NEPHROLOGY

NEPHROLOGY 2013; 18 (Supp. 1), 15–77 doi:10.1111/nep.12121

# ABSTRACTS

## 001

## INTERLEUKIN 17- RECEPTOR A (IL-17RA) ON LEUKOCYTES AND TISSUE CELLS MEDIATES INFLAMMATION IN A MURINE MODEL OF CRESCENTIC GLOMERULONEPHRITIS

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**Aim:** To explore the role of IL-17RA in experimental crescentic glomerulonephritis (GN).
**Background:** Interleukin (IL)-17A and IL-17F are inflammatory cytokines which signal through IL-17 receptor A (IL-17RA), expressed on many cell types, including renal tissue cells.
**Methods:** Necrotising, crescentic GN was induced by intravenous administration of sheep anti-mouse glomerular basement membrane globulin, thereby planting sheep globulin (SG) in glomeruli. Mice were culled at day 21. Wild type C57BL/6 (WT), IL-17RA-/- and bone marrow chimeric mice were used.
**Results:** IL-17RA-/- mice had reduced crescent formation (WT 17 ± 3 vs IL-17RA-/- 9 ± 3% $P < 0.05$), with fewer glomerular neutrophils (1.2 ± 0.1 vs 0.76 ± 0.04 cells/glomerular cross section [c/gcs]; $P < 0.05$), macrophages (2.0 ± 0.2 vs 1.1 ± 0.2c/gcs; $P < 0.05$) and a trend towards fewer T cells (0.25 ± 0.1 vs 0.15 ± 0.1c/gcs; P = NS). IL-17RA-/- mice had lower circulating anti-SG antibodies than WT mice ($OD_{450}$ 1:100; 0.3 ± 0.1 vs 0.2 ± 0.0; $P < 0.05$).

Bone marrow chimeric mice (chimerism 96%) were generated, permitting assessment of the effects of selective IL-17RA deficiency in either bone marrow (BM) or tissue cells (TC). BM-TC+ mice had reduced glomerular segmental necrosis (BM+TC+ 49 ± 5 vs BM-TC+ 27 ± 5; $P < 0.05$) and urinary protein: creatinine ratios (BM+TC + 2.0 ± 0.3 vs BM-TC + 1.1 ± 0.3 mg/mmol; $P < 0.05$). Mice with BM or TC IL-17RA deficiency had impaired cellular immunity (ELISPOT: BM+TC + 91 ± 19 vs BM-TC + 41 ± 6 IFNg+ spots/$2 \times 10^6$ SG-stimulated splenocytes; BM+TC + 91 ± 19 vs BM+TC- 43 ± 8; both $P < 0.05$).
**Conclusion:** IL-17A/F signalling promotes glomerular injury. Leukocyte-derived IL-17RA promotes immunity and injury, while IL-17RA on radio-resistant cells enhances antigen-specific systemic immunity.

## 002

## SHORT AND LONG TERM BIOLOGICAL VARIATION OF HIGH SENSITIVITY TROPONIN T (HS-TnT) AND N-TERMINAL B-TYPE NATRIURETIC PEPTIDE (NT-PROBNP) IN THE STABLE DIALYSIS POPULATION

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**Aims:** To determine the within-person(biological) variation of hs-TnT and NT-proBNP in stable dialysis patients, and derive the difference between serial measurements needed to detect a clinically significant change with 90% certainty(RCV).
**Background:** hs-TnT is frequently measured in the dialysis population for the diagnosis of acute cardiac events, and NT-proBNP is an emerging biomarker of long-term cardiac-risk, but their underlying biological variation in this setting is unknown; leading to misinterpretation of serial measurements.
**Methods:** Multicentre, prospective cohort study. 55 prevalent HD and PD patients(1:1) were assessed 10-times: weekly for 5-weeks then monthly for 4-months. Assessments were conducted at the same dialysis-cycle time point and entailed clinical review, bioimpedance spectroscopy, ECG, hs-TnT and NT-proBNP testing. Batched samples underwent duplicate analysis in a single-run. Patients were excluded if they underwent a change in cardiac medication, dialysis prescription, ischaemic symptomatology, extracellular volume >1 L, new arrhythmia or hospitalisation between visits. Between-person($CV_G$) and within-person($CV_I$) coefficients of variation were estimated using nested analysis of variance.
**Results:** 136-weekly and 113-monthly intervals from 42 patients were able to be included (age:59 ± 15 yrs, coronary-artery disease = 22%, LV ejection fraction = 60 ± 7%, diastolic dysfunction = 86%). For NT-proBNP: Median = 1974 pg/mL, $CV_G$ = 152%, $CV_{I\text{-weekly}}$ = 27% and $CV_{I\text{-monthly}}$ = 35%, $RCV_{weekly}$ = −46%–+84%, $RCV_{monthly}$ = −54%–+120%, $CV_I : CV_G$ = 0.23. For hs-TnT: Median = 34 ng/L, $CV_G$ = 81%, $CV_{I\text{-weekly}}$ = 7.9% and $CV_{I\text{-monthly}}$ = 12.6%, $RCV_{weekly}$ = −17%–+20%, $RCV_{monthly}$ = −25%–+34%, $CV_I : CV_G$ = 0.16. $CV_I$ was consistent across cardiac comorbidity subgroups.
**Conclusions:** Serial NT-proBNP levels need to double or halve and hs-TnT levels must increase by 20–34% or fall by 17–25% to confidently exclude change due to analytical & biological variation alone. The low $CV_I : CV_G$ implies the best strategy for applying these biomarkers in dialysis is relative change monitoring after a baseline estimate rather than comparing results to reference intervals.

## 003

## BLOCKING THE NADPH OXIDASE Nox4 ACTIVITY PROVIDES RENOPROTECTION IN LONG TERM DIABETIC NEPHROPATHY

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**Aim:** To examine the role of the NADPH oxidase Nox1 and Nox4 in diabetic nephropathy (DN) using genetic deletion and pharmacological inhibition approaches in streptozotocin induced diabetic mice.
**Background:** Chronic kidney failure is a major complication of diabetes. However, the underlying causes remain unclear. Oxidative stress is considered to be a major contributor to the development of diabetic nephropathy. NADPH oxidase is a major source of reactive oxygen species (ROS) in the kidney and contributes to renal damage in diabetes.
**Methods:** $Nox1^{-/y}ApoE^{-/-}$ or $Nox4^{-/-}ApoE^{-/-}$ and their respective wild type or $ApoE^{-/-}$ mice were rendered diabetic via streptozotocin injection. $ApoE^{-/-}$ non-diabetic and diabetic mice were treated with the specific NOX inhibitor (GKT137831). Animals were culled after 20 weeks and kidneys were removed for assessment of structural damage, oxidative stress markers, as well as protein expressions extracellular matrix (ECM), pro-fibrotic and pro-inflammatory markers. In vitro, Nox4 was silenced in human podocytes and exposed to high glucose and TGF-β for gene expression analysis and ROS measurements.
**Results:** Deletion of Nox4, but not of Nox1 resulted in renal protection from glomerular injury as evidenced by attenuated albuminuria, preserved renal structure, reduced glomerular accumulation of ECM proteins as well as attenuated glomerular macrophage infiltration. Administration of GKT137831 to diabetic $ApoE^{-/-}$ mice conferred a similar degree of renoprotection as did deletion of Nox4. In human podocytes, silencing of the Nox4 gene resulted in reduced ROS production and down-regulation of profibrotic markers that are implicated in diabetic nephropathy.
**Conclusions:** Collectively, these results identify Nox4 is a key source of ROS responsible for kidney injury in diabetes and provide proof of principle for an innovative small molecule approach to treat and/or prevent DN.

## 004

## EFFECT OF SODIUM RESTRICTION ON BLOOD PRESSURE, FLUID STATUS AND PROTEINURIA IN CKD PATIENTS: RESULTS OF A RANDOMISED CROSSOVER TRIAL AND 6-MONTH FOLLOW-UP

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**Background:** High-quality evidence to support the efficacy of sodium-restriction for reducing cardiovascular risk in CKD patients is needed.
**Aim:** The aim of this study was to examine in CKD patients 1) the degree of blood pressure (BP) and proteinuria reduction achievable on a low- versus high-sodium diet, and 2) whether these benefits are maintained with longer-term sodium-restriction.
**Methods:** The LowSALT CKD study was a double-blind randomised-crossover trial (period-1) with 6-month follow-up (observational arm; period-2). Stage III-IV CKD patients with BP 130–169/≥70 mm Hg consumed a low- and high sodium intake (median 75 [interquartile range (IQR) 58–112] versus

168 [146–219] mmol sodium/day) each for 2-weeks in random order (period-1). Participants were counselled to continue a low-sodium diet (target <100 mmol/day) with outcomes measured again at 6-months (period-2). Primary outcome was 24-hour ambulatory BP; secondary outcomes were proteinuria and extracellular fluid (ECF, bio-impedance). Outcomes were analysed using paired t-test where normally distributed and Wilcoxon signed-rank test with non-normal distribution.

**Results:** Twenty patients (age 68 ± 11 years and eGFR 31.6 ± 10.6 ml/min/1.73 $m^2$) completed the study. In period-1, mean ambulatory SBP/DBP was reduced by 9.8 [95% confidence interval (CI)] 4.5–15.1] /4.0 [1.6–6.4] mm Hg ($P < 0.01$), and ECF by 0.8 [95% CI 0.4–1.2] L ($P < 0.01$) from high- to low-salt period. At 6-months, SBP/DBP reductions were maintained (increase of 1.3 [95% CI -4.8-7.3]/1.2 [-1.5-3.9] mm Hg ($P > 0.05$) when compared with low-sodium period), as was ECF ($P > 0.05$). Median protein/albumin excretion were reduced by 40–50% in period-1 and this was maintained at 6-months ($P > 0.05$).

**Conclusions:** Sodium restriction considerably reduced BP, ECF and proteinuria in CKD patients, and, with the assistance of ongoing dietary-counselling by an accredited dietitian, these benefits were maintained at 6-months.

005

## BLOCKADE OF SPLEEN TYROSINE KINASE (Syk) INHIBITS ANTIBODY-MEDIATED REJECTION IN RAT RENAL ALLOGRAFTS

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**Aim:** To determine whether spleen tyrosine kinase (Syk) plays a role in acute renal allograft rejection.

**Background:** Kidney allografts induce strong antibody responses which contributes to graft rejection. Syk is involved in the antibody response (via B-cell receptor signalling) and antibody-dependent activation of macrophages and neutrophils (via FcγR signalling), whereas Syk is not expressed by T-cells. However, the role of Syk in these responses has not been investigated in allograft rejection.

**Methods:** Groups of 6 Sprague-Dawley rats underwent bilateral nephrectomy and an orthotopic transplant with a MHC mis-matched Wistar rat kidney. Groups of 6 recipient rats were treated with a Syk inhibitor (CC-482417, 30 mg/kg/bid) or vehicle from 1 hr before surgery until killed on day 5. Isografts controls were used.

**Results:** Vehicle treated recipients developed severe allograft failure (serum creatinine 304 ± 130 vs 46 ± 7 umol/L in isograft; $P < 0.001$). Histologic damage included glomerular and peritubular capillaritis, tubular injury (tubulitis, necrosis, dilation) affecting 90 ± 9% of tubules, and T-cell, macrophage and neutrophil infiltration. Immunostaining identified Syk activation in infiltrating leukocytes. Allografts showed IgG and C4d deposition and circulating donor-specific antibodies (DSA) were identified by flow cytometry. CC-482417 improved allograft function (serum creatinine 149 ± 18 umol/L; $P < 0.05$ vs vehicle), with reduced tubular damage (47 ± 19%; $P < 0.001$) and a reduction in capillaritis. CC-482417 treatment did not affect T-cell infiltration or activation (IL-2, granzyme B, IL-2Rα). However, CC-482417 reduced macrophage and neutrophil infiltration by 40 and 45%, respectively ($P < 0.05$ vs vehicle), and reduced macrophage activation (NOS-2, TNF-α, MMP-12). Interestingly, CC-482417 reduced serum DSA levels by 60% ($P < 0.01$).

**Conclusion:** This study establishes the involvement of Syk in antibody-mediated, but not T-cell mediated, acute renal allograft rejection. Further studies should examine Syk inhibition in a specific model of AMR.

006

## CALCIPROTEIN-ASSOCIATED FETUIN-A CONCENTRATION IS ASSOCIATED WITH ALL-CAUSE MORTALITY IN PATIENTS WITH PRE-DIALYSIS CKD

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**Aim**: To assess whether serum calciprotein-associated fetuin-A (CPP Fet-A) concentrations are predictive of death in a cohort of patients with pre-dialysis Chronic Kidney Disease (CKD).

**Background**: Serum CPP Fet-A concentrations have emerged as a potential marker of extraosseous mineralisation stress in patients with CKD or chronic inflammatory disease. *In vitro* studies in the macrophage suggest that CPP are pro-inflammatory and pro-apoptotic at high levels. In CKD, higher CPP Fet-A concentrations are associated with a pro-calcific milieu and aortic stiffness. Data relating CPP Fet-A concentrations to hard outcomes are lacking.

**Methods**: Serum CPP Fet-A concentrations were measured in a prospective cohort of 200 patients with Stages 3 and 4 CKD at enrolment. Participants were followed for a median 5.3 years until death or the observation period ended. Cox proportional hazards models were used to evaluate the association between serum CPP Fet-A and death, after adjustment for demographic, renal, mineral and inflammation-related risk factors.

**Results**: Mean ± SD age was 69 ± 11 years, estimated GFR (eGFR) was 33 ± 11 mL/min/1.73 $m^2$, serum phosphate was 1.08 ± 0.20 mmol/L and CPP Fet-A was 27.5 ± 21.2 mg/L. During follow-up 43 patients died. After adjustment for age, gender, eGFR, proteinuria, serum albumin, calcium, phosphate and intact parathyroid hormone concentrations, a 1SD increase in CPP-Fet-A was associated with 36% higher risk of all-cause mortality (Hazard ratio, HR 1.36, 95% confidence interval CI 1.06 to 1.74, $P = 0.017$). However, addition of high-sensitivity C-reactive protein to this model significantly attenuated the effect size (HR, 1.07 95% CI 1.01 to 1.14, $P = 0.040$).

**Conclusions**: Serum CPP Fet-A concentration is an inflammation-related risk marker for all-cause mortality in patients with pre-dialysis CKD.

007

## CX3CR1-DEC205 DC-TARGETED DNA VACCINE INDUCES SPECIFIC ANTIBODIES AND LIMITS ATHEROSCLEROSIS AND MACROPHAGE INFILTRATION IN THE Apo-E KNOCKOUT MOUSE MODEL OF ATHEROSCLEROSIS

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**Aim:** To assess the effect of Dendritic Cell (DC)-targeted CX3CR1 vaccination in the prevention of macrophage infiltration and attenuation of atherosclerosis in Apo-E-/- mice.

**Background**: Monocytes/macrophages are involved in the pathogenesis of atherosclerosis. CX3C chemokine ligand 1 (CX3CL1/Fractalkine) and its receptor CX3CR1 have been identified to have an important role in the migration and recruitment of monocytes during the pathogenesis of atherosclerosis.

**Methods:** DC-targeted and control vectors with CX3CR1 (DEC-CX3CR1/Con-CX3CR1) were generated. Apo-E -/- mice were vaccinated weekly (3x). Anti-CX3CR1 antibody was determined by ELISA. Whole aortas were dissected at 34 weeks of age. Severity of atherosclerosis, macrophage infiltration and lipid deposition were examined histologically.

**Results:** DEC-CX3CR1 vaccinated mice had high levels of anti-CX3CR1 antibodies (Abs 1.1), Con-CX3CR1 vaccinated mice also had increased antibodies (Abs 0.85), compared to controls (Abs 0.1) ($p < 0.001$). DEC-CX3CR1 and Con-CX3CR1 vaccinated mice demonstrated a decreased plaque size (39%&46% of luminal area) as compared to the control (58%) in brachiocephalic artery ($p < 0.001$, $p < 0.05$). In the aortic arch, DEC-CX3CR1 vaccinated mice showed a significantly decreased plaque size (7.5%) compared to Con-CX3CR1 vaccinated mice (16%) and control (18%), ($p < 0.05$, $p < 0.01$ respectively). Both DEC-CX3CR1 and Con-CX3CR1 vaccinated mice had a significantly decreased infiltration of macrophages (19%&21% of plaque area) into the atherosclerotic plaques in comparison to controls (40%, $p < 0.05$, $p < 0.001$ respectively). DEC-CX3CR1 vaccinated mice revealed a significantly lower lipid deposition level (9% of plaque area) within the atherosclerotic plaques compared to Con-CX3CR1 mice (14%, $p < 0.05$) and controls (16%, $p < 0.001$).

**Conclusions:** DC-targeted CX3CR1 vaccination induced specific antibodies that limit macrophage infiltration into atherosclerotic plaques suggesting a potential therapeutic role in atherosclerosis.

008

## BENEFITS AND COSTS OF AN ACCEPTABLE HUMAN LEUKOCYTE ANTIGEN MISMATCH PROGRAM IN AUSTRALIA

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**Aims:** To determine the benefits and costs of implementing an acceptable mismatch program in Australia.
**Background:** Implementation of an acceptable mismatch program in Europe has improved access to transplantation for highly-sensitised patients on the deceased-donor waiting list, but the benefits and costs of a similar program in Australia is unclear.
**Methods:** Using a third party perspective, two probabilistic decision analytical models were developed to compare 1) an eplet-defined acceptable mismatch and 2) and eplet/Luminex-defined acceptable mismatch program with the current deceased-donor allocation model in Australia (n = 10,000, age 18+). The model terminated when all transplant recipients were deceased.
**Results:** Compared with current allocation, an eplet-defined acceptable mismatch model reduces average waiting time for 4 of 28 (14%) highly-sensitised recipients by 34 ± 22 months (p = 0.056), with an average gain of 1.32 life-days and $622 savings per patient; whereas an eplet/Luminex-defined acceptable mismatch model reduces the average waiting time for 12 of 23 (52%) highly-sensitised recipients by 37 ± 33 months (p = 0.03), with an average 6.00 life-days gained and $2,805 savings per patient. Average increase in waiting time for reallocated recipients in the eplet and eplet/Luminex models were 12 ± 9 and 15 ± 18 months respectively. Among non-highly-sensitised patients on the waitlist, there was a reduction of 0.09 life-days and $59 excess cost in the eplet-defined acceptable mismatch model and a reduction of 0.60 life-days and $374 excess cost in eplet/Luminex-defined acceptable mismatch model.
**Conclusions:** The integration of an acceptable mismatch program into the deceased-donor kidney allocation reduces waiting-time and provides modest health benefits and cost savings for highly-sensitised patients without incurring significant reduction in overall health benefits and extra costs for non-highly-sensitised candidates on the waitlist.

009

## THE ASSOCIATION BETWEEN GLOMERULAR FILTRATION RATE ESTIMATED BY MULTIPLE METHODS AT DIALYSIS COMMENCEMENT AND PATIENT SURVIVAL IN THE IDEAL TRIAL

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**Background and Aims:** The Initiating Dialysis Early and Late (IDEAL) study demonstrated that planned early or late initiation of dialysis, based on the Cockcroft and Gault (CG) estimation of glomerular filtration rate (eGFR), was associated with identical clinical outcomes. This study was a pre-specified analysis examining the association of all-cause mortality with eGFR, measured by the CG, Modification of Diet in Renal Disease (MDRD) or the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formulae at the time of commencement of dialysis.
**Methods:** IDEAL trial participants were allocated into tertiles according to the CG, MDRD and CKD-EPI formulae at dialysis commencement. The patient survival was assessed using the Kaplan-Meier method.
**Results:** There was no difference in survival among patients when stratified into tertiles of GFR according to the CG formula. However, there was a significant survival benefit in the tertile of patients starting dialysis with the lowest eGFR when the MDRD or CKD-EPI was applied (p < 0.01), independent of correction for body surface area. An increased hazard ratio for death was observed in older females and patients with diabetes and cardiovascular disease independent of the formula used.
**Conclusion:** Discrepancies exist in the relationship between eGFR at dialysis commencement and mortality in patients with stage 5 CKD depending on the formula used. Patients commencing dialysis with a higher eGFR were more likely to be older, Caucasian and have a history of ischemic heart disease, suggesting that observational studies demonstrating a survival benefit in patients who start dialysis 'late' is due to reduced comorbidity.

010

## THE SLO-NIACIN TRIAL: A DOUBLE-BLIND PLACEBO CONTROLLED RANDOMISED CROSS-OVER TRIAL OF LOW DOSE SLOW-RELEASE NIACIN TO LOWER PHOSPHATE IN HAEMODIALYSIS PATIENTS

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**Aim:** Is low dose slow-release niacin better tolerated but still effective at lowering phosphate?
**Background:** Serum phosphate levels correlate with mortality in dialysis patients. Current phosphate binders often cause side-effects leading to poor compliance. Niacin has previously been shown to lower serum phosphate in patients with kidney disease. However, at doses previously used (≥1 g daily), it is poorly tolerated. Slo-niacin® is a slow-release low-dose formulation (500 mg) taken once daily.
**Method:** The study was a double-blind placebo-controlled randomised cross-over trial approved by the local ethics committee. Patients were on haemodialysis. All patients received both active treatment and placebo for 8 weeks each with intervening 2 week washout phase. All patients continued usual phosphate binders and Cinacalcet/vitamin D analogues, although no dose adjustments were allowed during the study. Patients were recruited if they were >18 yo, not pregnant and serum phosphate 4 weeks prior to commencement was ≥1.8 mM. All gave informed consent.
**Results:** 33 patients were recruited. 1 patient died following emergency cardiac surgery during placebo phase but had not taken trial medication for 2 weeks prior. 32 patients were analysed by intention to treat, including 3 drop-outs (2 Slo-niacin®, 1 placebo, p = NS). Mean change in serum phosphate over 8 weeks was –0.23 mM (95% CI –1.29 to 0.81) for niacin versus 0.13 mM (95% CI –0.82 to 1.08) for placebo (p = 0.021, paired t-test). Mean absolute change was thus >0.3 mM decrease in serum phosphate in favour of niacin. ANOVA of mean absolute change was also statistically significant at p < 0.007.

Slo-niacin® was well tolerated apart from early mild flushing.

**Conclusion:** Low dose slow-release niacin remains effective at lowering serum phosphate and is reasonably tolerated.

011

## BUTTONHOLE CANNULATION AND INFECTION OUTCOMES: SYSTEMATIC REVIEW AND META-ANALYSIS

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**Aims:** To summarise the current evidence on the impact of buttonhole cannulation on infection rates.
**Background:** Publications in the last decade have reported the utilization of buttonhole cannulation (BH) method for vascular access, especially in the home haemodialysis population. Some have reported an association with increased infections in comparison to ropeladder (RL) cannulation, although definitive evidence is lacking.
**Methods:** We searched Medline, EMBASE, the clinical trials registry (www.clinicaltrials.gov) and reference lists of review articles and trials for cannulation studies in maintenance haemodialysis patients comparing BH with alternative cannulation methods without language restriction. "Renal dialysis" and "catheterization" were used as MeSH terms while "buttonhole cannulation" as a text term. Randomised clinical trials (RCT's) and observational studies between 1950 and 15/Feb/2013 were included. The primary outcome was access-related infection. Relative risk (RR) or incidence rate ratios (IRRs) with associated 95% confidence intervals (CI) were calculated or reported IRR used. Random effects models were used to calculate overall effect estimate and 95% CI's.

**Results:** Thirteen studies, all published after 2006, met the inclusion criteria, 3 RCTS and 10 observational studies, studying a total of more than1472 patients. Of these, 9 reported total infections, 3 reported systemic infections only and 1 reported local infections only. The majority of studies were single center. Compared with RL cannulation, BH cannulation increased access-related infection 6-fold (RR 6.41, 95%CI 1.43–28.67) in RCT's, 3 fold (RR 2.95, 95%CI 1.85–4.71) in studies reporting outcomes before and after change of cannulation method and 3 fold (RR 3.27, 95%CI 1.44–7.43) in observational studies comparing units with different cannulation methods.
**Conclusions:** Buttonhole cannulation is associated with increased infection risk and should be used with caution.

012

## UTILITY OF "BACK UP" ARTERIO-VENOUS FISTULAS IN PATIENTS ON PERITONEAL DIALYSIS AND USE OF CENTRAL LINES: A COMPARISON BETWEEN TWO AUSTRALIAN CENTRES

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**Aim:** To study utility of back up arterio-venous fistulas (AVF) in patients initiated on peritoneal dialysis (PD) and to determine the rates of central venous catheter (CVC) use in patients requiring conversion to haemodialysis (HD).
**Background:** There is limited data on benefit of back-up AVF in patients treated with PD and it has been argued that these may not be useable at the time of HD transfer. There is therefore a high rate of CVC use in this population when they require transfer to HD.
**Methods:** We retrospectively analysed data on patients transferred to HD from PD, between January 2008 and December 2012 at both Royal Adelaide Hospital (RAH), where a policy of AVF in most PD patients is followed, and Princess Alexandra Hospital (PAH), where only patients at risk have back up AVF created.
**Results:** Of the142 patients at RAH, 33 (23%) patients required transfer to HD. 25 patients had back-up AVF, which was successfully used in 22 patients (88%). CVC had to be used in 3 patients (12%) as the fistula was dysfunctional. The CVCs used during transfer at RAH were 11 (33%).Of the 232 patients at PAH, 70 (30%) required transfer. AVF was utilized in 26 (37%) patients, whereas a CVC had to be used in 44 (61%) patients. Routine creation of AVF in PD patients was associated with a catheter usage rate of 24% (RAH) as compared to a rate of 61% (PAH) in a centre where this is not done (P = 0.0006, Fisher's exact test).
**Conclusion:** Routine creation of a back-up AVF in all PD patients is sustainable and results in a much lower rate of CVC use on HD transfer.

013

## FETUIN-CONTAINING CALCIPROTEIN PARTICLE LEVELS CAN BE REDUCED BY DIALYSIS, SODIUM THIOSULPHATE AND PLASMA EXCHANGE. POTENTIAL THERAPEUTIC IMPLICATIONS?

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**Aim:** Determine which, if any, clinical treatment strategies cause a reduction in Fetuin-A (Fet-A) calciprotien particles (CPP) in dialysis patients.
**Background:** Fetuin-A is an important regulator of physiological and pathological mineralisation. Fetuin-A (Fet-A) has been shown to protect from ectopic mineralisation. In patients with chronic inflammation and with chronic renal impairment, Fet-A is detectable within large macromolecular complexes called calciprotein particles (CPP). These are composed of nanocrystals of calcium phosphate surrounded by a predominantly Fet-A protein 'shell'. CPP formation may protect cells against the pro-inflammatory and pro-apoptotic effects of naked crystalline calcium phosphate, but may themselves be proinflammatory. We have previously demonstrated that in calciphylaxis, a condition associated with severe vascular calcification and a very poor prognosis, a very high proportion of serum fetuin-A circulates as CPP (CPP%). Treatment of the condition is hindered by the lack of a reliable target to monitor and we wonder if serum CPP% might be a useful biomarker.
**Methods:** We determined whether include increased duration/frequency of haemodialysis (HDx), sodium thiosulphate (STS) infusion , plasma exchange (PEx) or transplantation were associated with a sustained reduction in CPP%.
**Results:** HDx reduces serum CPP% but not sustainably so. The addition of STS infusion during HDx further reduced CPP%, but infusion between HDx sessions had no significant sustained reduction. PEx provided additional benefit, reducing CPP% between HDx sessions. Transplantation resulted in sustained lower levels of CPP%.
**Conclusion:** CPP% may be a modifiable marker of mineral stress. Experiments are being conducted to determine whether CPP are directly involved in the pathology of vascular calcification.

014

## USE OF STENTS IN HAEMODIALYSIS FISTULAE: SUCCESS AND LONG TERM FOLLOW-UP

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**Aim:** Endovascular stent deployment is used to treat dysfunctional haemodialysis fistulae characterized by resistant or recurrent stenosis and pseudoaneurysms. This study aims to report the procedural success, complication rate and long-term patency of stents in haemodialysis fistulae at a single centre.
**Background:** The use of self-expandable bare metal and covered stents have been described to treat resistant or recurrent stenosis, to obliterate large pseudoaneurysms and as a bailout technique to deal with complications related to angioplasty procedures. The effectiveness of these procedures has been described in the literature with varying degrees of success.
**Methods:** Between 2008 and 2012, 50 procedures (9 for pseudoaneurysms, 41 for resistant or recurrent stenoses) were performed in 42 patients at a single centre. Clinical and radiological information collected during this period was reviewed retrospectively. Post-intervention primary and secondary (cumulative functional) patency rates were determined using Kaplan Meier analysis. Patients were censored for death, loss to follow-up and transplantation.
**Results:** The clinical and anatomical success rate was 98% (49/50). Minor complications that did not affect procedural success occurred in 3 instances. A major complication leading to access loss occurred in one procedure. Post-intervention primary patency rates at 6, 12 and 18 months were 52%, 24% and 10% respectively. Post-intervention secondary patency rates at 6, 12 and 18 months were 98%, 92% and 92% respectively, with an additional 1.7 procedures per patient.
**Conclusion:** The use of stents in haemodialysis fistulae provides excellent function patency of the dialysis fistulae but repeated procedures are required to maintain secondary patency.

015

## UPPER ARM FISTULAE AND MULTIPLE STENOSES INFLUENCE HAEMODIALYSIS ARTERIOVENOUS FISTULAE PATENCY AFTER BALLOON ANGIOPLASTY

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**Aim:** Patency after percutaneous balloon angioplasty (PTA) for haemodialysis fistula stenosis is highly variable. This study aimed to assess factors associated with patency following first episode of treatment with PTA.
**Background:** Restenosis recurs commonly after PTA. Previous studies have shown that some intrinsic fistula and biochemical factors may influence patency after PTA.
**Methods:** We retrospectively reviewed all endovascular procedures performed by nephrologists between 2007 and 2012 at a single centre. Anatomical, clinical, biochemical and medication information was subjected to cox regression analysis to identify factors influencing post-intervention patency.
**Results:** 120 patients were identified as having first episode treatment with PTA. During a median follow-up period of 22.66 months (5.24–53 months), 171 follow-up procedures were performed. Post-intervention primary patency rates at 6, 12 and 18 months were 46%, 25% and 15% respectively. Cumulative (functional) patency rates at 6, 12 and 18 months were 97%, 94 and 92% respectively with 1.4 additional procedures per patient. In univariate cox regression analysis, the presence of multiple lesions (p = 0.037) was associated with early restenosis at 6 months, while upper arm fistulae were associated with early restenosis (p = 0.004) and shorter primary patency (p = 0.001). Other anatomical characteristics (fistula age, lesion length, pre-procedure stenosis), clinical history

(diabetes, coronary and peripheral artery disease), medications, and biochemical parameters (HbA1c, CRP, albumin and lipids) did not influence patency.
**Conclusion:** Multiple stenoses and upper arm fistulae may be associated with shorter patency after PTA. More large volume prospective studies are required to further assess factors associated with patency after PTA in haemodialysis fistulae, particularly the role of metabolic and inflammatory markers.

016

## CLINICAL OUTCOMES AFTER ARTERIOVENOUS FISTULA CREATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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**Aim:** Creation of an arteriovenous fistula (AVF) before initiation of haemodialysis (HD) is an important goal in chronic kidney disease (CKD) management. This study aims to determine outcomes and optimal timing for AVF creation in CKD patients.
**Methods:** We reviewed records of all CKD patients who had a first AVF creation for future HD at Austin Health from 01/01/2007–31/12/2009 and obtained follow-up data until 31/12/2011. Survival analysis was performed for the primary outcome of time from AVF creation to first HD treatment.
**Results:** In 100 patients who had a first AVF created, the mean age was 63.7 ± 13.7 years, 49 had diabetes and 39 were female. Mean time from AVF creation to first HD in 73 patients who commenced HD was 14.1 ± 12.7 (range: 0.2–47.7) months. Of these 73 patients, 21 (29%) required a radiological and/or surgical procedure before commencing HD and 26 (36%) required a procedure within 3 months of commencing HD. Despite AVF creation, 12 (16%) patients required a catheter to start HD and 2 (3%) required a catheter within 3 months of HD commencement. Median time to starting HD was 479 days. In patients with eGFR < 16 mL/min (the median) median time to starting dialysis was 321 days compared to 909 days for eGFR ≥ 16 ml/min (Log rank p = 0.018). At 3, 6 and 12 months respectively, 20%, 44% and 56% of patients with eGFR < 16 mL/min had commenced HD compared to 11%, 20% and 26% with eGFR ≥ 16 ml/min.
**Conclusion:** While early AVF creation is an important goal, we demonstrate that optimal timing of AVF creation is challenging, with half of our patients not using the AVF for over a year, and many requiring subsequent AVF procedures before becoming established on HD.

017

## OUTCOME OF PREDIALYSIS EDUCATION IN WESTERN SYDNEY: EARLY REFERRAL IS ASSOCIATED *WITH REDUCED RATE OF LINE USE AT FIRST DIALYSIS*

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**Aim:** To review characteristics and outcomes for patients referred to a comprehensive predialysis programme in Western Sydney.
**Background:** In 2005 the Western Renal Service (WRS) appointed a Predialysis coordinator to facilitate patient education, informed dialysis modality choice and facilitate access planning. This programme was developed to promote home dialysis therapies and minimise rates of unplanned dialysis commencement and haemodialysis catheter use as initial dialysis access.
**Methods:** Patients referred for predialysis education between 2005–2010 and who subsequently commenced dialysis were identified from the WRS predialysis database. The proportions of these patients who ultimately undertook a home dialysis therapy or commenced dialysis with permanent access were calculated and related to the GFR at referral to this programme.
**Results:** 965 patients were referred to the predialysis programme in this period. 546 of these patients subsequently commenced maintenance dialysis; 72% of this group ultimately undertook a home dialysis therapy. The average referral GFR was 12.5 mL/min/1.73 $m^2$, 74% were referred with a GFR of 15 mL/min/1.73 $m^2$ and 92% with a GFR of 20 mL/min/1.73 $m^2$ or less.

Patients who started dialysis with permanent dialysis access had a higher GFR at referral than patients who commenced dialysis with a haemodialysis catheter (13.4 vs 11.1, p < 0.01). Patients referred for predialysis interview with a GFR more than 10 ml/min/1.73 $m^2$ were more likely to commence dialysis with permanent dialysis access (p < 0.01). Rates of home dialysis did not appear to be affected by the GFR at time of referral.
**Conclusions:** Despite the referral GFR being lower than recommended levels, high rates of home dialysis uptake was achieved in patients referred to the predialysis programme at WRS. Earlier referral is associated with a higher chance of commencing dialysis with permanent access.

018

## FACTORS INFLUENCING HAEMODIALYSIS ARTERIOVENOUS FISTULA PATENCY AFTER BALLOON ANGIOPLASTY; A SYSTEMATIC REVIEW

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**Aim:** Percutaneous transluminal angioplasty (PTA) is an established treatment for haemodialysis fistula stenosis. This study aimed to systematically review evidence for factors associated with patency after percutaneous transluminal angioplasty (PTA).
**Background:** The effects of patient comorbidity, demographic, biochemical and anatomical characteristics, with initial PTA success and post-intervention patency have not previously been summarised.
**Methods:** We searched databases to identify studies assessing patency after PTA in haemodialysis fistulae. Studies of immature or thrombosed fistulae or other dialysis access were excluded. Quality of studies was assessed using a modified validated checklist. Outcomes assessed were post-intervention primary and secondary patency, restenosis at 6 months, technical and clinical success, assisted primary patency and mean interval or frequency of endovascular interventions during follow up. Findings were summarized descriptively.
**Results:** We included 12 single-centre studies of 1 120 participants with 1281 fistulae. Follow-up ranged from 3 days-10years. Shorter primary patency was seen with more recent fistulae (4 studies), longer stenosis length, upper arm fistulae (2 studies), small inflow artery diameter, arteriovenous anastomotic site and history of previous endovascular interventions (1 study each). Shorter secondary patency was seen with increased patient age (2 studies), and more recent fistulae (1 study). Early restenosis was associated with diabetes (3 studies), HbA1c, low-density lipoprotein, and asymmetric dimethylarginine (1 study each). Technical success was reduced for upper arm fistulae and high-grade stenoses (1 study), while clinical success of PTA was more likely in stenotic compared to thrombosed fistulae (1 study).
**Conclusion:** Fistula characteristics and diabetes may be associated with poor PTA outcomes, however evidence is inconclusive, and the role of metabolic and inflammatory markers is unclear.

