiver's mental health. Study materials were reviewed by two public contributors, informing the appearance of recruitment materials, and content of the participant information sheet and survey. Quantitative data analysis using descriptive statistics will be used to analyse survey responses.

Results: Participants are currently being recruited, with data collection projected to end in May 022. We aim to recruit approximately 150 participants, with 15 participants recruited as of mid-February

2022. Preliminary results describing participants' sociodemographic background, caregiving situation (e.g. condition of the person they care for, relationship to the person they care for), and current mental health status will be presented. Intervention content and delivery (e.g. intervention format; where, when, and by whom the intervention is delivered) preferences identified as most important by informal caregivers will be reported. Findings will be used to guide development of a CBT-SH intervention for informal caregivers of people with kidney conditions and will inform upcoming qualitative research with informal caregivers and health and social care professionals to continue the intervention development process.

Discussion: To our knowledge, this is the first study focused on the development of a CBT-SH intervention to support informal caregivers of people with kidney conditions. By incorporating informal caregiver's intervention preferences during intervention development, we aim to ensure the intervention meets their needs and preferences, and will be acceptable when implemented into practice. Results reflect the first step towards the development of a CBT-SH intervention for informal caregivers of people with kidney conditions.

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Track P - Living with kidney disease

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Supporting kidney friendly food boxes during the COVID-19 pandemic

Renal nutrition

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Introduction: In April 2020, when free food boxes became available for distribution by local authorities in England for people considered to be clinically extremely vulnerable, our patients raised concerns with our local Kidney Patient Association that most of the content of the food boxes was unsuitable for people with kidney disease who were diet-restricted. The KPA contacted our renal dietitians for help to replace foods with high potassium content with kidney-friendly items.

Method: People living with kidney disease, self-isolating at home could register with their local authority for a free weekly food box delivery. However, local authority food boxes contained multi-packs of tomato soup, baked beans, tomato-based pasta sauce, coffee and bananas, all of which have a high potassium content. KPA volunteers working in partnership with the renal dietetics team, replaced these items with lower potassium alternatives. Renal recipes were included in each food box to offer meal ideas with the food box items. The unsuitable foods from the government boxes were redistributed to local food banks for use. KPA volunteers delivered the weekly kidney-friendly free food boxes to the home of each patient until they no longer required it.

Results: From April 2020 to Dec 2021, 600 kidney friendly food boxes have been funded by the local KPA and delivered by volunteers to vulnerable renal patients in our catchment area.

Discussion: This community initiative successfully delivered kidney-friendly food boxes to our most vulnerable kidney patients. It is a great example of partnership working between a renal dietetics service and a local kidney patient charity making a difference to the local community during challenging times.

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Track P - Living with kidney disease

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The psychosocial impact of living with non-anaemic functional iron deficiency in individuals with non-dialysis kidney disease

Behavioural, psychological and quality of life, Patient outcome and experience

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Background: Anaemia is a well-recognised complication of chronic kidney disease (CKD), leading to symptoms such as overwhelming fatigue. One of the major underlying causes of anaemia is iron deficiency and iron replacement therapy is routinely provided for these patients. Iron availability is critical for numerous metabolic processes within the body, and when iron stores are low, in the absence of overt anaemia, “functional iron deficiency” can occur. In non-dialysis CKD, this under-recognised state may be associated with substantial symptoms, but iron replacement is not routinely offered. The Iron and Muscle study is a multicentre trial exploring impact of intravenous iron therapy on physical function in people with CKD Stages 3-4 with functional iron deficiency but without anaemia. Understanding the patient perspective and experience is an essential part of therapeutic strategy evaluation, thus a qualitative sub-study is included in Iron and Muscle. The aim of the initial phase of the sub-study was to understand the psychosocial impact of living with CKD and functional iron deficiency.

Methods: A sample of Iron and Muscle participants (stages 3-4 CKD, Hb 110-150 g/L, Ferritin < 100 µg/L and/or Transferrin Saturations (TSAT) <20%) were recruited upon entry to the trial, prior to receiving the therapeutic intervention (intravenous infusion of iron or placebo), to participate in an interview. An experienced researcher, not involved with the rest of the study, conducted semi-structured interviews face-to-face and via telephone. Topics explored included experiences of living with CKD and iron deficiency, symptoms, and quality of life. Interviews were audio-recorded and transcribed verbatim. Data were analysed using thematic analysis.

Findings: Twenty-one participants (6 males and 15 females, average age 59 years (range: 39-72 years)) were interviewed. Interviews lasted an average of 64 minutes (range: 37-98 minutes).

Six overarching themes were identified:

•Lack of awareness of iron deficiency

Participants had a lack of awareness and understanding of non-anaemic functional iron deficiency, their iron deficiency diagnosis, perceived causes and effects of low iron

•Overwhelming feelings of tiredness

Participants described overwhelming feelings of tiredness, energy management, consequences, and impact on daily activities

•Feeling limited

Participants felt limited and self-conscious about their ability to perform tasks and activities

•Balancing emotions

Managing the emotional consequences and conflict between feelings experienced and perceptions of how should feel were challenges participants experienced

•Low mood

Participants discussed feelings of low mood, sudden changes in mood, feeling overwhelmed and unmotivated

•Reduced social activities

Social activities and hobbies were impacted with participants unable to do their desired activities

Discussion: Findings highlight that people with CKD are unaware of their functional iron deficiency, and consequently lack understanding about the associated impact. People living with CKD and functional iron deficiency experience substantial psychosocial and physical burden. The impact of iron will be explored in these participants upon their exit of the Iron and Muscle study; if demonstrated to be of benefit, improved communication and support about the psychosocial impact and management of functional iron deficiency for individuals with CKD may be required, alongside effective interventions to improve fatigue management and resulting quality of life.

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Track P - Living with kidney disease

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

Renal nutrition

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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/m2; 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.

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/m2 and 74% reported doing minimal exercise. 74% of patients opted for a phone call rather than a video consultation.

At the three-month review, 14/19 patients were included (5 were excluded as they declined further input at baseline, could not be contacted by phone and did not respond to answerphone messages, or had become unwell making them unsuitable for weight management advice). Of the included patients, 71% had lost weight, with a significant mean weight loss of 5.2kg (5% of their baseline weight, $p<0.05$). 4 patients reported an increase in their physical activity.

At the six-month review, 14 patients were included. 11 patients had either maintained or lost further weight since their three-month review. Of the patients who had lost weight, there was a significant weight loss of 6.8% since baseline ($p<0.01$).

9-month and 12-month reviews are due in the coming months.

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.

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Track Q - Supportive care

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A two-question prognostic tool for patients receiving haemodialysis: initial implementation.

End of life and palliative care, Haemodialysis - quality improvement

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Introduction: Accurate prediction of survival on dialysis is helpful in making shared decisions about a patient's care. Whilst interventions aimed at minimising long-term cardiovascular risk, establishing effective venous access or working-up patients for transplantation are appropriate in those patients with a substantial predicted survival, steps to minimise treatment burden, prioritise quality of life, and even to consider withdrawal of dialysis are appropriate in those where prognosis is more limited. If prognostic judgements are inaccurate, perhaps because of unconscious bias on the part of clinicians, poor decision-making may result in patients being over- or under-treated.

Methods: We designed a simple two-question prognostic tool, comprising the 'surprise question' and a question asking clinicians whether they thought that a patient was in their last year of life. Combining these two questions allowed patients to be assigned to one of three prognostic categories: those in whom death in the next year was expected, those in whom death in the next year was unexpected, and an intermediate category for those patients in whom death in the next year was not expected, but would be considered unsurprising. Questionnaires were sent to all 18 haemodialysis consultants and 10 nurse managers working in our service, asking that for all patients under their care they should grade prognosis using these two questions, and assess frailty using the Rockwood clinical frailty score.

Results: Paired nurse and doctor responses were received for 1059 chronic haemodialysis patients, 95.5% of the eligible patient population. Nurses and doctors felt that a similar proportion of patients were in their last year of life (13.8% when assessed by nurses, 14.8% when assessed by doctors, $p=0.49$). However, doctors said they would be unsurprised if 37.3% of their patients died in the next year, a much higher proportion than among nurses, who would be unsurprised if 15.8% died ($p<0.0001$). Combining these results by pairing nurse and doctor scores resulted in 23.2% of patients being assigned to the 'expected death' category, 18.2% to the 'unsurprising death' category and 58.5% to the 'unexpected death' category, figure 1. These categories correlated with various known adverse prognostic factors including increasing age, duration on dialysis and frailty scores, figure 2. There were significant differences between sexes (men accounted for 65.9% of the 'expected death' group but only 59% of the whole cohort, $p=0.049$), and between ethnic groups (Asian patients were considered most likely to die, followed by white and black patients, $p<0.001$, figure 3).

Discussion: The two-point questionnaire proved simple to complete, readily assigning patients to three prognostic groups which correlated appropriately with age, duration on dialysis and frailty. We suggest that these prognostic categories fit naturally with patterns of clinical decision-making, and may help patients and clinicians balance long- and shorter-term priorities in care. We intend to evaluate these prognostic categories prospectively to determine how accurately they accurately predict 12-month mortality. This will also allow us to assess whether the observed differences in prognostic predictions between sexes and ethnic groups reflect accurate prognostication or unconscious bias by clinicians.

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Gender differences in considerations, experiences and expectations of haemodialysis in a frail and seriously-ill patient population

End of life and palliative care

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Background: Renal replacement therapy is increasingly offered to older, frailer patients and there are a growing number of seriously unwell patients on haemodialysis (HD). These patients tend to have multiple comorbidities and a high care burden, meaning a greater proportion of their time is spent managing healthcare issues or within a healthcare setting. Perceptions of these experiences can influence subsequent behaviour; illness perception has been associated with outcomes including treatment adherence, functional recovery and quality of life[1].

The impact of gender on patient experience is an area of growing interest. Females consistently report less positive experiences and lower scores for both physical and mental health[2]. As such, we sought to explore experiences and expectations of seriously-unwell patients whilst on HD, with a particular focus on gender differences.

Methods: Seriously unwell patients at three hospital-based HD units were invited to take part in the ePISTLE study[3]. 'Seriously unwell' was defined as a 1-year mortality risk of >20%[4]. Patients were invited to take either part in a semi-structured interview or to complete the same questions independently via a questionnaire. Analysis was undertaken using a thematic approach[5]. Ethical approval was granted (18/LO/1386).

Results: 43 patients were recruited into the study (14F, 29M). The median age of participants was 76 years (interquartile range, IQR 65-83) and they had been on HD for a median of 34 months (IQR 20-56). 37 patients took part in a semi-structured interview, 6 patients chose to complete the questionnaire independently.

Factors considered when starting dialysis. Seven master themes were identified: a strong desire to keep living, fear, exploration of alternative treatment options, impact on overall wellbeing, and a desire to achieve specific health goals. There were marked gender differences in the way people approached this decision-making process (Figure 1a) with males significantly more likely to consider alternative treatment options (P= 0.001) and females more likely to prioritise overall well-being and maintenance of autonomy.

Treatment expectations. To identify treatment expectations, participants were asked both at an individual level, “what do you hope to get out of treatment”, but also to consider more generally, “what does good treatment mean to you?”. Answers to both these sections were combined to identify master themes for treatment expectations.

Seven master themes were identified; A desire to achieve physical goals, to maintain autonomy and equipoise, to promote longevity, a sense of social normalcy, a feeling of wellbeing, and care expectations. Again, marked gender differences seen, with females more likely to prioritise a feeling of wellbeing and males more likely to want to achieve physical goals (Figure 1b).

Symptom burden: Participants were asked to complete the iPOS Renal survey[6] to capture their symptom burden. There were no statistical differences in total physical symptom scores or anxiety levels between genders, but females were more likely to report feeling depressed than males (P=0.001).

Discussion: There are marked gender differences in the experiences and expectations of seriously-unwell patients on HD. Recognising that different genders approach treatment decisions and prioritise treatment expectations differently will allow for more personalised care plans to be developed, and improve the experiences of our seriously unwell dialysis patients.