019

## IMPROVING VASCULAR ACCESS OUTCOMES AT GOLD COAST

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**Background:** A mature arteriovenous fistula (AVF) at the start of dialysis reduces morbidity, mortality and costs compared to a cental venous catheter (CVC). In 2005, less than 38% of our patients commenced haemodialysis with an AVF and Central Line Associated Blood Stream Infection (CLABSI) rate associated with our haemodialysis CVC's was 3.5/1000 catheter days.
**Aim:** A multi-pronged intervention was developed with focus on a renal access co-ordinator to expedite a "fistula first" approach and reduce complications associated with HD CVC use by targeting incident (first dialysis) catheter rates and CLABSI rates.
**Methods:** Outcome was assessed by 1. Proportion of patients starting dialysis with a CVC. 2. Tunnelled Haemodialysis associated CLABSI rates per 1000 catheter days. 3. Proportion of patients on maintenance dialysis with a CVC. 4. Non tunnelled haemodialysis catheter total yearly dwell days. 5. Proportion of prevalent patients and incident patients with AVF.
**Results:** The proportion of patients commencing haemodialysis via a CVC dropped from 62% in 2005 to 34% in 2012. The CLABSI Rate associated with tunnelled Haemodialysis catheter use dropped from 3.5/ 1000 days in 2005 to 0.35/ 1000 days in 2012. The percentage of patients on maintenance haemodialysis via a CVC dropped from 13% in 2005 to 9% in 2012. The non-tunnelled CVC line days per year dropped from 1330 line days/ yr in 2006 to 220 line days/ yr in 2012. The percentage of incident patients with AVF improved from 15% in 2007 to 35.7% in 2012, and prevalence rate from 76% to 88%.

**Conclusion:** A Coordinated MDT approach to vascular access care significantly improved dialysis starts with native AVF, reduction in the usage of non tunnelled CVCs and CLABSI.

020

## SERUM GENTAMICIN MONITORING IS NOT WARRANTED WITH USE OF GENTAMICIN CITRATE LOCKS FOR HAEMODIALYSIS CENTRAL VENOUS CATHETER (CVC)

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**Aim:** We analysed the clinical utility of serum gentamicin monitoring with the use of gentamicin–citrate locks (GCL) for central venous catheters (CVC) used for haemodialysis.
**Background:** GCL appear to prevent or reduce the incidence of CVC-associated blood-stream infections. Based on prior studies, ongoing serum gentamicin level monitoring has been advocated to minimise the risk associated with the long-term effect of systemic gentamicin concentrations. The clinical utility of serum gentamicin level monitoring using Gentamicin 10 mg, sodium citrate 31.4 mg in 3 mL sodium chloride 0.9%, which is available as a pre-mixed syringe preparation (Baxter Healthcare®) is unclear.
**Methods:** Retrospective cross sectional analysis was performed on haemodialysis patients using GCL for CVC. Serum gentamicin levels on haemodialysis patients using GCL at a single centre between March 2012 and February 2013 were analysed based on the indication for either lock-safety monitoring (CVC lock) or therapeutic drug monitoring (for treatment).
**Results:** CVC for dialysis access was used in 59 patients during the study period, in 303 cases serum samples for gentamicin levels were available. Of these, 16 patients (54 samples) received therapeutic gentamicin for documented systemic infections. Thus, 249 samples in the lock safety monitoring group were analysed. Only 2.6% of samples of GCL monitoring showed gentamicin levels ≥0.3 mg/L; whilst none of the samples in this group had >2 consecutive samples with levels ≥0.3 mg/L or levels above >0.5 mg/L. P 0.0). No patients recorded adverse events.
**Conclusions:** Routine monitoring of serum gentamicin levels with gentamicin-citrate lock for CVC is expensive and unnecessary.

021

## GLOBAL LONGITUDINAL STRAIN IS ASSOCIATED WITH OBESITY, INFLAMMATION, UREMIC TOXINS AND ARTERIAL STIFFNESS IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGES 3 AND 4

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**Aim:** To evaluate the relationship between global longitudinal strain (GLS) with traditional and renal specific risk factors of cardiovascular disease (CVD).
**Background:** Global longitudinal strain (GLS) is an easily measured echocardiographic technique which detects subtle and early changes in left ventricular (LV) function compared to ejection fraction (EF).
**Methods:** A cross sectional study of patients with moderate Chronic Kidney Disease (CKD) stages 3 and 4 (n = 136). Clinical characteristics, anthropometric, biochemical data including markers of inflammation (high sensitivity C-Reactive Protein (hsCRP), albumin, uremic toxins [indoxyl sulphate (IS), p-cresyl sulphate (p-CS)], and arterial stiffness [pulse wave velocity (PWV)] were measured. GLS was determined from 3 standard apical views using 2-Dimensional speckle tracking and EF was measured using Simpson's rule. Associations between GLS and traditional and renal specific risk factors were explored using multivariate models. Values are expressed as mean ± SD.
**Results:** Patient characteristics for this study population include age 59 ± 9.8 years, 58% male, estimated Glomerular Filtration Rate (eGFR) 44.4 ± 10 ml/min/1.73 $m^2$, GLS –18.3% ± 3.6, EF 65% ± 7.7. 34% of patients with EF > 45% had impaired GLS (>–16%). We demonstrated that GLS correlated with hsCRP ($r = 0.2$, $p = 0.03$), free IS ($r = 0.25$, $p = 0.004$) free p-CS ($r = 0.25$, $p = 0.003$), BMI ($r = 0.3$, $p = 0.002$), waist hip ratio (0.3, $p = 0.009$) and PWV ($r = 0.27$, $p = 0.003$). Following adjustment for demographic, baseline co-morbidities and laboratory parameters, GLS was independently predicted by hsCRP, free p-CS, waist hip ratio, diastolic blood pressure and arterial stiffness ($R^2$ for model = 0.36, $p < 0.0001$).
**Conclusion:** In the CKD cohort, LV systolic dysfunction was associated with inflammation, uremic toxins, obesity and vascular stiffness.

022

## THE ASSOCIATION BETWEEN QUALITY OF LIFE AND GLOBAL LONGITUDINAL STRAIN IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGES 3 AND 4

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**Aim:** To evaluate the relationship between Left Ventricular (LV) dysfunction and self reported functional health and well being in Chronic Kidney Disease (CKD).
**Background:** Patients with CKD have a significant burden of dyspnoea and fatigue in spite of normal Ejection Fraction (EF). Global longitudinal strain (GLS) is an easily measured echocardiographic technique which detects subtle changes in LV function compared to EF.
**Methods:** A cross sectional study of patients with moderate CKD stages 3 and 4 (n = 136). Clinical characteristics, anthropometric and biochemical data were measured. GLS was determined from 3 standard apical views using 2-Dimensional speckle tracking and EF was measured using Simpson's rule. QOL [physical function, physical role, pain, general health, vitality, emotional role, mental health, physical component scale (PCS) and mental component scale (MCS)] was assessed using validated Short Form-12 (SF-12). Associations between QOL, GLS and EF were explored using multivariate models. Values are expressed as mean ± SD.
**Results:** Patient characteristics for this study population include age 59 ± 9.8 years, 58% male, estimated Glomerular Filtration Rate (eGFR) 44.4 ± 10 ml/min/1.73 $m^2$, GLS –18.3% ± 3.6, EF 65% ± 7.7. In multivariate models, GLS was significantly related to vitality ($p = 0.04$), physical role ($p = 0.01$), mental health ($p = 0.003$) and MCS ($p = 0.01$) following adjustment of co-morbidities and biochemical data relevant to poorer health related outcomes. EF was only significantly related to mental health ($p = 0.004$). Body Mass Index (BMI) was consistently associated with a poorer outcome in all dimensions of QOL.
**Conclusion:** This is the first study to demonstrate a significant association between GLS and health related QOL. GLS may be a more sensitive marker compared to EF to detect early changes in physical and mental symptoms related to LV dysfunction.

023

## OXIDATIVE STRESS IS ASSOCIATED WITH POOR GRIP STRENGTH AND SARCOPENIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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**Aim:** To investigate the contribution of oxidative stress to reduced strength and lean mass in patients with CKD.
**Background:** Patients with chronic kidney disease (CKD) have impaired protein metabolism, resulting in sarcopenia. Oxidative stress has previously been identified as an important cause of sarcopenia in other populations. It was hypothesised that oxidative stress would be negatively associated with lean mass and independently associated with grip strength.
**Methods:** A cross sectional analysis was performed on 152 participants with stage 3 or 4 CKD (eGFR 25–60 mL/min/1.73 $m^2$). Measures of oxidative stress (plasma isoprostanes, glutathione peroxidase, total anti-oxidant capacity), grip strength, cardiorespiratory fitness ($VO_2$peak), albumin, CRP and standard biochemical analysis were performed. 75 patients underwent assessment of appendicular lean soft tissue mass as a percentage of total mass by dual energy x-ray absorptiometry (DEXA).
**Results:** Based on plasma isoprostanes, 22.4% of CKD patients (n = 34) had elevated oxidative stress levels (>250 pg/ml). Isoprostanes were negatively associated with grip strength ($r = –0.230$, $p = 0.007$) and lean mass ($r = –0.239$, $p = 0.040$). 82% of all patients were below their age predicted grip strength. Multiple linear regression identified isoprostanes as a predictor of grip strength independent of age, sex, diabetes status, haemoglobin, $VO_2$peak and phosphate ($r^2 = 67.8$, $p < 0.001$).
**Conclusions:** CKD patients have reduced muscle strength when compared to age-predicted normative values. Elevated oxidative stress was associated with lean mass, and independently associated with reduced strength in CKD patients.

024

## AST-120 (KREMEZIN) FOR DELAYING PROGRESSION IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW

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**Aim:** To determine the effectiveness of AST-120 (Kremezin) in delaying the progression of Chronic Kidney Disease (CKD).
**Background:** Conventional therapy for patients with chronic kidney disease includes dietary protein and salt restriction together with optimum blood pressure management. However, these treatments fail to stop disease progression in many patients. AST-120 (Kremezin), a spherical oral adsorbent, in addition to conventional therapy, may have a role in delaying the progression of CKD.
**Methods:** A randomized, controlled clinical trial using AST-120 (Kremezin) as intervention in delaying progression in patients with CKD. Three reviewers independently reviewed the studies. Data were gathered from published and unpublished articles, journals and clinical trials. Studies were critically appraised with regards to methods of minimizing bias. All seven studies included received a quality scale for systematic review overall score of not less than B.
**Results:** Seven studies showed that AST-120 (Kremezin) was effective in slowing the progression of CKD, as shown using different measures of renal function. (1 study used estimated glomerular filtration rate, 3 studies used estimated creatinine clearance, 4 studies used serum creatinine levels, and 3 studies used indoxyl sulfate levels), as compared with conventional therapy alone.
**Conclusions:** There is evidence supporting the efficacy of AST-120 (Kremezin) when combined with conventional therapy of dietary protein restriction and RAS blockade in delaying the progression of CKD compared with conventional therapy alone. We await the results of three large randomized controlled studies (EPPIC-1, EPPIC-2, and K-STAR) to confirm the results of this systematic review.

025

## KIDNEY DISEASE KNOWLEDGE AMONG NEW PATIENTS REFERRED TO A HOSPITAL NEPHROLOGY OUTPATIENT DEPARTMENT – 1 YEAR FOLLOW-UP

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**Aim:** To determine if chronic kidney disease (CKD) knowledge among patients one year after initial consultation in a nephrology clinic has improved.
**Background:** CKD health literacy among newly referred patients is limited. Little is known about CKD knowledge following informal education.
**Methods:** Newly referred patients to nephrology outpatients received education from doctors, and had access to pamphlets, internet sites, and patient support groups. Those with eGFR <20 ml/min/1.73 $m^2$ saw a CKD nurse. Knowledge was assessed by questionnaire at 12 months and compared with baseline.
**Results:** 95 patients were followed from 210 at baseline. Mean follow-up was 12.7 (+/–1.7) months. Those not surveyed included 59.1% discharged, 23.5% lost to follow-up, 7% deceased, 10.4% others. Median age was 70 (IQR 60–76) years, 54% male, 54% age pensioners. 50% were secondary school educated. Mean eGFR was 45.5 (+/– 22.4) ml/min/1.73 $m^2$, including 52% with CKD stage 3, 26% stage 4, and 0% stage 5. 80% had seen a nephrologist at least 3 times. 50% received pamphlets, 16% searched the internet, 8% saw a CKD nurse, 3% knew of Kidney Health Australia. 5 patients remained uncertain why they had been referred and 35 patients were uncertain what CKD means. CKD causes identified were unknown (n = 42), alcohol (n = 22), diabetes (n = 13), and hypertension (n = 11). Symptoms included other (n = 69), kidney pain (n = 8), haematuria (n = 7), and dysuria (n = 7). Management identified included uncertain (n = 36), dialysis (n = 33), other (n = 30). These results were comparable with baseline results.
**Conclusions:** After a year of attendance at nephrology outpatients, CKD health literacy remained poor. Visits to nephrologists and provision of pamphlets are insufficient. A more structured, individualized and repetitive education program by a multidisciplinary team may be more effective.

026

## NUTRITIONAL STATUS IS ASSOCIATED WITH THE FUTURE TREATMENT CHOICE – RENAL REPLACEMENT THERAPY VS. CONSERVATIVE CARE IN END STAGE KIDNEY DISEASE PATIENTS ATTENDING THE MULTIDISCIPLINARY PRE-DIALYSIS ASSESSMENT CLINIC

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**Background:** The aim of this study was to examine the relationships between nutrition status and patients' initial decisions for future renal replacement therapy (RRT) or conservative care (CC).
**Methods:** Retrospective analysis was performed on data obtained from patients' initial pre-dialysis clinic assessment records from April 2002 to March 2012. These included demographics (age and gender), clinical (GFR and co-morbidities) and nutritional [body mass index (BMI), serum albumin and subjective global assessment (SGA)] data and initial decision for RRT or CC.
**Results:** n = 501; mean age: 66.0 ± 14.7 years; 60.1%: M; mean GFR: 15.8 ± 5.5 mL/min/1.73 $m^2$ and diabetes: 44.9%. Patients who preferred CC (14.8%) over the RRT were older (77.3 ± 7.0 vs. 63.9 ± 14.7 years, $P < 0.0001$), had lower levels of GFR (17.5 ± 8.3 vs. 20.7 ± 8.6. mL/min/1.73 $m^2$, $P = 0.004$) and had higher prevalence of malnutrition rated by SGA score = B or C (64.6% vs. 39.6%, $P < 0.0001$). Among the patients who chose to start dialysis, patients who preferred hospital dialysis (HD) were older (68.7 ± 11.5 vs. 64.0 ± 14.2, $P < 0.0001$), had a higher prevalence of coronary artery disease (49.5% vs. 29.0%, $P < 0.0001$), diabetes (60.4% vs. 42.0%, P = 0.003), and malnutrition (52.1% vs. 32.7%, $P = 0.003$) compared to those preferred home dialysis (PD and HD). The two most elderly groups were those preferred CC and hospital HD. Apart from age (77.3 ± 7.0 vs. 68.6 ± 11.5 years, $P < 0.0001$) and BMI (28.1 ± 5.9 vs. 30.3 ± 6.8 kg/$m^2$, $P = 0.04$), there was no statistical difference for all other variables including the high prevalence of malnutrition (51.2% vs. 64.6%, $P = 0.11$).
**Conclusions:** Patients preferring CC and hospital dialysis were more advanced in age, had a higher prevalence of co-morbidities and nutrition abnormalities. Timely nutrition intervention should be considered in these groups in view of high nutrition risk.

027

## UREMIC TOXINS AND INFLAMMATION IN CHRONIC KIDNEY DISEASE

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**Background:** Indoxyl sulphate (IS) and p-cresyl sulphate (PCS) are nephro- and cardiovascular toxins which have pro-inflammatory properties in-vitro. However, the association between these putative uremic toxins and inflammation has not yet been investigated in the chronic kidney disease (CKD) population.
**Methods:** Serum concentrations of total and free IS and PCS, measured by ultra-performance liquid chromotography (an assay developed and validated by our group), and the inflammatory markers, interferon gamma (IFN-γ), interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α), were measured at baseline of a large randomised-control trial in CKD patients between March 2008 and September 2012. The relationships between toxin levels, inflammatory markers and exisiting vascular disease (previous stroke or transient ischemic attack, peripheral vascular disease, renovascular disease or vascular retinopathy) were evaluated by multiple linear regression and multivariable logistic regression.
**Results:** 149 CKD patients (59% male; age 60 ± 10 years; 44% diabetic) with a mean eGFR of 40 ± 9 ml/min/1.73 $m^2$ (range 25–59) were investigated. Following adjustment for eGFR, age and diabetes status, total and free IS were each significantly associated with IL-6 (p = 0.002 and p = 0.001, respectively), TNF-α (p = 0.004 and p = 0.031) and IFN (p = 0.006 and p = 0.007), whilst total and free PCS were associated with IL-6 (p = 0.006 and p = 0.033), but not with TNF-α or IFN. Although total PCS (OR 1.01, 95% CI 1.00–1.02, p = 0.016) and free PCS (OR 1.27; 95% CI1.03–1.63, p = 0.039) were associated with existing vascular disease on univariable logistic regression, neither IS nor PCS (free or total) were independently associated with vascular disease on multivariable analysis.
**Conclusions:** IS, and to a lesser extent, PCS were independently associated with inflammatory markers in CKD patients. These inflammatory associations may underpin some of their proposed nephro- and cardiovascular toxicity.

**028**
**Abstract withdrawn**

**029**

## *"I DON'T LIKE WHAT I READ ABOUT CHRONIC KIDNEY DISEASE, I MIGHT AS WELL JUST GO GET A GUN AND SHOOT MYSELF"*: FOCUS GROUP STUDY OF PATIENTS WITH EARLY STAGE CHRONIC KIDNEY DISEASE

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**Aim:** The aim of this study was to elicit patient perspectives on early stage chronic kidney disease and to identify their information needs.
**Background:** Chronic kidney disease (CKD) is a growing public health concern. Patients with CKD are at higher risk of cardiovascular mortality and progression to end-stage kidney disease requiring renal replacement therapy to survive. To prevent CKD progression, patients must make lifestyle modifications and adhere to treatment regimens.
**Methods:** Patients with CKD Stages 1–3 were purposively sampled from three major hospitals in Sydney, Australia to participate in focus groups. The focus group session were recorded with a digital voice recorder and transcribed verbatim. Data collection ceased when theoretical saturation was reached. Transcripts were thematically analysed.
**Results:** From nine focus groups including 38 participants, six major themes were identified: medical attentiveness (shared decision making, vigilant follow-up, rapport); learning self-management (diet and nutrition, barriers to physical activity, medication safety); contextualising comorbidities (prominence of chronic kidney disease, contradictory treatment); prognostic uncertainty (defeat and hopelessness, disease progression, disbelief regarding diagnosis); motivation and coping mechanisms (race against time, control, optimism, feeling normal); and knowledge gaps (practical advice, access to information, pathology results, diagnostic ambiguity, education for general practitioners).
**Conclusion:** Patients believe that their capacity to slow the progression of CKD is limited by the lack of knowledge of risk factors, treatment, lifestyle modifications and poor access to education. Development of multi-modal educational resources including practical lifestyle recommendations, such as adequate diet according to CKD stage and types of appropriate physical activities, combined with active physician engagement in prevention, are likely to promote patients' ability and motivation to make lifestyle modifications for prevention of CKD progression.

**030**

## IMPROVED PATIENT ACCESS TO DIETETIC SERVICES IN CHRONIC KIDNEY DISEASE USING A CATEGORISED REFERRAL TOOL

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**Aim:** To use the current status of dietetic appointments and reasons for referral to develop streamlined referral pathways that enable clear patient prioritisation.
**Background:** Over a 3-year period the number of CKD patients attending our hospital renal outpatient service increased dramatically from under 100 to over 400 patients. During this time dietetic resources remained unchanged, presenting challenges for meeting current practice guidelines and extending waiting times to see the dietitian.
**Methods:** A 4-week audit of appointments was conducted before (baseline) and after a 3-month trial of the new referral pathways. A new referral tool and booking procedures were developed from baseline data including: categorisation of dietetic priority (Category 1, 2 and 3); utilisation of community dietetic services where appropriate; and explanatory notes on who should take precedence in fully booked clinics. A questionnaire on nurses' perceptions was also conducted pre and post introduction of the new pathways.
**Results:** At baseline, 18 of 57 (31.6%) attempts to book timely dietetic appointments were not successful due to fully booked clinics: 7 new (6 for lifestyle-related reasons e.g. obesity, diabetes, cholesterol); and 11 review (6 for higher dietetic urgency e.g. hyperkalaemia and malnutrition). Following trial of the new system, only 4 of 58 (6.9%) attempts to book timely dietetics appointments were unsuccessful and all were considered low dietetic priority (Category 3), a significant improvement compared to baseline. Nurses' perceptions of improved appropriate patient access to dietetic services confirmed utility of the new tool.
**Conclusions:** Review of dietetic referral practices has led to development of an innovative referral tool and procedures, resulting in improved efficiency of existing dietetic resources and enhanced guidance to ensure high priority CKD patients are seen in a timely manner.

**031**

## IDIOPATHIC MEMBRANOUS NEPHROPATHY (IMN) TREATMENT AND OUTCOMES: A RETROSPECTIVE CASE REVIEW STUDY

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**Aim:** Review the management of IMN in a single centre to define current practices and outcomes.
**Background:** The clinical course and timing of treatment for IMN is complicated by the unpredictable occurrence of spontaneous remissions. Treatment regimens vary widely, prompting the need for audits for outcomes.
**Methods:** Demographics and clinical parameters for 49 patients with IMN at our institution between 2008–2012 were reviewed.
**Results:** At presentation, the cohort had mean creatinine 155 (52–1147) umol/L, mean proteinuria 6.1 ± 5.4 g/24 h, and mean albumin 24 ± 8.6 g/L: 80% had nephrotic syndrome. Immunotherapy was not used in 24 patients; 25% of patients had partial remission (proteinuria: 3.5g/24h with normal serum albumin), 21% had complete remission (proteinuria < 0.3 g/24 h), and 21% ESRF. Twenty-five patients received the following immunotherapies: prednisolone + cyclophosphamide (48%), prednisolone alone (24%), prednisolone + cyclosporin (20%), cyclophosphamide (4%), or cyclosporin (4%). In this cohort 28% had partial remission, 24% complete remission, and 16% ESRF. These patients had worse eGFR and worse proteinuria at initiation of treatment.
**Conclusions:** In our center, immunotherapy was reserved for patients with worse clinical parameters. A variety of treatment regimens were utilised. Remission rate is slightly higher in the immunotherapy group compared to patients without immunotherapy (52% vs. 46%). ESRF rate was higher in patients not treated with immunotherapy compared to patients on immunotherapy (21% vs.16%).

032

## ALPORT SYNDROME AND THIN BASEMENT MEMBRANE NEPHROPATHY IN THE QUEENSLAND CHRONIC KIDNEY DISEASE (CKD) REGISTRY

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**Aim:** To describe the characteristics of Australians with CKD due to Alport Syndrome (AS) and Thin Basement Membrane Nephropathy (TBMN).
**Background:** AS is due to mutations in genes encoding Alpha subunits of Collagen IV. Its population prevalence is ~1/50000. TBMN occurs in carriers of genes responsible for Autosomal Recessive AS and is estimated to affect ~1% of the population.
**Methods:** The CKD.QLD registry from four sites comprising 2167 patients was searched and analyzed for all cases of AS/TBMN.
**Results:** 3 cases of AS and 5 cases of TBMN were identified (0.4%). There was low prevalence at all sites (0–0.7%). Those with AS and TBMN were most commonly CKD Stage 2 (50%) while in the CKD.QLD registry overall, CKD 3B was most common (26.7%).

All patients with AS or TBMN were stages 2/3A. All AS and TBMN patients were female.

AS and TBMN patients were younger than the overall full CKD.QLD registry, with mean ages of 29.1 yrs, 55.4 yrs and 64.9 yrs respectively. The sole patient with CKD Stage 3A was the only patient >64 yrs.
**Conclusions:** AS and TBMN are rare in this CKD cohort consistent with prior descriptions. Those with AS and TBMN were younger and at earlier stages of CKD. The absence of identified males with AS is compatible with underlying inheritance patterns; though this is less clear in those with TBMN. Further expansion and refining of the CKD.QLD Registry are indicated to increase capture of AS/TBMN cases. Whilst there is optimism that early CKD follow-up may result in improved clinical outcomes, longitudinal review should be undertaken. A review of Renal Replacement Therapy Registries and potential genotypic studies may similarly increase understanding of these groups.

033

## CHARACTERISATION OF RARE GENETIC POLYMORPHISMS AND THEIR PATHOGENIC CONSEQUENCES IN THE DEVELOPMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background**: Systemic lupus erythematosus (SLE) is a clinically heterogenous disease in which renal failure strongly predicts mortality. Whilst genetic predisposition is a potent risk factor, few genetic mechanisms have been identified.
**Aim**: To identify mono- or oligo-genic causes of SLE.
**Methods**: We conducted whole exome sequencing of 5 SLE patients and their families (n = 20), selected by phenotype severity, familial clustering of SLE, or consanginous parentage. Rare non-synonymous single nucleotide polymorphisms (SNPs) in genes implicated in immune tolerance, DNA metabolism or apoptosis were investigated. Altered gene function due to these SNPs was interrogated by gene-specific assays.
**Results**: A novel R97H SNP, in the ubiquitous DNA exonuclease *three primer repair exonuclease 1* (TREX1), was identified in Family A resulting in a 16-fold reduction in exonuclease activity with associated increased IFN-α levels. In Family C we identified SNPs in two candidate genes: A rare W40C substitution in *B-cell scaffold protein with ankyrin repeats* (BANK1), a negative regulator of CD40 activation, was associated with B cell hyper-reactivity. Co-occurring mutations in *Interleukin-1 receptor-associated kinase 2* (IRAK2) increased Toll-like receptor-driven NF-kB activation. In Family D, a novel damaging mutation in *PTPN22*, known to T cell receptor signalling, is under investigation. As for Family E, a novel mutation in the *autoimmune regulator* (AIRE) gene abrogated expression of the tissue-restricted antigens insulin and involucrin, and is thus likely to impair T-cell negative selection.
**Conclusion**: Using whole exome sequencing we have successfully identified novel and rare SNPs with strong effects that are likely to be driving or contributing to SLE pathogenesis and would not have been identified by GWAS. This represents the first key step in personalised medicine for SLE patients.

034

## INHIBITION OF IL-6 RECEPTOR ATTENUATES AUTOIMMUNITY AND GLOMERULONEPHRITIS IN EXPERIMENTAL ANCA VASCULITIS

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**Aim:** To define the role of interleukin (IL)-6 signalling in anti-neutrophil cytoplasmic antibody (ANCA) vasculitis.
**Background:** The pleiotropic cytokine IL-6, critically required for Th17 immunity, is elevated in patients with ANCA vasculitis. IL-6 signaling occurs via the classic pathway using membrane bound IL-6 receptor (mIL-6R) and the trans-pathway via soluble IL-6 receptor (sIL-6R). Anti-IL-6R therapy has proven clinical effectiveness in treating rheumatological conditions.
**Methods:** We induced autoimmune anti-myeloperoxidase (MPO) glomerulonephritis (AIaMPOGN) by immunising C57BL/6 wild type (WT) mice with murine MPO. Renal injury was triggered after 14 days with administration of a sub-nephritogenic dose of nephrotoxic serum. We assessed the effect of IL-6 inhibition when administered during the induction phase (days −1 and 7) and during the effector phase (day 14) of injury using antibodies targeting IL-6 (classical and trans-pathway), mIL-6R (classical and trans pathway), and sIL-6R (trans-pathway).
**Results:** Early mIL-6R blockade diminished autoimmunity and attenuated glomerular injury in AIaMPOGN. Compared to mice administered isotype control immunoglobulin (IgG), total anti-MPO IgG levels were reduced in mice treated with IL-6R antibody (IgG:0.48+/–0.06, anti-mIL-6R:0.30+/–0.05$OD_{450}$ $P < 0.05$). Attenuated humoral immunity corresponded with attenuated cellular immunity (MPO-stimulated splenocyte IL17A: IgG:1.50+/–0.17, anti-mIL-6R:0.83+/–0.17$OD_{450}$ $P < 0.01$, MPO-stimulated splenocyte IFNγ: IgG:1.46+/–0.05, anti-mIL6R:0.47+/–0.14$OD_{450}$ $P < 0.0001$). Renal injury was also attenuated (abnormal glomeruli: IgG:44+/–6, anti-mIL-6R:21+/–2%, $P = 0.001$, 24 hour albuminuria: IgG:1052.0+/–201.1, anti-mIL-6R:252.8+/–54.6 μg/24 hours $P = 0.001$). No difference in humoral immunity (total anti-MPO IgG:1.18+/–0.06, anti-IL-6R:1.23+/–0.04, $P = 0.49$, IgG:0.73+/–0.33, anti-IL-6:0.46+/–0.21, anti-sIL-6R:0.49+/–0.15, $P = 0.08$) or renal injury (abnormal glomeruli: IgG:27.85+/–2.73, anti-IL-6R:31.50+/–2.24, $P = 0.32$, IgG:39.75+/–13.56, anti-IL-6: 32.60+/–17.65, anti-sIL-6R:33.89+/–10.54, $P = 0.51$) was seen following effector phase blockade of IL-6, mIL-6R and sIL-6R.
**Conclusion:** IL-6 critically directs development of cellular and humoral autoimmunity in ANCA associated glomerulonephritis but does not seem to play a major role as an effector cytokine.

035

## GLOMERULAR DEPOSITION OF MYELOPEROXIDASE AND NETS CORRELATE WITH THE PRESENCE OF DELAYED TYPE HYPERSENSITIVITY EFFECTOR CELLS IN ANCA VASCULITIS

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**Aim:** To provide evidence to support the hypothesis that glomerular injury in human ANCA associated vasculitis (AAV) is initiated by ANCA induced neutrophil accumulation, degranulation and formation of extracellular traps (NETs). A process exacerbated by the presence of anti MPO CD4 T cells recognizing extracellular myeloperoxidase (MPO) and directing delayed type hypersensitivity (DTH) effector macrophages.
**Background:** ANCA associated renal vasculitis is characterised by blood vessel inflammation and an association with circulating antibodies to ANCA. The autoantigenic targets of ANCA are MPO and proteinase 3. Loss of tolerance to MPO underlies most cases of AAV and glomerulonephritis.
**Methods:** Forty-eight renal biopsies from clinically active AAV patients positive for MPO were examined for the deposition of extracellular MPO, cellular origin of MPO (CD15+ Neutrophils and CD68+ Macrophages/monocytes), NETs and association with other leukocytes (CD4+ T cells, CD8+ T cells, FoxP3+T cells and Mast cell Tryptase+ Mast cells).
**Results:** Significant correlation was found for simultaneous glomerular infiltration of CD4 T cells and MPO positive cells ($P < 0.05$) and simultaneous infiltration of CD15 and MPO positive cells, and CD68 and MPO positive cells ($P = 0.004$, $P = 0.035$ respectively). Extracellular MPO was found in 93% of all

glomeruli and made up 23% of the total proportion of MPO observed within glomeruli and 31% of all the MPO in the interstitium. Neutrophil extracellular traps (NETs) were present in 61.3% of MPO-ANCA biopsies and there was significantly more CD15 cells, total MPO expression and extracellular MPO in the glomeruli of patients with the presence of NETs ($P < 0.05$).
**Conclusions:** This study provides evidence to support the hypothesis that neutrophil derived extracellular MPO acts as a planted autoantigen in glomeruli inducing T cell mediated DTH type injury.

036

## AN INTEGRATED CELL, TISSUE AND WHOLE ORGAN PROFILE OF KIDNEY MORPHOGENESIS

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**Aim:** To generate a comprehensive and quantitative spatial and temporal analysis of kidney morphogenesis in mouse that documents the relationship between progenitor populations within the nephrogenic niche and throughout the whole organ.
**Background:** There is good evidence that events occurring during fetal development that subtly alter organ structure influence predisposition to renal disease in adulthood. Understanding development is therefore critical for interpreting observed congenital defects or understanding the basis upon which disease arises. However, in the mammal, the size, opacity and complexity of organs has impeded systematic analyses of developmental processes critical to organ function.
**Methods:** Here, we employ a multiscale imaging approach to integrate optical projection tomography, single-cell resolution confocal and quantitative image analysis to comprehensively document kidney organogenesis across the entire developmental period in a mammalian model, the mouse. This included the quantification across time of ureteric epithelial (tip number, branch generation, branch angles, tree volume, tip volume, proliferation rate) and nephron progenitor parameters (number of niches, rate of niche formation, progenitor numbers, proliferation rate).
**Results:** Our analyses reveals temporally non-uniform process identifying three distinct morphogenetic phases; establishment, consolidation, and completion; that vary with respect to niche size, rates of cellular proliferation, dominant morphogenetic processes in the ureteric tree and spatial relationships between key cellular compartments.
**Conclusions:** The existence of distinct developmental phases during kidney development predicts differential temporal sensitivity to genetic and environmental insults, potentially enhancing our understanding of the mechanism of developmental anomalies. This approach will facilitate global quantitative analysis of even subtle perturbations to kidney development and is applicable to other organ systems.

037

## KIDNEY CD103+ DCs EXACERBATE RENAL INJURY THROUGH ACTIVATING CD8+ T CELLS IN ADRIAMYCIN NEPHROPATHY

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**Background:** CD103+ DCs, a newly described subset of DCs, have been investigated in diseases of lungs, intestine and skin. However, the characteristics and functions of CD103+ DCs in kidney remain unclear.
**Methods:** Adriamycin nephrosis (AN) was induced in BALB/c mice. The distribution, phenotype and function of kidney CD103+ DCs were assessed in normal and AN mice. CD103+ DCs were depleted by neutralizing CD103-saporin (SAP) antibody in AN mice to examine their role *in vivo*.
**Results:** CD103+ DCs were identified in kidney as CD45+/MHC-II+/CD11c+/CD103+/F4/80-/CD11b- cells. CD103+ DCs were distributed predominantly in cortex of normal and AN kidney. The number of CD103+ DCs was significantly increased in kidney of AN mice compared to that of normal mice. Depletion of kidney CD103+ DCs by CD103-SAP antibody improved renal function in AN mice, as evidenced by a decrease in proteinuria serum creatinine and increase in creatinine clearance. AN mice treated with CD103-SAP antibody also had less glomerulosclerosis, tubular atrophy and interstitial expansion than did AN control mice. The possible mechanisms underlying the pathogenic role of CD103+ DCs were examined. Kidney CD103+ DCs expressed high levels of IL-6 in AN mice, but not other inflammatory cytokines including IL-1beta, IL-12, IFN-γ, TNF-α and MCP-1. The co-stimulatory molecules CD80, CD86 and B7-H1 were highly expressed in kidney CD103+ DCs in AN mice compared to those of normal mice. Kidney CD103+ DCs displayed higher capability of cross-presenting antigen to CD8+ T cells than did CD103- DCs.
**Conclusion:** CD103+ DCs are present in kidney and induce renal injury in AN mice. The mechanism underlying the pathogenic role of CD103+ DCs in AN mice may relate to their ability to activate CD8 T cells.