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Track Q - Supportive care

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Healthcare professionals lack confidence and training in approaching advanced care planning discussions during renal inpatient admissions

Patient outcome and experience, Other

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Background: Renal inpatients often comprise a co-morbid and frail cohort that are vulnerable to clinical deterioration whilst in hospital 1. Risk factors include higher rates of major adverse cardiovascular events 2 and opportunistic infections, particularly in immunosuppressed patients with glomerulonephritis 3 or in those with a kidney transplant 4. Given that renal healthcare professionals frequently care for such a cohort as inpatients, it would seem plausible that they are confident and competent with advanced care planning (ACP) discussions particularly focussing on resuscitation and treatment escalation plans (TEP).

Aims: We sought to assess attitudes and practices, relating to ACP for inpatients, amongst healthcare professionals working in the renal department of the Royal Free Hospital in order to identify barriers to timely discussions on TEP.

Methods: A self-devised, anonymous survey of 22 questions on ACP was piloted and distributed to all healthcare professionals working within inpatient renal services.

Results: Preliminary results are available from 8 consultants, 7 junior doctors and 10 allied healthcare professionals, 84% of whom had been involved in ACP decisions in the last year (Feb 2021-22). Only 28% reported to have previously received relevant training. When asked who was best placed to contribute to ACP decisions, majority (88%) selected the admitting or ward doctors although a significant number also chose the nurse in charge of the ward (56%), intensive care team (32%) and palliative care teams (48%). Almost two thirds of respondents believed that the ideal time to establish a TEP was on admission (68%) and that an early TEP was essential to good patient care (64%). Three respondents felt that a do not resuscitate order resulted in poorer access to medical care. The COVID-19 pandemic was deemed by 92% to have had at least a moderate effect on TEP. A third of respondents demonstrated concern that TEP and resuscitation plans were not considered appropriately on a frequent basis for renal inpatients. The most common barriers cited to hindering ACP discussions were limited time to explore such issues and anxieties relating to inciting fear or anger in patients and key contacts. Most respondents felt very confident in their ability to explore current medical issues (80%) and co-morbidities (76%) but less than two thirds expressed similar confidence in assessments of physiological baseline (48%), functional baseline (56%), frailty (52%) and prognosis (24%). The survey also identified problems with documentation of TEP and resuscitation plans on our electronic patient record (EPR) system and access to community records for pre-existing ACP.

Conclusions and recommendations: Our results demonstrate under confidence and anxieties in healthcare professionals when approaching ACP in renal inpatients, with a significant proportion

concerned that TEP were not frequently considered appropriately. Training in recognising frailty and it's impact on prognosis may likely improve the confidence and quality of TEP completed. An audit of inpatient TEP discussion and documentation is currently in progress. Improvements in documentation and communication, achieved through local retraining, will be critical to improving TEP for renal patients and avoid unnecessary or harmful treatments in the frail and vulnerable.

Thursday 9th June, 14:10-15:10

Track Q - Supportive care

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Quality Improvement Project on Improving quality of life outcomes and awareness of Advance Care Planning in End stage Renal patients

Haemodialysis - quality improvement

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Introduction: Advance care planning (ACP) is an evidence-based practice shown to reduce suffering, hospitalisations and improve quality of life through shared patient centred decision making. This approach considers the patients' values and life goals when taking healthcare decisions and offers the opportunity for individuals to plan their care while they still have the capacity to do so. Family members also find this beneficial because it reduces their levels of anxiety and depression.

Until now, there have been few patient-centered studies showing that ACP improves quality of life in dialysis patients (1,2,3). Therefore, this study examines how ACP improves patient satisfaction.

Methods: We gave our questionnaire to patients aged over 50 years and not on the transplant waiting list or undergoing pre-transplant work up in our dialysis center. Our aim was to improve ACP satisfaction score amongst these individuals by at least 20%.

Our primary outcome measure, the ACP satisfaction score is defined as the score from a 10-point Likert scale, illustrated with 5x smiley faces, to the question: "How satisfied are you with your advance care planning?"

Using a questionnaire to study patients' understanding and opinion on ACP. We then used the following intervention tools to further educate patients about the advantages of ACP, and then repeated the questionnaire.

1. Posters placed around the dialysis unit and renal outpatients

2. Kidney Care UK Capacity Leaflet

Results: Baseline data was collected from 43 individuals at each stage of the process. Our data showed a slight improvement in the understanding of ACP, but no unexpected outliers were noted. Total of 4 sets of data were collected.

With our primary outcome measure, there has not been any exponential change, compared to the baseline data.

There has been an improvement in our outcome measures, (Do you know what an Advance care plan is?) with our interventions ranging from 3% to 15%. Understanding of the option to withdraw from dialysis also improved from 33% to 63% during our study period.

Discussion: This quality improvement project has shown limited success at improving the primary outcome measure. Although not a desired result, the score did not fall below the initial response.

Other factors which may have influenced the results are:

(1) Most patients surveyed did not know the definition of ACP. Despite repeated explanations during the survey, patients continued to struggle with the term.

(2) During the collection of data, we also noticed that most patients had poor eyesight and language or reading barriers.

(3) Involving family members may have been more receptive to discussions. If the patient was forgetful or if they did not want to discuss our intervention, then there may have been less desire for patients to proactively make any changes.

Despite multiple interventions, our study illustrates some barriers to effective ACP. Therefore, further interventions should be carried out to assess if ACP has a positive effect on patients' quality of life. Our study was small and a single centre-based study. Hence, further research may prove to be beneficial in this patient category.

Thursday 9th June, 14:10-15:10

Track Q - Supportive care

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The 'Difficult Conversations Booklet': a toolkit to support kidney health professionals have conversations with older adults about palliative and end-of-life care

End of life and palliative care, Staff education

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Introduction: Renal guidelines recommend the timely preparation of people with kidney failure for end-of-life. There is variation in how end-of-life and palliative care is provided dependent on treatment pathway. People undergoing dialysis are more likely to die in hospital and have more hospital admissions than people receiving conservative care. Providing accurate information about adjusting and stopping treatments, choosing not to commence dialysis and palliative care options, is a fundamental step in ensuring timely, reasoned decisions are made between patients and professionals about the type of care they wish to receive. We interviewed older adults with kidney failure and their families about their experiences and views of end-of-life care to inform the development of the 'Difficult Conversations' Booklet, a guide to help kidney health professionals have conversations with their patients about future care.

Methods: Design: survey using qualitative interview methods to explore views of older adults with kidney failure (n=17), family/carers (n=4) and bereaved family/carer (n=2) perspectives of important end-of-life care issues. Interviews took place on the telephone or via Zoom and lasted no longer than 1 hour. Audio recordings were transcribed verbatim, NVivo software managed the data, which was analysed using thematic analysis. Quotations from the interviews are included in the 'Difficult Conversations' Booklet.

Results: Most people had not discussed their future care with a kidney clinician. Peoples views varied in their preference for how, when and with whom conversations about end-of-life should take place. Although stopping dialysis results in death, most people learnt about the consequences of withdrawal from dialysis after they had commenced treatment. People accepted death as inevitable but were uncertain about how death occurred as a result of kidney disease. Most people

had made their own decisions and actioned them e.g., made a Will and/or nominated a Power of Attorney, often in discussion with their spouse. Family members were actively involved in conversations and decisions about care, and both provided and required support in this role.

Discussion: Conversations about end-of-life care are not part of routine kidney care management. Including the experiences of people with kidney failure and their families in the 'Difficult Conversations' booklet improves understanding and allows clinicians to hold timely discussions about future care options. Having an agreed plan about future care can help mitigate against 'crisis' management in acute situations. For services, holding these conversations can improve allocation and co-ordination of relevant services, i.e. palliative care. For patients, discussing end-of-life improves patient knowledge, increases realistic expectations, and reduces anxiety about future care, and supports decision making in line with patients preferences for care.

Thursday 9th June, 14:10-15:10

Track R - Glomerulonephritis and vasculitis

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A Single Centre Retrospective Analysis of the use of Rituximab in adult patients with Minimal Change Disease

GN, Pharmacology, medicines management including anaemia and MBD

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Introduction: Minimal Change Disease (MCD) accounts for 10-25% of cases of Nephrotic Syndrome (NS) in adults. Steroids can effectively induce complete remission (CR) in the majority of patients. Steroid sparing agents (SSAs) are considered when relapses are frequent or patients are steroid dependent. Rituximab (RTX) has emerged as an effective therapy for maintenance of remission in MCD and reduces the number of relapses in both paediatric and adult populations. However, questions remain on effective dosing regimens and maintenance of remission after prolonged follow-up.

Method: We performed a single-centre, retrospective analysis of 27 patients who received RTX for MCD between 2011 and 2021. 10 patients had paediatric-onset disease and 26 patients were treated with alternative SSAs before RTX initiation. 60% of patients were neither steroid-dependent nor frequently relapsing at the time of RTX. The primary outcome of interest was period of sustained, complete remission (months - m) after RTX.

Results: 27 patients underwent 45 courses of RTX, equating to 85 separate infusions. 17 courses constituted a high-dose regimen (375 mg/m2 weekly for 4 weeks or 1 gram two weeks apart) and 28 courses were administered as a low-dose regimen (single dose or 6 monthly doses for 2 years or 9 monthly/yearly dosing). RTX administration was intentionally deferred in patients with nephrotic range proteinuria; 40/45 courses were administered while patients were in remission (urine protein: creatinine < 350 mg/mmol). Seven patients were on SSAs at the time of RTX; all SSAs were stopped on RTX initiation or within the first 8 weeks.

During the observed follow-up period (range 6 – 122m, median 58m), 15 patients experienced a relapse (56%). The overall relapse rate was higher in individuals with paediatric-onset compared to adult-onset disease (65% Vs 48%). Relapse rate was similar when comparing high-dose vs low-dose regimens (59% Vs 56%). Relapse rates may be lower when RTX is administered when patients are in remission (80% Vs 53%). Median survival in CR for the whole cohort was 33m (range 3 – 104m) from the initial dose and 27m (range 0 – 103m) from the most recent RTX dose (accounting for multi-dosing regimens). Median steroid-free survival after RTX was 29 months (range 0 – 73m) in the 37 courses where steroids were fully withdrawn. Within the cohort, 5 patients with paediatric-onset relapsing disease, underwent a 6 monthly course of RTX for two years. There were no relapses in the dosing period; two patients relapsed within 2 years (12 and 16 months), two patients remain in complete remission (47 and 49 months).

Discussion: Our single centre analysis with extended follow-up suggests RTX can be an effective, but currently non-commissioned, therapy in patients with relapsing MCD, allowing withdrawal of other SSAs in all patients and steroids in all but one patient (1 patient taper ongoing). Although approximately a third of patients remained relapse-free at 5 years post-RTX, the majority of patients will relapse and respond to repeat dosing. A 6 monthly interval, low-dose RTX treatment regimen offers an attractive approach to maintain remission in patients with difficult to treat, relapsing MCD.

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The Clinical Importance of Frailty Assessments in ANCA associated Vasculitis

GN, Patient outcome and experience

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Introduction: Anti-neutrophil cytoplasmic autoantibody (ANCA) associated vasculitis (AAV) is a rare autoimmune condition. It typically affects those over 50 years old, with the incidence increasing until the age of 80 years old. Whilst the mortality associated with AAV has improved, it continues to carry a high degree of morbidity. Frailty is more prevalent in older populations and those with chronic disease; it is also independently associated with adverse health outcomes. Whilst frailty is not synonymous with older age, the higher prevalence of vasculitis in older age groups has created a need for frailty assessment to aid the management of AAV. This study aims to investigate the association between frailty status, assessed by a validated frailty risk score, and health outcomes in patients with AAV.

Methods: A retrospective cohort study of biopsy proven AAV patients was carried out between 2008 and 2021. Using electronic records The Hospital Frailty Risk Score (HFRS) was applied to patients aged over 75 years old. The score was calculated using inpatient coding that occurred in the 2 years prior to diagnosis, or within the same admission the diagnosis was made. Based on HFRS, patients were categorized into three categories: 'low' (<5), 'intermediate' (5-15) and 'high' (>15).

Results: In our cohort of 34 patients, there were 15 female and 19 male patients. There were 18 'low' risk (<5), 13 'intermediate' risk (5-15) and 3 'high' risk (>15) patients. Overall mean age was 79.6 ± 3.8 years. Remission induction treatment with cyclophosphamide and/or rituximab was given across all HFRS categories, with only 1 patient in the 'low' risk and 3 in the 'intermediate' risk group not receiving induction immunosuppression. Five significant adverse event episodes were identified with 3 (17%) in 'low' risk, 1 (8%) in 'intermediate' risk, and 1 (33%) in the 'high' risk groups, respectively. Four of the 5 adverse event episodes were infection-related, whilst the other was severe thrombocytopenia. No patient in the 'high' risk group received renal replacement therapy (RRT) on presentation, in comparison to 2 in the 'low' risk and 5 in the 'intermediate' risk groups.

Mortality across the HFRS groups was similar. Logistic regression analysis did not indicate significant associations with mortality at 1 year (OR 1.01, 95%CI 0.84-1.24, p=0.86) or 2 years (OR 1.08, 95%CI 0.91-1.28, p=0.38), and application of Cox regression analysis also did not indicate significant associations with mortality for the entire study follow-up period (HR 1.03, 95%CI 0.84-1.25, p=0.645) per 1 unit increase of HFRS. Median follow-up was 2.83 years. Table 1 summarizes the study findings.

Discussion: This study showed no significant associations between HFRS score and adverse events or mortality. Nevertheless, our findings suggest that patients with high HFRS scores should still be considered for remission induction treatment. Frailty assessment tools has been used to support shared decision making across various realms in clinical and geriatric nephrology. Further validation is required for larger AAV populations, with consideration given to evaluating the prognostic value of other frailty assessment methods. Given an aging population with multi-morbidities, the need for tailored vasculitis therapy is essential to ensure optimization of patient outcomes.

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Shared genetic risk factors in European patients with different presentations of non-monogenic idiopathic nephrotic syndrome

Genetic and rare diseases, GN

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Introduction: Idiopathic nephrotic syndrome (INS) is classified in children according to response to initial corticosteroid therapy into steroid sensitive nephrotic syndrome (SSNS) and steroid resistant nephrotic syndrome (SRNS) and in adults according to kidney histology into minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS). However, there is well-recognized phenotypic overlap between these entities and some evidence to suggest that they represent a spectrum of a single disease. Genome-wide association studies (GWAS) have shown a strong association between SSNS and variation at HLA, suggesting an underlying immunological basis. We sought to determine whether a risk score generated from genetic variants associated with SSNS could be used to gain insight into the pathophysiology of INS presenting in other ways.

Methods: We developed an SSNS genetic risk score (SSNS-GRS) from the five variants independently associated with childhood SSNS in a previous European GWAS. We quantified SSNS-GRS in independent cohorts of European individuals with childhood SSNS, non-monogenic SRNS, MCD, and non-monogenic FSGS.

Results: The SSNS-GRS was significantly elevated in cohorts with each of the above conditions compared with healthy participants and participants with membranous nephropathy (a different immune-mediated kidney disease that also presents with nephrotic syndrome).

Conclusions: The shared genetic risk factors among patients with different presentations of INS suggests a shared autoimmune pathogenesis. This suggests that in cases where an underlying monogenic defect is not detected, INS is caused by an autoimmune podocytopathy. Use of the SSNS-GRS may aid in further diagnostic criteria to classify patients with INS, in addition to testing for monogenic causes.

Thursday 9th June, 14:10-15:10

Track R - Glomerulonephritis and vasculitis

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Risk Factors for Venous Thrombosis in Anti-PLA2R+ve and -ve Primary Membranous Nephropathy

GN

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Background and Aims: Venous thrombosis (VT) is an established cause of increased morbidity and mortality amongst patients with nephrotic syndrome. Previous studies suggest primary membranous nephropathy (PMN) to be associated with the highest risk of developing VT amongst all nephrotic diseases. Antibodies to the phospholipase A2 receptor (anti-PLA2R) is identified as a pathogenic marker to the disease activity of PMN, and considered a strong prognostic marker towards disease progression and treatment response. Recent evidence cites the potential of anti-PLA2R as an independent risk factor of VT in PMN. Nevertheless, the pathophysiology of VT for anti-PLA2R+ve and –ve PMN is not fully known. Whether the common risk factors of VT remain as significant within the anti-PLA2R+ve and –ve PMN context is also not convincingly elucidated of yet. Our study aimed to evaluate and compare risk factors for VT in patients with anti-PLA2R+ve and –ve PMN.

Method: This is a retrospective analysis of patients diagnosed with PMN between Oct 2015 and Sep 2021. Patients included are age ≥ 18 years, have biopsy-diagnosed PMN and serum anti-PLA2R immunofluorescence assay testing following PMN diagnosis. Patients excluded from this study were those with secondary causes of membranous nephropathy, those who had kidney transplantation prior to or following PMN diagnosis, or where iatrogenic causes such as major surgery or prolonged immobilization led to VT. Study patients were screened until Nov 28th 2021 for any VT event, and were grouped between those with anti-PLA2R+ve and -ve antibody test results. Demographic and clinical parameters from age, gender, presence of co-morbidities and common risk factors associated with increased risk of VT (hypertension, diabetes mellitus, atrial fibrillation, CHA2DS2-VASC ≥3, BMI > 30, malignant disease, hormonal treatment and contraceptive pill use), serum and urine biochemical test results at PMN diagnosis (albumin, 24-hr proteinuria, proteinuria/albumin ratio, creatinine, eGFR, cholesterol, triglycerides and IgG) were collected. The comparison of demographic and clinical parameters for patients with and without VT in each of the anti-PLA2R+ve and –ve groups was conducted through Chi-Squared, t and Mann-Whitney U tests. Multivariate regression analysis determined the significance of association between each parameter and VT event occurrence.

Results: Seventy patients with PMN were included in this study, of which 39 patients are anti-PLA2R+ve and 31 patients are anti-PLA2R-ve. 8 patients (20.5%) had VT in the anti-PLA2R+ve group during follow-up whilst this was the case for 4 patients (12.9%) in the anti-PLA2R-ve group. In both groups, patients with VT were found to have higher serum cholesterol levels ($p<0.05$). Lower serum albumin levels, but greater 24 hour proteinuria and proteinuria/albumin ratio was observed in patients with VT within the anti-PLA2R-ve group ($p<0.05$). Full results from the multivariate regression analysis are presented in Tables 1 and 2. Serum cholesterol is demonstrated to be significantly associated with VT in the anti-PLA2R+ve (OR 1.42, 95%Cl 1.12-1.72) and anti-PLA2R-ve groups (OR 1.45, 95%Cl 1.15-1.76) respectively. Serum albumin (OR 1.41, 95%Cl 1.10-1.73), 24 hour proteinuria (OR 1.33, 95%Cl 1.03-1.63) and proteinuria/albumin ratio (OR 1.32, 95%Cl 1.04-1.59) are shown to be significantly associated with VT within the anti-PLA2R-ve group.

Conclusion: There is supporting evidence that serum cholesterol, albumin and proteinuria may all present as important markers of risk prediction for VT in patients with PMN, though this will require further validation in prospective multi-center studies with larger patient samples. Close monitoring of these markers, and early management in response to hypercholesterolemia, hypoalbuminemia and proteinuria with consideration of anti-PLA2R status should ensue as part of primary prevention strategies to reduce VT incidence in the PMN population.

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A preview to the Kidney Transplantation in Older People (KTOP) study; baseline prevalence of frailty and cognitive impairment.

Transplantation - research, Other

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Kidney transplantation (KT) in older people has mixed outcomes resulting in a highly variable impact on quality of life. Older people listed for and undergoing KT are particularly vulnerable to frailty and cognitive impairment, and the presence of these factors may explain some of the differences in outcomes observed.

The Kidney Transplantation in Older People (KTOP) study: impact of frailty on outcomes, is an active clinical research study. Here we present our study cohort at baseline and describe the prevalence of frailty and cognitive impairment observed in the older people listed for transplantation.

Methods: The KTOP study is a prospective, observational study being conducted at the Imperial College Renal and Transplant centre. From October 2019 all patients aged 60 or above, and either active on the waitlist or undergoing living KT, were eligible for recruitment. Each participant completed a combination of questionnaires assessing frailty, cognitive function, and quality of life. These questionnaires were repeated at defined time points whilst on the wait list or following a KT. Clinical data was concurrently collected. The study remains active, with recruitment closing in March 2022, followed by completion in March 2023.

Results: Thus far 208 patients have been recruited, 97 of whom have received a KT. Table 1 summarises the demographic characteristics of the study cohort. Baseline Montreal Cognitive Assessments (MOCA) are available for 174 participants; 72 (41.8%) have cognitive impairment (defined by a MOCA score of ≥ 26). Edmonton Frail Scale (EFS) scores were available for 184 participants; 30 (16.3%) were identified as being frail (EFS score of ≥ 8), with a further 37 (20.1%) identified as being 'vulnerable to frailty' (EFS score 6-7).

Discussion: Our baseline data has demonstrated that in the KTOP study cohort the prevalence of cognitive impairment was 41.8% and the prevalence of frailty was 16.3%, with a further 20.1% identified as being vulnerable to frailty. Current clinical practice does not routinely incorporate assessments of frailty or cognition as part of the transplant work up for older people. Follow-up data will determine the impact of these paramaters on quality of life and outcomes of those being

transplanted compared to those remaining on the wait list. Ultimately, the KTOP study will enrich our understanding of transplantation in older people and therefore guide the information available during shared decision making discussions and improvements in care of older people with kidney failure.

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Assessment of HLA incompatibility at the molecular compared to antigenic HLA level enables better prediction of graft function deterioration in paediatric kidney transplantation.

Paediatrics, Transplantation - research

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Introduction: HLA mismatching has a detrimental effect on graft survival after paediatric kidney transplantation. Assessment of HLA incompatibility at the molecular level (molecular HLA mismatch; molMM) has emerged as a promising method for predicting primary alloimmunity risk. In this study, we aimed to assess whether molMM compared to conventional antigenic mismatching (antMM) enables better prediction of graft function deterioration in paediatric kidney transplantation.

Methods: We performed a retrospective analysis of 177 paediatric patients from the ABMR study of the CERTAIN registry (median follow-up 4.5 (IQR 3-5) years). Only five patients experienced graft loss. Therefore, we used the time to 50% reduction in eGFR, from month-3 post-transplant baseline, as a surrogate endpoint for long-term graft loss (eGFR-50). HLA molMM was assessed using the Cambridge amino acid mismatch score (AAMS) which on a separate study was predictive of primary alloimmunity risk in this cohort. Survival analysis was performed using Cox models, adjusted for donor and recipient baseline characteristics.

Results: 27 (15%) patients met the primary outcome. In multivariable analysis, recipient and donor age, baseline eGFR, and re-transplant status had a significant association with eGFR-50. Importantly, only mismatches at HLA-DQα1β1, and not at other loci, were associated with the primary outcome (adjusted HR (aHR) 10.2; 95% CI, 10.1-10.4 per 10 AAMS increase, and aHR 1.8; 95% CI, 1.02-3.4 per antigen increase). There was a wide range of AAMS values (0-49) within each HLA-DQ antMM (0-2). We used a predetermined molMM score (AAMS=16 derived from analyses of donor-specific antibody risk) to classify patients according to HLA-DQα1β1 mismatch risk into “low/low”, “low/high” and “high/high” risk groups. Patient risk for eGFR-50 was associated with molMM stratification, regardless of their antMM. eGFR-50 risk was equivalent in patients with “low/low” risk mismatches (aHR 2.2, 0.2-23, p=0.5 for 2 v 0 antMM). Patients with “low/high” and “high/high” HLA-DQα1β1 mismatches had worse allograft outcomes (“low/high”: aHR 4.7, 1.9-11.4, p<0.05; “high/high” aHR 5.7, 1.4-22.7, p<0.05 versus “low/low”, Figure 1). Compared to antMM, molMM showed better stratification of outcomes whilst increasing the number of patients in the low risk group (“low/low” n=100, v 0 antMM n=65).