038

## SELECTIVE EPITHELIAL POTENTIAL OF A RENAL MESENCHYMAL STEM CELL-LIKE POPULATION DERIVED FROM MATURE COLLECTING DUCT EPITHELIUM

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**Aim:** To investigate the epithelial potential and origin of endogenous renal mesenchymal stem cell (MSC) – like cells.
**Background:** We have previously described an endogenous renal MSC-like population enriched in the papilla. While demonstrating immunophenotypic and differentiative capacity similar to bone marrow MSCs, this renal MSC-like population showed specific gene expression suggesting a collecting duct location. Here we sought to confirm the location of this population within collecting duct and to examine their capacity to switch between mesenchymal and epithelium.
**Methods:** Renal MSC-like cells were isolated and cultured from total kidney or from the collecting duct of Hoxb7GFP adult mice via FACS. Cultured renal MSC-like cells were injected into the neonatal kidney (P1) under ultrasound guidance. The location of injected cells was examined using immunofluorescence. *In vitro* epithelial potential was examined using a 3D collagen gel culture system.
**Results:** After microinjection into neonatal kidneys, renal MSC-like cells integrated specifically into $Aqp2^+$ collecting ducts within the medulla / papilla. This renal MSC-like population was enriched in the $GFP^+$ fraction of adult Hoxb7GFP mice where Hoxb7 marks the collecting ducts (CD). Reinjection of this CD-derived MSC-like population also showed selective integration back into CD. Such epithelial integration was never observed after injecting bone marrow MSCs. When cultured in a 3-D system, the Hoxb7/$GFP^+$ derived cells formed E-$cadherin^+$ tubular structures showing that they can switch fates *in vitro*.
**Conclusion:** Endogenous renal MSC-like cells are capable of epithelial differentiation *in vitro* and specific integration into the collecting duct *in vivo*. With these properties, such cells may play a role in normal tissue turnover or assist in the treatment of renal damage and disease.

039

## FMS-LIKE TYROSINE KINASE 3 LIGAND (FLT3-L) INDUCES REGULATORY T CELLS (TREGS), BUT DOES NOT PROTECT MICE FROM EXPERIMENTAL CRESCENTIC GLOMERULONEPHRITIS (GN)

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**Background:** FLT3-L is a growth factor that expands Tregs and plasmacytoid dendritic cells (pDC).
**Aim:** We hypothesised that FLT3-L-induced Tregs would protect mice from experimental crescentic GN.
**Methods:** Naive C57BL/6 mice were injected with FLT3-L 10μg or PBS (control) intraperitoneally daily for 10 days. To determine whether FLT3-L altered immune responses to foreign antigen, FLT3-L/PBS was injected for 10 days before mice were primed with sheep globulin (SG) and culled 4 days later. To induce GN, mice were primed with SG, given intravenous sheep anti-mouse glomerular basement membrane globulin at day 4 (planting SG in glomeruli), and culled at day 14.
**Results:** After FLT3-L administration, mice had increased splenic Treg proportions (CD4+Foxp3+/CD4+: FLT3-L 21.4 ± 1.9 vs PBS 11.1 ± 0.8%; $P < 0.05$). Four days after SG priming, FLT3-L-treated mice had higher proportions of lymph node pDCs (10.0 ± 1.6 vs 5.0 ± 0.9%; $P < 0.05$) and enhanced SG-specific dermal delayed type hypersensitivity (0.31 ± 0.08 vs 0.09 ± 0.02 mm; $P < 0.05$), without an increase in Tregs, suggesting that ceasing FLT3-L therapy enhanced cellular immunity.

Mice were treated with FLT3-L/PBS for 10 days prior to inducing GN. FLT3-L-injected mice were not protected from renal injury (segmental necrosis:

48.3 ± 15.3 vs 46.0 ± 13.2%; P = 0.91, crescents: 7.0 ± 3.4 vs 4.0 ± 2.0%; P = 0.48). When FLT3-L/PBS was administered daily throughout the GN model, FLT3-L-treated mice developed substantial mortality compared with controls (day 13: 87.5% vs 12.5%; P < 0.05). At day 9, FLT3-L-treated mice had enhanced cellular immunity, with greater IL-17A production (ELISPOT: 12.8 ± 1.8 vs 6.4 ± 0.8 spots/1x$10^6$ SG-stimulated splenocytes; P < 0.05) and higher proportions of activated T cells (CD4+CD25+/CD4+ spleen: 15.3 ± 0.8 vs 12.9 ± 0.5%; P < 0.05).
**Conclusion:** FLT3-L therapy in experimental crescentic GN enhanced systemic T cell responses, showing that attempts to selectively enhance protective immunity in GN may be harmful.

040

## LOSS OF *CRIM1* RESULTS IN RENAL PAPILLARY HYPOPLASIA VIA PERTURBATIONS TO Wnt/β-CATENIN SIGNALLING

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**Aim:** To elucidate the mechanism of normal papilla development in the context of the papillary hypoplasia seen in *Crim1* mutant mice.
**Background:** Congenital Abnormalities of the Kidney and Urinary Tract affects 1 in 500 individuals and represents the foremost cause of renal failure. While there has been significant focus on the genetic basis of defects in fetal kidney development, the regulation of postnatal papilla development and the functional impact of papillary malformation remain largely undefined. Our previous work established a link between *Crim1* deficiency and papillary hypoplasia as well as illustrating the association between this defect and functional obstruction. Here we characterise the molecular pathways involved in normal postnatal papilla development and investigate how these are altered in *Crim1* deficient mice.
**Methods:** Microarray profiling of wildtype mouse neonatal cortex versus medulla from birth (P0) to 3 months (P90) was performed to identify molecular pathways involved in medullary development. Activity of canonical Wnt signalling in wildtype and *Crim1* mutant mice was examined using qPCR and by examining BATGAL reporter mice.
**Results:** Microarray analyses identified Wnt signalling genes as differentially marking medulla development prior to P10, including Wnt4, Wnt5a, Wnt7b, Wnt9b ligands as well as genes associated with β-catenin mediated canonical Wnt signalling. LacZ staining of BATGAL mice localised canonical Wnt activity to the medullary interstitium and CD. Section *in situ* hybridisation confirmed the location of pathway members in interstitium or CD. qPCR revealed a reduction in expression of *Axin2* and *Lef1* in *Crim1* mutant mice, further implicating canonical Wnt signalling.
**Conclusions:** *Crim1* deficiency resulted in perturbations to the Wnt/β-catenin signalling during renal medulla development, thereby causing papillary hypoplasia preceding overt renal disease.

041

## INNATE IMMUNE CELLS PRODUCE INTERLEUKIN-17A, WHICH DRIVES AUTOIMMUNITY AND LUPUS NEPHRITIS

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**Aim:** To define the role of interleukin (IL)-17A in systemic lupus erythematosus (SLE) induced by pristane.
**Background:** SLE and lupus nephritis are significant causes of morbidity and mortality. Clinical studies have demonstrated that serum IL-17A levels are increased in disease, although direct evidence of pathogenicity is lacking.
**Methods:** We injected pristane (500 µl) intraperitoneally into C57BL/6 wild type (WT) mice and assessed IL-17A production after 6 days, using flow cytometry. Subsequently we treated WT and IL-17A-/- mice with pristane and assessed cellular immunity (8 weeks), humoral autoimmunity and renal injury, both functionally and histologically, after 7 months.
**Results:** After 6 days, IL-17A production was readily detected in pristane treated WT mice, but not in control (WT) mice. The majority of IL-17A producing cells were innate cells (macrophages 42.3 ± 5.2%, neutrophils 23.8 ± 2.7%, natural killer T cells 11.2 ± 1.3%, gammadelta T cells11.2 ± 1.3%) only 14.1 ± 1.5% were CD4+Tcells. After 8 weeks systemic IFNY (WT 591.3 ± 188.6 vs. IL-17A-/- 176.0 ± 15.8 ng/ml, P < 0.05) and TNF (WT 294.7 ± 11.6 vs. IL-17A-/- 196.6 ± 35.7 ng/ml, P < 0.05) production were decreased in IL-17A-/- mice, IL-17A was still readily detected in WT mice. After 7 months humoral autoimmunity was diminished in IL-17A-/- mice, with decreased levels of total IgG and anti-dsDNA, at serial dilutions. Glomerular IgG (WT 1.8 ± 0.1 vs. IL-17A-/- 1.1 ± 0.1 intensity score, P < 0.0001) and complement (WT 2.0 ± 0.1 vs. IL-17A-/- 1.3 ± 0.1 intensity score, P < 0.0001) deposition was decreased in the absence of IL-17A. Compared to WT mice, glomerular injury assessed by albuminuria (WT 271.5 ± 55.8 vs. IL-17A-/- 87.6 ± 15.9 µg/24 hours, P < 0.05) and histological injury (WT 32.0 ± 2.1 vs. IL-17A-/- 22.9 ± 3.1 abnormal glomeruli P < 0.05) were diminished in IL-17A-/- mice.
**Conclusions:** These results demonstrate that innate immune cells produce IL-17A, which drives autoimmunity and glomerular injury in experimental SLE.

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## INCREASED TUBULOINTERSTITIAL RECRUITMENT OF HUMAN CD141hi CLEC9A+ AND CD1C+ MYELOID DENDRITIC CELLS IN FIBROTIC KIDNEY DISEASE

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**Aim:** To identify, enumerate and phenotype human kidney DC subsets by multiparameter flow cytometry.
**Background:** Dendritic cells (DC) play critical roles in immune-mediated kidney diseases. Little is known, however, about DC subsets in diseased human kidneys, with previous studies restricted to a limited set of pathologies and to using immunohistochemical methods.
**Methods:** In this study, we developed novel protocols for extracting renal DC subsets from a wide range of human kidney diseases and characterised them by ten-colour flow cytometry.
**Results:** We detected significantly elevated numbers of total DC ($CD45^+$ $lineage^-$ $HLA\text{-}DR^+$), $CD11c^+CD141^{hi}$ and $CD11c^+CD1c^+$ myeloid DC (mDC) subsets in diseased biopsies with interstitial fibrosis than diseased biopsies without fibrosis or healthy kidney tissue. In contrast, $CD11c^-CD123^{hi}$ plasmacytoid DC numbers were significantly higher in the fibrotic group compared to healthy tissue only. Numbers of all DC subsets correlated with loss of kidney function. $CD141^{hi}$ DC expressed CLEC9A, whilst the majority of $CD1c^+$ DC lacked expression of CD1a and DC-SIGN, suggesting these mDC subsets may be circulating $CD141^{hi}$ and $CD1c^+$ blood DC infiltrating kidney tissue. Immunohistochemical analysis revealed $CLEC9A^+$ and $CD1c^+$ cells restricted to the renal tubulointerstitial compartment. Notably, DC expression of costimulatory and maturation molecule CD86 was significantly increased in both diseased cohorts compared to healthy tissue. Consistent with an inflammatory environment, significantly higher levels of chemokine IL-8 were detected in the dissociation supernatants of diseased biopsies with fibrosis than both non-fibrotic diseased biopsies and healthy tissue.
**Conclusion:** Collectively, our data indicate that activated mDC subsets recruited into the tubulointerstitium are positioned to play a role in the development of fibrosis and thus, progression to chronic kidney disease.

043

## DIRECTING THE DIFFERENTIATION OF HUMAN ES CELLS TOWARDS A RENAL FATE

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The goal of our project is to direct differentiation of pluripotent human ES cells (hESCs) to a renal progenitor state. It has previously been shown that mesendoderm differentiation can be induced via the addition of BMP4 and Activin A with the relative ratios of these factors determining the end of the primitive streak being induced (Tam PP, 2007). To find the optimum ratio of BMP4/ActivinA for mesoderm induction, hESCs were cultured with different combinations of BMP4/ActivinA ratios. qPCR results indicate that high BMP4 and low Activin A bias towards induction of posterior primitive streak, contributing to mesoderm formation. Next, we directed the differentiation from posterior primitive streak to intermediate mesoderm (IM) using several defined growth factors known to be involved in IM and metanephric mesenchyme (MM) development in vivo. With growth factors, the induced cells expressed the IM markers PAX2 and LHX1 as well as OSR1. In order to assess the commitment of these cells to

renal fate, induced IM were cultured up to 17 days. Time course RT-PCR analysis showed that gene expression changed in a stepwise manner from mesendoderm to IM then MM and ureteric epithelium. To assess the renal potential of these induced cells, we performed 3D aggregates which were cultured as explants. After culture, ECAD$^+$ tubular structures formed in these aggregates some of which were PAX2$^+$ whereas others were LTL lectin binding. Non-epithelial SIX2$^+$ cells were also maintained in these aggregates. In summary, we demonstrate a method for the stepwise induction of both the ureteric epithelium and the nephron progenitor populations of the kidney from human ES cells and show that these populations have appropriate renal tubulogenic potential in vitro.

044

## FEMALE MICE OFFSPRING ARE MORE SUSCEPTIBLE TO KIDNEY UNDERDEVELOPMENT AND DECLINE IN KIDNEY FUNCTION THAN MALE OFFSPRING DUE TO MATERNAL CIGARETTE SMOKE EXPOSURE DURING GESTATION AND LACTATION

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**Aim:** To investigate whether the gender of the offspring differentially impacts on renal development caused by maternal smoking during pregnancy and lactation.
**Background:** Maternal smoking during pregnancy can lead to underdeveloped kidneys in the offspring, which may lead to chronic kidney disease (KCD) later in life.
**Methods:** Female Balb/c breeder mice (6 weeks) were either exposed to tobacco cigarette smoke or sham exposed for 5 weeks prior to mating, during gestation and lactation. Male and female offspring were sacrificed at three different postnatal ages; postnatal day (P) 1, P 20 (weaning age) and 13 weeks (W13) (mature age). Blood and urine samples were collected to assess renal function. Kidneys were harvested to determine histological and molecular changes related to renal development.
**Results:** Maternal smoke exposure reduced body and kidney weights of the offspring in both genders at 13 weeks ($p < 0.05$). Males' offspring's kidneys from smoke exposed dams had fewer vascularised glomeruli and more immature glomeruli compared to the control at P1 and P20. mRNA of genes involved in renal development such as FGF2, GDNF and Pax2 were reduced in the kidneys of offspring from smoke exposed dams compared to control at P1 and P20. mRNA for genes involved in renal fibrosis (fibronectin and collagen IV) were downregulated in both genders, the inflammatory marker (MCP1) was upregulated in the female offspring at W13. Urinary albumin and creatinine clearance demonstrated functional in female offspring but not in male offspring at W13.
**Conclusion:** Despite male offspring having increased histological evidence of renal underdevelopment at birth and at weaning, female offspring of smoking mothers had greater evidence of CKD in adulthood as a consequence of maternal smoking.

045

## INTERLEUKIN-12 AND 18 STIMULATED T CELLS IN URAEMIC SERUM REDUCE PRODUCTION OF INTERFERON-GAMMA AND PROLIFERATION *IN VITRO*

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**Aim:** To determine the effect of uraemic serum on T cell function *in vitro*.
**Background:** Patients with chronic kidney disease (CKD) are immunocompromised and are at an increased risk of infections. Serum concentrations of interleukin (IL)-12 and IL-18 are at least 1.3-fold higher compared to age-matched healthy individuals but the effect of uraemic serum on T cell function remains unknown.
**Methods:** Immunomagnetic-bead isolated CD3-positive T cells from healthy blood donors were cultured in uraemic medium (UM) (10% v/v uraemic sera of stage 3–5 CKD patients) compared to complete medium (CM) (10% v/v sera of healthy individuals). T cell production of interferon-gamma (IFN-γ) by enzyme-linked immunosorbent assay, T cell proliferation by bromodeoxyuridine (BrdU) incorporation and messenger ribonucleic acid (mRNA) expression of IFN-γ receptor (R), IL-12R and IL-18R were assessed when cultured in UM and CM and in the presence of increasing concentrations of IL-12 and 18 (from 0.1 and 0.5 ng/mL respectively).
**Results:** T cells cultured in UM stimulated with 2.5 ng/mL and/or 12.5 ng/mL of exogenous IL-12 and 18 respectively produced over a 1.5-fold decrease in the production of IFN-γ, 1.2-fold reduction in BrdU proliferation and over a 2-fold reduction in IL-12R, IL-18R and IFN-γR mRNA expression compared to T cells cultured in CM ($p < 0.01$). T cell function and mRNA receptor expression were similar when cultured in CM or UM stimulated with phorbol myristate acetate and ionomycin or anti-CD3/28 with IL-12.
**Conclusions:** IL-12 and 18-stimulated T cells cultured in UM exhibited reduced T cell activation and proliferation, possibly related to a reduction in mRNA expression of IL-12R, IL-18R and IFN-γR *in vitro*. This observation may in part explain the immunocompromised state of CKD patients.

046

## NEW ZEALAND SURVEY OF GLOMERULONEPHRITIS

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**Background:** The incidence of glomerulonephritis is well documented but few studies have reported on outcomes. We report the long term outcomes of patients enrolled in the New Zealand Glomerulonephritis (NZGN) Study from 1970 to 1986.
**Aims**: To assess long term outcomes of GN in New Zealand focusing on progression to end stage renal disease (ESRD), renal replacement therapy and mortality.
**Methods**: We reviewed all records from the NZGN study. ANZDATA records were used for patient who had renal replacement therapy while medical notes and local laboratories records were used to retrieve recent serum creatinine values. Mortality data was obtained from the notes or from the national database.
**Results**: There were 850 patients, mostly Caucasians (78%) and male (69.1%). The median follow up was 30.1 years (1–42.3 years). There was no single predominant type of GN but IgA nephropathy (13.3%), acute diffuse proliferative GN (12.5%) and Focal GN (11.3%) were more common.

293 (34.5%) of the study population progressed to ESRD. 264 (90%) of these underwent dialysis. 181 (62%) of ESRD patients underwent renal transplantation. ESRD was more likely in patients with ESRD at diagnosis (78.5%), RPGN (92%), chronic GN (100%) and MCGN type II (dense deposit disease) (100%) and least likely in minimal change disease.

401 (47.2%) of the study population have died with the highest mortality rates in patients with RPGN 22 (88%), dense deposit disease 10 (83.3%) and end stage renal failure12 (85.7%) at time of biopsy.
**Conclusion:** We report the longest follow up of GN reported thus far with a median of 30.1 years. There was no predominant type of GN, but a third progressed to end stage renal failure.

047

## OUTCOMES OF CARDIAC SURGERY IN CHRONIC KIDNEY DISEASE

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**Aim:** To define predictors of early and late outcomes of cardiac surgery in patients with chronic kidney disease (CKD).
**Background**: CKD increases the risk of mortality in cardiac surgery. Since there is a wide variation in the co-morbidities in individual patients, providing prognostic data as well as evaluating their suitability for surgery is often a challenge.
**Methodology:** Patients (n = 545) with (serum creatinine ≥200 μmol/l or on renal dialysis) were identified from databases from the largest Sydney cardiothoracic surgical units with data consistent with the Australian and New Zealand Society of Cardiothoracic Surgeons data definitions. Patient data were matched against the National Dialysis Database and NSW Register of Births, Deaths and Marriages. Statistical analysis identified predictors of early and late outcomes.
**Results:** The Kaplan-Meier estimate of 1, 5 and 10 year survival for all patients was 82%, 60% and 39% respectively. Outcomes were similar after coronary bypass surgery and valve replacement, and were also similar for dialysis and non-dialysis patients both pre and post-operatively.

Odds ratio for significant independent predictors of outcomes were: Perioperative death: age /decade (1.4), emergency surgery (7.6), redo surgery (3.8), left

ventricular impairment (moderate: 2.6), (severe: 3.7); New early postoperative dialysis: serum creatinine >350 μmol/l (6.5), emergency surgery (3.5), tricuspid valve surgery (5.9); New permanent dialysis within 6 months of surgery: serum creatinine >350 μmol/l (13.1); late death: age /decade (1.5), female gender (1.4), serum creatinine >350 μmol/l (1.5), left ventricular impairment (moderate or severe 1.5).
**Conclusion:** Left ventricular impairment is a strong risk factor for early and late death in kidney disease patients. Following cardiac surgery, pre-operative dialysis dependent and dialysis free patients had similar long term outcomes.

048

## EXERCISE AND LIFESTYLE INTERVENTION IN CHRONIC KIDNEY DISEASE: EFFECTS ON CARDIOVASCULAR FUNCTION

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**Aim:** To determine the effect of exercise training and lifestyle intervention (LI) on cardiorespiratory fitness (CRF) and examine the impact on cardiovascular risk factors and cardiac function.
**Background:** Chronic kidney disease (CKD) is associated with poor cardiorespiratory fitness (CRF). Exercise can be effective in management of cardiovascular risk factors however there are few long term exercise studies in the CKD population.
**Method:** Pre-defined substudy of a larger randomized controlled trial. Between February 2008 and March 2010, 90 patients with stage 3–4 CKD were screened with an exercise stress echocardiogram prior to enrolment. Patients (n = 83) were randomized to standard care (control) or LI. LI included multidisciplinary care (CKD clinic), lifestyle program and aerobic and resistance exercise training for 12 mths. CRF ($VO_2$peak), left ventricular function, anthropometric, and biochemical data were collected at baseline and 12 mths.
**Results:** Ten percent of randomized patients had subclinical myocardial ischemia at screening and completed the study without incident. There was no baseline difference among 72 patients who completed follow-up (LI = 36, control = 36). The intervention increased $VO_2$peak (2.8 ± 0.7 ml/kg/min versus –0.3 ± 0.9 ml/kg/min p = 0.004). There was small weight loss (–1.8 ± 4.2 kg versus 0.7 ± 3.7 kg p = 0.02) but no change in BP or lipids. Diastolic function improved (increased e', 0.75 ± 1.16 cm/s versus –0.47 ± 1.0 cm/s p = 0.001). Systolic function was well preserved and improved to a lesser extent (global longitudinal strain, –0.4 ± 0.7 versus 1.3 ± 0.5% p = 0.05) and change in arterial elastance was attenuated (0.11 ± 0.76 mmHg/ml versus 0.76 ± 0.96 mmHg/ml, p = 0.006). Delta $VO_2$ peak was associated with group allocation and improved body composition.
**Conclusion:** Exercise and LI in patients with CKD can produce improvements in CRF, body composition and cardiac function.

049

## A RANDOMISED, CONTROLLED TRIAL OF EXIT SITE APPLICATION OF MEDIHONEY FOR THE PREVENTION OF CATHETER-ASSOCIATED INFECTIONS IN PD PATIENTS – HONEYPOT STUDY

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**Aim:** To determine whether, when compared with standard topical mupirocin prophylaxis of nasal S. aureus carriers, daily exit site application of antibacterial honey resulted in a longer time to catheter-associated infection in peritoneal dialysis (PD) patients.
**Background:** There is a paucity of evidence to guide the optimal strategy for preventing catheter-associated infections in PD patients. Antibacterial honey shows promise as a cheap, effective topical prophylactic agent without inducing microbial resistance.
**Methods:** In this multi-centre, open-label, parallel-groups, randomized controlled trial, 371 PD patients were randomized to daily topical exit-site application of antibacterial honey plus standard exit-site care (N = 186) or intranasal mupirocin prophylaxis (in nasal Staphylococcus aureus carriers only) plus standard exit-site care (control, N = 185). The primary endpoint was time to first catheter-associated infection (exit-site infection, tunnel infection or peritonitis).
**Results:** The median catheter-associated infection-free survival times were not significantly different between the honey (16.0 months) and control groups (17.7 months; unadjusted hazard ratio [HR] 1.12, 95% CI 0.83–1.51, P = 0.47). In the subgroup of diabetic patients, allocation to honey increased the risks of both the primary endpoint (HR 1.85, 95% CI 1.05–3.24) and peritonitis (HR 2.25, 95% CI 1.16–4.36). There were no significant differences between the honey and control groups with respect to mupirocin-resistant staphylococcal isolates (0/34 versus 2/27, P = 0.1), serious adverse events (298 versus 327, P = 0.2) or deaths (14 versus 18, P = 0.9). Patients receiving honey were more likely to withdraw from the trial (29% vs 9%, P < 0.001) and 11 (6%) experienced local skin reactions.
**Conclusion:** Daily topical exit-site application of antibacterial honey was not superior to nasal mupirocin prophylaxis for the prevention of catheter-associated infection in PD patients and may have been inferior in diabetic patients.

050

## GLOBAL LONGITUDINAL STRAIN IS AN INDEPENDENT PREDICTOR OF ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE

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**Aim:** To evaluate the prognostic value of Global Longitudinal Strain (GLS) in patients with Advanced Chronic Kidney Disease (CKD).
**Background:** Left ventricular (LV) systolic dysfunction is an important predictor of cardiovascular death. Global longitudinal strain (GLS) is a widely available echocardiographic technique proven to be more sensitive than conventional ejection fraction (EF) in detecting subtle changes in LV function.
**Methodology:** We followed 183 patients (57.4% male, 61.2% on dialysis) with stage 5 and end stage kidney disease(ESKD) for a mean of 7.8 ± 4.4 yrs. 112 (61%) of patients died within this time and 46 (25%) deaths were due to cardiovascular (CV). GLS was calculated using 2 dimensional speckle tracking and EF was measured using Simpson's biplane. Cox proportional hazard model was used to assess baseline variables, laboratory values and measures of LV function as predictors of all- cause and CV mortality.
**Results:** The mean GLS was –13.7 ± 4.1% and EF was 44 ± 11%. 53% of patients with EF ≥ 45% had detectable abnormal GLS (>–16%). GLS was a significant predictor of all-cause [Hazard Ratio (HR) 1.08 95% Confidence Interval (CI) 1.01–1.15] and CV mortality (HR 1.13 95%CI 1.01–1.15) following adjustment for age, diabetes mellitus, hypertension, previous cardiac events, parathyroid hormone, EF and allowing for transplant as a competing risk. In this cohort, EF (as a continuous variable) or EF < 45% was not a significant predictor of patient survival.
**Conclusion:** GLS is an important predictor of all-cause and CV mortality in CKD patients. GLS is known to detect subtle cardiac changes such as myocardial hypertrophy and fibrosis and therefore may be a more sensitive discriminator for LV dysfunction.

051

## COMPARISON OF ESTIMATED GLOMERULAR FILTRATION RATE BY THE CKD-EPI EQUATIONS WITH AND WITHOUT CYSTATIN C FOR PREDICTING CARDIOVASCULAR MORTALITY IN ELDERLY WOMEN

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**Aim:** To evaluate the predictive value of the creatinine-derived Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI-Cr) equation, CKD-EPI-cystatin C (CKD-EPI-cystatin) and combined CKD-EPI-creatinine-cystatin C (CKD-EPI-Cr-cystatin)-derived estimated glomerular filtration rate (eGFR) equations and clinical events.
**Introduction:** eGFR using serum creatinine equations are predictive of cardiovascular disease (CVD) mortality among the general population and those with chronic kidney disease. Newly developed CKD-EPI-cystatin and

CKD-EPI-Cr-cystatin-derived eGFR equations appear to be superior in predicting measured GFR but the association with clinical events remains unknown.
**Methods:** This was a prospective observational study of 1,165 women over the age of 70 from the Calcium Intake Fracture Outcome Study. Complete verified 10-year records for CVD mortality were obtained using the Western Australian Data Linkage System.
**Results**: Mean (SD) eGFRs of participants derived from CKD-EPI-Cr, CKD-EPI-cystatin and CKD-EPI-Cr-cystatin equations were 67 (13), 65 (15) and 66 (13) mL/min/1.73 $m^2$ respectively. In the adjusted Cox regression models, each SD decline in eGFR by CKD-EPI-Cr, CKD-EPI-cystatin and CKD-EPI-Cr-cystatin equations was associated with a similar increased risk of CVD mortality (adjusted hazard ratio [HR] 1.15, 95%CI 1.04–1.46; adjusted HR 1.33, 95%CI 1.12–1.59; and adjusted HR 1.32, 95%CI 1.12–1.57 respectively). Receiver operating characteristic (ROC) curve analysis demonstrated that the sensitivity and specificity of the three equations were similar. Compared to CKD-EPI-Cr equation, there was no net reclassification improvement (NRI) above or below 40% estimated risk for CVD events using eGFR derived from CKD-EPI-cystatin (NCI 0.3%, P = 0.867) or from CKD-EPI-Cr-cystatin (NRI 0.2%, P = 0.876) equations.
**Conclusion**: The newly-developed and validated CKD-EPI-cystatin and CKD-EPI-Cr-cystatin equations did not improve the prediction of CVD mortality compared with the commonly-used CKD-EPI-Cr equation.

052

## THE IMPACT OF HAEMODIAFILTRATION, HAEMOFILTRATION AND HAEMODIALYSIS ON CLINICAL OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Aim:** To compare the impact of convective therapies and haemodialysis on clinical outcomes in end stage kidney disease (ESKD).
**Background:** Convective modalities of dialysis, including haemodiafiltration and haemofiltration, may improve patient outcomes and mortality compared with haemodialysis.
**Methods:** A systematic review and meta-analysis were performed examining all randomised controlled trials that assessed convective therapies compared with haemodialysisin participants with ESKD. Medline, EMBASE and the Cochrane Library database were searched to February 2013. The primary outcome was cardiovascular events (defined where possible as cardiovascular mortality, myocardial infarction and stroke, otherwise as defined by study author) with multiple secondary outcomes. Summary estimates of relative risk (RR) or weighted mean difference (WMD) with 95% confidence interval (CI) were calculated using random effects models.
**Results:** The search yielded 24 trials (3356 participants) with a median follow-up of 12 months. Compared with haemodialysis, convective therapies did not reduce cardiovascular events (RR 0.84, 95%CI0.59–1.19, 3 trials, 2402 participants) or all-cause mortality (RR 0.84, 95%CI0.66–1.06, 9 trials, 2961 participants). Convective therapies reduced symptomatic hypotension (RR 0.49, 95%CI0.31–0.78, 5 trials, 422 participants). There was no impact on small molecule clearance (WMD 0.05 kt/v ratio, 95%CI-0.08-0.18, 12 trials, 629 patients). Clearances of β2-microglobulin were improved (WMD 19.94 ml/min, 95%CI11.58-28.30, 4 trials, 157 patients). Participants allocated to convective therapies were more likely to be transplanted (RR 1.24, 95%CI1.04-1.47). Overall trial quality was low. There was variation in follow-up principles among trials with some censoring at transplant, some at non-adherence and some not specified.
**Conclusions:** The advantages of convective modalities over conventional haemodialysis for cardiovascular events and mortality remain inconclusive. Further high quality studies are needed to clarify the role of these modalities.

053

## GENDER DIFFERENCES IN TREATMENT PATTERNS OF END-STAGE KIDNEY DISEASE IN INDIGENOUS AUSTRALIANS

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**Aim:** To examine gender differences in treatment patterns of end-stage kidney disease (ESKD) in Indigenous Australians.
**Background:** Gender disparity is a nonmedical factor that may affect treatment patterns in patients with ESKD. Ethnic disparities in the treatment of Indigenous and non-indigenous ESKD patients in Australia have been documented. However gender differences in treatment patterns among Indigenous Australians have not been investigated.
**Methods:** Patients were men ($n = 908$) and women ($n = 1,114$), aged ≥18 years, recorded in the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) as commencing renal replacement therapy in Australia 2001–2010. Indigenous status (Australian Aboriginal and Torres Strait Islander) was self-reported. We used Poisson regression with robust standard errors to calculate relative risks (RR) and 95% confidence intervals (CI) adjusted for relevant clinical and sociodemographic covariates to examine differences between groups.
**Results:** Compared to men, women were older (mean age; 52.0 versus 50.9, $p < 0.05$), were more likely to be obese (35.9% versus 30.3%, $p < 0.05$), were less likely to be current or former smokers (55.1% versus 75.3%, $p < 0.001$) and were less likely to have been referred to nephrological care within only 3-months of commencing treatment (29.8% versus 34.6%, $p < 0.05$). The majority (around 80%) of both men and women received haemodialysis in hospital however women were around 40% less likely to receive haemodialysis a satellite facility (RR = 0.58, 95%CI 0.41–0.86, $p < 0.01$). Of note, women were around 45% less likely to have received a renal transplant during the study period compared to men (RR = 0.54, 95%CI 0.38–0.75, $p < 0.001$).
**Conclusions:** Results indicate that gender differences in the treatment of Indigenous Australians with ESKD exist. Research examining gender disparities in dialysis and transplantation in Indigenous Australians with ESKD is clearly indicated.

054

## GENDER DIFFERENCES IN TREATMENT PATTERNS OF END-STAGE KIDNEY DISEASE IN NON-INDIGENOUS AUSTRALIANS

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**Aim:** To examine gender differences in treatment patterns of end-stage kidney disease (ESKD) in non-indigenous Australians.
**Background:** Gender disparity is a nonmedical factor that has been shown to affect treatment patterns in patients with ESKD. However gender differences in treatment patterns in ESKD patients in Australia have not yet been comprehensively explored.
**Methods:** Patients were non-indigenous men ($n = 12,247$) and women ($n = 7,471$), aged ≥18 years, recorded in ANZDATA as commencing renal replacement therapy in Australia 2001–2010. We used Poisson regression with robust standard errors to calculate relative risks (RR) and 95% confidence intervals (CI) adjusted for relevant clinical and sociodemographic covariates to examine differences between groups.
**Results:** Compared to men, women were younger (mean age; 61.6 versus 62.1, $p < 0.05$), had fewer medical comorbidities (mean number, 1.21 versus 1.46, $p < 0.001$), were less likely to be ever smokers (35.8% versus 61.9%, $p < 0.001$) and were more likely to be obese (28.5% versus 25.7%, $p < 0.001$). Women were less likely to access haemodialysis (RR = 0.93, 95%CI 0.91–0.96, $p < 0.001$) and more likely to access peritoneal dialysis (RR = 1.23, 95%CI 1.14–1.33, $p < 0.001$) as their initial modality compared to men. In regards to initial dialysis facility, there were no gender differences in those being dialysed in hospital/outpatient care however women were less likely to be dialysed in a satellite facility (RR = 0.80, 95%CI 0.65–0.98, $p < 0.05$) and more likely to be receiving home (peritoneal) dialysis (RR = 1.86, 95%CI 1.28–2.68, $p < 0.01$). While there were no gender differences in preemptive transplants, women were significantly less likely to receive a subsequent transplant (RR = 0.86, 95%CI 0.82–0.89, $p < 0.001$).
**Conclusions:** Results indicate that gender disparities in the treatment of non-indigenous ESKD patients exist. Research examining gender biases and preferences in dialysis and transplantation is indicated.

055

## OUTCOMES IN RURAL VERSUS URBAN END STAGE KIDNEY DISEASE IN NEW SOUTH WALES USING DATA LINKAGE

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**Aim:** To compare mortality of end stage kidney disease (ESKD) patients in rural and urban NSW using data linkage.

**Background:** There is international evidence suggesting higher mortality with increasing remoteness from health services, however this has not been explored in an Australian setting.
**Methods:** The ANZDATA Registry was used to identify all incident patients living in NSW receiving renal replacement therapy between 01/07/2000 and 31/07/2010. These patients were linked to the NSW admitted patient data collection (NSW APDC) and the NSW Registry of Births Deaths and Marriages, allowing measurement of hospital usage and mortality. Postcodes and the ARIA index were used to separate patients into urban (living in highly accessible areas) and rural residents (living out of highly accessible areas). We compared all-cause mortality between the two groups.
**Results:** ANZDATA identified 11,036 patents, 209 did not match within NSW APDC, leaving 10,827 patients with 2,403,678 hospitalisation records. After accounting for missing data and non-NSW residence, 10,329 patients remained. Of these, 8,832 patients were classified as urban and 1,497 as rural residents. Follow-up was to a median of 4.41 years (IQR 2.24 to 7.82 years). The median unadjusted survival in the urban residents was 4.47 years and in the rural residents was 3.93 years (p = 0.006). There was no difference in 1 year survival (89% in the rural vs. 90% in the urban) or in rates of late referral 23% in rural vs. 22% in the urban, p = 0.28) between the two groups.
**Conclusions:** Urban ESKD residents have a significant unadjusted mortality advantage compared to rural residents in NSW. Further adjustment for patient and system characteristics is required to explore factors contributing to this mortality difference.