Conclusion: Assessment of HLA incompatibility at the molecular level enables better stratification of graft deterioration risk compared to conventional serology-based HLA mismatching. Further validation of molMM in independent cohorts is required before clinical implementation.

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Does serum from patients with CKD induce protein loss from human skeletal muscle cells in vitro?

CKD

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Introduction: Chronic kidney disease (CKD) promotes loss of skeletal muscle mass and function, which increases patients' risk of hospitalisation and death. Circulating factors, e.g. elevated inflammatory cytokines and muscle growth suppressors, are putative causes for muscle loss in CKD. Historically, studies in this field have often relied on animal models and animal-derived tissues with apparent limitations for translation. This study examines whether serum from patients with CKD induces a negative protein balance in human skeletal muscle cell cultures relative to serum from healthy control (HC) individuals.

Methods: Individuals without CKD donated quadriceps muscle samples during elective orthopaedic surgery. After isolation of myoblasts, cells were proliferated and differentiated in vitro to obtain desmin-positive multinucleated myotubes. Myotubes were treated in triplicate with pooled serum from individuals with CKD or HC at concentrations of 2%, 6% or 20% for 24 hours before obtaining readouts. We measured total protein content of cultures with a colorimetric Bradford assay. Protein synthesis rate and protein degradation rate were measured separately using radiolabelled tyrosine as a tracer of amino acid incorporation and release. Finally, we used rtPCR to examine mRNA expression levels of anabolic, catabolic and inflammatory signal mediators.

Results: Serum samples came from 10 healthy volunteers (age range: 68-83 years, male/female: 4/6, eGFR range: 64-86 ml/min/1.73 m2) and 11 patients with CKD (age range: 69-90 years, male/female: 6/5, eGFR range: 16-37 ml/min/1.73 m2). Mean protein content of myotube cultures was lower after treatment with 2% CKD serum compared to 2% HC serum (37.4µg vs. 43.5µg respectively, p=0.03). However, myotube protein was not significantly different for HC vs. CKD serum treatment at 6% and 20% serum concentration. Rates of protein synthesis and rates of protein degradation were not significantly different between HC vs CKD serum treatment at any serum concentration. As a control measure, we observed significantly higher total myotube protein, elevated protein synthesis and suppressed protein degradation with serum concentration rising from 2% to 6% to 20% in a stepwise fashion irrespective of serum type. mRNA expression of catabolic genes (FOXO1, TRIM63, FBXO32),

anti-anabolic genes (MSTN), anabolic genes (IGF1, IGF2, IRS1, MYOG) and inflammatory genes (TNFA, IL1B, IL6) was not significantly different for myotubes treated with CKD serum or HC serum.

Discussion: Serum from patients with pre-dialysis CKD reduced protein content of human skeletal muscle cells in vitro relative to serum from healthy individuals at 2% concentration, but not at higher concentrations. No differences in protein synthesis rate, protein degradation rate or mRNA expression of catabolic and anabolic genes were observed in relation to serum type over 24 hours. Acute exposure of skeletal muscle to circulating factors may not be as important as chronic exposure or non-circulating factors for muscle loss in CKD.

Thursday 9th June, 14:10-15:10

Track S - Laboratory and translational science

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Outcomes of Renal Transplant Recipients with BK virus Infection: A single-centre experience

Transplantation - research

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Aim: Post renal transplant BK virus reactivation/ infection is on of the important and common causes of allograft failure. Our aims were understanding the the incidence and clinical outcome associated with BK virus infection/ reactivation, identify risk factors for BKN and BK viraemia development, defining the natural progression of BK virus infection in renal transplant recipients, as well as evaluation of the effect of BKV infection on graft and patient survival in renal transplant recipients between Jan 2010 – October 2017.

Methods: A single-center retrospective analysis of 492 patients who received their renal transplant between Jan 2010- October 2017.

Results: In a cohort of 492 patients (337 males, 155 female) with a mean age of 54.1 years +/- 13.7. Seventy three (14.8%) patients had BK Viruria out of which 33 patients developed BK viremia. Ten patients were biopsy-proven BKVN and 3 of them had graft loss.

The mean duration between transplantation and viruria was 8- 19 months, between viruria and development of viremia was 2.83 - 6 months, duration between viremia and development of BKVN was 3.29 – 8 months, lastly, duration between BKVN and development of graft failure as a result of BKVN was 14.49 – 23 months. There was no statistically significant difference between the overall graft survival or patient survival for patients with positive BKV infection and that of negative BKV infection. No statistically significant difference in the incidence of acute rejection between both BKV infected group and the non- infected group.

Conclusion: Patients who developed BKV infection have a poorer graft function when compared to other renal transplant patients who did not. However, no significant statistical difference between both groups regarding both graft and patient survival.

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Perioperative major adverse cardiovascular events with kidney transplantation

Transplantation - research

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Introduction: Perioperative major adverse cardiovascular events (MACE) following kidney transplantation are not well quantified. Yet, an elaborate work-up including cardiac stress testing and revascularisation are routinely performed to prevent such events. We audited all kidney transplant procedures to determine the incidence of perioperative MACE and possible predictive factors in a large inner-city kidney transplant centre.

Methods: Data on demographics, biochemical parameters and cardiovascular events, including myocardial infarction, heart failure, stroke and cardiovascular deaths during hospital admission were collected on all 313 patients undergoing kidney transplantation between 01/1/2019 to 31/12/2021 in one centre. A multivariable binary logistic regression determined whether being high risk was associated with MACE. Models were adjusted for age, sex, BMI, diabetes status, IHD, Heart failure, and CVA, and results are expressed as odds ratios (OR) with 95% confidence intervals (95% CI). Models passed statistical assumptions.

Results: Seven out of 313 patients (2.2%) experienced MACE in the post-operative period. The clinical characteristics of the cohort were: age (51.6 ± 13.5) years, 56.5% were male, 17.3% had diabetes, 84.7% had hypertension, and 29.7% had BMI>30 Kg/m2.

The patients with MACE were more likely to be >60 years of age compared to patients without MACE (42.9% vs 31.7%; p=0.255), more likely to be male (85.7% vs 55.7%; p=0.372), diabetic (28.6% vs 17.3%; p=0.955), hypertensive (100% vs 86%; p=0.998), and have ischaemic heart disease (14.3% vs 7.7%; p=0.610). [see table 1]. No significant individual predictive variables were identified. Furthermore, there was no significant relationship between the modified Lee Index risk stratification scoring system and MACE incidence. [see table 2]

Discussion: The study shows that the incidence of perioperative MACE during kidney transplant is low. The patients with MACE were more likely to be older, male, diabetic, hypertensive, and have IHD. However, no independent risk factor could be established in this analysis. A larger study may be necessary to identify the high-risk patients who may benefit cardiovascular work up prior to transplantation.

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Pre- and peri-operative heart failure in kidney transplant recipients: a single-centre experience

Transplantation - research

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Introduction: Heart failure (HF) is a major adverse cardiac event (MACE) in the peri-operative period following kidney transplantation. Simultaneously pre-existing HF is of concern in patients awaiting kidney transplantation. Considerable pre-transplant cardiovascular (CV) screening involves invasive and non-invasive tests, although there is no consensus as to the predictive value of these tests – or other key risk factors – for anticipating a MACE within 30 days of operation.(1) This single-centre observational study characterises ten renal transplant patients with pre- and peri-operative HF.

Methods: Data on demographics, past medical history, pre-transplant CV screening and CV outcomes in the peri-operative period (0¬–30 days post-transplant) were collected for the 313 patients (mean age 51.6 ± 13.5 years, 56% male, 17% diabetes, 29.7% BMI>30 Kg/m2) undergoing kidney transplantation between 1st January 2019 and 31st December in one centre.

Results: Five transplant patients were identified with known pre-existing HF and five who developed de novo peri-operative HF (Table 1). Pre-existing HF patients had a mean age of 48.6 years, whilst those who developed peri-operative HF had a mean age of 62.8 years. Mean BMI was 30.4 kg/m2 in the pre-existing HF group, compared to 25.5 kg/m2 in the peri-operative HF group. No pattern was identified in ethnicity or prevalence of co-morbidities in between the groups. Of those with pre-existing HF, no patients had positive findings in pre-transplant CV screening tests; 3 suffered from HFmrEF and 2 HFpEF, none suffered from diabetes of CV disease; 4 were on haemodialysis and 1 on peritoneal dialysis; two received living donor transplant. Of those who developed peri-operative HF, none had diabetes or CV disease; only one patient had a positive CV screening test: an angiogram demonstrating a >50% lesion. This patient had undergone two primary cutaneous interventions for ischaemic heart disease. Following development of HF, this patient died due to multi-organ failure.

Discussion: In this limited cohort, pre-existing HF was not predictive of post-operative adverse CV outcomes. Conversely, pre-transplant CV screening did not identify abnormalities in 4/5 patients who then developed peri-operative HF. Patients with peri-operative HF appeared to be older, and less likely to be obese than those with pre-existing HF. Further study to elucidate the risk factors for peri-operative MACE is needed to better identify high risk patients and guide pre-transplant CV screening.

Reference:

1.Hart A, Weir MR, Kasiske BL. Cardiovascular risk assessment in kidney transplantation. Kidney Int. 2015 Mar 1;87(3):527–34.

Table 1: Comparing kidney transplant patients with pre-existing and de novo peri-operative heart failure. Demographic data, past medical history, and cardiovascular outcomes in five patients with pre-existing HF and five patients who developed peri-operative HF. Pre-transplant CV screening tests include dobutamine stress echocardiogram and angiogram. Peri-operative adverse CV outcomes include acute coronary syndrome, cerebrovascular accident, heart failure and CV death. BMI, body mass index; CV, cardiovascular; HF, heart failure; SD, standard deviation.

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Regulatory T cells supress memory IFN-gamma and IL-17A production in highly sensitised patients with end-stage renal disease

Transplantation - research

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Introduction: Highly sensitized patients (HS) present worse long-term outcome after transplantation compared to those non-sensitised. It has been hypothesised that regulatory T cells (Tregs) could regulate memory immune alloresponses, however Tregs populations have not been studied in HS populations. IL-17A and IFNγ are cytokines which have been strongly associated with acute and chronic rejection, respectively. In vitro anti-donor IFNγ production correlates with graft dysfunction and fewer Tregs in patients with chronic rejection. Therapy using autologous expanded Tregs has been demonstrated to be safe. This project aims to understand Tregs phenotype in HS patients and to test the hypothesis that Tregs could be used in sensitised patients to suppress memory IFNγ/IL-17A responses.

Methods: We prospectively recruited HS patients on haemodialysis (HD), phenotyped their PBMCs, isolated their Tregs and expanded them using established protocols (Interleukin-2 + Rapamycin). We compared the Tregs and Teffectors (Teffs) phenotype with non-sensitised patients on HD and healthy volunteers (HV). IFNγ/IL-17A production by CD8-depleted peripheral blood mononuclear cells (PBMC)(+/- additional depletion of CD25hi cells) in response to Human Leucocyte Antigen (HLA) proteins (PureProt) was tested in FluoroSpot to assess the memory immune alloresponses at baseline and when expanded autologous Tregs were added.

Results: Out of 16 patients recruited, 10 (63%) had a background of transplantation with a nephrectomy in 4/10 and 4/10 (25%) were still receiving immunosuppressive drugs. Tregs from HS patients shared similarities with Tregs from HV (Figure 1A), but had a smaller proportion of CD45RA-CCR7- effector memory Tregs (1B) and a higher proportion of GATA-3+ Tregs (1C) compared to HV. Stimulation of CD8-depleted PBMCs from HS patients showed HLA specific reactivity (HLA SR) for IFNγ (3/16) and IL-17A (5/16) in response to HLA proteins they have been sensitised to.

Autologous ex vivo expanded Tregs managed to regulate IFNγ production in 1/3 patients (Figure 2A). When CD19- were depleted, 5/10 patients presented an increase of IFNγ production (4 of those with no response from CD8-depleted PBMC) (Figure 2B). Interestingly, autologous ex vivo expanded Tregs managed to regulate IFNγ production in all these patients (5/5, 100%).

In 4/5 patients with IL-17A HLA SR (80%), IL-17A production was regulated by ex vivo expanded Tregs (Figure 3A). Moreover, in 4/11 (36%) patients, Tregs depletion was associated with and increase in IL-17A production, which was suppressed in 3/4 when expanded autologous Tregs were added (3B).

Discussion: HS patients display a smaller proportion of CD45RA-CCR7- Tregs compared to HV. This was associated with the lack of spontaneous regulation of IFNγ production when stimulated with HLA they have been sensitised to. Autologous ex vivo expanded Tregs are able to regulate IFNγ production in HS patients only when the B cells are depleted. When challenged with an HLA they have been sensitised to, IL-17A production could be inhibited by autologous ex vivo expanded Tregs in 80% of HS patients. The Phase IIa trial GAMECHANgER-1 will test whether these findings are reproducible in vivo in highly sensitised patients awaiting kidney transplantation.

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Searching for druggable targets in HNF1B mutant kidney organoids

Genetic and rare diseases

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Background. Heterozygous mutations of hepatocyte nuclear factor 1B (HNF1B) cause a spectrum of human kidney disease, from congenital dysplastic organs containing poorly formed nephrons to tubulopathies featuring electrolyte wasting into the urine. Despite the clinical importance of HNF1B kidney disease, research into this topic has been hampered by the difficulty of accessing mutant kidney tissues because biopsies and nephrectomies are rarely undertaken in affected individuals. Moreover, most genetic mouse models only exhibit a dysmorphic kidney phenotype when both Hnf1b alleles are mutated. We reasoned that studying HNF1B heterozygous mutant organoids derived from human pluripotent stem cells would reveal dysregulated molecular pathways and also identify potential druggable targets.

Methods. We introduced a heterozygous frameshift mutation in exon 1 of HNF1B using CRISPr/Cas9 gene editing in the human embryonic stem cell line Man13. We compared the capacity of this mutant line to generate nephron organoids with the non mutant isogenic line. RNA sequencing (RNAseq) was used to document the transcriptional landscape as the cell lines underwent renal differentiation.

Results. Using an established kidney differentiation protocol, both lines generated organoids. Observing these transparent organoids in culture, mutants appeared to have a less complex internal structure. Histology confirmed that wild type organoids were dominated by regular tubule profiles with their walls composed of a cell monolayer, whereas a subset of dysmorphic tubules in mutant organoids were multilayered. As assessed by Western blot, protein levels were lower in mutant organoids than in wild type organoids. As assessed by immunostaining, dysplastic mutant tubules showed a patchy HNF1B pattern, contrasting with the uniform staining of nuclei in wild type tubules. Upregulated transcripts in HNF1B mutant organoids included NCAM1, LHX1, and PAX8, each expressed by nephron precursors. Downregulated transcripts included: anti-cystic molecules CYS1 and PKDH1; and HNF1 family members HNF1A and HNF4G; and GREM1, a BMP antagonist. Also notable, given electrolyte abnormalities in HNF1B patients, was downregulation of several Mendelian tubulopathy genes: AGT, angiotensinogen, mutated in renal tubular dysgenesis; CLCN5, a Cl channel mutated in Dent disease; CLDN19, a tight junction protein mutated in renal hypomagnesaemia 5; LRP2, encoding megalin, an endocytic receptor mutated in Donnai-Barrow syndrome; and SLC4A4, a transporter mutated in proximal tubule acidosis. Bioinformatic analysis of RNAseq data indicated an aberrant cAMP signalling pathway in mutant organoids, and HNF1B

mutant kidney tubules were resistant to forskolin, an adenylyl cyclase activator, whereas this chemical resulted in dilatation of wild type tubules. Bioinformatics also indicated glutaminergic receptor signalling defects, and levels of glutamate ionotropic receptor kainate type subunit 3 (GRIK3) were increased on Western blot of mutant organoids, with the protein prominent in dysplastic tubules as assessed by immunostaining.

Summary. Our strategy, involving biochemical analyses of HNF1B mutant dysplastic kidney organoids compared with isogenic organoids lacking the mutation, reveals several aberrant pathways and specific druggable targets. Studies are ongoing to determine whether manipulating these will ameliorate the dysmorphic and dysfunctional phenotypes of HNF1B mutant organoids.

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Using personalised pluripotent stem cell technology to study inherited genetically-defined renal dysplasia

Genetic and rare diseases

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Background. Kidney malformations, including renal dysplasia where organs contain immature and metaplastic tissues, are the commonest cause of kidney failure in young children. Malformations also account for an important subset of young adults with chronic kidney disease. Heterozygous mutations of hepatocyte nuclear factor 1B (HNF1B), encoding a transcription factor expressed in developing kidney epithelia, are the commonest genetically defined cause of human kidney malformations. It is rare to access kidney tissues from affected individuals, and this is a barrier to understanding the pathobiology of this disease. We hypothesised that human induced pluripotent stem cell (hiPSC) and kidney organoid technologies could recreate HNF1B associated dysplasia.

Methods. We studied a family that carried a heterozygous deletion of exon 9 of HNF1B. Over three separate pregnancies, three fetuses had bilateral renal dysplasia detected on ultrasound screening. One sibling, with oligohydramios, underwent termination of pregnancy. Two male siblings survived and are currently young adults with eGFRs 60-70 ml/min, and each has evidence of tubulopathy (hyperuricaemia treated with allopurinol in both, and one with renal glycosuria). Their HNF1B mutation was inherited from their father who has milder kidney disease and gout. After consent (ethics REC 11/H1003/3) hiPSCs were generated from peripheral venous blood samples donated by the two surviving children and their unaffected non-mutant mother. hiPSCs were induced to differentiate over several weeks using a well-established protocol, and resulting organoids compared.

Results. As expected, the hiPSCs that did not carry the mutation differentiated to form organoids that were rich in nephrons, glomeruli and proximal tubules, with a lesser proportion of distal tubule and collecting duct-like structures. Similar results were obtained using an unrelated control iPSC line. In contrast, although hiPSCs from each affected patient formed organoids, these were of significantly greater area than those derived from their mother's cells. During the period in 3D culture, the HNFIB+/-Δexon9 mutant organoids expressed lower levels of HNF1B mRNA than the mother's organoids, as assessed by primers over exon 9. On histology, mutant organoids contained dysmorphic glomeruli with poorly formed glomerular tufts, identified by synaptopodin immunostaining, and aberrant tubules with walls comprised of multiple layers of epithelia, identified

by CDH1 immunostaining. To test the functionality of tubules, organoids were exposed to 8-bromo-cyclic AMP, a chemical known to enhance the accumulation of fluid within lumens of healthy developing kidney tubules. As expected, tubules in control organoids dilated over a several days. In marked contrast, mutant tubules were resistant to this chemical, consistent with a delayed or an otherwise aberrant differentiation.

Summary. hiPSCs and organoid technology can model dysmorphic and dysfunctional HNF1B mutant kidneys in a dish. We have generated hiPSCs from several other HNF1B mutant families followed in our clinics. In future, such models will be used to study the molecular pathobiology of this disease and also as test beds for drug therapies to enhance normal differentiation.

Thursday 9th June, 14:10-15:10

Track S - Laboratory and translational science

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HIV+ end-stage renal disease patient with immunosuppressive drug-drug interactions received successful transplantation after Ibalizumab suppressed switch

Pharmacology, medicines management including anaemia and MBD, Transplantation - research

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This case represents the first known use of ibalizumab in an HIV+ patient on hemodialysis undergoing kidney transplantation. The patient is a 67-year-old black male diagnosed with HIV in 2003 who had been on hemodialysis for a number of years, the challenge was to find an HIV antiretroviral (ARV) regimen to maintain viral suppression while eliminating drug-drug interactions (DDIs) between his ARV regimen where viral drug resistance significantly limited treatment options and his immunosuppressive medications post-transplant. The patient's HIV treatment blocked his ability to receive kidney transplant due to DDIs with tacrolimus and mycophenolate mofetil.

Diagnoses:

Chronic kidney disease

HIV-1 infection

Cerebrovascular disease

Seizure disorder – secondary to cerebrovascular accident (CVA) in 2002

Hypertension

Type 2 Diabetes Mellitus

Surgical and Procedure History

Right heart catheterization – 2021

Renal transplant (non-familial allograft) – 2019

Lung biopsy – 2011 – negative

Arteriovenous fistula placement - 2012

Family History: Mother, father, and sister are all deceased of complications related to diabetes, hypertension, and/or kidney disease.

Physical exam was remarkable for gait disorder from past CVA and vision changes from diabetic retinopathy. Hypertension is controlled.

HIV history includes a CD4 nadir <200 cells/mL pre-transplant with the only known opportunistic infection of oral candidiasis.

ARV history was determined by patient and physician recall. See Table 1 in appendix

ARV Resistance Profile

Due to inability to recover previous treatment records, past resistance tests were unavailable. Given patient's long period of viral suppression from 2008 to 2018, the only available sequencing pre-transplant was proviral DNA.

Patient viral resistance profile and level of resistance can be seen in Tables 2 & 3 in appendix

The patient's concomitant medications, pre-transplant and post-transplant regimens can be seen in Table 4 in the appendix.

Successful kidney transplantation occurred in June 2019. His recovery was prolonged by anemia as he refused transfusions. Transient dysphagia required temporary PEG tube placement for enteral nutrition and medications. Ibalizumab infusion was important as other ARV absorption may have been impacted until return to PO intake.

Anemia resolved 2 months post-transplant and other labs were unremarkable during this time period.

A summary of treatment can be seen in Table 5 in the appendix

Discussion: HIV-positive donor organs can now benefit HIV-positive recipients enabling life-saving transplants for our patients. While the current possibility of transplant is welcome, the complexity of managing ARV regimens that are limited due to resistance and DDIs poses significant clinical challenges.

Pre-transplant, the combination of ibalizumab, emtricitabine/tenofovir disoproxil fumarate and raltegravir maintained viral suppression successfully. Post-transplant, raltegravir was changed to dolutegravir and 2 years after transplantation, HIV suppression has been maintained. Patient's quality of life has improved dramatically.

Ibalizumab is the first monoclonal antibody approved for the treatment of HIV-1 infection. With no expected DDIs or cross resistance with other ARVs, it became a key option for this patient. Also, ibalizumab is not dependent on renal or hepatic clearance as all of the ARV medications. Importantly, this case represents the first known use of ibalizumab in an HIV+ patient undergoing kidney transplantation.

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Surface Plasmon Resonance interrogation of the Alternative Pathway regulatory Trimolecular complex reveals a C3 variant with resistance to Factor H regulation

Genetic and rare diseases

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Introduction: A 9 year old girl was referred to the NRCTC having presented with aHUS at the age of 16 months. Following initial treatment with plasma exchange she had been commenced on Eculizumab and remained on this treatment. Genetic analysis had identified a homozygous point mutation in C3, p.L1109V (c.3325C>G:p.Leu1109Val).

Mutation screening in aHUS is challenging, because most of the disease-associated mutations are individually rare, and a significant proportion of variants consist of missense mutations of unknown significance. The definitive interpretation of a variant of unknown significance is of importance to allow counselling of family members and to assess risk of relapse following Eculizumab withdrawal-seen almost exclusively in those with functionally significant complement mutations.

Methods: Healthy donor (WT) C3 and the rare variant L1109V C3 were purified from plasma using standard affinity chromatography techniques. Standard alternative pathway (AP) complement protein functional tests were undertaken. These included fluid phase C3b binding cofactor activity assays and In vitro modelling of cell surface regulation using standard plasmon resonance. A novel technique was employed to analyse the formation of the AP regulatory Tri-molecular complex (TMC) in real-time.