056

## RENAL REPLACEMENT THERAPY (RRT) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS IN AUSTRALIA AND NEW ZEALAND

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**Aim:** To analyse the epidemiology, dialysis, transplantation and pregnancy outcomes of patients with end-stage renal disease secondary to SLE from 1986–2009 in Australia and New Zealand.
**Background:** There has been no review of outcomes of SLE patients on RRT in Australia and New Zealand since newer immunosuppressive protocols.
**Methods:** Data were retrieved from Australia and New Zealand Dialysis and Transplant Registry (ANZDATA). Patients entering RRT January 1986 until December 2009 were analysed in four age groups (<19, 19–39.9, 40–59.9 and 60+ years). Data included demographics, dialysis modality, transplantation outcome, pregnancy and mortality. Comparisons were made between SLE, other glomerulonephritis (GN) and other causes of primary renal disease (PRD).
**Results:** SLE patients entering RRT tended to be female (79.8% vs. 33.7% GN, 41.5% PRD), younger and non-Caucasian (38.2% vs. 24.7% all other). The percentage remained stable over time (1.3% of RRT). More SLE and GN patients were transplanted (both 53.7% vs. 25.1% PRD). 10 year patient survival in SLE and GN (30.8% and 27%) was better than PRD (12.6%). Survival advantage of haemodialysis over peritoneal dialysis seen in GN and PRD was not seen in SLE. There was no significant difference in graft survival; 10 year transplanted patient survival was better in SLE and GN (79.3% and 77.3%) than PRD (72.1%). Cardiovascular disease accounted for the majority of deaths in all groups (53.7%), but significantly more in paediatric SLE (64.7% vs. 42.4% in all other <19 years). Parenthood data (1968–2010) shows decreasing surgical terminations and increasing live births; SLE patients had significantly more spontaneous abortions (16%).
**Conclusions:** Outcomes for SLE patients on RRT are comparable to other GN and better than PRD.

057

## PREGNANCY OUTCOMES ACCORDING TO DIALYSIS COMMENCING BEFORE OR AFTER CONCEPTION IN WOMEN WITH END-STAGE KIDNEY DISEASE

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**Background:** Pregnancy in end-stage renal disease is a rare occurrence, posing substantial risk for mother and baby. Timing of pregnancy and residual renal function are potential factors affecting outcomes. Aims: We describe one of the largest series of pregnancies in women receiving chronic dialysis treatment, and review maternal and fetal outcomes specifically comparing women who had conceived before and after starting chronic dialysis.
**Methods:** We analysed all pregnancies reported to the Australian and New Zealand Dialysis and Transplantation Registry from 1963 to 2011 (n = 115).
**Results:** Between 1963–2000, 32 women had 38 pregnancies, with 11 live births, a high rate of surgical termination (27%) and miscarriage or stillbirth (45%). Between 2001–2011, there were 77 pregnancies among 73 women. Of these, 53 pregnancies were conceived while established on long-term dialysis and 24 conceived before dialysis was commenced (during pregnancy). The overall live birth rate was 60% (73% after excluding elective terminations). Women who conceived before dialysis commenced had significantly higher GFR at entry onto dialysis, and higher live birth rates (91% vs. 63%, p = 0.03), but their infants had similar birth weight and gestational age. Overall, the median gestational age was 33.8 weeks (IQR 30.6–37.6 weeks) and median birth weight was 1750 g (IQR 1130–2417 g). Over 40% of pregnancies reached 35 weeks gestation; prematurity <28 weeks was low (11.4%) and 28 day neonatal survival was 98%.
**Conclusions:** Women with kidney disease who start chronic dialysis after conception have superior live birth rates to those already established on dialysis at the time of conception, although these remain high-risk pregnancies. This is of relevance when discussing the options for pregnancy in women facing end-stage kidney disease.

058

## A CROSS SECTIONAL DESCRIPTIVE STUDY OF PALLIATIVE CARE OUTCOME SCALE -SYMPTOMS IN END STAGE RENAL DISEASE (POS-S-RENAL) REPORTED BY HAEMODIALYSIS PATIENTS AND STAFF

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**Background:** The Palliative care Outcome Scale-Symptoms (POS-S-Renal) is a validated instrument to measure patients' physical and psychological needs in end stage renal disease.
**Aim:** To describe the symptom burden in haemodialysis patients, as self-reported by patients and as assessed by staff.
**Method:** All prevalent haemodialysis patients from five dialysis centers and the staff were invited for this cross-sectional study in March 2013. The participants simultaneously completed POS-S-Renal in the same week. Symptoms were assessed using this 18-item questionnaire, which was offered in several languages. Higher scores were associated with higher disease burden. Data were analyzed by paired *t* test and multivariate analysis using SPSS v21 and *p* considered significant if <0.05.
**Results:** A total of 148 haemodialysis patients were recruited (88% response rate), 57% were males, age 63 ± 14 years, dialysis vintage 36 ± 28 months (mean ± SD). There was no difference in age, gender, race, religion and language spoken between the responders and non-responders. There was a significant difference in total scores between patients with 3 or more comorbidities compared to those with fewer comorbidities (score 11.6 vs. 8.8, $p = 0.04$, 95% CI 0.83 to 5.89). Similarly, In-Centre dialysis patients had higher scores compared with Satellite patients after adjusting for age and sex ($p = 0.006$). In addition, there was a significant difference in POS-S total score between patients and Nursing staff; 9.71 vs. 5.8, $p = 0.001$ (95% CI 2.81 to 4.99). Staff under-reported patients' symptoms in pain ($t(145) = 4.48$, $p < 0.001$), shortness of breath ($t(145) = 4.18$, $p < 0.001$, lack of energy ($t(144) = 4.38$, $p < 0.001$) and constipation ($t(144) = 3.75$, $p < 0.001$).
**Conclusion:** In-Centre haemodialysis patients and patients with multiple comorbidities had higher disease burden however staff tended to underestimate patient symptoms.

059

## RENAL REPLACEMENT THERAPY DUE TO LITHIUM TOXICITY IN AUSTRALIA

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**Aim:** To analyse the annual incidence of renal replacement therapy (RRT) due to lithium-induced nephropathy (LiN) and to correlate this with the quantities of lithium carbonate dispensed in Australia.

**Background:** Lithium has been used to treat bipolar disorders since 1949, becoming more popular in the 1960s. Evidence that long-term (e.g. >15 years) use can lead to irreversible kidney damage has been mounting since the 1980s, however associations between lithium use and RRT have never been investigated on a national scale.
**Methods:** We compared rates of commencement, demographics and comorbidities for patients who commenced RRT due to LiN as a primary renal disease with all other causes 1991–2011, using the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA). We also investigated quantities of lithium dispensed using Australian Pharmaceutical Benefits Scheme (PBS) data 1992–2011.
**Results:** LiN caused 187 people in Australia to commence RRT 1991–2011; the incidence per million population per year increased from 0.12 (95%CI 0.00–0.49) in 1987–1991 to 0.78 (95%CI 0.67–0.90) in 2007-20011 ($P < 0.001$). Neither a tendency to treat older and sicker patients nor demographic changes accounted for this increase. LiN patients were more likely than non-LiN patients to be female, Caucasian, to smoke, and to have a higher body mass index; and less likely to be biopsied or to have coronary disease, peripheral vascular disease or diabetes. The per capita quantity of lithium dispensed increased markedly 1992–2000.
**Conclusions:** Rates of ESKD due to LiN are increasing rapidly. The increases in lithium dispensed during the 1990s, and the time lag involved in the development of LiN suggests incidence will continue to increase. We therefor encourage discretion when prescribing lithium salts.

060

## PREDICTING DIALYSIS START DATE – THE CHRISTCHURCH EXPERIENCE

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**Aims:**
1) Do Christchurch nephrologists accurately predict dialysis start date?
2) Which patient variables are associated with dialysis start date?
**Background:** Since March 2008, we have predicted dialysis start date for outpatients referred for dialysis education. Prediction accuracy and impact of patient variables on dialysis start date were unknown.
**Methods:** We analysed dialysis start date predictions for patients referred March 2008–October 2012. Prediction categories were "0–3 months", "3–12 months", or "12–18 months". Age, sex, ethnicity, comorbidities, renal diagnosis, estimated glomerular filtration rate (eGFR) decline in year prior to referral, eGFR, haemoglobin, calcium, phosphate, albumin, and proteinuria were recorded for all patients. Correct predictions were patients who started dialysis or died in the predicted window. We performed Kaplan-Meier survival analysis and Cox regression analysis to determine variables associated with hazard of starting dialysis or death.
**Results:** 332 patients were followed for median 401 days. 5–21% of patients started dialysis or died within their prediction category window. Hazard of starting dialysis or death was associated with prediction category (HR = 5.2 (95% CI 3.1–8.7) for "0–3 months" vs. "12–18 months", $p < 0.0001$; HR = 2.8 (95% CI 1.9–4.3) for "3–12 months vs. "12–18 months", $p < 0.0001$) in univariate analysis. In multivariate analysis eGFR (HR = 0.89, $p < 0.0001$), hypocalcaemia (HR = 2.1, $p = 0.01$), anaemia (HR = 2.4, $p = 0.001$), and proteinuria > 1 g/day (HR = 5.5, $p < 0.0001$) at referral, but not prediction category (HR = 0.9, $p = 0.9$), were significant predictors of starting dialysis or death.
**Conclusions:** Christchurch nephrologists are inaccurate and conservative when predicting dialysis start date. However, patients are triaged appropriately, with earlier prediction groups starting at greater hazard. Dialysis educators could consider eGFR, serum calcium, haemoglobin, and level of proteinuria when triaging dialysis education sessions.

061

## BENCHMARKING PREVALENCE OF MALNUTRITION ACROSS QUEENSLAND DIALYSIS UNITS

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**Aim:** To benchmark malnutrition prevalence across dialysis units in Queensland.
**Background:** Malnutrition is a strong predictor of morbidity and mortality in dialysis patients. Benchmarking of malnutrition rates across dialysis units is considered essential to provide feedback on performance relating to prevention and treatment of malnutrition.
**Methods:** A state-wide approach to annual malnutrition audits in Queensland dialysis units commenced in 2010. Established dialysis patients (≥3months) were assessed, at least once annually, using the validated tool, Subjective Global Assessment (SGA) to diagnose malnutrition as indicated by a rating of B or C.
**Results:** Public dialysis units representing 84% (n = 882/1052) of in-centre haemodialysis patients and 48% (n = 172/358) of home dialysis patients in Queensland submitted data over three years (2010–2012). Malnutrition rates among in-centre patients remained stable, averaging 19.6% (19.0% to 20.0%) from 2010–2012, however notable trends were identified across individual units with an average change of 7.8% (−18.0% to 13.6%) over the three years.

In 2012 average malnutrition prevalence in peritoneal dialysis patients was 23.7% (range 16.7% to 28.6%) and 7.9% in home haemodialysis units (range 0% to 12.5%).

Completion rates of malnutrition audits across in-centre haemodialysis (75%, 83% 87%) and home dialysis units (58%, 83%, 76%) have increased over the three years of data capture.
**Conclusions:** High completion rates (84%) of malnutrition audits for in-centre dialysis patients provide a representative data set (20% malnutrition), compared with variable completion and reported rates in home dialysis across Queensland. Benchmarking state-wide malnutrition data for in-centre dialysis patients is feasible and proved useful in identifying trends or issues at a local level. Limited audit data from home dialysis units likely reflects the access difficulties experienced by clinicians servicing this patient group.

062

## WHAT IS HAEMODYNAMIC STABILITY? THE IMPORTANCE OF 'TIME' IN 'CHANGE OVER TIME'

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The concept of haemodynamic stability is not readily defined by quantitative measures. During haemodialysis (HD) significant hypo or hypertension is arbitrarily defined by a symptomatic change in systolic pressure (SBP) ≥20 mmHg. Such definitions are heavily reliant upon patient self-report, ignoring the importance of appropriate intraobservation time-periods to frame the diagnosis.
**Method:** The comprehensive beat-to-beat SBP record of 38 HD sessions was recorded in asymptomatic HD outpatients (68% male, 18% diabetic). The continuous SBP time-series (~16,000 observations/HD) was analysed in the context of 3 time-windows; 'short', 'medium', and 'long' by the pulse-period lengths of 100, 500 and 1,000 heart-beats respectively. To define 'significant' BP variability the absolute cutoff of 20 mmHg systolic was used. A rate-of-change momentum oscillator dynamically compared the magnitude and direction of SBP change against a continuously moving baseline for each respective timeframe.
**Results:** 37 HD treatments (97%) recorded ≥1 significant, asymptomatic swings in SBP over one-or-more time-windows. The total number of captured events was 193, 369 and 316 for 100, 500 and 1,000 beat observation widths respectively. Peak sensitivity for capturing intradialytic SBP swings occurred in the medium term. The frequency of suprathreshold episodes was (mean ± SEM) 5.08 ± 1.08, 9.71 ± 0.98, and 8.31 ± 0.76 for the respective periods. Over the shortest timeframe, sudden rises were more common than sudden fall (57% Vs 43%) however this ratio reversed with lengthening of the framing period. Despite the frequency of significant SBP variability, only a single episode was associated with clinical symptoms.
**Conclusion:** Clinically silent SBP variability during 'stable' HD is exceedingly common and unrecognised in clinical practice when strict pressure criteria are applied. Appropriate timing between observations is paramount to framing the diagnosis.

063

## A NOVEL METHOD TO PROFILE THE CARDIOVASCULAR STABILITY OF DIALYSIS PATIENTS BY CONTINUOUS MEASUREMENT USING A MEDIAN HYBRID PREPROCESSING FILTER ALGORITHM

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The detection of significant haemodynamic instability is a challenge during haemodialysis (HD). The sensitivity of research-grade devices applied in the

clinical setting creates a signal degraded by outliers, artifact and noise, a common obstacle in real-time physiological analysis. The solution would yield an uncontaminated dynamic regression reflecting the underlying Blood Pressure (BP) profile.
**Method:** A continuous BP dataset was captured in 10 stable 'short-break' HD outpatients. Simulations using progressively complex moving-average (MA), control-chart and median-hybrid (MHF) filters were applied to determine the best technique to extract an analyzable series. Outputs were compared to the parent signal and validated by Bland-Altmann analysis against a simultaneously collected brachial-cuff dataset from each patient. Validation of signal integrity was performed using white-noise analysis by Fisher's Kappa and Bartlett's KS methods.
**Results:** A continuous BP record from HD yields ≥ 16,000 separate observations. MA filters performed well at white-noise exclusion but were susceptible to impulsive artifact and sustained measurement error where duration exceeded MA subset length. Intraindividual variation in optimal subset size saw no uniform metric. Control chart methods improve resistance to extreme outliers at the expense of poor noise attenuation and signal edge detection. Tighter control limits incrementally reduced integrity of the output signal, eventually rendering a self-propagating loop of uninterpretable data. The MHF output performed well to exclude outliers and create a series free of white-noise ($p < 0.001$). 46/50 (92%) time-coincident paired BP values met agreement limits, confirming intercept equivalence to routine clinical practice. In all ten patients, absolute BP peaks and troughs revealed by continuous monitoring were not captured by arm-cuff observations.
**Conclusion:** This paper represents the first design and application of MHF methodology to clinical time-series data.

064

## EARLY VERSUS LATE REFERRAL TO SPECIALIST NEPHROLOGY SERVICES – A SYSTEMATIC REVIEW

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**Aim**: To determine the effect of early versus late nephrology referral on clinical outcomes in people with chronic kidney disease (CKD).
**Background**: Later referral to specialist nephrology services results in significant morbidity and mortality.
**Methods**: A systematic literature search was performed to identify relevant studies to February 2012. Studies compared adult patients with CKD (eGFR <30 mL/min/1.73 $m^2$) referred for evaluation to nephrology services early versus those referred later. Two authors independently assessed study eligibility and extracted data. Risk of bias was assessed using the Newcastle-Ottawa Scale for non-randomised studies. Meta-analyses were performed using a random effects model, expressed as relative risk (RR) with 95%CI.
**Results**: Forty cohort studies (9 prospective and 31 retrospective) of 63,887 participants were included. There were no existing randomised control trials. Mortality was reduced in early referrals at all time points with RR 0.47 (95%CI 0.29–0.76) at 3 months, RR 0.58 (95%CI 0.42–0.79) at 6 months, RR 0.56 (95%CI 0.47–0.67) at 12 months and RR 0.71 (95%CI 0.54–0.94) at 5 years. Initial hospitalisation duration was also reduced in early referrals by 9.1 days (95%CI 7.3–10.9). Early referrals were approximately 60% more likely to start dialysis with a peritoneal catheter (RR 1.59 95%CI 1.23–2.05) and 60% less likely to start with a temporary vascular catheter (RR 0.41 95%CI 0.30–0.56). Late referrals were 78% less likely to start with permanent vascular access (RR 0.22 95%CI 0.12–0.40).
**Conclusions**: Preventing one patient starting haemodialysis with temporary vascular access and to achieve one more patient starting with permanent access, requires just three early CKD referrals. Early referral of 12 CKD patients was enough to prevent one death within the first year of renal replacement therapy.

065

## AN AUSTRALIAN SCORED SALT QUESTIONNAIRE: DEVELOPMENT AND VALIDATION IN CHRONIC KIDNEY DISEASE

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**Aim:** To develop and evaluate feasibility, reliability and validity of a self-administered scored salt questionnaire (SSQ) for use in clinical care of Chronic Kidney Disease (CKD) patients.
**Background:** A low salt diet (<100 mmol sodium) is recommended for all CKD patients. Traditional methods of assessing intake are time consuming, complex, with inherent problems of accuracy and applicability. Nor are there enough dieticians to provide individualised education to all patients given the expanding CKD population. Therefore, clinicians require a rapid and robust method to identify high sodium consumers and guide advice at the point of usual care.
**Methods:** Phase 1 – development of SSQ from convenience sample of previously collected dietary history data (n = 30 renal patients). Phase 2 – cross-sectional study to evaluate the SSQ in multidisciplinary community-based outreach clinics (n = 47; CKD stages 3–5). Participants completed the SSQ and feasibility survey; 24-hr urinary sodium excretion; 24-hr food record; and diet history interview.
**Results:** The SSQ score correlated significantly with 24-hr urinary sodium ($r = 0.371$; $p = 0.031$) and the correlation between 24-hr food record and diet history confirmed habitual intake ($r = 0.701$; $p = <0.001$) on the day of data collection. A cut point of >65 in SSQ score was validated to correctly identify high sodium consumers: sensitivity 58%, specificity 80%, positive predictive 88%, negative predictive value 44%. Cronbach's alpha coefficient (0.729) demonstrated good overall reliability. Acceptance and feasibility by patients and the multidisciplinary team was greater than 80% and majority of patients (74.5%) completed the SSQ in <10 minutes.
**Conclusions:** The SSQ is valid, reliable, and feasible to assess habitual sodium intake for our Australian CKD cohort, to triage patients based on high sodium intake for individual dietetic intervention, and to direct counselling/education on a low salt diet.

066

## CHRONIC KIDNEY DISEASE AND RISK OF STROKE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Aim:** To determine the independent and combined effects of reduced glomerular filtration rate (GFR) and proteinuria on risk of stroke.
**Background:** The association between chronic kidney disease (CKD) and stroke is poorly described.
**Methods**: Systematic review and meta-analysis of observational studies and interventional trials using Meta-analysis Of Observational Studies in Epidemiology and Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. We searched MEDLINE and Embase for studies and trials which prospectively measured GFR, proteinuria or both, and quantified subsequent risk of stroke. Reviewers abstracted relative risk (RR) of stroke and synthesized data using a random-effects model. We assessed study or trial quality using the Newcastle-Ottawa scale or Cochrane risk of bias tool.
**Results**: We included 65 reports: 46 studies, 19 trials (2344852 participants). Stroke increased by 45% in patients with an estimated GFR (eGFR) <60 ml/min/1.73 $m^2$ (25 reports, 1230445 participants, RR1.45 95%CI1.33-1.57). Haemorrhagic stroke increased by 65% (8 reports, 80321 participants, RR1.65, 95%CI1.09-2.50) and ischaemic stroke by 32% (7 reports, 74528 participants, RR1.32, 95%CI1.17-1.49). In patients with proteinuria, stroke increased by 84% (19 reports, 89110 participants, RR1.84, 95%CI1.65-2.04) though this association was only seen for ischaemic stroke (6 reports, 49785 participants, RR1.75, 95%CI1.52-2.02) and not for haemorrhagic stroke (4 reports, 29281 participants, RR1.43, 95%CI0.98-2.09). Considering both eGFR and proteinuria, patients with an eGFR < 60 ml/min/1.73 $m^2$ were not at increased risk of ischaemic stroke when proteinuria was absent (2 reports, 10174 participants, RR1.56, 95%CI0.66-3.65) and at highest risk of ischaemic stroke when proteinuria was present (1 report, 3205 participants, RR2.24, 95%CI1.50-3.35).
**Conclusions**: CKD affects risk of haemorrhagic and ischaemic stroke differently depending upon eGFR and degree of proteinuria. Optimal preventative treatments require urgent evaluation in patients with CKD.

067

## ASSOCIATION BETWEEN FLAVONOID INTAKE, RENAL FUNCTION AND RENAL OUTCOMES IN ELDERLY WOMEN

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**Aim**: To explore the association of habitual intake of total flavonoids and flavonoid classes with renal function and risk of renal disease events in elderly women.

**Background**: Oxidative stress and endothelial dysfunction may contribute to progression of chronic kidney disease (CKD) and atherosclerosis in the general population and patients with CKD. In addition to their known antioxidant properties, flavonoids have been shown to improve endothelial function, improve nitric oxide homeostasis and reduce platelet aggregation and therefore, flavonoids may have a role in the maintenance of healthy renal and vascular function.
**Methods**: This was a prospective observational cohort study of 1,068 women aged over 75 years without prevalent renal disease. Serum cystatin C concentrations were measured at baseline. Flavonoid consumption was assessed using the United States Department of Agriculture Flavonoid, Flavone and Proanthocyanidin databases. Complete verified 5-year records for renal disease-associated hospitalisations and mortality were obtained using the Western Australian Data Linkage System.
**Results**: Compared to participants in the lowest tertile of total flavonoid intake, participants in the highest tertile of total flavonoid consumption had lower Cystatin C concentration (1.14 ± 0.02 vs 1.24 ± 0.02 mg/day, $p < 0.001$). Similar associations were observed with flavonol and flavan-3-ol intake, with the strongest association observed with proanthocyanidin intake (1.13 ± 0.02 vs 1.24 ± 0.02 mg/day, $p < 0.001$). Participants in the highest tertile of proanthocyanidin intake was associated with a significantly lower risk of renal disease-associated hospitalisations and mortality (adjusted hazard ratio 0.34, 95%CI 0.15–0.78; $p = 0.022$).
**Conclusion**: Increased consumption of total flavonoids, in particular proanthocyanidin, may have a protective effect on preventing or ameliorating age and vascular related impairment of renal function and renal events.

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## RETINAL ARTERIOLAR NARROWING CORRELATES WITH MEAN SYSTOLIC WAKING BP AND LVH

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**Aims:** This study determined whether retinal small vessel changes correlated with poor blood pressure (BP) control, as assessed by clinic or ambulatory BP readings, and end-organ damage.
**Background:** Fifty % of all patients undergoing treatment for hypertension have BP that is inadequately controlled because current monitoring methods are inadequate.
**Methods:** Participants had clinic and 24 hour BP readings, and end-organ damage was assessed on echocardiography. Retinal imaging was performed with a non-mydriatic camera (KOWA, Japan), and small vessel abnormalities were graded (Wong and Mitchell classification), and calibre measured at the RetVIC grading centre, Centre for Eye Research Australia, as described previously. Statistical analysis was performed using Stata software (StataCorp, Texas).
**Results:** One hundred and thirty-one individuals (mean age, 62 ± 14.5 years, 59 [45%] male) participated in the study. Ninety-nine (76%) had a clinic BP ≥ 140/90 mm Hg, and 81 (62%) had a mean 24 hour systolic daytime BP > 136 mmHg. Twenty-three (23/69, 33%) had LVH, and 58 (58/69, 84%) had diastolic dysfunction.

All participants had signs of mild (89%) or moderate (11%) microvascular retinopathy. A reduced arteriovenous ratio correlated with increased clinic BP ($p = 0.01$), and LVH ($p = 0.03$).

Retinal arteriolar calibre was reduced in patients with a mean ambulatory BP ≥ 140 mm Hg ($p = 0.04$), mean systolic awake BP > 136 mm Hg ($p = 0.02$) and with LVH ($p = 0.01$). Arteriole narrowing predicted LVH (AUC = 0.69) compared with mean ambulatory systolic BP (AUC = 0.63) and mean awake systolic BP (AUC = 0.62).
**Conclusions:** Retinal arteriole narrowing correlates with elevated mean ambulatory BP, mean systolic awake BP and LVH.

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## RELATIONSHIP BETWEEN URINARY PHOSPHATE WITH CARDIOVASCULAR DISEASE AND MORTALITY IN THE AUSDIAB COHORT

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**Aim:** To assess the association between urinary phosphate excretion and outcomes in a large population-based cohort.
**Background:** Serum phosphate is associated with cardiovascular disease (CVD) and mortality in the general population. Greater dietary phosphorus intake may lead to higher serum phosphate and adverse outcomes. Urinary phosphate excretion is a marker of intestinal phosphorus absorption and may be a more reliable marker of phosphate homeostasis. Studies report good correlation between urine phosphate-creatinine ratio (uPiCr) and 24-hour urinary phosphate excretion, but whether uPiCr is associated with risk of CVD or mortality is uncertain.
**Methods:** Using the nationally representative AusDiab cohort, uPiCr was determined from available urine samples (n = 11,116). Participant baseline characteristics were compared across quartiles of uPiCr and regression analysis was used to determine associations. Relationships between uPiCr and all-cause mortality were determined using Cox proportion hazards regression with uPiCr modelled using fractional polynomials.
**Results:** Mean age 51+/–14 y, 45% males and 9.6% chronic kidney disease (CKD-Epi equation). During a median follow-up 12.1 years there were 1265 deaths. Mean uPiCr was 1.45+/–0.7 mmol/mmol. Participants with higher uPiCr were older, more likely female, had higher albuminuria, lower GFR, greater prevalence of CVD and hypertension (all $p < 0.001$) and higher BMI ($p = 0.002$). With increasing quartiles of uPiCr the hazard ratios (HR) for all-cause mortality were 1.27 [95%CI 1.07,1.52], 1.54 [1.30,1.83], and 2.07 [1.76,2.44] (compared to the lowest quartile). When modelled as fractional polynomial, both low and high urine phosphate were independently associated with an increased risk of mortality.
**Conclusion:** Low and high uPiCr is associated with increased all-cause mortality in a general population cohort and may serve as a useful marker for interventions aimed at improving phosphate balance.

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## CHRONIC KIDNEY DISEASE (CKD) PATIENT OUTCOMES: A LONGITUDINAL REPORT FROM THE CKD.QLD REGISTRY

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**Aim:** To describe longitudinal outcomes of patients with CKD managed in a metropolitan Renal Unit, through the CKD.QLD registry.
**Background:** Nearly half (46.7%) of prevalent CKD patients at Royal Brisbane and Women's Hospital (RBWH) Renal Unit have consented for inclusion in the CKD.QLD Registry.
**Methods:** Outcomes were assessed for RBWH CKD patients enrolled in the registry ≥= 12 months prior to this analysis. Outcomes included deaths, start of RRT and hospitalisations, exclusive of dialysis, and/or antedating start of RRT.
**Results:** Of 960 RBWH patients enrolled, 612 qualified for inclusion. At time of analysis, 33 had started RRT (5.4%), 14 had died (3.2%), all prior to RRT commencement (if planned), and 12 were discharged or transferred. Cause of death was ESRD (4), cardiovascular (5), malignancy (3), other/unknown (2). 553 patients remained in the RBWH CKD care stream.

Pathways for the 33 commencing RRT were: transition (7), haemodialysis (8), home haemodialysis (2), peritoneal dialysis (13) or transplantation (3).

286 patients (47%) had at least one RBWH hospitalisation, with a range of 1 to 25 episodes, and a median of 2 each. There was a total of 919 hospitalisation episodes, with a length of stay (LOS) from 1 to 47 days, and total LOS of 3110 days. Admitting units were renal (26.7%), general medical (22%), surgical (18.1%), specialist medical (12.1%), urology (7.9%), vascular (3.3%) and "others" (9.9%).
**Conclusion:** This is the first report of longitudinal outcomes in CKD.QLD. Rates of death and of RRT, which appear relatively low, will be further followed

over time. However, the burden of hospitalisations and the implied costs, are very considerable. Further definition of the high frequency users and precipitants of hospitalisations is obviously important.

071

## PREVALANCE OF SARCOPENIC OBESITY AND RELATIONSHIP WITH INFLAMMATION IN CHRONIC KIDNEY DISEASE

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**Aim:** To investigate the prevalence of sarcopenic obesity and the relationship with inflammatory markers in chronic kidney disease (CKD).
**Background:** It is postulated that an association of obesity, inflammation, and atherosclerosis (OIA syndrome) is highly prevalent in CKD and associated with increased cardiovascular (CV) mortality.
**Methods:** Investigations of anthropometric data and inflammatory markers were conducted in baseline data analysis of CKD patients enrolled in a large randomised-control trial with at least 1 CV-related risk factor and complete body composition, assessed via Dual-energy X-ray absorptiometry (DXA), BMI and waist circumference. The prevalence of obesity defined by WHO cut-offs and sarcopenic obesity defined by muscle mass index <7.26 kg/m$^2$ in men and <5.45 kg/m$^2$ in women. Data analysis involved investigating correlations between obesity and sarcopenic obesity with markers of inflammation (log-transformed CRP, IL6).
**Results:** 84 Stage 3–4 patients (52.4% male (n-44), average age 58.5 (SD 10.6) years old, eGFR 40.1 (9.1), BMI 33.9 (6.0) kg/m$^2$) were included in the analysis. The prevalence of obesity was 73.8% (62/84) by BMI; 85.7% by waist circumference and 89.3% by (%) body fat. All 84 patients met the criteria for sarcopenia. BMI and waist circumference were associated with inflammatory markers CRP ($r = 0.364$ $p = 0.001$ and $r = 0.317$ $p = 0.005$)) and IL-6 ($r = 0.322$ $p = 0.005$; and $r = 0.267$ $p = 0.022$). Body fat (%) and muscle-mass index was associated with CRP only ($r = 0.307$ $p = 0.006$; and $r = 0.358$ $p = 0.001$).
**Conclusions:** Sarcopenic obesity is highly prevalent in CKD patients with existing CV-risk factors and is associated with increased inflammation. Further investigation into effect of weight loss on inflammation and subsequent CV-risk in this high-risk group is warranted.

072

## KEY TO GOOD HEALTH: ASSESSING THE EFFECTIVENESS OF COMMUNITY SCREENING FOR CHRONIC KIDNEY DISEASE

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**Aim:** Assess the effectiveness of three different approaches to community screening for chronic kidney disease (CKD).
**Background:** Kidney Health Australia partnered with a range of community organisations in Victoria to provide the KEY to Good Health Program.
**Methods:** Eligibility was restricted to anyone over 50 (or age over 35 years if of Aboriginal or Torres Strait Islander origin) and to anyone over 18, with at least one of the recognised risk factors for CKD. The participants were assigned to receive either a Kidney Health Check and QKidney risk assessment (Model 1), urine tests and QKidney (Model 2) or QKidney only (Model 3). Half of the participants were randomly selected for telephone follow-up two months later.
**Results:** 1314 participants were recruited between February and October 2012. Urine dipstick detected proteinuria in 7% of participants, and urine albumin : creatinine ratio tests were abnormal in 14%. High blood pressure was recorded in 56% of participants, and results indicative of CKD were present in 29%. The QKidney risk calculator revealed up to 21% of participants were at high risk of developing kidney disease in the next five years. Follow-up telephone calls were successful in reaching 49% of participants. Further tests were ordered in up to 50% of participants who were referred to their doctor. There were no significant differences between the three models in the level of engagement with a general practitioner following KEY.
**Conclusions:** KEY was effective in detecting markers of, and risk factors for, CKD. Despite the different intensities of screening approaches, the three models were equally effective in encouraging people at risk of CKD to engage with health professionals.

073

## A PRAGMATIC TRIAL OF A POLYPILL-BASED STRATEGY TO IMPROVE ADHERENCE TO INDICATED PREVENTIVE TREATMENTS AMONG PEOPLE AT HIGH CARDIOVASCULAR DISEASE RISK

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**Aim:** To determine whether a treatment strategy using fixed dose combinations of preventive drugs ("polypills") improved adherence amongst people at high cardiovascular disease (CVD) risk.
**Background**: Individuals at high CVD risk benefit from long-term preventive drug therapy. Practice audits indicate that many high-risk patients do not take recommended medications.
**Methods:** The Kanyini Guidelines Adherence with the Polypill trial was a randomised, open-label, blinded-endpoint trial. Eligibility was established CVD or estimated 5-year CVD risk ≥15%, with participants randomised to a "polypill-based strategy" or "usual care". Polypill group participants received a fixed-dose combination pill (aspirin 75 mg, simvastatin 40 mg, lisinopril 10 mg and either atenolol 50 mg or hydrochlorothiazide 12.5 mg). No attempt was made to influence management of usual care participants. Three primary outcomes were defined – self-reported adherence to antiplatelet, statin and ≥2 blood pressure (BP) lowering drugs (defined as "combination treatment"), and changes in systolic BP and total cholesterol from baseline.
**Results:** 623 participants were recruited from 33 primary care practices. At baseline, 50% reported use of combination treatment, mean systolic BP was 143 mmHg and mean total cholesterol was 4.4 mmol/L. After median follow-up of 18 months, the polypill-based strategy was associated with improvement in adherence to combination treatment compared to usual care (70% vs. 47%; RR 1.48, [95% CI 1.29, 1.71] $p < 0.0001$), without differences in systolic BP (−1.5 mmHg, [95% CI −4.0, 1.0], $p = 0.24$) or total cholesterol (0.08 mmol/L, [95% CI −0.06, 0.22], $p = 0.26$).
**Conclusion:** Provision of a cardiovascular polypill improved self-reported adherence to recommended treatments. The lack of differences in BP and total cholesterol may reflect limited study power and lesser potency of individual components of the polypill used in the trial.

074

## CHRONIC KIDNEY DISEASE (CKD) IS NOT RENAL REPLACEMENT THERAPY (RRT): THE CKD.QLD REGISTRY DATASET

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**Background:** CKD is the most common chronic disease in Australia. Data about its natural history are minimal and rely on extrapolations from mortality and RRT datasets.
**Aim:** To describe how characteristics of CKD patients in a tertiary hospital setting differ from those of RRT populations and the National Mortality Dataset (NMD), analysed by AIHW.
**Methods:** Age, sex and primary diagnosis of the first 960 RBWH patients in the CKD.QLD Registry (RBWH.CKD) were analysed and compared with RRT groups from the RBWH (RBWH.RRT), QLD (QLD.RRT) and ANZDATA (ANZ.RRT) and the AIHW dataset of people dying with ESKD not on RRT (AIHW.ESKF).
**Findings:** Healthcare providers, and presumably their coding propensities, were the same in the RBWH.CKD and RBWH.RRT groups. All RRT groups were male dominated, in contrast to the RBWH.CKD and AIHW.ESKF, where the sexes were equally represented. RBWH.CKD patients were older than the RRT groups, with means of 65.4 vs 60–61 years respectively, while the deceased AIHW.ESKF group was older again with a mean age >70 yr. There were notable differences in aetiologies of CKD. Only 17% of the RBWH.CKD group had diabetic nephropathy, contrasting with 38% in ANZ.RRT, while 25% of RBWH.CKD had renal vascular aetiology recorded, vs 13% in ANZ.RRT. These differences did not reflect diagnostic uncertainty, which was recorded in only 2% in RBWH.CKD compared to 12% in ANZ.RRT. Diagnostic weightings of RBWH.RRT were intermediate between RBWH.CKD and ANZ.RRT.
**Conclusions:** Age, sex and primary diagnosis describe different weightings of characteristics in populations of patients with CKD from those on RRT. The

natural history of CKD is imperfectly understood if viewed through the prism of RRT, highlighting the importance of datasets like CKD.QLD.