Results: The co factor activity assays showed no difference in fluid phase regulation of L1109V C3 when compared to WT C3. Using surface plasmon resonance we used a novel assay to interrogate the alternative pathway regulatory trimolecular complex formation on surfaces demonstrating reduced binding of the regulatory protein FH and FI. To probe this difference in fluid vs surface complement regulation we used FH fragments: CCP1-4 the regulatory domain responsible for cofactor activity and the surface localisation domains of Factor H (CCP 19-20)

In keeping with normal fluid phase activity, the binding of the regulatory domain of FH (CCP1-4) to the C3 variant was normal. In stark contrast, L1109V C3b had a clear attenuation of binding of surface localisation domains of Factor H (CCP 19-20)

The reduced efficacy (around 50%) to build the TMC implies that L1109V is resistant to cleavage of FI when FH is serving as the co-factor on the cell surface.

Discussion: The functional characterisation of L1109V clearly shows this variant is resistant to regulation of FH and this behaviour arises from an impairment of binding of FH CCP 19-20, impairing regulation of C3b when bound to the cell surface and disables FH from serving as a co-factor to FI when building the TMC for surface regulation. This novel assay provides a highly sensitive assay of complement activity to allow analysis of variants of uncertain significance in aHUS.

Wednesday

AKI

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Can just telling people they've had an AKI improve their outcomes.

AKI

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Acute kidney injury (AKI) is a common health issue. It is a sudden episode of kidney failure that is almost entirely associated with episodes of acute illness. AKI is common with as many as 20% of patients arriving at hospital having an AKI, with up to 15% of patients developing AKI in a postoperative period. Patients who have an episode of AKI are more likely to have a further episode of AKI and require readmission to hospital. This project aimed to provide patients with AKI education for self-care and management, with the hope of reducing AKI readmissions. Using quality improvement methodology, the AKI patient discharge and readmission pathway was reviewed, and information about AKI was given to patients. This was in the form of verbal information and a patient information leaflet. This information was provided on discharge from acute care. Baseline data were collected that showed more than 80% of patients reported that they were not given information about AKI prior to their discharge from hospital. Due to higher readmission rates, the focus of this improvement project was on acute medical wards. Following implementation, there was a sustained reduction in AKI patient readmission rates. This reduction led to a significant reduction of inpatient bed days and a shorter length of stay for those patients who were readmitted. Quality improvement methods have facilitated a successful reduction in acute AKI readmission to hospital.

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Epidemiology and definitions of ESA hyporesponsiveness among patients with anemia due to chronic kidney disease: a targeted literature search

Pharmacology, medicines management including anaemia and MBD

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Introduction: Current management of anemia associated with chronic kidney disease (aCKD) involves administration of supplemental iron and erythropoietin-stimulating agents (ESAs). However, some patients experience inadequate response to ESAs, termed ESA hyporesponsiveness (ESA-H) or resistance. ESA-H is associated with increased risk for cardiovascular events, morbidity, and all-cause mortality, representing an important clinical challenge. The objective of this study was to identify and synthesize recent literature on the definitions and epidemiology of ESA-H among patients with aCKD.

Methods: We performed a targeted literature search on PubMed, supplemented with searches of clinical guidelines and key publications, to identify and summarize operational definitions of hyporesponsiveness and the epidemiology of ESA-H.

Results: Six clinical guidelines, 23 observational studies, and 9 clinical trials, published since 2007, were included in the review. Cohort size varied from 99 to 138,688 patients.

Definitions of ESA-H varied across guidelines and studies, as different approaches, thresholds, and criteria were used to classify patients as ESA hyporesponders. The definitions of ESA-H provided by clinical guidelines were rarely used in the identified observational and clinical studies. In these studies, the most commonly used measures were either the ESA resistance index (ERI) or a combination of ESA dose and target hemoglobin level. ESA doses varied by country and type of dialysis received and were expressed as U/treatment, U/week, or U/kg/week. However, there was no consensus on the ERI values or ESA doses considered indicative of ESA-H. In studies reporting U/week, ESA doses above which patients were considered hyporesponsive ranged from 4000 U/week to 12,000 U/week (Figure). Prevalence estimates for ESA-H among dialysis-dependent patients with aCKD ranged from 2.8% to 39.1%. In some patients, ESA-H was transient, although this finding was not commonly cited among studies. Three publications categorized patients as acute or

chronic hyporesponders. The proportion of patients considered chronic hyporesponders ranged from 20.7% to 31.8%, and the proportion considered acute hyporesponders ranged from 24.4% to 68.2%. Although predictors of ESA-H related to patient characteristics and treatments across study types were not consistently identified, variables frequently associated with ESA-H were high C-reactive protein levels (8 of 32 studies) and lower serum albumin levels (6 of 32 studies).

Discussion: There is a lack of alignment between clinical guideline definitions of ESA-H and definitions used in clinical studies. This could be due in part to difficulty in applying guideline definitions to administrative databases or available clinical data. Guidelines and definitions also vary by country, likely due to variability in recommended ESA dose and hemoglobin thresholds among countries and differing practice patterns. Differences in definitions of ESA-H, cohort size, and dialysis dependence are likely to contribute to the variability in prevalence estimates and predictors identified. This study highlights the need for a consistent definition of ESA-H that can be used in randomized controlled trials and observational studies. A universal definition would facilitate improved clinical management of patients who may be ESA resistant, support the understanding of prevalence and risk factors across practice settings, and form the basis of future research focused on potential treatments for ESA hyporesponders.

Wednesday

Anaemia

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Evaluation of time and activities associated with ESA administration for anemia in CKD: a systematic review

CKD, Pharmacology, medicines management including anaemia and MBD

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Introduction: While use of erythropoiesis-stimulating agents (ESAs) is widely accepted for management of anemia in patients with chronic kidney disease (CKD), use of these injectable therapies presents a time and cost burden. We sought to identify and synthesize evidence on time-and-motion (T&M) of ESA procurement, prescribing, administration, and monitoring and associated costs to better understand the operational complexities associated with ESAs for anemia in CKD.

Methods: Embase/MEDLINE databases were searched on 28-Oct-2021. Search terms included indexed and free-text terms related to CKD, dialysis, anemia, ESAs, T&M, and costs. Additionally, searches of Google Scholar, conference proceedings, healthcare organization websites, and bibliographic searches were conducted. English-language publications reporting T&M of ESA treatment for CKD-related anemia, published from Jan 2001 onwards were eligible. Narrative synthesis of the data was performed.

Results: We included 11 T&M studies (from 1,583 citations). Most were conducted in Europe (5 studies). Ten investigated dialysis-dependent (DD) patients treated in hemodialysis units, and one evaluated non-dialysis dependent (NDD) patients in physician offices. Numbers of sites assessed ranged from 1–21. Seven studies reported on healthcare personnel (HCP), in general, who performed ESA tasks; nurses were the main HCP carrying out tasks in four studies. ESAs assessed included epoetin (alpha and beta), darbepoetin alfa, and CERA. Dosing schedules ranged from thrice-weekly, once-weekly, to once-a-month.

In the DD-CKD studies, eight reported observed overall time across ESA-related tasks, two reported time only for specific tasks, and three for both overall and by individual task(s). Specific tasks tracked and reported varied between studies; most often reported tasks were injecting drug (6 studies), reviewing patient chart (5), collecting the drug from a fridge (5), record-keeping (4). Mean HCP time per single drug preparation ranged from 0.97–5.06 min (4 studies). Time per single drug distribution was 0.25 min (short-acting; 1 study) and 0.49 min (long-acting; 1 study), per injection 0.26–1.63 min (5 studies), and record-keeping 0.32–2.2 min (2 studies). For combined ESA administration tasks,

mean total HCP time per patient per year (PPPY) was 0.33–20.3 h (6 studies). In the NDD-CKD study, routine injection visit time was 21 min/patient.

Mean total HCP time costs PPPY for combined ESA administration tasks were reported by 4 studies. In Panama (2018 US$), mean single administration cost was $82.68 (short-acting ESAs) and $4.44 (long-acting ESA), translating to $16,287.96 (short-acting ESAs) and $874.68 (long-acting ESA; 1 study) annually. In a US study (2005 US$), PPPY costs were $395 (95% CI, 368–424), extrapolated to an annual cost of $39,546 for a hypothetical scenario of 100 patients. An Australian study reported PPPY costs from AU$55.75–90.49 (short-acting) and $11.17–20.38 (long-acting). A study conducted in 12 hemodialysis units in Germany and UK estimated total costs of €4,786 (Germany) and £7,696 (UK) per centre with 100 patients/year (cost year 2006).

Conclusion: There is substantial time and cost burden associated with the reported tasks for needle-based administration of ESAs in patients with anemia in CKD. The introduction of an oral treatment can help lower healthcare resource use and associated costs.

Wednesday

Anaemia

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Kidney Disease Burden – A take on Host-Pathogen Communication and Visualization

AKI, Pharmacology, medicines management including anaemia and MBD

Muhammad Shahid[1], Pizon Kacper[1]

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Introduction: Apart from affecting the upper respiratory tract, severe acute respiratory syndrome-coronavirus (SARs-CoV) and SARS-CoV-2) can target kidneys resulting in disease burden. Where there is a lack of effective treatment for SARs-CoV and SARS-CoV-2, a more indirect approach should be considered to lower probable risk and onset of disease amongst immunocompromised and immunosuppressed individuals and patients. Angiotensin Converting Enzyme Inhibitor 2 (ACE2) has promising impact including acting against symptoms accompanied to that of SARs-CoV and SARS-CoV-2. Literature informs that ACE2 is expressed across several physiological systems, including lungs, cardiovascular, gut, kidneys, and central nervous, and across endothelia. Aims: This work seeks to investigate causes and potential mechanisms during SARS infection (CoV-2), renal interaction, and the effects of Acute Kidney Injury (AKI).

Objectives: The authors seek to provide an understanding of Microscopy and Visualization of Host-Pathogen Communication and principles of ACE2 in context of Immunology and Infection to understand burden of kidney disease.

Design: The authors seek to provide basic principles of activity within the kidney and the analysis of the effect of immunology and pathological components, which would be important in the treatment and prevention of infection.

Discussion: There has been a surge in literature surrounding mechanisms attributing to SARs-CoV and SARS-CoV-2 action on immune response to pathogen. There is possible advantage to implementing ACE2 treatment to improve immune response against infection.

Conclusion: ACE2 may provide appropriate strategies for the management of symptoms that relate SARs-CoV and SARS-CoV-2 in most immunocompromised or immunosuppressed patients. Visualization of ACE2 action can be achieved through microscopy to understand Host-Pathogen communication.

Keywords: Nephrology, Immunology, Microbiology, Host-Pathogen, Visualization, Biomedical Sciences,

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Evaluating a multidisciplinary kidney genetic clinic, 2010 to 2020

Genetic and rare diseases

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Background. Paediatric nephrologists encounter a rich variety of kidney diseases. Many of these rare disorders have genetic bases but how efficient are we at defining genetic causation in NHS hospital practice?

Methods. Accordingly, we analysed all results from our kidney genetic clinic undertaken from early in 2010, its inception, to Spring 2020. This multidisciplinary clinic comprised three physicians (a clinical geneticist, a paediatric nephrologist and an adult nephrologist) who together assessed each referral. All records of clinic visits, and results received by the Summer of 2020, were reviewed. We compared these results with historical data from a kidney genetic clinic (2006-2009) run by one of the authors.

Results. Two hundred and twenty two children were referred over 10 years. Twenty were not brought to the clinic, leaving 200 index cases (half male and half female). Half of the referrals came from paediatric nephrologists, with the remainder mostly from geneticists, paediatric urologists and general paediatricians. A definitive genetic diagnosis was made in 91 (45%). The commonest, in 24 cases, were COL4A3/4/5 variants in the Alport syndrome/thin basement membrane spectrum. Twenty three were diagnosed using the NHS Gene Testing Network; the exception was a deep intronic COL4A5 in found through the 100 Thousand Genomes Project. One family co-inherited COL4A5 and MYO1E variants, accentuating kidney disease. Eleven index cases were born with kidney malformations and carried heterozygous mutations of the transcription factor HNF1B; in two, the biliary system and the foregut were also severely malformed, and a third had hypothyroidism. Six index cases had digit and skeletal signs of nail patella syndrome, five with proven LMX1B mutations, but none had a decreased eGFR, and only one had mild proteinuria. Five index cases had Bardet-Biedl syndrome, mostly BBS1 mutations; all had malformed urinary tracts but only one had impaired kidney function. Several novel observations were made including: brothers with developmental delay and urinary tract malformations carried JARID1 histone demethylase mutations; a child with bright fetal kidneys and oligohydramios had biallelic PKD1 variants - one inherited from father who had a few cysts, and the other from mother who had normal kidneys; Senior Loken syndrome presenting with end stage renal disease and IQCB1 nephrocystin-5 mutation; an infant with atypical HUS carried biallelic CFH variants - in the extended family those carrying one mutant allele had a low penetrance of HUS; cat eye deletion syndrome with cystic kidneys; and a child with kidney and

skeletal malformations (Sensenbrenner syndrome) with mutation of the cilia gene WDR35. Our historical clinic assessed 91 referrals, with 27 (30%) assigned specific genetic diagnoses; the current clinic was significantly (P=0.01) more successful in this regard.

Summary. Our multidisciplinary clinic had notable success of making genetic diagnoses, thus providing families with an answer to their often long-sought question “Why does our child have (often devastating) kidney disease?” Nevertheless, the genetic diagnostic success rate remains low for children born with severe kidney malformations and here it is hoped that the introduction of whole genome sequencing will be informative.

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Long-term multisystemic efficacy with migalastat in ERT-naive and ERT-experienced patients with amenable GLA variants

Genetic and rare diseases

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Fabry disease (FD) is an X-linked, multisystemic disorder caused by GLA variants resulting in α-galactosidase A deficiency. Migalastat has demonstrated multisystemic efficacy and is approved for treating FD in adults with amenable GLA variants. We report incidence of predefined cerebrovascular, cardiac, and renal Fabry-associated clinical events (FACEs) as a measure of long-term efficacy of migalastat.

Phase III placebo-controlled FACETS (NCT00925301, enzyme replacement therapy [ERT] naive), active-controlled ATTRACT (NCT01218659, ERT experienced), and open-label extension (OLE) studies (N=97; mean age: 46.4 years; males, 38%) data were integrated. FACE incidence (events per 1000 patient-years) was assessed in all patients. Historical comparative data on FACE incidence was obtained from literature review.

Over median (Q1–Q3) follow-up of 5.1 (2.3–6.8) years, 17 (17.5%) patients experienced 22 FACEs with migalastat: an incidence of 48.3/1000. FACE incidence in ERT-naive classic males (<3% α-galactosidase A activity; multiorgan involvement) was 61.5/1000. Separately, incidence of cerebrovascular, cardiac, and renal events was 13.2/1000, 30.7/1000, and 4.4/1000, respectively. Following LVMi reduction in Phase III, LVMi remained stable with continuing migalastat in the OLE (N=84; mean (SD) migalastat exposure 2.7 (1.0) years (range: 0.1–4.3). Cox proportional hazards identified baseline estimated glomerular filtration rate (eGFR) as a predictor of FACEs, highlighting the importance of preserved renal function. Patients on migalastat for median (Q1–Q3) 5.9 (4.7–7.0) years (N=78) had stable eGFR (SD) of –1.57 (3.33) mL/min/1.73m2/year. ATTRACT subjects were randomised to receive migalastat or ERT for 18 months before switching to open-label migalastat. Migalastat (N=49) was associated with lower FACE incidence versus continued ERT (N=15; 66.0/1000

vs 326.6/1000, respectively). ATTRACT patients continued migalastat in the OLE (N=49) and experienced sustained low FACE incidence of 47.9/1000 over median (Q1–Q3) 4.9 (3.0–5.7) years, comparing favourably with historical reports of ERT. Low FACE incidence in migalastat-treated patients with amenable variants supports long-term multisystemic efficacy with migalastat.

Supported by Amicus Therapeutics.

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A systematic literature review on the costs and healthcare resource utilization associated with dialysis and anemia management by dialysis modality in patients with end-stage kidney disease

Haemodialysis - service delivery, Home therapies - service delivery

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Introduction: End-stage kidney disease (ESKD) is associated with a high clinical and economic burden and may be treated through varying dialysis modalities, including in-center hemodialysis (ICHD), home dialysis (home hemodialysis [HHD], or peritoneal dialysis [PD]). The prevalence of anemia associated with ESKD is estimated to be >50% and may present an increased risk of comorbidities and lower quality of life. Healthcare resource utilization (HCRU) and costs of dialysis care, in the general and anemia-associated ESKD population, is an essential aspect of the value of home dialysis. This review assessed the extent to which the economic burden of dialysis in ESKD and management of anemia in ESKD have been characterized in the literature based on dialysis modality.

Methods: A systematic literature review was conducted to characterize costs and HCRU in patients receiving ICHD, HHD, or PD in the general and anemia-associated ESKD populations. Outcomes included, but were not limited to, cost of dialysis, hospitalizations, and costs and use of erythropoiesis-stimulating agents (ESAs). Databases, including Embase and Medline, were searched between 2011 and 2021.

Results: Of 1105 records identified, 43 met the inclusion criteria for this review (costs=26, HCRU=8, costs and HCRU=9). Most studies were conducted in Europe (n=18) or North America (n=14). Studies were either observational database analyses (n=15) or economic evaluations (n=28). Comparisons in the studies included costs, both direct (eg, medical and pharmacy) and indirect, and/or HCRU between ICHD, HHD, and PD (n=22); between ICHD and HHD (n=11); or between ICHD and PD (n=10).

Most studies found that ICHD was more expensive than home modalities. Fourteen primary cost studies reported that total dialysis costs for ICHD were higher than HHD/PD per patient per year. Thirteen of 16 economic models reported that ICHD is more costly than HHD/PD, with 11 concluding

that HHD/PD is cost-effective or dominant compared with ICHD. Seventeen studies reported HCRU, with hospitalizations as the most frequent cost-related component (n=12). Findings contradicted one another as to which modality reduced HCRU across studies.

Limited evidence for anemia-related outcomes was available, with only 11 studies showing either costs and/or HCRU relating to ESA or iron use. Five reported that use and dose of ESAs were higher in ICHD patients than in HHD/PD patients (Figure). ESA costs were reported across 8 studies, with 4 reporting equivalent ESA costs across modalities and 4 reporting a higher ESA cost for ICHD patients. Three of these latter 4 studies related higher ESA costs with differences in dosage and use of ESAs. One economic evaluation modeled that ESA and iron costs were higher for HHD than ICHD, though not statistically significant.

Discussion: Most studies reported a higher total dialysis cost for ICHD compared with HHD; however, there was a paucity of evidence characterizing anemia-associated HCRU and costs. From the limited studies included, ICHD patients used ESAs more frequently and at higher doses than HHD/PD patients, thus incurring a higher cost. As global interests highlight increasing HHD penetration, understanding the cost differences and drivers of these differences in ESKD patients with anemia is increasingly important.

Wednesday

Quality Improvement, patient reported outcomes and experience

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Improving patient education, empowerment and access to specialist vasculitis services

Patient education, Patient outcome and experience

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Introduction: Anti-neutrophil cytoplasmic autoantibody (ANCA) associated vasculitis is an autoimmune condition characterised by multi-organ disease that can be life threatening. Over recent years the mortality associated with ANCA vasculitis has improved (1) but it is still associated with significant morbidity, requiring ongoing follow up and specialist input(2).

More recently, patients are using social media to learn about and manage their health conditions (3,4). A rise in telehealth, exacerbated by the COVID-19 pandemic has seen the role of digitalised health care being brought to the forefront. We examined how our cohort of ANCA vasculitis patients feel about access to the vasculitis service, as well as identifying ways to engage and encourage patient education using social media platforms.

Methods: A small, focused cohort survey of randomly selected ANCA vasculitis patients was conducted from a single centre in the North West, UK. Questionnaires were sent to patients and their primary carers. The survey consisted of 14 questions which included how often they contact the vasculitis team, whether they already use social media or digitalised health apps to manage and seek information on their condition and if they would be willing to engage with social media platforms to get information in the future.

Results: Of the twenty questionnaires sent out, 13 replied; 10 patients and 3 carers. The median age was 71 years (IQR 62-78) and all patients had a diagnosis of ANCA vasculitis, with diagnosis dates ranging from 6 months to 10 years.

The majority (91.6%, n =11) were aware that they could contact the vasculitis team between clinic appointments, with all patients choosing email or telephone as the primary method. Most patients were ‘very satisfied’ with the access to clinician advice between appointments stating the service was ‘friendly and quick to respond’. Patients contacted the team on average 2-3 times a year between appointments. When asked about improving access to the service, eleven said they would be willing to use a mobile number to text message on a non-urgent basis.

Nine patients (69 %) stated they use a digital device or app to manage their health conditions, with the majority using it for hospital appointments and prescriptions. Four patients use social media to access information about their condition or treatment. Of those that would be willing to use social

media as a way of receiving information (n=8), Facebook, Twitter and WhatsApp were the preferred platforms.

Discussion: We have demonstrated that all a large proportion of vasculitis patients contact us between appointments, highlighting the need for a specific service to meet the needs of these patients. We identified that improving access to the service will not only to provide prompt replies to patient queries but also promote communication, patient education and shared decision making.

This small study shows patients are keen and willing to engage with social media as way of receiving accurate information about their condition and treatment. We believe that social media can play a positive role in the management of chronic conditions and we aim to incorporate this into our service.

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Wednesday

Quality Improvement, patient reported outcomes and experience

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When the world was seemingly falling apart- our Support Group stood firm & became a shelter.

Patient and public involvement, Other

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Background: Our kidney patient support Group was set up in 2015 for patients and family members. Pre the covid-19 pandemic , this was run bi-monthly, across two geographical areas to ensure equity of access to all our patients, alternating dates to cater for the two dialysis shifts. Meeting face to face in community halls, sports facilities, and clubs. A communication list was established to ensure that those that could not make the meetings could still access information shared and send in questions to be asked ahead of any meeting. When covid struck, suddenly our members were being asked to shield, classed as clinically extremely vulnerable, left feeling isolated and unable to socialise How could we help in this situation?

Aim: Trying to maintain the aims of the group to be open to all patients, their families/carers known to renal services; provide an opportunity for patients and their families to have a voice; share experiences in a safe environment and offer peer support became an enormous challenge.

Immediately we thought how could we provide this now? Our patients are clinically extremely vulnerable- where would be safe? What could we do differently?

Method: Zoom meetings were proposed, although not quite the same the technology enabled us to continue with an additional source of comfort, reinforcing our mantra- you are not alone.

We had always worked in partnership with our local Kidney Patients Association , who generously funded the venues for our face to face meetings. We approached them for ideas and they enabled us to use their zoom account to host meetings

Invitations were sent to all our members on the communication list.

At our first virtual meeting it was decided because of shielding and people feeling isolated it would be beneficial to meet monthly at the usual time, still alternating days for the dialysis shifts.

Results: We were able to seamlessly transition into virtual meetings and have had 21 meetings to date. We have invited guest speakers: CEO of Polycystic Kidney Disease charity, local water company to help with the priority register, Renal Dietitian, National Kidney Federation Liaison Officer to name some. In addition promoted access to national patient webinars

We currently have 138 members on the communication list. The number of people at the meeting varies from 6-11. We have been privileged to be a part of our members/ members family's journey as they transition into dialysis, celebrate successes with passing exams and moving onto university, get married, work up to & have a transplant and also sharing anniversaries of 24 years & 5 years transplanted. We also remember our, members lost through this very difficult time.

We are now at a stage where we can explore together how to "venture back out into a world" that feels comfortable.