075

## EVALUATING THE CHARACTERISTICS OF NEWLY DIAGNOSED RENAL CELL CARCINOMA TO IMPROVE PATIENT OUTCOME

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**Aim:** To determine the clinical predictive parameters of localized and advanced renal cell carcinoma (RCC) at diagnosis.
**Background:** Although there has been an increase in incidental diagnosis of RCC, many patients still present with the typical clinical signs and symptoms; and 20–30% of patients have advanced RCC at diagnosis.
**Methods:** The medical records of 147 RCC patients diagnosed at University of Malaya Medical Centre (UMMC) from 2003–2012 were assessed. Symptoms at presentation included the classical triad (macro-hematuria, loin pain, abdominal mass), para-neoplastic (fever, loss of weight/appetite [LOW/LOA], lethargy), and blood tests (albumin, alkaline phosphatase [ALP], calcium, hemoglobin, platelets, lymphocytes, neutrophils). Logistic regression analysis was carried out to determine odds ratio (OR) of advanced/localized RCC, based on the clinical parameters.
**Results:** Among the classical triad symptoms, only abdominal mass (OR 2.94; $p = 0.003$) was significantly predictive for advanced RCC. Patients with all the triad symptoms were more likely to have advanced disease (OR 6.77; $p = 0.011$). Fever (OR 2.57; $p = 0.068$), LOW/LOA (OR 3.47; $p < 0.001$) and lethargy (OR 3.16; $p = 0.022$) were predictors of advanced disease. A combination of at least two para-neoplastic symptoms had stronger predictive value (OR 6.98; $p = 0.001$). Among the blood tests, elevated ALP (OR 5.84; $p = 0.001$), calcium (OR 12.77; $p = 0.018$), low albumin (OR 4.90; $p < 0.001$), hemoglobin (OR 4.58; $p < 0.001$) and lymphocyte count (OR 3.89; $p < 0.001$) were indicators of advanced RCC.
**Conclusion:** Clinical symptoms and blood tests can be useful predictors, alongside medical imaging, in assessing whether a patient has localized or advanced RCC. However other tools, such as biomarkers, may need to be developed to assist with identifying localized or advanced RCC.

076

## VASCULAR DYSFUNCTION IN ALBUMINURIA: ROLE OF ENDOTHELIAL GLYCOCALYX DISRUPTION

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**Aims:** Widespread vascular dysfunction accompanies albuminuria in diabetic and non-diabetic nephropathies. This vascular dysfunction includes accelerated atherosclerosis, impaired vasodilatation, decreased nitric oxide bioavailability, and increased permeability. We aim to determine whether endothelial glycocalyx disruption underlies widespread vascular dysfunction in kidney disease.
**Background:** Endothelial glycocalyx is a gel-like matrix covering the luminal surface of all blood vessels. Experimental disruption of endothelial glycoclayx causes the same pattern of abnormalities as seen in nephropathy (altherosclerosis, impaired vasodilatation, decreased NO, increased permeability). Restoring the endothelial glycocalyx is feasible, and improves the function of damaged capillaries (Salmon, Cardiovasc Res, 2009).
**Methods:** I have used single capillary permeability techniques in vivo to measure capillary wall permeability coefficients directly, in structurally distinct capillary beds (fenestrated capillary: glomeruli, and continuous capillary: gut mesentery), in adult male Sprague-Dawley rats 7 days after streptozotocin (45 mg/kg iv). Animals were anaesthetised, the gut mesentery exteriorised, single microvessels cannulated and perfused, and hydraulic conductivity (LP) calculated. Single glomeruli were subsequently harvested from the same animals, and volume-corrected ultrafiltration coefficient (LPA/Vi) measured using an oncometric technique (Salmon, J Physiol, 2006).
**Results:** Mesenteric $L_P$ and glomerular $L_PA/V_i$ were both increased in proteinuric diabetic animals (both $p < 0.05$, unpaired t-test). In non-diabetic nephropathy (Munich-Wistar-Fromter rats), we have also demonstrated identical widespread alterations in permeability of mesenteric and glomerular microvessel (both $p < 0.05$, unpaired t-test), and novel confocal/multiphoton microscopy techniques revealed accompanying endothelial glycocalyx disruption in mesenteric and glomerular capillaries.
**Conclusion:** Widespread alterations in permeability occur early in these diverse forms of kidney disease, and coupling single vessel permeability and confocal/multiphoton microscopy studies identifies altered endothelial glycocalyx as a potential link between albuminuria and widespread vascular dysfunction.

077

## IDENTIFICATION OF A NOVEL PATHWAY PROMOTING SALT-RETENTION IN OBESITY

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**Aim:** Identification of pathways promoting renal salt-retention in obesity.
**Background:** Obesity leads to salt-sensitive hypertension. Mechanisms promoting renal salt-retention at a tubular level are poorly defined.
**Methods:** C57Bl/6 mice were fed 40% (high fat, HFD) or 12% (control, CD) fat diets for 14 weeks. Abundance and phosphorylation of proteins were determined by western blotting. Surface expression was determined using immunofluorescence and confocal microscopy. *In vitro* studies used stimulation of AMPK with A769662 in murine embryonic fibroblasts (MEF's).
**Results:** HFD mice gained weight and developed hyperinsulinaemia and hyperleptinaemia. Cortical expression of NKCC2 was reduced but activating phosphorylation (T96/T101) was increased, a finding seen in other models of salt-sensitive hypertension. No change in expression or phosphorylation of NCC, or expression of α- and γ-ENaC was found. Surface localisation of transporters was unchanged. SPAK/OSR-1 is known to phosphorylate NKCC2 on T96/T101. Phosphorylation of SPAK/OSR-1 on T373/T325 was increased, consistent with increased activity. Inhibition of AMPK has previously been shown to be involved in mediating obesity-related renal injury. Thr172-phosphorylated-AMPK was reduced in HFD mouse cortex. Furthermore, SPAK/OSR-1 and AMPK were found to co-immunoprecipitate with NKCC2, indicating a possible kinase-kinase interaction. *In vitro*, activation of AMPK led to a reduction in T373/T325-phosphorylation of SPAK/OSR-1 in MEF's from β1-AMPK +/+ mice, but no effect was seen in MEF's from β1-AMPK –/– mice, indicating an AMPK-mediated effect.
**Conclusions:** NKCC2 is the most important sodium co-transporter in this model of obesity-related hypertension. Increased activation of SPAK/OSR-1 is likely responsible, which may itself be linked to suppression of AMPK activity. These data suggest that NKCC2, SPAK/OSR-1 and AMPK are important therapeutic targets in obesity-related hypertension, and identify a novel pathway promoting salt-retention in obesity.

078

## RESOLVIN D1 PROTECTS PODOCYTES IN ADRIAMYCIN-INDUCED NEPHROPATHY THROUGH MODULATION OF 14-3-3β ACETYLATION

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**Aim:** This study examined whether Resolvin D1 (RvD1) has renoprotective effects upon podocytes.
**Background:** RvD1 is a lipid-derived mediator generated during the resolution inflammation. While the immunoresolvent effects of Resolvins have been extensively studied in leukocytes, actions of Resolvins on intrinsic kidney cells have received little attention. The podocyte plays a central role in glomerular function, and podocyte damage can lead to proteinuria and glomerulosclerosis.
**Methods:** RvD1 was administered in a mouse model of adriamycin (ADR) nephropathy. Mice ($n = 6$) were given once daily RvD1 treatment (4ng/g/day) starting either 30 min (early treatment) or 14 days (late treatment) after ADR injection and continued until mice were killed on day 28.
**Results:** A progressive loss of synaptopodin expression over a 28 day time-course of ADR nephropathy was associated with increased acetylation of 14-3-3β and reduced synaptopodin phosphorylation. Early, but not late, RvD1

treatment attenuated ADR-induced proteinuria, glomerulosclerosis and tubulointerstitial fibrosis, modified macrophages from M1 to M2-type, prevented down-regulation of synaptopodin expression, and prevented changes in 14-3-3β acetylation and synaptopodin phosphorylation. In cultured podocytes, RvD1 prevented TNF-α-induced down-regulation of synaptopodin expression, a decrease in synaptopodin phosphorylation, an increase in acetylation of 14-3-3β and disassociation between 14-3-3β and synaptopodin. Thus, RvD1 prevented TNF-α-induced post-translational modification of synaptopodin and 14-3-3β proteins, and maintained the synaptopodin/14-3-3β interaction. Furthermore, replacement of lysine K51, or K117+K122 in 14-3-3β with glutamine, to mimic lysine acetylation, significantly reduced the interaction between 14-3-3β and synaptopodin.
**Conclusions:** Our studies provide the first evidence that RvD1 can protect against podocyte damage by preventing down-regulation of synaptopodin through inhibition of 14-3-3β/synaptopodin dissociation. RvD1 treatment may have therapeutical potential in chronic kidney disease.

079

## CURCUMIN ATTENUATES GROWTH OF ESTABLISHED RENAL CELL CARCINOMA THROUGH SUPPRESSION OF NUCLEAR FACTOR-KAPPA B

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**Aim:** To investigate the anti-cancer effects of curcumin, a nuclear factor-kappa-B (NF-κB) inhibitor, on human metastatic renal cell carcinoma (RCC) cells using cell culture and animal models.
**Background:** Enhanced activation of the transcription factor NF-κB has been implicated in development and progression of RCC.
**Methods:** Human metastatic RCC cell lines (Caki-1, 786-0, ACHN, SN12K1) were treated with curcumin (50 μM in ethanol) and analysed 24 h later for cell viability (MTT), apoptosis (ApopTag labelling and morphology), and NF-κB expression and transcription activity (Western blotting and ELISA). SN12K1 RCC was inoculated unilaterally into kidneys of severe combined immunodeficient mice and allowed to establish for 4 weeks, without (1 group) or with curcumin (100 mg/kg, delivered by gavage). Contralateral kidneys were used as controls. There were 2 curcumin dose regimens: curcumin 2 h before the SN12K1 injection, then for 5 days/week for 4 weeks; or the first dose of curcumin delivered one week after SN12K1 injection, then for 5 days/week for 3 weeks. Kidneys were compared for: weight; histology; and NF-κB expression and transcription activity.
**Results:** Curcumin significantly decreased cell viability in all cell lines by approximately 50% ($p < 0.01$), increased apoptosis ($p < 0.01$), and decreased expression and transcription of NF-κB (p65 and p50) ($p < 0.05$). In the animal model, pre-treatment with curcumin significantly attenuated tumour growth compared with no treatment. We had previously demonstrated that SN12K1 cells had established growth in kidneys by 1 week post-inoculation. Significantly, curcumin attenuated growth of established tumours. NF-κB expression and activation were decreased in all curcumin-treated tumour material. Curcumin did not induce any toxicity to normal cells.
**Conclusion:** These data suggest that curcumin has the potential to be an anti-cancer agent for some forms of RCC.

080

## A HEAD TO HEAD COMPARISON OF THE ANTI-FIBROTIC PROPERTIES OF RELAXIN AND ENALAPRIL IN EXPERIMENTAL CARDIAC AND RENAL FIBROSIS

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**Aim:** To determine the relative anti-fibrotic effect of relaxin and angiotensin blockade alone and in combination.
**Background:** Fibrosis is the final common pathway in chronic kidney and cardiac disease. Direct inhibition of the renin angiotensin system (RAS) is the most effective anti-fibrotic strategy currently available, but only slows progression modestly. Although exogenous relaxin has consistently been shown to be anti-fibrotic, its efficacy relative to current RAS blockade, and its ability to treat established fibrosis (the most clinically relevant scenario) are unknown.
**Methods:** We compared the individual vs combined anti-fibrotic effects of relaxin and the angiotensin converting enzyme inhibitor (ACEi) enalapril in preventative (started before injury) and therapeutic (treatment of established fibrosis) strategies, in mouse models of isoprenaline (ISO)-induced cardiac injury (at 17 days) and unilateral ureteric obstruction (UUO)-induced tubulointerstitial renal injury (at 5 days). Changes in blood pressure (SBP), tissue fibrosis (hydroxyproline content), and TGF-β1 expression and signaling were assessed.
**Results:** Pre-treatment with relaxin (0.5 mg/kg/day) alone, and in combination with enalapril (200 mg/L), reduced cardiac fibrosis more than enalapril (both $p < 0.05$ vs other groups). Relaxin was at least as efficacious as enalapril in preventing fibrosis post-UUO. Delayed treatment with relaxin +/– enalapril ameliorated further progression of both cardiac and renal fibrosis when started at day 10 and 2, respectively. In the cardiac model, enalapril +/– relaxin reduced SBP, relaxin alone did not. Cardiac histochemical staining for TGF-β1 and phosphorylation of its downstream regulator Smad2 were reduced by enalapril ($p < 0.05$), and even more by relaxin +/– enalapril (both $p < 0.05$ vs enalapril alone).
**Conclusion:** Relaxin alone and in combination with ACEi is an effective anti-fibrotic in both heart and kidney in clinically relevant experimental scenarios.

081

## APOPTOSIS SIGNAL-REGULATING KINASE 1 (ASK1) PROMOTES RENAL FIBROSIS AND APOPTOSIS IN THE OBSTRUCTED KIDNEY

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**Aim:** To determine whether apoptosis signal-regulating kinase 1 (ASK1) plays a pathogenic role in renal fibrosis and apoptosis.
**Background:** ASK1 is a member of the mitogen-activated protein kinase kinase kinase (MAP3K) family which can activate various signalling pathways, including the stress-activated protein kinases p38 and JNK. However, little is known of which MAP3K enzymes regulate p38 and JNK signalling in kidney disease. Since ASK1 is activated by oxidative stress, a common factor promoting kidney disease, we investigated ASK1 function in renal damage.
**Methods:** Groups of 8 Sprague-Dawley rats underwent surgical unilateral ureteric obstruction (UUO) and received the ASK1 inhibitor (GS-444217, 30 mg/kg/po/bid), vehicle or no treatment (NoTx), beginning 1 hr before surgery and continued until rats were killed on day 7. Tissues were analysed by immunohistochemistry, PCR and Western blotting.
**Results:** The α-SMA+ myofibroblast accumulation and increased collagen IV deposition seen in vehicle and NoTx UUO were reduced by 30–50% with GS-444217 treatment ($P < 0.001$ vs. both groups). Increased mRNA levels for pro-fibrotic molecules (collagen I, collagen IV, fibronectin, α-SMA, TGF-β1, CTGF and PAI-1) in vehicle and NoTx UUO was also reduced by GS-444217 (all $P < 0.05$ vs. controls). Western blot analysis identified a 6–15 fold increase in p38, JNK and ERK activation in UUO. GS-444217 abolished the increase in p-p38 and reduced p-JNK levels by 50% ($P < 0.01$ vs. controls), but had no effect upon p-ERK. GS-444217 reduced TUNEL+ apoptotic tubular cells in the UUO kidney by 50% ($P < 0.01$ vs. controls) and directly inhibited oxidative stress-induced apoptosis of cultured tubular cells in vitro.
**Conclusion:** This study establishes ASK1 as an important signalling molecule in renal fibrosis and apoptosis which operates as an upstream activator of p38 and JNK pathways.

082

## RELAXIN INHERENTLY REQUIRES THE ANGIOTENSIN II TYPE 2 RECEPTOR TO ABROGATE RENAL FIBROSIS

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**Aim:** To determine if the anti-fibrotic hormone relaxin interferes with the angiotensin II (Ang II) – transforming growth factor-β1 (TGF-β1) axis at the angiotensin II type 2 receptor ($AT_2R$) level.
**Background:** Fibrosis is a hallmark of chronic kidney disease. Current therapies slow but do not prevent this process. The hormone relaxin is emerging as a potential therapy, however, its mechanism of action remains poorly understood. Recent studies in renal fibroblasts have demonstrated that relaxin disrupts profibrotic actions of TGF-β1 by signalling through its cognate receptor, Relaxin Family Peptide Receptor 1 (RXFP1), extracellular signal-regulated kinase phosphorylation (pERK)1/2 and a neuronal nitric oxide (NO) synthase (nNOS)-NO-dependent pathway to abrogate Smad2 phosphorylation (pSmad2). Given that relaxin also inhibits Ang II activity, and that $AT_2R$ activation antagonises TGF-β1 activity, we hypothesised that there is a relaxin–$AT_2R$ interaction in renal fibroblasts.
**Methods:** The effect of the $AT_2R$ antagonist PD123319 on relaxin activity was examined in primary rat kidney fibroblasts, and in tissue from relaxin-treated male wild-type ($AT_2R^{+/+}$) and $AT_2R$ knockout ($AT_2R^{-/y}$) mice subjected to unilateral ureteric obstruction.
**Results:** Relaxin's ability to increase pERK1/2, pnNOS and matrix metalloproteinase levels, and inhibit TGF-β1 and pSmad2 expression, myofibroblast differentiation and collagen concentration (all $p < 0.05$ vs untreated cells or injured mice) was blocked by PD123319 in vitro and in vivo (all $p < 0.01$ vs relaxin alone), and by the absence of the $AT_2R$ ($AT_2R^{-/y}$ mice). Relaxin did not directly bind to $AT_2R$s, but mediated cross-talk through RXFP1-$AT_2R$ heterodimer complexes to induce its anti-fibrotic actions.
**Conclusion:** Results highlight a hitherto unrecognised interaction between relaxin and the $AT_2R$ which may mediate its anti-fibrotic actions.

083

## BLOCKADE OF ANGIOTENSIN II TYPE I RECEPTOR (AT1) AND CC CHEMOKINE RECEPTOR 2 (CCR2) HETEROMERS IN PROGRESSIVE CHRONIC KIDNEY DISEASE

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**Aim:** To test the hypothesis that blockade of the AT1-CCR2 heteromer with a combination of Irbesartan and Propagermanium (CCR2 pathway inhibitor) would have an additive benefit on progressive renal injury in subtotal nephrectomised (STNx) rats.
**Background:** Progressive chronic kidney disease (CKD) is associated with pathological fibrosis and podocyte loss, characteristic features that correlate closely with declining renal function and development of proteinuria. Both AT1 and CCR2 receptors have been consistently implicated in this disease progression. The combination of AT1/CCR2 blockade has been shown to inhibit the heteromer of these receptors and potentially increase the therapeutic effects in CKD.
**Methods:** STNx rats (n = 12) were randomly assigned to receive daily either Irbesartan (Irb; 10 mg/kg) or a combination of Irb (10 mg/kg) and Propagermanium (PPG; 30 mg/kg) or vehicle (V) for 12 weeks. In addition to renal function and histopathology examination, podocyte loss and the concentration of urinary MCP-1 were also measured.
**Results:** Without affecting body weight and blood pressure, the combination of Irb and PPG therapy in STNx rats was associated with significantly less proteinuria (V: 372 ± 52, Irb: 287 ± 32, Irb + PPG: 136 ± 16 mg/day), urinary MCP-1 (V: 4048 ± 587, Irb: 2533 ± 409, Irb + PPG: 2105 ± 538 pg/ml) and podocyte loss (V: 9 ± 0.8, Irb: 10 ± 0.6, Irb + PPG: 13 ± 0.7 podocytes/glomerulus) when compared to vehicle or Irbesartan treatment. Both mono and combination therapy attenuated tubulointerstitial fibrosis (V: 5.69 ± 0.8, Irb: 3.72 ± 0.41, Irb + PPG: 4.10 ± 0.7 %/area) and glomerulosclerosis (Veh: 1.37 ± 0.13, Irb: 0.52 ± 0.08, Irb + PPG: 0.66 ± 0.13), along with improved glomerular infiltration rate (V: 0.43 ± 0.13, Irb: 0.91 ± 0.12, Irb + PPG: 0.90 ± 0.16 ml/min/kg) when compared with vehicle treated STNx rats.
**Conclusion:** Blockade of the AT1-CCR2 heteromer with Irbesartan and Propagermanium was superior to Irbesartan alone in reducing proteinuria and podocyte loss in the STNx rat model of CKD.

084

## KCA3.1 MEDIATES RENAL INFLAMMATION IN MOUSE MODELS OF DIABETIC NEPHROPATHY

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**Aim:** To investigate the role of KCa3.1 in the inflammatory responses of diabetic nephropathy.
**Background:** Inflammation plays a key role in the development and progression of diabetic nephropathy. KCa3.1, a potassium channel protein, is associated with vascular inflammation, atherogenesis, and proliferation of endothelial cells, macrophages, and fibroblasts. We previously demonstrated that blockade of KCa3.1 ameliorated renal fibrosis in diabetic nephropathy through inhibition of TGF-β1 pathway. The present study aimed to identify the role of KCa3.1 in the inflammatory responses of diabetic nephropathy.
**Methods:** Two animal models of diabetes induced with streptozotocin were used in this study: (1) wild type verse KCa3.1-/- mice, and (2) diabetic eNOS-/- mice treated with or without a selective inhibitor of KCa3.1 (TRAM34). After mice were sacrificed, the expression of proinflammatory cytokines Chemokine (C-C motif) ligand 20 (CCl20), IL-6 and TNF-α were examined by real time PCR and immunohistochemistry staining. The activity of NF-kB and markers of inflammation (CD68 and CD45) were measured by immunohistochemistry staining.
**Results:** Both mRNA and protein levels of CCL20, IL-6 and TNF-α significantly decreased in kidneys of diabetic KCa3.1-/- mice compared to diabetic wild type mice. Similarly, TRAM34 reduced the expression of inflammatory markers described above in diabetic eNOS-/- mice compared to diabetic vehicle groups. Furthermore, blocking the KCa3.1 channel in both animal models led to the reduction of phosphorylation of NF-kB.
**Conclusions:** KCa3.1 mediated renal inflammation under diabetic condition through the NF-kB pathway.

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## THE PATHOGENIC ROLE OF TXNIP IN THE DEVELOPMENT OF TUBULOINTERSTITIAL FIBROSIS IN DIABETIC NEPHROPATHY – OPPORTUNITIES FOR NEW THERAPIES

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**Aim:** To examine a potential therapeutic role for targeted tubulo-epithelial cell TXNIP inhibition in experimental diabetic nephropathy, using a TXNIP DNAzyme to cleave TXNIP mRNA to abrogate tubulointerstitial fibrosis in a rodent model.
**Background:** Thioredoxin-interacting protein (TXNIP), an endogenous inhibitor of the antioxidant thioredoxin, is thought to be a mediator of progressive fibrosis in diabetic nephropathy (DN).
**Methods:** Transgenic (mRen-2)27 rats with streptozotocin-induced diabetes were randomly assigned to receive TXNIP DNAzyme or control (scrambled DNAzyme) delivered by implanted minipump. Site of activity of renal DNAzyme activity was measured immunohistochemically using fluorescent-labelled DNAzyme. Renal injury was assessed with biochemical measures of kidney function and histological changes. Renal gene expression of TXNIP, Collagen IV and TGF-β was assessed with RT-PCR, and peptide expression and localization measured by semi-quantitative immunohistochemistry.
**Results:** Fluorescently labelled TXNIP DNAzyme was demonstrated to be widely present in tubulo-epithelial cells, but not in glomeruli, endothelial cells or interstitium. Elevated TXNIP mRNA and protein expression in the renal cortex of diabetic animals were shown to be significantly attenuated by TXNIP DNAzyme compared with control scrambled DNAzyme and non-treated animals ($p < 0.05$). Downstream markers of TXNIP activity, particularly tubulointerstitial fibrosis and collagen deposition, were also dramatically attenuated in the tubulointerstitium of animals treated with TXNIP DNAzyme. The effects of the TXNIP inhibition was limited to tubulo-interstitial compartment, as there was no change

in the up-regulation of glomerular TXNIP expression, the amount of glomerulosclerosis or differences in renal function measures in the TXNIP DNAzyme treated animals.
**Conclusions:** This study supports the role of TXNIP as an important mediator of progressive tubulointerstitial fibrosis in DN, and further suggests TXNIP may represent a potential new therapeutic target for DN.

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## LONG-TERM MODULATION OF LITHIUM-INDUCED NEPHROGENIC DIABETES INSIPIDUS BY AMILORIDE

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**Aim:** To elucidate the long-term effect of amiloride on lithium-induced nephrogenic diabetes insipidus.
**Background:** Lithium induces nephrogenic diabetes insipidus (NDI) predominantly by preventing translocation of the aquaporin 2 channel (AQP2) into the apical membrane of the principal cells of the collecting duct, as well as down-regulation of AQP2 synthesis. Lithium enters the principal cells via epithelial sodium channel (ENaC). Short-term (3 weeks) administration of the ENaC inhibitor amiloride has been shown to partially reverse lithium-induced NDI. The main objective of this study was to examine the long-term (5 months) effects of amiloride in a lithium-induced rat NDI model.
**Methods:** 3 groups of male wistar rats, control, lithium alone and lithium plus amiloride, were studied. The rats were fed a diet containing lithium for 6 months (60 mmol $kg^{-1}$ food). Amiloride was added in the drinking water (0.2 mmol $L^{-1}$) after one-month of lithium treatment and continued for 5 months. At 6 months 24 hour metabolic studies were performed following which the rats were euthanised and the kidneys were processed for immunohistochemistry and western blotting.
**Results:** Urine osmolality decreased significantly after lithium treatment (199 mosm $kg^{-1}$ vs 2334 mosm $kg^{-1}$). Amiloride partially corrected the urinary concentrating ability to 590 mosm $kg^{-1}$. This was associated with a reduction in urine volumes (lithium alone 413 ± 67 µl min $kg^{-1}$ vs amiloride/lithium 128 ± 17 µl min $kg^{-1}$ vs control 14 ± 3 µl min $kg^{-1}$). Immunostaining and immunoblotting confirmed that amiloride restores the expression of AQP2 in the collecting tubules.
**Conclusions:** Chronic amiloride administration sustains the partially reversed NDI previously seen with short-term administration, accentuating its potential clinical significance in patients with lithium-induced NDI.

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## PYRROLIDINE DITHIOCARBAMATE ATTENUATES KIDNEY ENLARGEMENT IN EXPERIMENTAL POLYCYSTIC KIDNEY DISEASE

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**Aim:** To determine whether a small molecule dithiocarbamate inhibitor of nuclear factor (NF)-κB prevents the progression of kidney enlargement in polycystic kidney disease (PKD).
**Background:** PKD is characterised by cell proliferation, renal interstitial inflammation and fibrosis. The NF-κB system, which controls the transcription of multiple genes involved in growth and inflammation, is upregulated in experimental PKD. Pyrrolidine dithiocarbamate (PDTC) prevents the proteasomal degradation of Inhibitor of κB (IκB) proteins, thereby preventing NF-κB proteins from entering the nucleus and modifying gene transcription.
**Methods:** Groups of 4-week old male Lewis Polycystic Kidney rats received intraperitoneal injections of vehicle (saline) or PDTC 40 mg/kg once daily (40 × 1), or twice daily (40 × 2) (n = 8–9 each), and were sacrificed 7 weeks later. Magnetic resonance imaging (MRI) was performed at baseline and at +the study's completion to assess total kidney volume (TKV) progression.
**Results:** The percentage kidney weight to body weight was significantly lower in PDTC-treated than in vehicle-treated rats (vehicle 6.4 + 0.7%, PDTC(40 × 1) 5.0 + 0.9%, PDTC(40 × 2) 4.8 + 1.4%, $p < 0.01$ at both doses). By MRI, the relative within-rat increase in TKV over 5 weeks was 1.33-fold greater in vehicle compared to PDTC(40 × 2) (95%CI 1.10-1.60-fold, $p = 0.010$). This was accompanied by a reduction in week 10 proteinuria (65.9% reduction compared to vehicle, $p < 0.05$), but not in creatinine clearance. By histological analysis in whole coronal paraffin sections, percentage cyst area and interstitial monocyte accumulation were not different among groups.
**Conclusions:** Prophylactic treatment with PDTC attenuated kidney enlargement and proteinuria but not renal inflammation. These data suggest that PDTC may have renoprotective effects in PKD which involve the suppression of cystic epithelial cell.

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## NUMBERS OF PODOCYTES AND PARIETAL EPITHELIAL CELLS IN THE NORMAL HUMAN KIDNEY: ASSOCIATIONS WITH GLOMERULAR SIZE

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**Aim:** To determine associations between numbers of podocytes and parietal epithelial cells (PECs) and glomerular size.
**Background:** Recent evidence suggests that podocyte depletion is a direct cause of renal pathology and that PECs may give rise to podocytes. However, associations between these cell types and glomerular size remain unclear.
**Methods:** 14 Caucasian American males, who were autopsied at the University of Mississippi Medical Center, were selected based on their age at time of death: (2 infants, ≤3 years old) and 12 adults (≥18 years old). We used unbiased stereology to estimate individual glomerular volume (IGV), numbers of podocytes (labelled with Wilms' Tumour 1, WT-1) and PECs, including cell densities. Data were analysed in 3 categories (n = 12 glomeruli per category): infants, small adult glomeruli and large adult glomeruli.
**Results:** Glomeruli from infants were small and contained an average of 432 ± 107 podocytes, 169 ± 61 PECs and a podocyte density of 761 per $10^6$ $um^3$. Small adult glomeruli were 40% larger than those from term infants, and while they contained the same number of podocytes and PECs, they showed significantly lower podocyte density. Large adult glomeruli contained more podocytes (818 ± 115), more PECs (807 ± 231) and markedly lower podocyte density than infant and small adult glomeruli. 92% of the large adult glomeruli contained WT-1+ PECs, while WT-1+ PECs were not observed in infant glomeruli and were present in 42% of small adult glomeruli.
**Conclusions:** Large adult glomeruli show an increase in podocytes, exceeding the possible upper limit of congenital endowment. This increase may be associated with PECs and merits further assessment. However, the increase in podocyte number doesn't match the increase in glomerular volume, leaving these glomeruli with relative podocyte depletion.

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## γδ T CELLS ARE ESSENTIAL FOR THE DEVELOPMENT OF MPO AUTOIMMUNITY AND GLOMERULONEPHRITIS

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**Aim:** To explore the role of γδ T cells in the pathogenesis of autoimmune anti myeloperoxidase (MPO) anti-neutrophil cytoplasmic antibody (ANCA) associated glomerulonephritis (GN).
**Background:** Most circulating T cells express a TCR composed of αβ heterodimers, however a small population of T cells express the γδ TCR (unconventional γδ T cells). γδ T cells exhibit characteristics that enable them to participate in innate host defence and regulating αβ T cells in adaptive immune responses.
**Methods:** We compared autoimmunity and GN between WT and TCRδ-/- (γδ T cell deficient) mice. Autoimmunity was induced by MPO immunisation in Freund's Adjuvant and GN triggered using a subnephritogenic dose of anti-glomerular basement membrane antibody.
**Results:** Renal injury was significantly attenuated in TCRδ-/- mice compared with WT mice (proteinuria; 3.2 ± 0.3 vs 2.3 ± 0.2 mg/24 hr, $p < 0.05$ and abnormal glomeruli; 34.4 ± 2.9 vs 20.0 ± 3.1%, $p < 0.005$). Associated with decreased glomerular leukocyte accumulation (macrophage; 5.3 ± 0.7 vs 1.3 ± 0.7cells/glomerular cross section [c/gcs], neutrophils; 1.4 ± 0.2 vs 0.3 ± 0.06 c/gcs and CD4 cell; 1.4 ± 0.3 vs 0.3 ± 0.06 c/gcs, all $p < 0.05$). Antigen specific draining

node lymphocytes showed that the absence of γδ T cells resulted in decreased frequency of IFNγ producing CD4 T cells (Elispot 82.2 ± 19.0 vs 20.1 ± 7.1cells, $p < 0.05$) and reduced dermal MPO induced delayed type hypersensitivity swelling (0.24 ± 0.04 vs 0.02 ± 0.01 Δmm, $p < 0.05$). No difference in the development of MPO ANCA Ig was observed (0.3 ± 0.03 vs 0.3 ± 0.05$OD_{450nm}$, $p = 0.7$). Analysis of dendritic cells (DC) in lymph nodes draining immunisation sites showed significantly reduced DCs ($6.3 \times 10^4 \pm 7.4 \times 10^3$ vs $4.2 \times 10^3$cells/draining LN, $p < 0.05$) with increased percentage of DC apoptosis (1.6 ± 0.3 vs 3.4 ± 0.6%, $p < 0.05$) TCRδ-/- mice.
**Conclusion:** γδ T cells affect pathogenic adaptive autoimmune anti MPO responses by optimising the development of CD4 T effector adaptive autoimmune responses.

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## SYSTEMIC OVEREXPRESSION OF ENDOGENOUS SECRETORY RAGE (esRAGE) ATTENUATES DIABETIC KIDNEY INJURY IN MICE

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**Aim:** To determine whether systemic expression of endogenous secretory RAGE (esRAGE) after the induction of diabetes can prevent the development of diabetic nephropathy (DN) in mice with streptozotocin (STZ)-induced diabetes.
**Background:** We have reported that activation of TLR2 or 4 by their endogenous ligands (eg. HMGB1) mediates diabetic kidney injury. esRAGE is a soluble decoy receptor that can competitively bind ligands for TLRs/RAGE, including HMGB1. Here we test the hypothesis that blocking the interaction between TLRs/RAGE and HMGB1 will attenuate kidney injury in STZ induced DN.
**Methods:** A liver-specific rAAV encoding human esRAGE (rAAV-esRAGE) and a control vector encoding human serum albumin (rAAV-HSA) were created. Expression was quantitated using ELISAs specific for human esRAGE or HSA. DN was induced in WT Balb/c mice by intraperitoneal injection of STZ. At 2 weeks after STZ injection, mice received an IP injection of $5x10^{11}$ vector genome copies (VGC) encoding either rAAV-esRAGE or rAAV-HSA, or non-treatment. Samples were collected at week 12 post-induction of diabetes.
**Results:** Diabetic mice that received rAAV-esRAGE, rAAV-HSA or non-treatment developed equivalent degrees of hyperglycaemia. Both rAAV-HSA treated and untreated diabetic-mice developed significant albuminuria versus normals (ACR:309 ± 213&313 ± 215), whilst rAAV-esRAGE treated-diabetic-mice were protected (118 ± 42). WT diabetic-mice developed histological damage including glomerular hypertrophy, macrophage accumulation and interstitial fibrosis. These changes were significantly attenuated by rAAV-esRAGE treatment compared to rAAV-HSA ($p < 0.05$-0.01). mRNA expression of cytokine (TNFα), chemokine (MCP1) and pro-fibrotic (fibronectin) genes were significantly up-regulated in rAAV-HSA treated and untreated diabetic kidney versus normals but significantly diminished by rAAV-esRAGE treatment.
**Conclusion:** High-level expression of serum esRAGE after the induction of diabetes provided partial protection against the development of diabetic nephropathy in mice with STZ-induced diabetes.

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## MACROPHAGE-MYOFIBROBLAST TRANSITION – A MECHANISM CONTRIBUTING TO MYOFIBROBLAST ACCUMULATION IN HUMAN AND EXPERIMENTAL RENAL FIBROSIS

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**Background:** Macrophage infiltration is common feature in active fibrosis and can promote these lesions through production of pro-fibrotic molecules. However, it is unclear whether macrophages can directly contribute to fibrosis by transitioning into myofibroblasts.
**Aim:** To determine whether macrophage-myofibroblast transition (MMT) is involved in renal fibrosis.
**Methods:** Macrophages in transition to myofibroblasts (MMT cells) can be detected by co-expression of markers of macrophages (CD11b, F4/80, CD68) and myofibroblasts (α-SMA). We examined biopsies of human kidney disease and the mouse unilateral ureteric obstruction (UUO) model of renal fibrosis.
**Results:** Analysis of biopsies of various types of kidney disease identified CD68+α-SMA+ co-expressing MMT cells in active fibrotic lesions, but not in acute inflammatory or late-stage fibrotic lesions. Confocal analysis identified MMT cells on day 7 UUO on the basis of co-expression of F4/80/α-SMA or CD11b/α-SMA. MMT cells were also identified in enzyme digested day 7 UUO kidney using flow cytometric analysis of single cell suspensions, with F4/80 or CD11b expressed by 10–30% of α-SMA+ cells. CD11b+ cells isolated from the UUO kidney showed significantly increased mRNA levels of a panel of pro-fibrotic molecules (α-SMA, col I and III, fibronectin, HSP47, PAI-1) compared to CD11b+ isolated from the contralateral control kidney. Next, CD11b+ cells isolated from bone marrow were dye-labeled and injected into mice on day 2 UUO and then isolated from the day 7 UUO kidney. These transferred macrophages showed marked up-regulation of the panel of pro-fibrotic molecules compared to the freshly isolated cells prior to injection. Finally, TGF-β1 was shown to induce MMT in bone marrow-derived macrophages in vitro.
**Conclusion:** We have identified macrophage-myofibroblast transition as a significant source of myofibroblasts in human and experimental fibrosis.

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## A FUNCTIONAL ROLE FOR SPLEEN TYROSINE KINASE (SYK) IN INFILTRATING MYELOID CELLS IN HUMAN AND EXPERIMENTAL ACUTE GLOMERULAR DISEASE

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**Background:** Syk is essential for immunoglobulin-based signalling via the Fcγ-receptor on myeloid cells.
**Aim:** To identify Syk signalling (Tyr525/526 phosphorylation) in glomerulonephritis biopsies, and whether conditional Syk gene deletion in neutrophils and macrophages ($Syk^{f/f}LysM^{Cre}$) suppresses mouse anti-GBM disease.
**Methods:** Immunostaining for p-Syk was performed in 96 patients: MCD (3), TBMD (8), PIGN (5), SLE-IV (19), ANCA vasculitis (13), IgAN (31), MN (7) and FGS (10). Anti-GBM disease was induced in primed $Syk^{f/f}LysM^{Cre}$ and control $Syk^{f/f}$ mice. Mice were killed at 3 hrs (n = 4) or Day 9 (n = 13) after anti-GBM serum injection.
**Results:** p-Syk was seen in infiltrating glomerular leukocytes, mainly neutrophils and some macrophages, in 36/40 cases of crescentic GN. Glomerular p-Syk staining correlated with neutrophil infiltration ($r^2 = 0.71$, $p < 0.0001$). However, p-Syk staining was largely absent in other forms of GN. Anti-GBM disease in control $Syk^{f/f}$ mice provoked the glomerular influx of p-Syk+ neutrophils at 3 hrs (6.28 ± 0.77 vs 0.13 ± 0.05 GR1+ cells/gcs in normals, $p < 0.05$); and by D9 exhibited 58 ± 5% crescents, marked up-regulation of KIM-1, renal impairment (serum cystatin 1462 ± 90 vs 260 ± 29 ng/mL in normals, $p < 0.0001$), and heavy proteinuria. In contrast, $Syk^{f/f}LysM^{Cre}$ mice had an 85% reduction in glomerular neutrophils at 3 hrs ($p < 0.05$). At Day 9 $Syk^{f/f}LysM^{Cre}$ mice had a 67% reduction in crescent formation ($p < 0.01$) and improved serum cystatin levels (808 ± 89 ng/mL, $p < 0.0001$). $Syk^{f/f}LysM^{Cre}$ mice had reduced tubular injury, KIM-1 mRNA levels and glomerular macrophage infiltration (reduced by 79%, 90% and 71% respectively, all $p < 0.01$). There was no difference in proteinuria between the groups.
**Conclusion:** Syk is activated in infiltrating leukocytes in acute glomerulonephritis and Syk gene deletion is protective in experimental disease. These findings support the therapeutic use of Syk inhibitors in rapidly progressive glomerulonephritis.

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## HOW MISSENSE MUTATIONS IN THE *COL4A5* GENE CAUSE ALPORT SYNDROME

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**Aim:** This study examined whether missense mutations in X-linked Alport syndrome slowed cell growth, and increased ER stress, and whether these changes were corrected with chaperone treatment.
**Background:** Forty % of mutations in X-linked Alport syndrome are missense variants in the *COL4A5* gene. These typically produce an abnormal chain that is retained in the ER, and increases ER stress.
**Methods:** Cell lines were produced from skin fibroblasts from two males and two females with X-linked Alport syndrome due to missense mutations, and from non-haematuric normals.

Growth curves were examined over 72 hours. Levels of intracellular collagen IV α3, α4 and α5 protein were measured using western blots, and the corresponding mRNA quantitated using RT-PCR (Applied Biosystems 7500). Levels of mRNA corresponding to ER stress (BiP, CHOP and ATF6), and the pro- and antiapoptotic pathways (caspase 3, BAD and Bcl2) were quantitated.
Collagen IV α1 – α6 mRNA levels, and the markers of ER stress and apoptotic pathways, were compared before and after treatment with chaperones (10 mM 4-PBA, 100 mM TMAO, 2%DMSO, 10% glycerol).
**Results:** Cell growth rates were reduced in the affected male cell lines. Levels of the collagen IV α5 chain mRNA and protein were the same in affected and normal cell lines. There was no increase in ER stress mRNA. Treatment with chaperones did not increase intracellular collagen IV α5 chain, or ER stress or apoptotic marker mRNA.
**Conclusions:** Missense *COL4A5* mutations have an adverse effect on cell growth but do not increase ER stress detectably. Chaperone treatment had minimal impact on collagen IV α5 chain levels.
This work was supported by a grant from the Alport Syndrome Foundation of Australia.

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## INTERLEUKIN 17A DRIVES ACUTE KIDNEY INJURY THROUGH THE RECRUITMENT OF INNATE EFFECTOR CELLS

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**Aim:** To define the role of Interleukin (IL)-17A in cisplatin induced acute kidney injury (AKI).
**Background:** AKI is a major cause of morbidity and mortality. Clinical and experimental data demonstrate that cytokines and leukocytes promote renal inflammation and injury.
**Methods:** We administered cisplatin (15 mg/kg) to C57BL/6 wild type (WT) mice and measured kidney inflammation and injury. For reconstitution studies, CD4+ T cells were isolated using magnetic beads and injected into RAG1-/- mice, which lack adaptive immune cells.
**Results:** Kidney mRNA expression of IL-17A increased significantly after cisplatin treatment. Compared to WT mice treated with cisplatin, functional (serum urea: WT 72.2 ± 10.7 vs. IL-17A-/- 28.2 ± 8.2 mmol/L, $P < 0.01$) and histological injury (score: WT 3.3 ± 0.2 vs. IL-17A-/- 1.0 ± 0.2, $P < 0.001$) was decreased in IL-17A-/- mice. While interstitial neutrophil recruitment (1.8 ± 0.1 vs.1.0 ± 0.1, cells/high power field, $P < 0.001$) decreased in the absence of IL-17A, CD4+ T cell recruitment remained intact. Pre-emptive administration of anti-IL-17A antibodies to WT mice attenuated renal injury, serum urea (control antibodies: 54.6 ± 10 vs. anti-IL-17A 25.9 ± 11.2 mmol/L, $P < 0.05$). Neutrophil depletion prior to cisplatin treatment did not significantly reduce renal injury, which only decreased after additional IL-17A neutralization in neutrophil deficient mice. Depletion of both neutrophils and natural killer T cells significantly protected from AKI, but Injury was not further reduced after additional anti-IL-17A treatment, linking these cells with IL-17A induced AKI. While reconstitution of RAG1-/- mice with CD4+ T cells prior to cisplatin treatment increased renal injury, there was no difference after reconstituting with WT or IL-17A-/- CD4+T cells, demonstrating that IL-17A- producing CD4+ T cells did not enhance AKI. Mice deficient in gammadelta T cells were not protected from AKI.
**Conclusion:** IL-17A drives AKI and represents a new therapeutic target.

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## SOCIO-ECONOMIC DISPARITIES IN THE UPTAKE OF HOME DIALYSIS

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**Aim:** We investigate associations between area socio-economic status (SES) and home dialysis in Australia.
**Background:** Home dialysis – peritoneal dialysis (PD) or home haemodialysis (HHD) – is associated with better quality of life and outcomes than in-centre haemodialysis. In many developed countries socio-economically advantaged patients are more likely to commence home dialysis, but this has not been investigated in Australia.
**Methods:** We analysed 21,061 non-Indigenous adults who commenced chronic renal replacement therapy in Australia 2000–2010, using ANZDATA records. The main predictor was area SES, using standard indices for postcodes, grouped into quartiles. We investigated uptake of PD and HHD, using cure models to estimate both the time to commencement and the proportion of patients who will ever commence these modalities. All results are adjusted for age, gender, smoking status, BMI, comorbidities, state, primary kidney disease, race, residence in a major city, and late referral.
**Results:** Patients from advantaged areas were less likely to commence PD and more likely to use in-centre haemodialysis (satellite and hospital). Adjusted odds ratio for PD uptake in the most advantaged versus the most disadvantaged quartile (Q4 v Q1) was 0.73 (95%CI 0.66–0.80). SES was not associated with uptake of HHD (OR Q4vQ1 0.97, 95%CI 0.80–1.17). Rural areas were more disadvantaged and had higher rates of peritoneal dialysis than major cities (OR 1.38, 95%CI 1.28–1.49), however socio-economic gradients existed within major cities (OR Q4vQ1 0.75, 95%CI 0.67–0.85).
**Conclusions:** The lower incidence of home dialysis among advantaged patients contrasts with other countries, where advantaged patients are more likely to use home dialysis. Further research into the mediators of these gradients is required.

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## FETUIN-A-CONTAINING CALCIPROTEIN PARTICLES IN PERITONEAL DIALYSIS FLUID

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**Aim:** To determine whether fetuin-A (Fet-A) containing calciprotein particles (CPP) are present in PD fluid.
**Background:** In serum, Fet-A is present as high molecular weight complexes (100–200 nm) with calcium phosphate nanocrystals, called CPP. Clearance of CPP by macrophages may cause inflammatory cytokine and oxidant species generation. CPP have also been reported in the PD fluid of patients with calcific peritonitis. Since these particles are too big to pass even through large peritoneal membrane pores (~25 nm), it is possible they are formed *in situ*. Therefore, we tested whether CPP might be present generally in peritoneal fluid.
**Methods:** We measured CPP in spent dialysate fluid (PDF) and in the serum of 20 stable PD patients. Ultrastructural analysis of CPP was also undertaken by cryo-TEM.
**Results:** Mean (SD) Fet-A concentrations were found to be higher within PDF than might be expected by simple diffusion from the circulation [68(48) vs 45(13) mg/L, $p < 0.05$]. There was also a significantly higher ratio of Fet-A to albumin in PDF fluid than in serum [81(44) vs 5(1) mg/g, $p < 0.0001$]. The CPP present in PDF have a strikingly different morphology in PDF (smaller and spherical) compared to those in the circulation (elongate spindle shaped).
**Conclusion:** Fet-A-containing CPP are present at high concentrations in spent PDF from stable, asymptomatic PD patients. Their morphology differs substantially from those found in the circulation. CPP interaction with peritoneal macrophages may contribute to inflammation.

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## LIFESTYLE, SEXUAL FUNCTION AND PERITONEAL DIALYSIS

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**Aim and Background:** To assess the impact of Peritoneal Dialysis (PD) on patient lifestyle and sexual intimacy to assist clinicians in counseling of dialysis candidates.
**Methods:** An anonymous, paper based survey of all patients treated with PD for >6 months during the last 5 years. Four domains (lifestyle, body-image, personal relationships and sexual function) were assessed, prior to starting and whilst on PD.
**Results:** The response rate from 62 patients was 47% (n = 29). 55% of responders were aged 56–70
**Employment:** 72% were working prior to starting PD and 83% had no change in their employment whilst on PD. Average time at work was 30 hrs/week.
**Travel:** 48% travelled whilst on PD, the majority 1–2 times per year.
**Recreation:** 69% maintained regular exercise whilst on PD.
**Body image:** 45% reported a negative impact of PD on body image.
**Personal relationships:** 72% were in long-term relationships prior to starting PD. Of those who were not, 66% reported a neutral (33%) or positive (33%) impact of PD on forming new relationships, 22% reported a negative impact.

**Sexual Intimacy:** 34% were sexually intimate with another person during the period they were treated with PD. The most significant factor influencing sexual function was being connected to a machine overnight (average 3.27 on a scale of 1–5, 5 = major impact), followed by having a PD catheter (2.78) and additional fluid in the abdomen(2.66). Responders reported a deterioration in all four domains of sexual function assessed (libido, confidence, performance, and overall satisfaction), with the largest deterioration in sexual confidence.
**Conclusions:** The majority of responders maintained work and regular exercise whilst on PD, and almost half travelled regularly. Our survey highlights the potential negative impact of PD on body-image and sexual function, particularly sexual confidence.

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## PSYCHOLOGICAL FACTORS ASSOCIATED WITH SUCCESSFUL OUTCOMES IN HOME HAEMODIALYSIS

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**Aim:** Performing haemodialysis therapy at home has been associated with improved survival for end stage kidney disease patients and can generally be delivered at a lower cost to the health care system when compared to centre and satellite unit dialysis. However, only a minority of dialysis dependent ESKD patients successfully sustain haemodialysis at home. Current practice for determining dialysis treatment modality and location takes into account medical suitability and social situation, but infrequently formally examines the contribution of psychological factors. This study explores demographic, health, and psychological factors that may predict patients' ability to learn and sustain home haemodialysis.
**Methods:** One hundred and thirteen successful and unsuccessful home haemodialysis users were recruited to the study, and 55 responded to self-report measures. Demographic (age, gender, education level, carer support), health (co-morbidities, diabetes, psychiatric condition) and psychological (locus of control beliefs, coping styles) information was used as predictor variables for the participants' time maintaining home therapy (Home Time).
**Results:** In a 3-step regression, the model explained 32% of variance in Home Time. Coping styles significantly contributed 16% of the variance in Home Time after accounting for other variables. Adaptive Coping was significantly correlated with the length of time sustaining home therapy.
**Conclusions:** The presence of adaptive coping strategies is associated with improved ability to sustain home haemodialysis therapy. Evidence-based psychological approaches are available to help patients develop more adaptive coping strategies. More research is needed to assess whether instituting these psychological interventions will assist patients to adopt and sustain dialysis therapies which require increased patient self management.

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## END-STAGE KIDNEY DISEASE – SUPPORTING THE TREATMENT OPTION DECISION MAKING PROCESS

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**Aim:** To develop a decision aid with supportive educational materials for Australian patients who have end-stage kidney disease (ESKD).
**Background:** Shared decision making encompasses informed consent principles. It facilitates choice of the most appropriate treatment option, enhancing compliance and quality of life. In 2010 the Kidney Health Australia (KHA) consumer perspectives survey found that only 49% of patients were aware of all their treatment options.
Whilst decision aids are a proven adjunct to decision making for cancer treatment and surgery options there was no decision aid for ESKD in Australia, and only three in use worldwide.
**Methods:** A taskforce comprising nephrologists, psychologists, nurses, social workers and consumers from Australia and New Zealand collaborated to complete a literature review translating the best practice principles found into the development of a decision aid. An information tool about the decision aid for health professionals was also produced.
**Results:** The decision aid meets relevant key criteria of the International Patient Decision Aid Standards Collaboration. The five sections lead the patient through from determining the need for education, assessing and documenting their life priorities, understanding and evaluating the treatment options and then completing the actual decision-making process.
**Conclusions:** The decision aid is now available for patients to use at the commencement of education, and considered complete when the decision is made. Additional educational tools, developed through the KHA, ESKD project including a website, new DVDs and new written education materials have also been made available to support the new model of a decision aid led education process.

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## INTRODUCING NXSTAGE HAEMODIALYSIS IN THE AUSTRALIAN HOME

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**Background:** NxStage haemodialysis machine, although widely used overseas, has recently been approved for use in the Australian setting. Advantages for use at home include: a simpler user interface; compact size; inbuilt water purification system and capacity to use premade dialysate bags; excellent water efficiency and potential portability which may broaden the appeal of home haemodialysis. This abstract describes a single centre experience introducing NxStage into the Australian home.
**Methods:** Between January 2012 and February 2013 14 NxStage haemodialysis machines were acquired. We aimed to recruit patients from centre/satellite haemodialysis units, failing renal transplants or peritoneal dialysis, new start dialysis and those wanting to travel already established on home haemodialysis. A 5–6 sessions weekly, 3–4 hours/session prescription was recommended.
**Results:** Fourteen (7 centre haemodialysis, 1 peritoneal dialysis, 1 failed renal transplant, 3 new start dialysis, 2 other home haemodialysis machine) were recruited. All successfully trained. Three ceased Nxstage haemodialysis: 1 poor problem solving and unsafe to continue at home with previous failed attempt to train previously, 1 social issues and non compliance, 1 cannulation difficulties. Five patients have successfully taken Nxstage on holidays within Australia and New Zealand. Biochemistry and fluid balance parameters have been safely maintained provided frequent or extended hours dialysis is performed. Challenges with machine reliability, compliance with Australian electricity safety standards costs and logistics of portability have been experienced.
**Conclusions:** NxStage haemodialysis system can be successfully used in the Australian home. Local portability is possible although challenging logistically. The more simple system has not markedly increased our ability to maintain marginal candidates at home. Extended hours dialysis regimens are required to maintain good electrolyte balance due to lower efficiency of clearance.

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## BARRIERS TO HOME DIALYSIS THERAPIES

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**Aim:** To identify the barriers to home dialysis uptake.
**Background:** Understanding and responding to the perspectives and experience of dialysis patients is a key step in improving uptake of home dialysis therapies.
**Methods:** We conducted a qualitative study of 29 dialysis patients in the Alfred Health Renal Service. Forty patients were randomnly chosen from the home, satellite and incentre dialysis populations, to complete the Kidney Health Australia questionnaire utilised in the national census of consumer perspectives on dialysis. Patients were interviewed in person enabling elaboration of ideas suggested in the questionnaire.
**Results:** A response rate of 72% was achieved. 34% of respondents were on home dialysis therapies (10% peritoneal dialysis, 24% haemodialysis), 35% satellite and 31% incentre haemodialysis. The mean age was 65 years with 76% male. The majority of patients had been on dialysis for 1–5years. 83% & 90% of patients indicated they had no desire to change their dialysis modality or location respectively, with 90% of patients satisfied with their treatment. 59% & 48% of respondents were given no choice in their dialysis modality or location respectively, of whom 60% were given no reason. Only 30% of respondents were given information on all dialysis modalities. Surprisingly, 80% of respondents were satisfied with the information given and only 34% suggested improvements.
**Conclusions:** Overwhelmingly, patients were committed to the dialysis modality and location on which they were commenced and felt the information they received, despite being incomplete and late, was satisfactory. There was a large proportion of patients who had no choice in their modality and location who were satisfied with their management. These results suggest a lack of patient ownership and involvement in their medical condition which is likely to be a major factor in low uptake of home dialysis.

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## eGFR-BASED COMPARISON OF DIALYSIS ADEQUACY BETWEEN NOCTURNAL HOME-BASED AND CONVENTIONAL FACILITY-BASED HAEMODIALYSIS

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**Aim:** To show that nocturnal home-based dialysis (NHD) maintains a significantly greater mean eGFR (MDRD-derived) than conventional dialysis (CHD).
**Background:** When assessing dialysis adequacy (DA), urea kinetics (Kt/V and/or PRU) is traditionally used, while eGFR is the main quantifier of renal function in CKD, where a higher eGFR is associated with lower morbidity and mortality. However, eGFR is not used for DA in maintenance HD models, perhaps because of concerns about eGFR variability in the non-steady-state of acute kidney injury (AKI) models. We postulate these criticisms may not apply in maintenance HD, where the recurrent nature of the changing eGFR introduces comparability through reproducibility.
**Methods:** In a 2 year retrospective single centre study (1/2011–12/2012), a random sample of 60 patients (17 NHD vs. 43 CHD; M 36; F 24; mean age NHD 61.8 years; CHD 68.3 years; mean measurements per patient (pre+post): 20) was assessed for pre- and post-dialysis urea, creatinine and eGFR. Statistical analysis was by the two sample t-test.
**Results:** Mean NHD pre-eGFR = 11.84 +/– 3.16; CHD pre-eGFR = 7.95 +/– 2.97; NHD post-eGFR = 46.06 +/– 9.58; CHD post-eGFR = 25.58 +/– 8.03. The mean post- minus pre- NHD eGFR was 28.95 +/– 18.73 while the mean post- minus pre- CHD eGFR was 16.77 +/– 10.71. All comparisons were statistically significant: $p = 0.001$.
**Conclusion:** NHD patients sustain a significantly higher eGFR (low stage 3 to high stage 4) than CHD patients (low stage 4 to stage 5) based on eGFR CKD classification. eGFR may be a valid comparator by which to judge DA in maintenance dialysis models.

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## PLASMA CYSTATIN C IS ELEVATED IN THE ABSENCE OF ACUTE KIDNEY INJURY FOLLOWING CISPLATIN WITH CONTEMPORARY ANTIEMETICS

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**Aim:** To evaluate the clinical utility of plasma cystatin C (pCysC) to diagnose toxicant-induced acute kidney injury (AKI).
**Background:** A 50% increase in pCysC concentration has been proposed as an alternative to serum creatinine (sCr) to diagnose AKI because pCysC is less influenced by confounding factors including gender and age.
**Methods:** We studied 26 incident patients without chronic kidney disease receiving cisplatin-based chemotherapy including dexamethasone, aprepitant and palonosetron antiemetics. We measured selected urine and blood biomarkers over 8 timepoints before and for 2 weeks after chemotherapy.
**Results:** pCysC increased above baseline in all patients between days 3 and 7 post-cisplatin. 9 patients (35%) exhibited a ≥50% increase in pCysC whereas only 2 (8%) exhibited a ≥50% increase in sCr (i.e. Stage 1 AKI) ($p = 0.04$). Similarly, 16 patients (61%) experienced a ≥25% increase in pCysC whereas only 3 (12%) exhibited a ≥25% increase in sCr ($p < 0.001$). The mean difference between the percentage increase in pCysC and sCr was 25.0% (95% CI: 15.8%–34.3%).

A Wilcoxon signed-rank test was conducted to compare baseline and peak urinary biomarker concentration after chemotherapy. Between days 3 and 7 there was a significant elevation ($p < 0.05$) in each of kidney injury molecule (KIM)-1, clusterin, interleukin-18 and neutrophil gelatinase-associated lipocalin. Peak KIM-1 and clusterin significantly correlated with the rise in sCr suggesting subclinical injury. Increase in pCysC was not correlated with any urinary biomarker.
**Conclusions:** pCysC concentrations rise independently of sCr and kidney injury biomarkers in patients treated with cisplatin and contemporary antiemetics. This suggests clinically significant interference by corticosteroids, neurokinin-1 receptor antagonists or serotonin antagonists warranting further study. Increases in pCysC cannot be used to diagnose AKI in these patients.

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## ACE INHIBITOR USE AND AKI OUTCOMES: AN ANALYSIS OF THE RANDOMISED EVALUATION OF NORMAL VS. AUGMENTED LEVEL OF REPLACEMENT THERAPY (RENAL) TRIAL

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**Aim:** To assess the association of angiotensin converting enzyme inhibitor (ACEI) use and acute kidney injury (AKI) outcomes.
**Background:** AKI is associated with increased mortality. While ACEI use is known to slow progression of chronic kidney disease, its role in AKI remains unclear.
**Methods:** Outcomes from the Randomised Evaluation of Normal vs. Augmented Level Replacement Therapy (RENAL) study were analysed according to ACEI use during study data collection. The primary outcome was all-cause mortality at 90 days following randomisation. Secondary outcomes included 28 days mortality, renal replacement therapy (RRT)-free days, intensive care unit (ICU)-free days, and hospital-free days. Multivariate Cox regression adjusted for baseline characteristics was employed. Sensitivity analyses included logistic regression and propensity score adjustment.
**Results:** Of the 1463 participants with available data on ACEI usage, 142 participants (9.7%) received ACEI at least once during study data collection. Participants receiving ACEI were older ($P = 0.02$), had lower disease severity as assessed by APACHEIII score ($P = 0.03$), and had less sepsis at baseline ($P = 0.0002$). Multivariate cox regression analyses showed an association of ACEI use with lower mortality at 90 days (HR 0.34, 95%CI 0.23–0.49, $p < 0.0001$) and 28 days (HR 0.28, 95%CI 0.18–0.44, $p < 0.0001$). ACEI usage was also associated with prolonged RRT-free days ($P < 0.0001$), ICU-free days ($P = 0.0002$) and hospital free-days ($P = 0.003$). Sensitivity analyses using logistic regression and propensity score adjustment yielded similar results.
**Conclusions:** In the RENAL study, ACEI use was not common during study data collection and patients receiving these agents differed from other study participants. ACEI use was associated with reductions in mortality and requirement for renal supportive care. These findings are limited by the possibility of residual confounding due to baseline differences between the patient groups.

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## DIAGNOSTIC TEST LEVELS OF URINE INTERLEUKIN-18 AS AN EARLY BIOMARKER OF ACUTE KIDNEY INJURY (AKI) IN ICU AT MUHAMMAD HOESIN HOSPITAL PALEMBANG

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**Background:** Inflammation plays a role in the pathophysiology of AKI, wherein Interleukin-18(IL-18) is obtained high levels in AKI patients's urine. This study aims to determine whether level of urinary IL-18 has a high diagnostic value as an early biological marker for diagnosing AKI in critically ill patients in the ICU RSMH Palembang..
**Method:** Urinary IL-18 were measured at 0 and 24 hours with the ELISA method in 40 critically ill patients admitted to ICU RSMH Palembang, 2012. Diagnostic test performed on some of the cut-off point of urinary IL-18 levels compared with serum creatinine levels according to the AKIN criteria 2005.
**Result:** AKI frequency is 75%, with frequency in male 70%. Median age was 47 years, while no AKI is a 38.8 years. There is a significant increased levels of IL-18 urine in AKI patients($p = 0.02$), whereas in non AKI patients levels of IL-18 urine not significant statistically. Median urinary levels of IL-18 in 0 hour among patients with AKI and no AKI is not significant statistically ($p = 0.11$) and urinary levels of IL-8 in 24 hours also ($p = 1.00$). The diagnostic value of urine levels of IL-18 with a cut-off point of 100 pg/mL was sensitivity 83%, specificity 30%,70% accuracy and AUC 0.50.
**Conclusion:** Urine IL-18 has a high sensitivity value in AKI, and it has the ability AKI screening in the group of patients with high risk factors for AKI. However, the specificity and the AUC values were low, so the urine IL-18, can't be used as an early biomarker for diagnosing AKI in critically ill patients in the ICU RSMH Palembang.
**Key words**: AKI, Critical illness, IL-18, Diagnostic test.

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## THE INCIDENCE OF ACUTE KIDNEY INJURY ASSOCIATED WITH BROAD SPECTRUM ANTIBIOTICS

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**Aim:** To review the incidence of inpatient acute kidney injury (AKI) associated with broad spectrum antimicrobial therapy.
**Background:** AKI is common in septic patients. In 2012 a point prevalence survey at St Vincent's Hospital showed that the combination antibiotic Tazocin (pipercillin–tazobactam) was the most commonly prescribed intravenous antimicrobial therapy, with vancomycin being fifth most common. These antibiotics are often prescribed together empirically in septic patients and hospital acquired infections.
**Methods:** A retrospective audit of electronic medical records of acute inpatients with a discharge diagnosis including AKI admitted during 2012 was undertaken. Records from patients with known end stage kidney disease (dialysis and transplant) or where critical medical charts were absent were excluded. AKI was defined as an acute rise in serum urea and creatinine, the validity of this definition was confirmed using the AKIN criteria.
**Results:** In all, 1238 patients were admitted during 2012 with a discharge diagnosis including AKI. Overall, 1112 (90%) received at least one dose of antibiotic, 229 (18%) pipercillin-tazobactam, 201 (16%) vancomycin, and 97 (8%) received both. Only four patients receiving pipercillin-tazobactam alone or pipercillin-tazobactam and vancomycin concomitantly showed clinical features of acute interstitial nephritis such as ongoing fever, rash or urinary eosinophils. Two of these patients underwent a renal biopsy, one confirmed mild chronic tubulointerstitial damage with cast nephropathy, the other severe acute tubular necrosis (ATN). Nineteen patients needed short term renal replacement therapy and none needed ongoing dialysis.
**Conclusions:** The majority of patients in this audit were presumed to have ATN in the context of sepsis, because renal function recovered with antibiotic therapy and few patients fitted temporally or clinically with antibiotic mediated injury. As diagnostic renal biopsy in this context is uncommon, the underlying pathogenic mechanisms of AKI in the setting of sepsis treated with pipercillin-tazobactam and vancomycin is unclear.

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## DRUG DOSING IN THE ELDERLY: THE IMPACT OF AGE AND TUBULAR FUNCTION

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**Aim:** To explore the influence of age and renal pathology on drug handling in the elderly using simultaneous measurement of GFR, anion and cation secretion and reabsorption.
**Background:** Estimated GFR is typically used to modify dosage of renally excreted drugs. Age is a primary variable of GFR equations. Many drugs are weak organic anions or cations, predominantly handled by proximal tubular transport so eGFR may not reflect the alterations in tubular handling with age.
**Methods:** 40 subjects were investigated using a modified drug cocktail protocol with anion transport (urate), cation transport (pindolol), reabsorption (fluconazole) and GFR determinations (isotopic and estimated)
A: healthy controls: 20–40 years, plasma creatinine (Cr) <105 μmol/L (n = 10),
B: age > 65 years, no pathology, Cr <105 μmol/L (n = 11)
C: age > 65 years, Cr <105 μmol/L plus co-morbidities (n = 11)
D: age > 65 years, Cr >105 μmol/L plus co-morbidities (n = 8)
**Results:** The clearance equations (Cockcroft Gault, MDRD CKD-EPI) significantly underestimated (-32-54 mL/min) the measured GFR for those with normal renal function. In established CKD these were more accurate (-2-10 mL/min).

GFR had a moderate correlation ($R^2 = 0.40–0.43$) with anion transport and reabsorption. Cationic secretion showed poor correlation to GFR ($R^2 = 0.11$). Mild hypertension and vascular disease without CKD was associated with greater clearances of the markers than in age-matched normals, suggesting hyperfiltration.
**Conclusion:** In healthy elderly, GFR does not necessarily decline with age compared to calculated estimates for GFR. Tubular function does not decline in parallel with GFR with disproportionate relationships between filtration and tubular cation drug transport. Furthermore mild pathology (hypertension) appears to impact on all aspects of the nephron function in the absence of changes in GFR.

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## ACUTE KIDNEY INJURY, ANALGESIC NEPHROPATHY AND TOXIN-MEDIATED KIDNEY INJURY IN AN AUSTRALIAN CHRONIC KIDNEY DISEASE (CKD) COHORT

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**Aim:** To describe CKD attributed to Acute Kidney Injury (AKI), Analgesic Nephropathy (AN) and Toxin-mediated Kidney Disease/Injury (TMI) as seen in public nephrology practice.
**Background:** AKI is etiologically heterogeneous with an incidence of 2000-3000/million-population/yr. Some are caused by extrinsic toxic agents. Many toxins also result in CKD in the absence of known AKI.
**Methods:** The CKD.QLD registry from four sites, comprising 2167 patients, was searched for all cases of CKD related to AKI or extrinsic toxins.
**Results:** 80 (3.7%) had AKI, 58 (2.7%) had AN and 103 (4.7%) had TMI, constituting a total of 241 (11.1%) in this analysis. TMI subgroups were NSAID (23.3%), lithium (18.4%), chemotherapy (11.7%), calcineurin inhibitors (10.7%), renin-angiotensin system inhibitors (7.8%), antibiotics (6.8%), toxin not otherwise specified (NOS) (6.8%), contrast medium (3.9%), proton pump inhibitors (2.9%), supplements (2.9%) and biologic agents (1.9%). AKI subgroups were prerenal (18.8%), AKI NOS (16.3%), cardiac (12.5%), sepsis (12.5%), vascular (12.5%), interstitial nephritis (7.5%), infective (non-sepsis) (5%), post-infective glomerulonephritis (5%), obstructive (3.8%), hemolytic uremic syndrome (2.5%), non-renal trauma (2.5%) and envenomation (1.3%).

In the AKI/AN/TMI cohort the female : male ratio was 53:47. There were markedly more women in the AN cohort (67:33).

The most common age group was 65–74 yrs (32.4% vs 38.7%) with mean ages 66.6 yrs. Those with AN were older (74.5 yrs) and TMI younger (53.9 yrs).

AKI, AN, TMI and CKD.QLD populations were most commonly CKD Stage 3B (26.7%-39.7%).
**Conclusions:** AKI, AN and Toxin-mediated were significant causes for CKD with similar CKD Stage distribution despite heterogeneous etiology. Women more commonly had AN. Those with AN were older and with TMI younger. Ongoing registry-based surveillance may reveal changing etiologies.

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## A JUSTIFICATION FOR LESS RESTRICTIVE GUIDELINES ON THE USE OF METFORMIN IN RENAL FAILURE

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**Aim:** To utilise available evidence to rationalise the use of metformin in renal failure.
**Background:** Metformin is associated with a significantly lower incidence of cardiovascular events and mortality compared to other hypoglycaemic agents. Guidelines recommend against using metformin when the estimated glomerular filtration rate (eGFR) <30 ml/min, because of the risk of metformin associated (MA) lactic acidosis (LA). However there is no evidence of an increased incidence of LA with metformin and in the patients with LA other contributory factors confound the issue.
**Methods:** Studies on intentional metformin overdose and metformin bioavailability, renal clearance and plasma metformin (pM) in renal impairment provide evidence of pM and plasma lactate (pL) in likely MALA. And predict a likely 'safe' pL and pM, based on eGFR and metformin dose.
**Results:** In metformin overdose (n = 22): LA was not inevitable with pM > 40 mg/l (therapeutic range 1–2 mg/l): Severe LA (pH ≤ 7.21, pL ≥ 11 mmol/l, n = 8) did not occur unless pM > 40 mg/l: And pL was a more consistent predictor of pH than pM, with pH = 7.47–0.02×pL, R = 0.95, and pL ≤ 4.7 being associated with a pH ≥ 7.34. Predicted pM (mg/l), with metformin 1700 mg/day, was 4.8 (eGFR 40 ml/min), 7.4 (eGFR 20 ml/min) and 15 (eGFR 10 ml/min). Reported pM in renal failure (n = 13) was always less than predicted pM.
**Conclusions:** Metformin accumulates in renal failure and, although accumulation does not always lead to LA, dose modification is recommended. Predicted pM levels suggest a dose of 1700 mg/day is justifiable with an eGFR >20 ml/min and 850 mg/day with an eGFR 10–20 ml/min: Monitoring venous pL (target ≤3 mmol/l) is a recommended safeguard with these dosage suggestions.