Conclusion: Despite the abrupt disruption to services around us, we were able to continue meeting. Members were able to support each other and celebrate milestones/ share in their grief. A consistent base – protection from this storm called COVID-19.

Implications for service: Going forward, we have recognised the need to develop a hybrid approach- when our members feel safe, to return to face to face, we will also offer the opportunity to join the meeting virtually.

Thursday

Living with kidney disease

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Working with frailty: the value of renal social work input within the renal MDT

Behavioural, psychological and quality of life

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Introduction: Frailty is hard to define, identifying a group of vulnerable mainly older adults at high risk of adverse outcomes, and for the severely frail, it can take a comparatively minor external stressor such as a fall to lead to a major loss of independence. The demographic of people with end-stage kidney disease is becoming increasingly elderly, with a resultant growth in frailty and all its consequences. These include difficulties completing tasks of daily living, falls and declining cognition, all of which may lead to an increase in hospital admissions, as well as worries about planning for the future and an impaired ability to carry out patients' own caring responsibilities. Younger patients often have multiple comorbidities and can display features of severe frailty at a much earlier stage than their contemporaries. This paper explores the contribution that a renal social worker can make to tackle these areas of concern.

Methods: Over the last year we had noticed an increase in the number of referrals of patients with complex needs, and so we audited this group by looking back over the reasons for referrals and the actions taken. We then drew up a list of all the issues identified in order to establish how diverse they were and what impact our presence embedded within the MDT makes on this group of patients. We drew conclusions from this and, together with other MDT members, considered ways of further improving our service.

Results: Of the 116 referrals received over the period in question, nearly half (50) concerned issues around frailty, mostly relating to older people, but with a proportion of younger patients with multiple comorbidities. The most common issues identified were mobility problems/falls, reduced appetite/weight loss, cognitive impairment, low mood and motivation, continence problems and UTIs, fatigue and exhaustion, poor sleep, ageing carers and worries about the patient's own caring responsibilities.

Discussion: Having a renal social worker as part of the MDT has the following benefits for frail patients: a preventative and person-centred approach to maximising quality of life; the ability to liaise with key professionals such as GPs, community therapists, housing, DWP, other local authorities and voluntary agencies as well as our own MDT; carrying out Care Act assessments and arranging support in a timely manner for both hospital discharge and outpatients; completing mental capacity assessments and carers assessments and offering follow-up support; referring for equipment to maximise safety within the home; helping patients claim benefits and applying for grants to improve material circumstances; advocating for rehousing by writing supporting letters; assisting with advance care planning and arranging end of life support.

Ideas for improving our MDT response included regular patient screening, appointing a frailty champion and establishing a wellbeing team to co-ordinate our endeavours.

Thursday

COVID-19

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An exploration of adjustment experiences among people with chronic kidney disease who continued attending in-centre haemodialysis during the COVID-19 pandemic

Behavioural, psychological and quality of life, COVID-19 including vaccination

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Introduction: In the United Kingdom, there are over 25,000 people with Chronic Kidney Disease (CKD) receiving in-centre haemodialysis (ICHD). Individuals with this long-term condition have been classified as clinically extremely vulnerable from COVID-19 (Ikizler, 2020; Raab, 2020), and data from the UK Renal Registry (2020) has also shown higher rates of infection and increased risk of mortality among this patient population. However, people with CKD must adhere to their treatment regime and continue to attend clinical centres for dialysis despite the risk of contracting COVID-19 with potentially serious consequences. This has had a detrimental impact on people's experiences of ICHD and increased their risk of psychological distress and disturbance. Therefore, the aim of this study was to investigate the impact of COVID-19 on ICHD patients' coping, adjustment and wellbeing, as well as to explore how people experienced ICHD during the pandemic and gain insights into how those experiences affected their psychological adjustment and mental health.

Methods: This study utilised a mixed-methods design, by collecting questionnaire surveys and conducting qualitative semi-structured interviews with people with CKD receiving ICHD in the UK during the COVID-19 pandemic. Forty people (18 female, 22 male) completed a questionnaire survey and reported COVID-19-related adverse impacts on treatment and rated their COVID-19-related concerns. They then completed the Depression, Anxiety and Stress Scale (DASS-21) and four scales of the Kidney Disease Quality of Life Short-Form (KDQLS). Fourteen respondents also took part in a semi-structured interview following completion of the questionnaire to discuss their experiences. The interviews were audio-recorded and transcribed verbatim, before being analysed using thematic analysis (Braun & Clarke, 2006).

Results: The questionnaire results detailed that the most common adverse impacts were staff shortages/changes and impaired interaction with staff/patients. Of the respondents, 32.4% were severely depressed, 14.7% severely anxious and 18.9% severely stressed. Participants who had tested positive for COVID-19 were more depressed and reported more adverse impacts. Older and married/cohabiting participants had better adjustment and wellbeing. The thematic analysis identified four themes: perceptions of the threat of COVID; impacts on treatment; impaired

communication; and coping and positive adjustment. Participants' experiences extended understanding of how they were affected by measures taken to mitigate for COVID-19 and gave insights into ways that psychological impacts of COVID-19 could be mitigated by additional informational and supportive measures within dialysis units.

Discussion: The findings show how the impact of the COVID-19 pandemic on patients' experiences of dialysis treatment influenced their coping, adjustment and wellbeing. Adjustment and wellbeing among participants were low, and levels of depression, anxiety and stress were higher than for pre-COVID studies of ICHD patients using the same measure. Participants indicated having a lower quality of life, and their experiences demonstrated that those undergoing ICHD during the pandemic understood their vulnerability to disease, which combined with lockdown mitigations significantly heightened their risk of adverse mental health impacts. The results can help to identify the additional psychological support that dialysis patients need to maintain positive adjustment and wellbeing and inform enhanced clinical practice for ICHD during outbreaks of infectious disease.

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Moving more associates with reduced risk of cardiovascular disease and death across all stages of chronic kidney disease: a UK Biobank study

Rehabilitation, exercise and lifestyle

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Background and Aims: Physical activity (PA) is widely recommended for prevention of chronic conditions including cardiovascular (CV) disease. In chronic kidney disease (CKD), it is unclear whether PA confers similar benefit. We examined whether duration and intensity of PA is associated with risk of CV disease and mortality and whether the relationship differs in CKD.

Method: Participants were from UK Biobank: a prospective cohort study with over 500,000 participants. Estimated glomerular filtration rate was calculated using cystatin C (eGFRcys). CKD was defined according to the KDIGO guidelines and participants were categorised as no CKD (eGFRcys >90mL/min/1.73m2), CKD G1-2 (eGFRcys 60-89mL/min/1.73m2) or CKD G3-5 (eGFRcys <60mL/min/1.73m2). Exercise duration and intensity was self-reported using the international physical activity questionnaire (IPAQ) and participants categorised into 4 groups: inactive (reference), low, moderate and vigorous PA, according to World Health Organisation (WHO) weekly PA recommendations. Cox proportional hazards models tested associations between PA category and a composite endpoint of CV disease (myocardial infarction or stroke) or all-cause mortality across CKD categories. Models were adjusted for other known risk factors for CV disease and death including age, smoking status, blood pressure, eGFRcys and albuminuria.

Results: Of 502,460 participants in UK Biobank, 123,167 were excluded because of missing biochemistry or IPAQ data and a further 21,084 were excluded because of pre-existing CV disease: 358,209 participants were included in the analyses. Of these 182,457 (51.0%) were classed as no CKD, 162,621 (45.4%) as CKD G1-2 and 13,131 (3.7%) as CKD G3-5. 48,369 (13.5%) of participants were classed as inactive and 211,591 (16.5%) as undertaking vigorous PA. In participants without CKD, any PA above inactivity was associated with reduced risk of reaching the combined endpoint by approximately 20% (low: HR 0.77, CI 0.67-0.89; moderate: HR 0.80, CI 0.70-0.91; vigorous: HR 0.81, CI 0.73-0.90, $p<0.001$). This relationship is maintained in CKD G1-2, but in CKD G3-5, moderate (HR 0.75, CI 0.61-0.93) and vigorous (HR 0.77, CI 0.66-0.89, $p<0.001$) activity are associated with reduced risk of the combined endpoint. (Table 1) Interestingly across all categories of CKD, the majority of participants considered that they undertook more than the WHO minimum recommended PA per week.

Conclusion: Achieving the minimum weekly targets for PA set by WHO is associated with a significantly reduced risk of a combined endpoint of CV disease and death. This relationship is preserved in those with CKD G1-2, even when adjusted for other recognised risk factors. The benefit is seen in CKD G3-5 with increased intensity of PA, above the WHO minimum. PA data is self-reported which limits the accuracy and association does not prove causality. However, patients with CKD have a much higher risk of CVD and death and PA is a simple, low-cost intervention which warrants further study to improve CV morbidity and all-cause mortality amongst people with CKD.

Thursday

Glomerulonephritis and vasculitis

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A comparative study of Plasma and Interstitial fluid composition of uremic retention solutes and protein distribution

GN, Other

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Introduction: Uraemic retention solutes accumulate in the extracellular fluid (ECF) space of patients with kidney disease. Whilst these are well studied in plasma, assumption is made of their free circulation and hence equilibration in the entire ECF, despite anatomical barriers between plasma and interstitial fluid (IF) and the significant variability in the characteristics of these solutes, including molecular weight (MW), charge and solubility. We hypothesize that there may be differences in composition of these two compartments based on solute physicochemical characteristics, which may have implications for understanding uraemic pathophysiology including effective toxin removal.

Methods: A microneedle array and suction device was used to extract epidermal & subcutaneous IF patients with oedema of various aetiologies (kidney failure, liver failure and heart failure). Venepuncture was performed simultaneously. Paired plasma and IF samples were analysed using Roche COBAS 8000 c701 (Roche Diagnostics, Germany). Molecules measured were Creatinine, Urea, Sodium (NA), Potassium (K), Phosphate (PO4), Chloride (CL), Bicarbonate (TCO2), Urea, PTH, Total Protein, Albumin and Cystatin-C.

Results: Paired samples were obtained from 11 patients; 5 with kidney failure, 2 heart failure, 2 liver failure and 2 with other aetiologies. 9 out of 11(82%) patients had a serum creatinine greater than 100(µmol/l). Analytes were grouped into standard uraemic toxin categories.

Small Water soluble molecules: Mean creatinine was 318±265µmol/L in IF compared to 309±232 µmol/L in P (p=0.76); urea 16.2±11 in IF compared to 14.2±7 in P (p=0.20). No significant difference was found for between plasma and IF for sodium, potassium, and chloride. Small but less soluble molecules such as phosphate 1.02±4mmol/L in IF vs 1.23±0.6mmol/L in Plasma (p=0.24), urate 475±139.9 in IF vs 417.9±129.7µmol/L in plasma (p=0.11) showed no significant difference, including TCO2 that showed a trend for higher interstitial levels (p=0.07). Interestingly, sodium (148.1±20.4 mmol/L in IF vs 137.7±7.1 in plasma; p=0.07) and chloride (p=0.21) concentrations were higher in IF in 73% of paired samples but overall, there was no statistical difference between paired samples.

Middle and large molecules: There was a marked difference in the mean concentration of total protein and albumin between IF (total protein 6.76g/l, albumin 3.62g/l) and plasma (total protein 64.6g/l, albumin 26.9g/l, p<0.01).This was also true for PTH which had much higher plasma concentrations; 14.9±11.6pmol/L compared to IF; 0.73±0.3pmol/L; p<0.01 and cystatin C; 3.4±1.4mg/L in plasma and 2.39±1.1mg/L in F; p<0.05

Conclusion: The findings provide evidence of significant equilibration between IF and plasma at steady states for a range of small water-soluble ions or molecules although IF sodium seemed higher. Less soluble small analytes like urate showed a trend towards a difference and there was marked plasma-IF difference in larger molecules such as albumin, PTH and cystatin C. Further research with larger patient numbers in steady states and during dialysis will throw more light in interstitial uraemic pathophysiology.