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## SURVIVAL AFTER CUTANEOUS MELANOMA IN KIDNEY TRANSPLANT RECIPIENTS: A NATIONAL POPULATION-BASED MATCHED COHORT STUDY

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**Aim**: We examined tumour characteristics and risk factors for mortality after melanoma diagnosis in kidney transplant and matched non-transplant recipients.
**Background:** Early detection and tailored treatment algorithms have resulted in improved outcomes for people with melanoma. People with kidney disease are at elevated risk of melanoma, but whether they have poorer outcomes than non-transplant recipients is not known.
**Methods:** Using ANZDATA and state cancer registries we conducted a national, population-based, matched cohort study of de novo invasive cutaneous melanoma in Australian kidney transplant recipients and in randomly selected members of the general population matched for age, sex, state of residence, and year of diagnosis (1982–2003). Melanoma histopathological characteristics were extracted from cancer registry notifications and date of death data obtained by linkage with the National Death Index (1982–2011). Conditional Cox proportional hazard models were used to analyse the overall and melanoma-specific survival of transplant and non-transplant recipients adjusted for histopathological characteristics.
**Results:** Compared to non-transplant recipients (n = 202), melanomas in transplant recipients (n = 75) were more likely to have a higher pathologic stage at diagnosis (P = 0.003). During 3072 years of follow-up, 57 (76%) transplant recipients died and 61 (30%) non-transplant recipients died. Pathologic stage (P < 0.001) and histological type (P = 0.009) independently predicted risk of death. Transplantation was associated with a significantly increased risk of death (adjusted hazards ratio 8.06; CI 3.92–16.6, P < 0.001) and the burden of excess mortality was predominantly with stage I melanoma.
**Conclusions:** Transplant recipients have a markedly poorer outcome than non-recipients after melanoma diagnosis. Treatment algorithms developed for the general population with melanoma may not benefit transplant recipients. A review of screening guidelines and treatment algorithms is warranted.

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## LONG-TERM OUTCOMES FOLLOWING ACUTE REJECTION IN KIDNEY TRANSPLANT RECIPIENTS: AN ANZDATA ANALYSIS

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**Aim**: We compared cause-specific rates of graft loss and death for kidney transplant recipients with and without acute rejection (AR).
**Background**: Declining rates of AR, and an apparent dissociation between acute rejection incidence and 1 year graft survival, have raised questions as to the importance of AR as an outcome. However, AR and its treatment have the potential directly or indirectly to affect longer-term outcomes.
**Methods**: Analysis of the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, including all recipients of a primary kidney-only transplant between 1997–2011 (n = 8376). The associations between AR during the first 6 months post transplant and cause-specific graft loss and death were determined using competing-risk survival analyses adjusted for baseline donor, recipient and transplant characteristics.
**Results**: Those with AR had significantly more graft loss attributed to chronic allograft nephropathy (CAN) (subhazard ratio (SHR) 1.38, 95% CI 1.16–1.64), death with a functioning graft (SHR 1.32, 95% CI 1.12–1.56) or AR beyond month 6 (SHR 2.70, 95% CI 1.46–4.98), and nonsignificantly higher graft loss due to non-compliance and other causes. Graft losses attributed to glomerulonephritis recurrence were not increased. Among causes of death, cardiovascular (SHR 1.47, 95% CI 1.16–1.87) and cancer deaths (SHR 1.39, 95% CI 1.05–1.82) were significantly increased whereas infectious deaths were not. Sensitivity analyses restricted to biopsy-proven AR and vascular AR produced similar results.
**Conclusions**: Although graft loss due to AR is uncommon in the modern era of kidney transplantation, AR is associated with increased rates of long-term graft failure attributed to AR, CAN or death with function, and increased rates of death from cardiovascular disease and malignancy. AR therefore remains an important short-term outcome in kidney transplantation.

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## URINARY CLUSTERIN PREDICTS GRAFT RECOVERY WITHIN FOUR HOURS OF KIDNEY TRANSPLANTATION

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**Aims:** To evaluate the ability of urinary biomarker concentrations to predict graft recovery early after kidney transplantation.
**Background:** The utility of urinary neutrophil gelatinase-associated lipocalin (NGAL), interleukin-18 (IL-18), kidney injury molecule-1 (KIM-1) and clusterin for predicting graft recovery is poorly defined.
**Methods:** Serial urine and plasma biomarkers were prospectively studied for 7d in 60 kidney transplant patients. Urinary biomarker concentrations were normalised to creatinine. Delayed graft function (DGF) was defined by dialysis within 7 post-operative days, slow graft function (SGF) by a serum creatinine reduction ratio (CRR) < 0.7 and immediate graft function (IGF) by CRR ≥ 0.7.
**Results:** 16 patients had DGF, 22 SGF, and 22 IGF. Clusterin concentration increased in patients with SGF and DGF by 4 h (ANOVA, p = 0.01; Tukey's post-hoc tests: p < 0.05). IL-18, NGAL and KIM-1 were increased (p < 0.05) across groups by 8 h, 12 h and 1 d respectively.

At 4 h, elevated clusterin was predictive of non-IGF (AUC-ROC: 0.78, 95% CI: 0.68–0.88). sCr, fall in sCr from baseline (delta sCr), IL-18, NGAL, and KIM-1 were not predictive (p > 0.05). In multivariate analysis, after adjustment for clinical variables, the combined metric [elevated clusterin or anuria] predicted non-IGF (OR: 5.2, 95% CI: 1.17–23.0) but other biomarkers did not.

Clusterin performed best at 12 h (AUC: 0.84, 95% CI: 0.76–0.93). At 12 h delta sCr improved the logistic regression model: AUC-ROC increased from 0.86 to 0.93, and Integrated Discrimination Improvement (IDI) was 0.21 (p < 0.001). Addition of [clusterin or anuria] further improved prediction (AUC: 0.94; IDI 0.06, p < 0.05).
**Conclusions:** Urinary clusterin predicted graft recovery at 4 h, and improved prediction in combination with sCr at 12 h. Urinary clusterin outperformed NGAL, IL-18 and KIM-1.

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## LIVING KIDNEY DONOR ASSESSMENT: THE CHALLENGES, UNCERTAINTIES AND CONTROVERSIES AMONG 110 TRANSPLANT NEPHROLOGISTS AND SURGEONS FROM 12 COUNTRIES

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**Aim:** To ascertain the perspectives of transplant nephrologists and surgeons on the challenges in living kidney donor assessment.
**Background:** Living kidney donation has been accepted in most transplant units worldwide, but donor evaluation policies and practices vary. The organ scarcity has stimulated emerging types of donation including paired-exchange programs, and expanded criteria for donor acceptance.
**Methods:** Semi-structured, face-to-face interviews were conducted with 110 transplant nephrologists and surgeons from 43 transplant units in 12 countries from Europe, Asia, and North America.
**Results:** Sixty-four transplant nephrologists and 46 surgeons participated. Five themes were identified: burden of responsibility (including concepts of personal accountability, policing morality, democratic decision making, meeting legal obligations, optimising outcomes and innovation, relinquished control); medical protectiveness (prognostic uncertainty, scepticism of donor risk perception, avoidance of undue coercion, concerns for dubious motivations and coercion, safeguard donor well-being, ethical information disclosure); respecting donor autonomy (facilitate informed-decision making, concede to donor risk acceptance, giving benefit of the doubt, donor mandate to maintain health, acceptable altruism); driving ideologies (preserving equity, championing living donation, cognisance of anti-paternalism); and contextual pressures (evolving donor demographic, resource limitations).
**Conclusions:** Defining acceptable risk is central to decision making regarding living kidney donors, with apparent differences among units and countries. Living kidney donor assessment involves complex negotiations between safeguarding donors and donor autonomy, as well as contending with ideological and contextual influences. Authoritative and comprehensive position

statements would support decision-making and make explicit that which is often implicit, the uncertainties and challenges of living kidney donor assessment.

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## THE BENEFITS AND COSTS OF LUMINEX TESTING FOR PREFORMED ANTIBODIES IN RENAL TRANSPLANTATION

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**Aim:** To compare the benefits and costs of using Luminex as an add-on test to CDC-crossmatch for screening donor-specific antibodies (DSA) prior to kidney transplantation.
**Background**: The Luminex technique is a useful add-on test to the CDC-crossmatch for identifying immunologically significant DSA because of improved test performance characteristics compared to CDC alone. However, the costs and benefits of Luminex as an add-on test to CDC in predicting antibody-mediated rejection (AMR) and/or graft loss are unclear.
**Methods**: A probabilistic Markov model was developed to estimate costs and benefits for Luminex as an add-on test to CDC compared with CDC alone (n = 10,000, starting age = 18+). The model terminated when all transplant recipients were deceased.
**Results**: Compared with CDC-crossmatch alone, the incremental benefits of screening DSA with Luminex as an add-on test to CDC were 0.0123 LYS and 0.0263 gain in QALYS, with savings of $7,094 over the lifetime of a transplant recipient at a selected Mean Fluorescence Intensity > 500. When varying the most influential variable (the false negative rates of Luminex) between the most and the least favourable scenario, the incremental health benefits ranged from a gain of 0.01 QALYS to a loss of 0.007 QALYS, with incremental costs ranging from a cost saving of $5,279 to an extra cost of $4,335.
**Conclusions**: Compared with CDC alone, our model analyses suggested screening with Luminex as an add-on test to CDC is cost-saving and improves the overall patient survival. However, uncertainties exist in the model's most influential variables including the test sensitivity of Luminex techniques for identifying immunologically significant DSA.

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## THE IMPACT OF DIABETES MELLITUS ON ARTERIAL STIFFNESS AFTER TRANSPLANTATION

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**Background**: Cardiovascular disease (CVD)-associated mortality is the most common cause of death with functioning graft in kidney transplant recipients (KTR) with pre-existing diabetes mellitus (DM) and new onset of diabetes after transplantation (NODAT). The development of NODAT is relatively common with a 1-year incidence of up to 39% using the American Diabetes Association diagnostic criteria. This study aims to determine whether the early development of NODAT is associated with higher arterial stiffness.
**Methods**: A prospective cohort study of 92 KTR was conducted in a single-centre between 2008 and 2012. At 3 months post-transplant, all KTR underwent an oral glucose tolerance test (OGTT, pre-transplant diabetics excluded) and measurements of arterial stiffness (aortic augmentation index [AIx] and pulse-wave velocity [PWV]) using SphymoCor system®.
**Results:** Of 92 KTR, 9 (10%) had pre-existing DM, 40 (43%) recipients developed abnormal glucose regulation post-transplant (14 [15%] had NODAT and 26 [28%] had IFG/IGT) and 43 (47%) had a normal OGTT. After adjusting for the effects of age, gender, anti-hypertensive medications, immunosuppression, blood pressure, BMI and eGFR, recipients with pre-existing DM had significantly higher log-PWV (mean difference −0.22 m/s, 95% CI −0.44, −0.02; p = 0.03) and log-AIx (mean difference −0.44%, 95% CI −0.77, −0.12; p < 0.01) compared to recipients with normoglycaemia. Log-PWV and log-AIx were similar between recipients with normoglycaemia and recipients with IFG/IGT or NODAT.
**Conclusions**: Pre-transplant diabetes but not early post-transplant IFG/IGT or NODAT was associated with higher PWV and AIx, established surrogate markers of CVD. Early identification and appropriate management of abnormal glucose regulation post-transplant may reduce long-term CVD events in these recipients.

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## GLYCAEMIC PROFILE EARLY AFTER KIDNEY TRANSPLANTATION: HIGHS, LOWS AND DIAGNOSTIC DILEMMAS

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**Aim**: To characterise the glycaemic profile early after kidney transplantation, and to assess the correlations between glycaemic profile, oral glucose tolerance test (OGTT) and HbA1c.
**Background**: The pathogenesis of hyperglycaemia after kidney transplantation differs from diabetes in the general population. Diagnostic and monitoring strategies extrapolated from general population studies may therefore not be appropriate.
**Methods**: We recruited patients undergoing kidney transplantation at a single centre over 2011–13, and measured glucose with a continuous glucose monitor (CGM) that samples interstitial glucose every 5 minutes. CGM was performed during the first 6 days post transplant and at months 3 and 6. We defined hypoglycaemia as glucose < 3.5 mmol/L and hyperglycaemia as glucose ≥ 11.1 mmol/L.
**Results**: CGM recordings were available for 27 patients at transplant (mean age 44 ± 16.2), 23 at month 3 and 18 at month 6. At transplant 7/27 had ≥1 hypoglycaemic episode and 24/27 had ≥1 hyperglycaemic episode. At month 3 7/23 had ≥1 hypoglycaemic episode, none associated with hypoglycaemic therapy; and 13/23 had ≥1 hyperglycaemic episode. Three of these 13 patients had a normal OGTT. At month 6 4/18 had hypoglycaemia (3 not on hypoglycaemic therapy) & 3/18 had hyperglycaemia. OGTT results at month 3 correlated with nocturnal (P = 0.03) but not peak glucose (P = 0.09). HbA1c correlated poorly with mean glucose at month 3 (P = 0.1) but well at month 6 (P = 0.004).
**Conclusions**: Hypoglycaemic and hyperglycaemic excursions are very common early after kidney transplantation. A normal 3-month OGTT does not exclude hyperglycaemia. HbA1c should not be used to monitor glycaemic control in the first 3 months post-transplant.

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## CONVERSION FROM CALCINEURIN-INHIBITOR TO MAMMALIAN TARGET OF RAPAMYCIN INHIBITORS FOR MAINTENANCE IMMUNOSUPPRESSION IN KIDNEY TRANSPLANT RECIPIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED TRIALS

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**Aim**: A systematic review of randomized trials where maintenance immunosuppressive regimens containing mammalian target of rapamycin inhibitors (mTOR-I) were compared with regimens containing calcineurin-inhibitors (CNI) for kidney transplant recipients.
**Background**: Trials comparing the *de novo* use of mTOR-I to the use of CNI in kidney transplantation have largely been disappointing. The clinical benefit of the conversion from CNI to mTOR-I remains unclear.
**Methods**: Databases (2000–2011) and conference proceedings (2009–2011) were searched. Results are expressed as relative risk (RR), and for continuous outcomes are expressed as weighted mean difference (WMD), both expressed with 95% confidence intervals (CI).
**Results**: Twenty-two trials were included (13 trials of sirolimus and 9 of everolimus). Compared with CNI, mTOR-I was associated with higher mean estimated glomerular filtration rate (eGFR) at 12 months with WMD of 3.68 mL/min (95%CI 1.67, 5.70; p < 0.01; intention to treat analysis [ITT]), with similar findings for early (<12 months) and late conversion. In the on-treatment analysis up to 5-years post-transplant, mTOR-I was associated with higher mean eGFR compared to CNI with WMD of 14.37 (95%CI 9.69, 19.05; p < 0.01). Biopsy proven acute rejection was higher in the mTOR-I group at 12 months (RR 1.96; 95%CI 1.46, 2.62; p < 0.01), but not beyond 5 years. For graft loss between 2 and

5 years post-conversion, mTOR-I was associated with a lower risk of graft loss (RR 0.45, 95%CI 0.22, 0.95; p = 0.04). For adverse events, there was a greater relative risk of drug discontinuation, oedema, proteinuria, pneumonitis and hyperlipidemia at 12 months with mTOR-I.
**Conclusions**: This meta-analysis has demonstrated that surrogate endpoints for graft survival favoured mTOR-I but risk of adverse events and drug discontinuation is higher for mTOR-I.

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**Abstract withdrawn**

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## LIFETIME RISK FOR END STAGE RENAL DISEASE IN A REMOTE ABORIGINAL COMMUNITY: EFFECT OF DIABETES

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**Aim**: The aim of this study was to assess the effect of diabetes on the lifetime risk of ESRD in Aboriginal people.
**Background:** The incidence of end stage renal disease (ESRD) in Aboriginal Australians in remote regions is among the highest in the world.
**Methods:** In this cohort study, 1390 participants in a remote Aboriginal community (>85% ascertainment) who were free from ESRD at baseline, were followed for up to 20 years. Participants with diabetes before developing ESRD and those with diagnosed ESRD during the follow-up period were identified through hospital records. Lifetime risks of ESRD in people with and without diabetes were estimated after adjusting for the competing risk of death due to non-ESRD causes.
**Results:** Among participants, 235 were diagnosed with diabetes at baseline or before the diagnosis of ESRD and 67 developed ESRD during the follow-up period. The overall lifetime risk of ESRD was 19% (95%CI: 14, 23). The lifetime risk for those without diagnosed diabetes was 7% (95%CI: 4, 11) while the estimates of lifetime risk for those with diabetes were 41% (95%CI: 32, 50). The population attributable risk associated with diabetes was as high as 62% (95% CI: 44, 74).
**Conclusions:** About 1 in 5 in the study population will have ESRD during their lifetime in comparison to 1 in 40 to 60 Canadians and white Americans. The lifetime risk of ESRD among people with diabetes in this remote Aboriginal population is very high, about 1 in 2. Our findings imply that a large proportion of ESRD in such a high risk population are associated with diabetes. Thus they are potentially preventable by appropriately managing and preventing diabetes.

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## QUANTITATIVE ANALYSIS OF TOTAL KIDNEY VOLUME IN ADPKD USING 3D SLICER

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**Aim:** To determine the feasibility of quantifying total kidney volume (TKV) using 3D SLICER in human autosomal dominant polycystic kidney disease (ADPKD).
**Background:** TKV, as determined by magnetic resonance imaging (MRI) is a surrogate marker of disease severity and risk for progression in ADPKD. However, the method and difficulty of calculating TKV is not well described in the literature. 3D Slicer is an open source medical image computing platform that may be suitable for the analysis of TKV.
**Method**: Renal MRI was performed in a prevalent ADPKD population from Western Sydney (GFR stages 1–3, n = 18). MRI was performed at 4 mm sequences, and images were transferred to a workstation where the renal outline of each cross-sectional sequence was manually traced, and processed using 3D Slicer. TKV was also calculated by ultrasound (US) using the ellipsoid formula.
**Results**: The mean time taken to perform the analysis using 3D SLICER by a single operator was 9.4 ± 0.45 minutes per kidney (mean ± SD). The mean TKV and height-adjusted TKV (ht-TKV) were 1409 ± 801.5 and 849.3 ± 34.9 $cm^3/m$ respectively, and volumes were similar on both sides (right:739.9 ± 473.4; left:702.9 ± 330.0 $cm^3$). There was a strong negative correlation between ht-TKV and eGFR (CKD-EPI, r = 0.653 p = 0.02). Values for ht-TKV estimated by MR and US were similar, and strongly correlated with each other (r = 0.973, P < 0.001).
**Conclusion**: The analysis of MR images by 3D SLICER is a rapid and simple method to quantify ht-TKV that has strong inverse correlation with eGFR. Although TKV estimated by MR and US are similar, the former is more suitable for monitoring disease progression in ADPKD due to its greater technical precision.

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## TRENDS IN HEALTH STATUS AND CHRONIC DISEASE RISK FACTORS OVER 10–14 YEARS IN A REMOTE AUSTRALIAN ABORIGINAL COMMUNITY: A MATCHED PAIR STUDY

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**Aim:** To determine trends in health status over a 10-year interval in a remote Australian Aboriginal community.
**Background:** Remote-living Australian Indigenous people have high rates of chronic disease. There is limited systematic evidence of trends in risk factors and disease markers over time.
**Methods**: Health screens were performed between 1992–1997 and 2004–2006 in one high risk community, with >85% ascertainment of people age ≥5 years. Outcomes were compared across age and sex-matched pairs.
**Results:** 1209 subjects were matched. In both sexes, on the second screen, there were significant increases in birthweight, in adolescent and young adult height, and in HDL-c levels, and 30.4% and 34% of adults had prescriptions for angiotensin-covering enzyme inhibitors and hypoglycaemic agents, respectively. Furthermore, the census showed higher numbers and proportions of people age 55+ years in the community. Males age 15–44 yrs had lower weight, BMIs, waist and waist-hip ratios, SBP and DBPs, and levels of overt albuminuria and triglycerides. However, on the second screen, females more often drank alcohol, had higher weight, waist and WHR, high proportions of diabetes, especially in those aged 45+ years. Over the same interval, we know that death rates have fallen substantially, especially in those aged 55+ years.
**Conclusions:** There are many encouraging trends in these data. The weight increase in females, in theory undesirable, might reflect better food access. Higher proportions of diabetes in older females probably reflect the recent reductions in

death rates in middle-age subjects, achieved through better chronic disease treatment, and improved overall health. The trade-off for this welcome improved longevity is older people needing chronic disease treatment.

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## SCREENING AND STAGING OF CHRONIC KIDNEY DISEASE: AN AUDIT IN ABORIGINAL PEOPLE OF THE GOVE REGION IN 2011–2

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**Aim:** To audit the screening and staging of chronic kidney disease (CKD) against the Kidney Health International (KHI) guidelines in an Aboriginal health service in the Gove Region of the Northern Territory in 2011–2.
**Background:** Under the KHI guidelines, all people of Aboriginal origin over the age of 30 should receive kidney health checks (blood pressure, eGFR, urine ACR) at least every two years. If problems are detected, the guidelines specify how to stage the disease.
**Methods:** Electronic records of current Aboriginal patients >30 years old were queried for blood pressure, eGFR and ACR readings, and whether elevated ACR results had been followed up as per KHI guidelines. Where patients had an existing diagnosis of CKD with albuminuria, the validity of the staging was assessed.
**Results:** A total of 310 individuals met the audit criteria for inclusion. Comprehensive screening for CKD was conducted in 45% of eligible patients. Albuminuria was detected in 108 patients (35%), and persistent albuminuria confirmed in 68 (22%). In patients with no history of CKD, screening revealed 22 had an elevated ACR. Of these, 68% received adequate follow-up to confirm or rule out persistent albuminuria, revealing 45% had previously undiagnosed CKD. Of 86 patients with existing diagnoses of CKD, 22% needed their stage adjusted, 17% had diagnoses with inadequate evidence, and 11% had adequate evidence to revoke their diagnoses.
**Conclusions:** Screening and management of CKD could be improved by regular in-service training to ensure staff are familiar with and correctly applying the guidelines. Diagnoses of CKD should include the evidence on which they were based, and patients with CKD should be reviewed regularly to ensure their staging remains accurate.

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## INCIDENCE AND CLINICAL SYNDROME OF IgG4-RELATED TUBULOINTERSTITIAL NEPHRITIS IN 2 TERTIARY HOSPITALS IN SOUTH WESTERN SYDNEY

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**Aim:** To describe the clinical syndrome of IgG4-related tubulointerstitial nephritis (IgG4 TIN) (without membranous nephropathy) in South Western Sydney.
**Background:** Although systemic IgG4 related disease is rare, IgG4 TIN is the most common renal manifestation. The disease is usually associated with diffuse organ involvement, multiple renal low attenuation lesions, immune activation and elevated serum IgG4 levels. The incidence of IgG4 TIN may be underestimated as staining for IgG4 is not routinely performed on renal biopsies.
**Methods:** A retrospective review (2002–2012) of renal biopsies with prospective specimen staining to diagnose IgG4 TIN was done. Biopsies with a primary diagnosis of interstitial nephritis were selected and those with glomerular disease were excluded. Sections were stained using an established technique with an IgG4 specific monoclonal antibody. Simultaneous demographic and clinical details were collected. This study was approved by Sydney South West Local health district (SSWLHD) ethics committee.
**Results:** There were 89 cases of interstitial nephritis from 1238 renal biopsies (2002–2012). In 2012, 11/124 renal biopsies had interstitial nephritis. 3/11 cases stained positive for IgG4. Of these 3 patients, 2 were south Asian females-aged 22, asymptomatic with serum creatinine (sCr) 167 umol/L and aged 46 undergoing treatment for tuberculosis with sCr 180 umol/L respectively. The third patient was a 74 year old Caucasian male with interstitial lung disease who required renal replacement therapy (sCr 700 umol/L). A presumptive diagnosis of drug related interstitial nephritis was made before treatment and corticosteroids was given resulting in overall improvement of renal function (sCr < 100 umol/L).
**Conclusion:** A significant proportion of IgG4 TIN which is thought to be drug related. IgG4 staining would impact on patient management when routinely done in TIN.

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## A COMPARISON OF PBS MEDICATIONS IN TWO REMOTE CENTRAL AUSTRALIAN ABORIGINAL COMMUNITIES

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**Aim:** To compare costs of medications related to chronic disease care supplied through the PBS S100 program in two remote Aboriginal communities, from data provided by Medicare.
**Background:** Special arrangements exist to provide to clients in remote communities access to medications listed in the PBS at no cost (S100). These have been in place since 1999 and approximately 170 community controlled and state/territory operated remote health services participate. There are few reports on conduct or outcomes of this program.
**Methods:** Data were obtained from Medicare comprising PBS numbers for, and costs of, items dispensed in two remote Northern Territory Aboriginal health services (C1, population > 600; C2, population > 4500) from October 2011 through September 2012. We determined dispensing costs per drug and for all drugs for each community. Profiles of drug issuance by drug type were developed using associated WHO-published Anatomical Therapeutic Chemical (ATC) Classification System codes and a purpose-oriented coding system (WH) developed in house.
**Results2:** In C1 and C2, total costs were $165,596.85 and $1,434,134.80, respectively, of which lipid-lowering drugs were 21.1% and 16.9%, diabetes-related drugs 16.7% and 22.5%, BP-lowering drugs 14.7% and 8.8% (60% of these being ACEi or ARBs), and lung disease-related drugs 8.3% and 7.8% respectively using WH codes. Cardiovascular System and Alimentary Tract and Metabolism drugs accounted for >50% of costs in both communities (ATC); >60% of costs were CD-related (WH). Anti-infection drugs represented 12–16% of costs in these communities.
**Conclusions:** The high proportions of dispensing costs for chronic-disease related drugs and the relatively low proportions of anti-infection drugs mark the transition in health status in these remote Aboriginal communities and the gratifying strengthening of systematic chronic disease services.

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## THE RELATIONSHIP BETWEEN BODY BUILD, COMPOSITION AND KIDNEY DAMAGE IN ABORIGINAL AND TORRES STRAIT ISLANDER PEOPLES

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**Background:** In order to address morbidity related to chronic kidney disease in Indigenous Australians, it is important to understand key risk markers, including obesity. In other populations, abnormal adipokine profiles are linked with cardiovascular disease risk.
**Methods:** In a cohort of non-dialysing adults, 465 Aboriginal and 128 Torres Strait Islander (TSI) adults voluntarily provided: serum creatinine, CRP, adiponectin, leptin, urine (albumin to creatinine ratio), anthropometry and resistance. eGFR, body mass index (BMI) and waist to hip ratio (WHR) were calculated.
**Results:** Participant characteristics were: age (mean (SD)) 45(15) years; 40% diabetes, 18% eGFR < 60 ml/min/1.73 $m^2$; 45% albuminuria (although Aboriginal v TSI = 48 v 34%, p = 0.01).

Mean differences between groups in weight (10 kg), BMI (3.7 $kg/m^2$) and resistance (100 ohms (all $p < 0.001$) was consistent with Aboriginals having lower lean mass for size than TSI group. A more centralised pattern of fat distribution in Aboriginal than TSI men and women was seen.

Aboriginal participants had higher median CRP (Aboriginal v TSI = 6 v 3 mg/L, $p < 0.0001$). Higher adiponectin and leptin concentrations were observed in females (than males, $p < 0.001$), and with kidney damage (higher ACR, $p < 0.001$; lower eGFR, $p < 0.001$).

BMI, waist, WHR, low adiponectin and high leptin clustered together in factor analysis in non-diabetic adults. Multivariate regression analysis indicated

adiponectin concentrations was linked to kidney impairment (low eGFR, high ACR, eGFR*ACR) and inversely with CRP, WHR, waist and male gender ($R^2 = 0.25$).
**Conclusion:** Aboriginal participants had a stronger tendency to central obesity, and showed lower lean mass for size than TSI group. Total and central adiposity most strongly associated with an abnormal adipokine profile, even after controlling for kidney damage. Weight management is therefore an important modifiable risk marker in Indigenous Australians.

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## MOLECULAR CHARACTERISTICS OF RENAL CELL CARCINOMA – A STUDY USING TRAF-1 AND A MALAYSIAN PATIENT COHORT

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**Aim:** To compare tumour necrosis factor receptor-associated factor-1 (TRAF-1) expression in normal kidney, renal cell carcinoma (RCC) tissue, and serum from control and RCC patients from the University of Malaya Medical Centre (UMMC).
**Background:** RCC generally has poor prognosis because of late diagnosis and metastasis. Development of new RCC biomarkers identifying and predicting progression of RCC is necessary. We have described decreased TRAF-1 in an RCC patient cohort from Princess Alexandra Hospital, compared with normal kidney. The TRAF-1 signalling pathway is necessary for immune response and apoptosis regulation. A Malaysian patient population was sourced to commence a multi-centre study.
**Methods:** Immunohistochemistry with automated batch staining, and Aperio ImageScope morphometry (positive pixel counts/PPC) were used to compare TRAF-1 in 75 RCC patients from UMMC (69 clear cell RCC/ccRCC, 4 papillary, 1 chromophobe, and 1 oncocytoma) with normal kidney tissue. Serum from 15 ccRCC and 15 healthy people were tested for TRAF-1 (ELISA). ANOVA with Tukey's post-hoc (tissue) and Mann-Whitney U-test (serum) were used (mean ± SEM).
**Results:** Compared with normal kidney (168512 ± 6166 PPC), ccRCC was lower (82591 ± 5646) and chromophobe was higher (324959 ± 8267) ($p < 0.05$). There was no significant difference with papillary (182405 ± 13314) or oncocytoma (216386 ± 24985). There was a significant difference between chromophobe and oncocytoma, two kidney cancers that are difficult to differentiate. TRAF-1 in serum from ccRCC patients was significantly increased over normal serum (202.28 ± 74.58 vs 50.63 ± 13.56; $p = 0.012$).
**Conclusion:** Lower TRAF-1 in ccRCC, seen previously, was confirmed. Significantly increased serum TRAF-1 may indicate the protein is actively secreted from developing ccRCC. Serum TRAF-1 may be a useful non-invasive indicator of RCC development. Results from other RCC subtypes, like the distinctly-increased expression in chromophobe RCC, need further study.

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## SURVEY OF RENAL TRAINING IN METROPOLITAN VS NON METROPOLITAN AREAS

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**Aims:** Assess the overall experience of advanced renal training in rural areas on future career pathways. To give future trainees realistic information regarding training in a rural setting and potentially change perceptions of training in non-metropolitan settings.
**Background:** The recent increased interest in nephrology training has resulted in insufficient training positions in metropolitan areas. This has resulted in trainees looking further afield for training opportunities. Information on training in rural areas is limited. This is the first survey of renal physicians who have trained in non-metropolitan hospitals and will provide information regarding their training experience in non-metropolitan hospitals.
**Methods:** All non-metropolitan units were asked to provide names of trainees over the last ten years. A web-based questionnaire on various aspects of nephrology training was sent to identified physicians who had trained in non-metropolitan units as well as placed in the ANZSN newsletter. A total of 12 out of 15 Physicians responded.
**Results:** In the domains of hypertension, CKD, Haemodialysis, Conservative care pathway and AKI > 50% thought rural training experience was similar to metropolitan training. In the domains of chronic transplant, GN, Obstetrics medicine 45% thought management of was inferior while 36% found it similar. PD was thought to be similar or inferior by 36% while 27% thought it was superior. Indigenous health and general medicine rated superior (63–72%). 75% were involved in research. 100% trainees performed native renal biopsies with 66% transplant biopsies and 8.3% CT guided biopsy.75% inserted non cuffed catheter and 66% cuffed catheters. 16% inserted PD catheters. 75% performed renal ultrasound and 50% performed fistula ultrasound.16.6% performed fistulogram / fistuloplasty. 83% thought rural training was a positive experience and for 66.6% it enhanced their career prospects. 27% had a negative impact on their personal life. Although 41% thought rural training should be mandatory while 50% did not.
**Conclusions:** The majority of trainees found rural training a positive experience and enhanced their career pathways.

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## AUDIT COMPARING ULTRASOUND GUIDED PERCUTANEOUS NATIVE KIDNEY BIOPSY PERFORMED BY INTERVENTIONAL RADIOLOSIST WITH THOSE PERFORMED BY NEPHROLOGISTS AND NEPHROLOGY TRAINEES

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**Aim:** To compare ultrasound guided percutaneous native kidney biopsies performed by Interventional Radiologists with those performed by Nephrologists and Nephrology Trainees.
**Background:** Percutaneous Kidney biopsies have been performed by Nephrologists since 1951. Recent widespread availability of real-time imaging guidance using ultrasound has improved perceived safety of the procedure. There has been a change in practice with ultrasound guided kidney biopsies being performed increasingly by Interventional Radiologists resulting in deskilling of Nephrologists and reduced opportunities for Nephrology Trainees.
**Methods:** Retrospective audit was done comparing all ultrasound guided percutaneous native kidney biopsied performed by Interventional Radiologists at Auckland hospital from February 2010 to December 2011 with those done by the Nephrologists and Nephrology trainees at Northshore Hospital from December 2010 to January 2013. Data collected and compared included age, sex, ethnicity, weight, indication for biopsy, renal function test, needle size, number of passes, side and site of biopsy, number of glomeruli obtained, complications, risk factors for complication, outcome of complication, length of stay and diagnosis.
**Results:** There were 97 patients in Radiologists group and 74 patients in the Nephrologists group. Complication rates were 13.4% in Radiologists group and 8.1% in Nephrologists group; there were no statistical difference in complication rate between the groups. 2 patients in Radiologist group with perinephric hematoma required renal artery embolisation. No patients in Nephrologists group required any intervention. Complication rates noted in both groups were similar to published data.
**Conclusions:** Biopsies done by both Radiologists and Nephrologists meets the standards in published data. Kidney biopsy can be safely and successfully done by Nephrologists and Nephrology trainees under ultrasound guidance. Only minor complications noted with careful selection of patients.

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## AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE IN AN AUSTRALIAN CHRONIC KIDNEY DISEASE (CKD) POPULATION

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**Aim:** To describe characteristics of CKD due to Autosomal Dominant Polycystic Kidney Disease (ADPKD) in four public renal specialty practices in Queensland.
**Background:** ADPKD is the most common potentially lethal Autosomal Dominant condition with a prevalence of 1/400-1000. Those with CKD are not well described within Australasia.

**Methods:** The CKD.QLD registry from four sites, comprising 2167 patients, was searched for all cases of ADPKD.
**Results:** 83 cases of ADPKD were identified (3.8% of all patients). Prevalence was similar at each site (3.5%-4.3%). Those with ADPKD in the CKD.QLD registry more broadly were most commonly CKD Stage 3B. Those with ADPKD were more commonly CKD Stages 1 and 2 compared to the CKD.QLD cohort (33.7% vs 13.6%).

Gender was equal in the ADPKD (M : F 49% vs 51%) and CKD.QLD (51% vs 49%) cohorts. Women with ADPKD were most commonly CKD stages 4, 2 and 1 (28.6%, 26% and 19% respectively). Men were most commonly CKD Stages 3B, 3A and 2 (31.7%, 19.5%, 17%).

ADPKD patients were younger than the overall CKD.QLD cohort (mean 53.7 vs 64.9 yrs). The most common ADPKD age group was 45–54 yrs (21.7%) whereas in the CKD.QLD cohort it was 65–74 yrs (28.7%). Women with ADPKD were older than men (M : F 49.4 vs 58 yrs). ADPKD patients ≥75 yrs only had CKD Stages 3B-5. Conversely, ADPKD patients <24 yrs only had CKD Stages 1–2.
**Conclusions:** Those with ADPKD are younger than the general CKD population with a unique pattern of CKD Stage related to both age and sex. These require further investigation, including assessment against ADPKD patients in Renal Replacement Therapy Registries. Genotypic studies will increase understanding of subgroups of ADPKD patients.

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## PATIENTS' ATTITUDES TOWARDS LIVING KIDNEY DONATION: SYSTEMATIC REVIEW AND THEMATIC SYNTHESIS OF QUALITATIVE RESEARCH

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**Aim:** To describe the beliefs, attitudes, and expectations of patients with chronic kidney disease (CKD) towards living kidney donation.
**Background:** Living kidney donation can yield better clinical outcomes for recipients compared with deceased kidney donation or dialysis. However, the risk to donors means patients face complex decisions regarding living kidney donation.
**Methods:** We conducted a systematic review of qualitative studies of patients' attitudes towards living kidney donation using a comprehensive literature search to February 2013. Thematic synthesis was used to analyse the findings related to living kidney donation prior to transplantation.
**Results:** Thirty-five studies involving 1456 patients with CKD (stages 1–5) were included. We identified five major themes: prioritising health (better graft survival, urgency and desperation); shifting relationship dynamics (strengthened bonds, alleviating family burden, unrelenting indebtedness, tension and conflict); burden of responsibility (perceived minimal risk, jeopardising donor health, imposing financial burden, overwhelmed by prognostic uncertainty and anticipating donor regret); respecting socio-cultural norms (religious altruism, trust in doctors and medicine, violation of God's creation, family loyalty); and an onerous request (vulnerability, honesty and respect, disappointment of rejection, uncertainty in method of approach and decisional pressure and coercion).
**Conclusions:** Patients with CKD believe that living kidney donation can offer a lifesaving treatment with minimal medical risk to themselves or donors. However, patients anticipate burdens of guilt and responsibility, particularly if graft failure and donor complications occur. Also, they express concerns about donor-recipient relationship tensions caused by indebtedness. Some patients had reservations about the concept of living kidney donation and initiating discussions with potential donors. Clarifying, validating and addressing these concerns, coupled with education and psychosocial support can empower patients to make informed decisions about living kidney donation.

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## VALUE OF 3- AND 12-MONTH SURVEILLANCE RENAL TRANSPLANT BIOPSY: A SINGLE CENTRE 5-YEAR STUDY

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**Aim:** To evaluate the benefit of renal transplant surveillance biopsy (SB) at 12 months (M) in patients with stable renal function and normal 3M SB.
**Background:** Our patients routinely undergo SB at both 3 and 12M to evaluate graft function.
**Methods:** Retrospective analysis included all patients transplanted between 2007 and 2011, with both 3- and 12M SBs on-site. Immunosuppression protocols were constant. The primary endpoint was histological evidence of rejection at 12M (Banff criteria).
**Results:** Of 592 transplant recipients, 241 fit inclusion criteria. Mean age was 48.4 ± 12.6 years, 65.6% male and 85.5% were first grafts. Major reasons for exclusion were: transfer to another centre (149/351), patient declining either SB (109/351) and medical decision against SB (93/351).

41 (17%) had subclinical acute cellular rejection (ACR) ± glomerulitis (g1) at 3M and were treated. At 12M SB, 30/41 had no rejection but 11/41 had subclinical ACR.

12M SB in 200 patients with normal 3M SB was normal in 181, with subclinical ACR detected in 19 (9.5%). Treatment was modulated in response to the normal 12M SB in 22.7%; usually with calcineurin inhibitor dose reduction. SB complication rate was 2.7%. No patient refused 12M SB after complication at 3M.

Estimating SB cost at $3000/episode, our total cost of 12M SB in patients with normal 3M SB was $600,000, and found treatable pathology in 19 patients. Per patient, this is less than the differential 1-year cost between transplantation and return to dialysis.
**Conclusion:** 3M SB revealed unsuspected pathology in 17% of patients. After a normal 3M SB, 12M SB was abnormal in 9.5% of patients. These results justify unit SB policy, provided the procedural complication rate is low.

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## PUBLIC AWARENESS AND ATTITUDES TO LIVING ORGAN DONATION: SYSTEMATIC REVIEW AND INTEGRATIVE SYNTHESIS

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**Aim:** To synthesise studies on public awareness and attitudes toward living organ donation.
**Background:** The deceased donor organ shortage has driven widespread adoption of living donor transplantation. Yet, public views on living donation are not well understood.
**Methods:** Electronic databases and reference lists were searched to September 2012. Summary estimates from survey data were obtained by random effects meta-analysis. Qualitative descriptive synthesis of each study was performed.
**Results:** Forty-seven studies involving 34 610 respondents were included. The proportion of respondents aware of living organ donation was 76.7% (4 studies, n = 3248; [95%CI: 46.2% to 97.0%], $I^2$ = 99.7%). The majority were in favour of living directed donation (85.5% (11 studies, n = 15,836; [CI: 81.6% to 89.6%], $I^2$ = 98%), with recipient and community benefit as the rationale provided. However, barriers included fear of surgical and health risks, lack of knowledge, respect for cultural norms, financial loss, distrust in hospitals, and avoiding recipient indebtedness. The public voiced concern about possible risks or an obligatory pressure exerted on the donor. Many supported reimbursement for out-of-pocket expenses, paid leave, waitlisting priority, health insurance and donor acknowledgement. There was strong opposition to financial incentives which they believed risked exploitation, inequity, and diminished voluntary altruistic donation.
**Conclusions:** The public is generally supportive of living donation and articulated important equity and ethical considerations for protecting the health and safety of living donors. This supports increased public engagement and strengthening of a shared view among professionals and the public in living donation practice and policy.

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## RACIAL VARIATION IN PAEDIATRIC TRANSPLANT OUTCOMES

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**Aim:** To investigate racial disparities in post-transplant outcomes for paediatric patients in Australia.
**Background:** Disadvantaged racial groups have lower transplantation rates and poorer post-transplant outcomes in Australia and elsewhere. Disparities in transplant outcomes for paediatric patients have been found in the USA and Canada, but have not been investigated in detail in Australia.
**Methods:** We used Cox models with baseline hazard stratified by donor source to investigate patient and graft survival, and time to first rejection episode for all patients who received a primary transplant when aged <18 in Australia 1990–2011, using ANZDATA. We also investigated uptake of second transplant among patients with a failed graft.
**Results:** In total, 524 Caucasian, 20 Indigenous and 87 paediatric patients of other races received a primary graft during the study. Only 53 patients died. Caucasian patients were most likely to receive a live-donor graft, were less sensitised, had fewer HLA mismatches and spent less time on dialysis before transplantation ($P < 0.03$). After adjusting for these effects, death-censored graft survival did not vary between races for the first 3 years (HR = 0.3, 95%CI 0.4–2.0, P = 0.2), but after that, Indigenous patients were more likely to lose a graft (HR = 4.8, 95% CI 2.3–9.8, $P < 0.001$), compared to Caucasian patients. Indigenous patients were possibly at increased risk of rejection (HR = 1.9, 95%CI 0.8–4.6, P = 0.1), but not of death (HR = 0.5, 95%CI 0.1–2.3, P = 0.4). Indigenous patients were less likely than Caucasians to receive a second graft after graft failure (unadjusted HR = 0.1, 95%CI 0.0–0.6, P = 0.01).
**Conclusions:** Indigenous paediatric transplant recipients are more likely to suffer graft failure, and less likely to receive a second graft. Further research is required to identify and address the causes of these disparities.

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## PREFERRED OUTCOMES FOLLOWING IMMUNOSUPRESSION AMONG KIDNEY TRANSPLANT RECIPIENTS

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**Aim:** To evaluate transplant recipient preferences for outcomes after transplantation using a best-worst scale survey.
**Background**: Patient-centred research and clinical care requires knowledge of the priorities and trade-offs individuals are willing to make to achieve important outcomes.
**Methods**: Kidney transplant recipients were shown 20 scenarios which contained a list of 9 outcomes including graft survival and the risk of dying before graft failure, serious adverse events and drug related side effects and asked to choose the best and the worst outcome for each scenario. Surveys have been mailed, handed out with explanation, emailed with an option to complete on-line and structured interviews from a convenience sample. Responses are analysed using: a multinominal logit (MNL) model to evaluate relative importance and trade-offs between outcomes.
**Results**: To date 63 recipients (35–73 years) have been recruited. The time since transplantation ranged from <6 months to 18 years with 52% receiving living donor organs and only 8% being pre-emptively transplanted. The MNL model suggests that a 10% increased risk of cancer, cardiovascular disease or serious infection is equated to 4.5 to 5 years of graft survival, diabetes to 3 years and drug related side effects to 1.9 years for nausea and diarrhoea and less than 1 year for excessive weight gain and appearance. The risk of dying with a functioning graft was equated to 2.6 years graft survival.
**Conclusion**: Transplant recipients are willing to accept a high probability of serious outcomes and side effects to maximize graft survival. Aversion of returning to dialysis is reflected in the low importance placed on the risk of dying with a functioning graft and the trade-off between graft survival and overall survival.

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## OBESITY AS A BARRIER TO RENAL TRANSPLANTATION: A MULTIDISCIPLINARY WEIGHT LOSS STUDY

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**Aim:** To pilot a group weight loss program for CKD patients who had previously failed to lose weight independently.
**Background:** For dialysis patients, renal transplantation is the goal due to its advantages over dialysis in survival, quality of life and morbidity. This study aimed to facilitate weight loss using a multidisciplinary approach in patients, whose only barrier to transplantation was their BMI, based on the current requirements for transplantation workup.
**Method:** This was a longitudinal, single centre, prospective, cohort study. Nine patients (Age M = 43.2 years, range: 32–56) with a BMI > 30 kg/m$^2$ (M = 36.6 kg/m$^2$, range: 33.2–40.7) were enrolled in the study. The group attended monthly assessments with a dietitian and physiotherapist and four group education sessions. At baseline, six and twelve months, participants completed the Fatigue Severity Scale, Kidney Disease Quality of Life questionnaire and a six-minute walk test.
**Results:** Seven participants lost weight and reduced BMI. Average individual weight and BMI change was –4.8 kg (range: –11.0–0.8) and –1.8 kg/m$^2$ (range: –4.3–0.4), respectively, at 12 months. Average waist circumference change was –4.6 cm (range: –12–1.5). This was achieved despite a concurrent increase in fatigue, reduction in exercise capacity and deterioration in some domains of the KDQOL. Four patients achieved transplantation and one patient is active on the transplant list.
**Discussion:** Implementing a diet and lifestyle modification program using a multidisciplinary approach, resulted in successful weight and BMI reduction in seven patients. These outcomes were achieved despite participants experiencing multiple barriers related to disease progression and co-morbidity. This suggests the need for potential transplant recipients to commence weight reduction in earlier stages of CKD.

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## SOUTH AUSTRALIAN AND NORTHERN TERRITORY INDIGENOUS TRANSPLANT OUTCOMES, 2001–2011

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**Aim:** To identify factors contributing to indigenous renal transplant recipient (RTR) outcomes in the first two years post transplantation.
**Background:** Indigenous RTRs have worse outcomes than non-indigenous recipients following renal transplantation, particularly in the first two years post transplantation.
**Methods:** Retrospective review of outcomes in the first two years post transplant for indigenous RTRs from the Northern Territory (N.T.) and South Australia (S.A.) transplanted between 2001 and 2011.
**Results:** 95 indigenous RTRs received 97 renal allografts during this period, at a mean age of 46.6 years. 44 and 53 grafts were transplanted in S.A. and N.T. patients respectively. Pretransplant comorbidities included ischaemic heart disease 32/95 (34%) and diabetes mellitus 55/95 (58%). 45/97 (46%) of renal transplant episodes experienced at least one episode of rejection including vascular rejection in 26/97(27%). 18/97 (19%) of renal transplant episodes received anti thymocyte globulin for treatment of rejection. 23/97 (24%) of renal transplant episodes had cytomegalovirus viraemia +/– disease. After the first two years post transplant19/95 (20%) of indigenous RTRs were deceased and an additional 6/95 (6%) had returned to dialysis. 14/19 (74%) of deaths and 1/6 (17%) of returns to dialysis were secondary to infection. Infectious deaths were due to bacterial 5/14 (36%), fungal 5/14 (36%), viral 1/14 (7%) infections and no organism was isolated in 3/14 (21%).
**Conclusions:** In the first two years post renal transplant, mortality is high, predominantly due to infectious causes. A greater understanding of the contributing factors to transplant outcomes with a focus on infection is required to improve transplant outcomes in indigenous RTRs.

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## OUTCOMES OF TASMANIAN LIVING KIDNEY DONORS

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**Aim:** To examine the clinical outcomes of Tasmanian living kidney donors.
**Background:** Use of living kidney donors is common in Australia. Awareness of local, long-term donor outcomes is critical. Tasmania has the highest rate of living kidney donation of all Australian states, however it also boasts poor health determinates and a high rate of chronic kidney disease. This study examined the health outcomes of Tasmanian kidney donors.
**Methods:** We performed a retrospective review of all Tasmanian living kidney donors from 1 January 1978 till 31 December 2012. Names and follow up data were obtained from three sources; the treating hospitals (Royal Hobart Hospital and Launceston General Hospital), the transplant unit of the Royal Melbourne Hospital, and the Australia and New Zealand Dialysis and Transplant living kidney donor Registry (ANZDATA).
**Results:** We identified 108 donors, 65% (n = 70) were female and median age at donation was 52 years (range: 26–72).

Follow-up data was available on 82% (n = 89) of patients. Median time since donation was 4 years (range: 1–24). Two (2%) had died (non-renal related), nine (10%) developed new hypertension, and one (1%) developed microalbuminuria. No donors required renal replacement therapy. Median eGFR at last follow-up was 59.6 ml/min (range: 38–121). Forty-one (47%) had an eGFR 45–60 mls/min and six patients (7%) had an eGFR <45 mls/min.
Follow-up eGFR was negatively associated with age ($r = -0.30$, $p < 0.01$).
**Conclusions:** The majority of Tasmanian kidney donors have reasonable GFR at follow-up. New onset hypertension and microalbuminuria suggests long-term annual follow-up is vital for prompt detection and management of chronic disease risk factors.

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## LIVING DONOR KIDNEY TRANSPLANTATION: A COMPARISON BETWEEN PRE-EMPTIVE AND DIALYSIS-DEPENDENT PATIENTS

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**Aim:** To compare the outcomes of pre-emptive live donor kidney transplants with those performed after the commencement of dialysis.
**Background:** 35% of live donor kidney transplants are performed pre-emptively in Australia. Registry data shows that shorter duration of dialysis prior to transplantation is associated with improved allograft survival with the best survival seen in those transplanted pre-emptively. We investigated to determine whether improved graft survival was evident in recipients of a pre-emptive transplant at our centre.
**Methods:** A retrospective study of all living donor transplants at RMH between Jan 2000 and Oct 2012 was performed to assess differences in graft function and survival.
**Results:** Of 394 living donor transplants (including 49 ABO incompatible), 135 (34%) were pre-emptive and 259 (66%) were for those on dialysis. Pre-emptive patients had a mean eGFR of 9.11+/–3.6ml/min/1.73 at time of transplantation and dialysis-dependent patients had a median dialysis duration of 20 mths (IQR 8,40). Pre-emptive and dialysis-dependent living transplants had similar mean recipient age (45.3 vs 44.9 yrs), donor age (54.3 vs 53.5 yrs), and proportion of males (60 vs 66%), diabetics (8 vs 6.5%) and living-related grafts (55 vs 56%). Renal function was similar at 12 months post-transplant in pre-emptive and dialysis-dependent recipients (eGFR 51.3+/–15.3 vs 48.5+/–16.9 ml/min/1.73 $m^2$) and at 5 years (45.6+/–21.6 vs 45.7+/–19.6 ml/min/1.73 $m^2$). After median 5.3 yrs follow-up, rates of rejection and graft failure were also similar.
**Conclusion:** No difference in allograft outcome was evident in recipients of pre-emptive kidney transplants compared to other live donor transplants.

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## HOW WELL DO WE FOLLOW-UP LIVING KIDNEY DONORS?

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**Aim:** To determine the completeness of clinical follow-up of Tasmanian living kidney donors.
**Background:** Living kidney donation is common in Australia. Current guidelines suggest donors have yearly follow-up with a nephrologist to monitor their kidney function and manage chronic disease risk factors.
**Method:** We performed a retrospective review of the follow-up of all Tasmanian living kidney donors from 1 January 1978, till 31 December 2012. Names and follow-up data were obtained from three sources; the treating hospitals (Royal Hobart Hospital and Launceston General Hospital), the transplant unit of the Royal Melbourne Hospital, and the Australia and New Zealand Dialysis and Transplant living kidney donor Registry (ANZDATA).
**Results:** We identified 108 donors; 66% of which were female. Median age at last follow-up was 56 years (range: 35–78), and median time since donation was 4 years (range: 1–28).

Considering the entire cohort overall (n = 108); median yearly follow-up was 33% (range: 0–100).

77% have had at least one nephrologist follow-up, thus subsequently 23% appear to have had no post-donation nephrologist follow-up. Of those not seen by a nephrologist (n = 25); 24% have had follow-up by their General Practitioner only and the remainder no recorded follow-up.

Of the group with at least one follow-up (n = 83), median yearly follow-up was 50% (range: 8–100), with only 17 % having achieved follow-up of once a year or more.

Lower annual follow-up (every 4 year or less) was associated with longer time since donation (median 6 years) and younger age at last follow-up (median 52 years).
**Conclusion:** Since donation, the majority of Tasmanian kidney donors have had nephrologist follow-up fewer than every 2 years. This is less than suggested by clinical guidelines.

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## HIGH PREVALENCE OF DE NOVO HLA ANTIBODIES POST TRANSFUSION IN RENAL TRANSPLANTATION

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**Background:** Blood transfusion in kidney transplantation is considered as a major risk for sensitisation. We studied the prevalence of transfusion during the transplantation period and analysed the impact on HLA antibody status.
**Method:** We retrospectively analysed all adult kidney recipients from a single centre transfused with red blood cells and platelets during the first 48 hours of transplantation surgery. HLA tissue typing was performed by single antigen Luminex bead assay (Tepnel). HLA antibodies and donor specific antibodies (DSA) pre and post-transplantation between days 14 and 31 were analysed. All patients received prednisolone, tacrolimus and MMF.
**Results:** 189 patients underwent kidney transplantation during the study period (2010–13). 69 (36%) received blood transfusion during peri-transplantation period [mean of 3 units (range 2–14)]. Mean recipient age of transfused patient was 51 +/– 12 years (36M/54F). Prior to transplantation 40/69 recipients had non-donor specific HLA antibodies and 9/69 had pre-existing DSA. We observed the formation of de novo HLA antibodies (MFI > 1500) in 18/69 (26%) patients with 8 HLA Class I, 5 HLA class II and 5 for both classes. The HLA antibody specificity for class I Ab was HLA B (n = 11) and the HLA class II Ab was DR (n = 7). We also found 4 de novo Cw locus Ab and 1 DP Ab. 5 patients developed de novo DSA after transplantation.
**Conclusions:**
1) High prevalence of transfusion in peri- transplantation period (36%)
2) 26% of transfused KTR developed clinically significant HLA antibodies-(MFI > 1500)
3) High prevalence of transfusion and sensitization in young patients may potentially impact future transplantation.

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## ANGIOTENSIN 2 TYPE 1 RECEPTOR ACTIVATING ANTIBODIES IN TRANSPLANT GLOMERULOPATHY

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**Background:** Transplant glomerulopathy (TG) is associated with poorer kidney graft survival. Angiotensin 2 type 1 receptor antibodies (ATR1Ab) have been implicated in antibody mediated rejection, both in association with donor specific antibodies (DSA) and in isolation. We aim to define the prevalence and the consequence of AT1RAb in graft outcomes in a cohort with TG.
**Materials and Methods:** From January 1990 to January 2011, 141 TG patients were investigated. Patient demographics, DSA, AT1RAb titre (tested before and/or at and/or after transplantation) and graft failure were reported. A positive result for AT1RAb was considered to be greater than 10 U/mL.
**Results:** In the entire cohort, the mean time from transplant to TG diagnosis was 4.5 years, 78 patients had failed grafts, 74 had a definitely positive value of AT1RAb and 63 had DSA. At time of transplantation 51 patients had negative AT1RAb results, and 38 were positive. No difference was observed according to donors/recipient's characteristic, time of TG diagnosis, presence of DSA and graft survival between both groups. Graft survival was independently affected by the presence of DSA but associations with AT1AbR were not straightforward. Patient survival was poorer in patients with DSA and high value of AT1RAb (>17 U/mL). Cause of death was not associated with AT1RAb.
**Discussion:** AT1AbR positive patients comprised 52.5% of the TG patients, compared to that of the general transplant population (11%). Presence of DSA AT1R affects graft and patient survival whereas high titre of AT1RAb affects patient survival. We suggest that AT1RAb at transplantation should have an impact in TG patients.

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## $VEGF_{165}b$ IS PROTECTIVE IN DIABETIC NEPHROPATHY

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**Aim:** Diabetic nephropathy is a leading cause of renal failure. Harnessing endogenous protective factors within capillary walls offers new opportunities to halt diabetic complications.
**Background:** We have recently found that $VEGF_{165}b$, when selectively overexpressed in podocytes or injected systemically, reduces albuminuria and slows progression of diabetic nephropathy in DBA2J, db/db and C57Bl6 mice. Glomerular $VEGF_{165}b$ is increased in diabetic patients with non-progressive nephropathy (Oltean, Qiu et al, unpublished).
**Methods:** The potential utility of $VEGF_{165}b$ in human diabetic nephropathy was examined by measuring the permeability (ultrafiltration coefficient; $L_PA$, $nl.min^{-1}.mmHg^{-1}$) of single glomeruli isolated from untransplantable human kidneys from diabetic and non-diabetic donors, and testing whether diabetic glomerular function can be improved through direct modulation of the capillary wall.
**Results:**
[1] Human glomerular $L_PA$ was 6.2 ± 0.8(25/3) {mean ± sem (glomeruli/donors)}, significantly greater than $L_PA$ of rat {1.0 ± 0.1(135/17} and mouse {1.2 ± 0.1(67/14} glomeruli ($p < 0.001$). When corrected for glomerular volume ($L_PA/V_i$, $min^{-1}.mmHg^{-1}$), human and rat glomerular function was indistinguishable (0.93 ± 0.08 vs 0.99 ± 0.05, $p > 0.05$), but both were significantly different from mouse glomerular $L_PA/V_i$ (2.03 ± 0.15, $p < 0.001$).
[2] $L_PA/V_i$ of human glomeruli from diabetic donors {2.3 ± 0.4 (16/3)} was higher than $L_PA/V_i$ of glomeruli from non-diabetic donors {1.0 ± 0.1 (25/3)} ($p < 0.001$).
[3] Treatment with 1 nM $VEGF_{165}b$ (1 hr) restored $L_PA/V_i$ to normal in diabetic human glomeruli {1.0 ± 0.2 (13/3); $p < 0.001$}.
**Conclusion:** These are the first measurements of the permeability of diabetic human glomeruli, and demonstrate altered single glomerular function (increased $L_PA/V_i$). This disrupted glomerular function in human diabetic nephropathy can be normalised by $VEGF_{165}b$. Long-term systemic treatment with $VEGF_{165}b$ also reduced albuminuria and improved histology in multiple animal models of diabetic nephropathy. $VEGF_{165}b$ holds promise as a tool to improve capillary function in diabetic complications.

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## GLYOXALASE-1 INHIBITION LEADS TO DIABETIC KIDNEY DISEASE ASSOCIATED WITH PODOCYTE INSULIN RESISTANCE

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**Aim:** To examine the effects of a GLO-1 inhibitor on podocyte insulin signalling and renal function under diabetic conditions.
**Background:** The plasma concentration of the reactive carbonyl, methylglyoxal (MGO), is elevated in diabetes. Increased accumulation of MGO may contribute to insulin resistance at peripheral sites of glucose uptake. A deficiency in podocyte insulin signalling impairs podocyte function resulting in chronic kidney disease. Glyoxalase-1 (GLO-1) is an enzyme considered to detoxify MGO.
**Methods:** Human podocytes were exposed to a GLO-1 inhibitor and insulin sensitivity assessed using pAKT/AKT and membranous GLUT4 protein expression. Male db/db mice (reminiscent of human type 2 diabetes) and db/H control mice were administered with GLO-1 on alternate days from weeks 6 to 9 of life (50 mg/kg body weight) and renal function and glycaemic control were assessed.
**Results:** Human podocytes exposed to an inhibitor of GLO-1 showed reduced insulin signalling with lower pAKT/AKT ratios and GLUT4 membrane translocation. In the db/db mouse, serum cystatin C was elevated at 9 weeks, and this was exacerbated with GLO-1 inhibition. Peripheral insulin resistance in db/db mice however, was not different in the presence of GLO-1 inhibition. Decreased insulin signalling and expression of GLUT4 in human podocytes exposed to an inhibitor of GLO-1 were consistent with the degree of renal dysfunction in diabetic mice.
**Conclusions:** Alterations to the glyoxalase system in diabetes may contribute to renal impairment by adversely affecting podocyte insulin sensitivity.

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## SEMICARBAZIDE-SENSITIVE AMINE OXIDASE INHIBITOR INHIBITS EXTRACELLULAR MATRIX DEPOSITION IN KIDNEY FIBROSIS

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**Aim:** To determine the role of a semicarbazide-sensitive amine oxidase (SSAO) inhibitor (PXS4728A) as an antifibrotic agent using *in vitro* and *in vivo* models of kidney fibrosis.
Background: Novel anti-inflammatory agents targeting early phases of cellular response to injury are increasingly recognised to have a role in tubulointerstitial fibrosis. SSAO is a protein enzyme known for its role in inflammation by mediating the migration of leukocytes and producing reactive oxygen species. However, the role of SSAO inhibitors in kidney fibrosis is unclear.
**Method:** In vivo, 6–8 week old male C57BL/6 (20–25g; n = 4) were subject to a 7-day unilateral ureteric obstruction (UUO) model. PSX4728A (2 mg/kg) was orally gavaged and Telmisartan (3 mg/kg), a clinically used angiotensin receptor blocker, was administered in the drinking water. In vitro, human proximal tubular cells (HK2) cells were exposed to transforming growth factorβ1 (TGFβ1) (1 ng/ml) for 48 hours with or without PXS4728A. Semiquantitative morphometric analyses of glomerulosclerosis and tubuloinsteritial fibrosis were performed. Kidney tissue & cell lysate were analysed for fibrotic and inflammatory mRNA and protein expression.
**Results:** The mRNA expression of Collagen-IV (C-IV) and Fibronectin (FN) in kidney tissue was lower in PXS4728A groups (6.4 ± 0.0 and 7.6 ± 0.1) as compared to the vehicle (PBS) (9.9 ± 0.3 and 12.6 ± 0.5). The mRNA expression of TGFβ1 and monocyte chemoattractant protein-1 were effectively suppressed by PSX4278 and Telmisartan alone, but not when used in conjunction. Mice treated with PXS4782A had reduced tubular dilatation and glomerulosclerosis as compared to control groups. This was supported by our in vivo findings, as PXS4782A inhibited TGFβ1-induced C-IV and FN protein expression in HK2 cells.
**Conclusion:** PSX4728A is as effective as Telmisartan as an antifibrotic agent in both *in vivo* and *in vitro* models of fibrosis.

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## NOTCH SIGNALING MEDIATES MMP-9-DEPENDENT ENDOTHELIAL-MESENCHYMAL TRANSITION DOWNSTREAM OF TGF-β IN HUMAN RENAL GLOMERULAR ENDOTHELIAL CELLS

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**Aim:** To examine the effect of MMP-9 on endothelial-mesenchymal transition (EndoMT) downstream of TGF-β1.
**Background:** EndoMT has been shown to contribute to myofibroblast formation in kidney fibrosis. Our previous study showed a profibrotic role for MMP-9 in kidney disease by inducing epithelial EMT. Inhibition of MMP-9 activity reduced kidney fibrosis in murine unilateral ureteral obstruction. This study investigated whether MMP-9 also plays a role in EndoMT.
**Methods:** Human renal glomerular endothelial cells (HRGEC) were treated with TGF-β1 to induce EndoMT. EndoMT was assessed by morphological changes, immunofluorescence staining (IF) and western blot (WB) of endothelial (CD31 and VE-cadherin) and mesenchymal markers (α-SMA, and vimentin). Notch signaling was examined by RT-PCR and WB.
**Results:** TGF-β1 (10 or 20 ng/ml) induced EndoMT in HRGEC as evidenced by morphological changes, and by significant downregulation of VE-cadherin & CD31 and upregulation of α-SMA & vimentin. RT-PCR showed an upregulation of Snail, a known inducer of EMT. TGF-β1-induced EndoMT was abrogated by MMP inhibitor GM6001. Zymography showed that MMP-9 was upregulated in TGF-β1-treated HRGECs. Recombinant MMP-9 (2 μg/ml) also induced EndoMT in HRGECs with an upregulation of Notch signaling evidenced by an increase of Notch intracellular domain (NICD) accompanied by a decrease of Notch 1. Inhibition of MMP-9 activity demonstrated a dose-dependent reduction in TGF-β1-induced α-SMA and NICD in HRGECs. Inhibition of Notch pathway by gamma-secretase inhibitor in HRGECs also prevented TGF-β1-induced upregulation of α-SMA and NICD and downregulation of CD31 and VE-cadherin.
**Conclusions:** Notch signaling plays an important role in MMP9-dependent EndoMT downstream of TGF-β1 in HRGECs.

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## ADENINE-INDUCED CHRONIC KIDNEY DISEASE IS ASSOCIATED WITH ARTERIAL MACROPHAGE INFILTRATION AND MEDIAL VASCULAR CALCIFICATION

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**Aim:** To establish a model of chronic kidney disease (CKD) in ApoE-/- mice using high adenine diet and assess the effect on aortic vascular calcification and macrophage infiltration.
**Background**: Vascular calcification is strongly associated with cardiovascular morbidity and mortality. In patients with CKD, lesions comprised of calcium deposits are commonly found in arteries and are known as arteriosclerosis. Several studies have suggested that monocytes/macrophages are involved in uraemic arterial vascular calcification.
**Methods:** ApoE-/- mice were fed with diet containing 0.25% adenine for 4 weeks, followed by 8 weeks feeding with normal chow and then sacrificed. Urine and serum were collected for biochemical testing of renal function and several hormones. Kidneys were collected for examination of injury by histochemistry. Whole aortas were dissected. Macrophage infiltration and vascular calcification were examined by immunohistochemistry.
**Results:** Serum creatinine level and 25 hydroxyvit D were higher in adenine fed mice (36 μmol/L, 95 nmol/L) compared to control (19 μmol/L, 78 nmol/L, $p < 0.05$). Adenine fed mice had a significantly higher GT fibrosis score (3.2) and PAS tubular damage score (3.5) compared to control (1.2 & 1.2, $p < 0.001$). Adenine-fed mice demonstrated significantly higher calcium deposition in aortic arch and thoracic aorta (1.8% & 3.2% of vessel area) compared to control (1.2% & 2.0%, $p < 0.05$). Adenine-fed mice also had a greater macrophage infiltration in aortic arch (26% of vessel area) compared to control (15%, $p < 0.05$) as well as in thoracic aorta (31% & 18%, $p < 0.01$).
**Conclusions:** Adenine-induced kidney failure exacerbated vascular calcification with increased infiltration of macrophages in apoE-/- mice. These data suggest a potential role for macrophages in uraemic vascular calcification.

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## EARLY INTERVENTION WITH APYRASE AMELIORATES FIBROSIS AFTER UNILATERAL ISCHEMIA REPERFUSION INJURY (IRI)

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**Background:** Apyrase, a form of soluble CD39, protects acutely against renal ischemia reperfusion injury (IRI). Apyrase hydrolyses ATP released from injured cells and leads to increased generation of peri-cellular adenosine which is anti-inflammatory.
**Aim:** To evaluate the impact of apyrase in the development of fibrosis after IRI using a mouse model of renal IRI with or without right nephrectomy.
**Methods:** Intraperitoneal injection of apyrase (0.4 U/g) or vehicle was given 30 mins before the mice were anaesthetised. In the "IRI" model, the right kidney was left *in situ*; in the unilateral IRI ("UIRI") model, a right nephrectomy was performed prior to clamping of the left renal pedicle for 23.5 minutes. Mice were euthanised 24 hours or 4 weeks after reperfusion and the kidneys were harvested for histological examination.
**Results:** In the UIRI model, serum creatinine was significantly lower at 24 hours reperfusion in mice treated with apyrase compared to vehicle 63.53 ± 6.557 μmol/L (n = 5) vs. 101.3 ± 8.105 μmol/L (n = 5), $p = 0.0068$. In the same model, mice treated with apyrase had significantly lower fibrosis score at 4 weeks post IRI than vehicle treated mice 0.06966 ± 0.01377 (n = 7) vs. 0.1340 ± 0.008112 (n = 3), $p = 0.02$. In the IRI model with a normal kidney in situ, apyrase did not reduce the development of fibrosis at 4 weeks 0.2433 ± 0.03712 (n = 3) vs 0.2250 ± 0.04555 n = 4, $p = 0.78$.
**Conclusions:** Early intervention with apyrase reduces acute ischemic renal injury. This translates to less fibrosis at 4 weeks in a solitary kidney. However, the effect is lost if the contralateral kidney is *in situ* causing delayed recovery of the injured kidney which is not ameliorated by treatment with apyrase.

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## PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR-Y ACTIVATION DOES NOT PROTECT HUMAN KIDNEY PROXIMAL TUBULAR EPITHELIAL CELLS AGAINST OXIDATIVE STRESS

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**Aim:** To determine the role of peroxisome proliferator-activated receptor-gamma (PPARγ) in protecting kidney proximal tubular epithelium (PTE) against mitochondrial destabilisation and oxidative stress.
**Background:** Despite a wealth of knowledge about PPARγ function, mechanism(s) underlying the ability of PPARγ agonists to be renoprotective in diabetic nephropathy are not well-understood. Mitochondrial dysfunction and oxidative stress contribute to diabetic nephropathy. PPARγ upregulates proteins required for mitochondrial biogenesis.
**Methods:** HK-2 cells were treated with 0.2–1.0 mM hydrogen peroxide ($H_2O_2$) for 2 h and 18 h. Treated and untreated cells were compared for: apoptosis, mitosis (morphology/biomarkers); cell viability (MTT); superoxide (dihydroethidium /DHE); mitochondrial function (MitoTracker Red; JC-1); ATP (luminescence); and mitochondrial ultrastructure (electron microscopy). Western immunoblotting was used to study PPARγ, phospho-PPARγ, PPARγ-coactivator-1α (PGC-1α; mitochondrial biogenesis marker), and pak2, p62 and LC3-II (mitophagy markers). PPARγ agonists (rosiglitazone, pioglitazone, troglitazone) and the inhibitor (GW9662) were used to modulate PPARγ.
**Results:** At 2 h and 18 h, mitochondrial destabilisation increased with $H_2O_2$ concentration: MitoTracker Red and ATP decreased ($p < 0.05$); JC-1 fluorescence altered red→green; and DHE increased (18 h; $p < 0.05$). Mitochondria were sparse and had disrupted cristae. Pak2 increased, p62 decreased (2 h), and p62 and LC3-II increased (18 h) (all $p < 0.05$) indicating increased defective

mitochondrial autophagy. PPARγ expression did not alter but phospho-PPARγ increased and PGC-1α decreased (2 h) indicating aberrant PPARγ activation and reduced mitochondrial biogenesis. Cell viability decreased (18 h; $p < 0.05$), with further cell death when PPARγ agonists were used. PPARγ inhibition had negligible effect.
**Conclusions:** Oxidative stress promoted mitochondrial destabilisation in kidney PTE, in association with PPARγ activation. PPARγ agonists failed to protect the cells. Despite positive effects in other tissues, PPARγ activation appears to be detrimental to kidney PTE health when oxidative stress induces damage.

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## INHIBITION OF TUBULAR ALBUMIN DEGRADATION IS A COMMON FEATURE IN PROTEINURIC DISEASE MODELS

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**Background:** Endocytosis and degradation of glomerular filtered albumin is a constitutive function of normal kidney. We have found that tubular albumin degradation is inhibited in type 2 diabetic nephropathy. The current study investigates whether this is unique to diabetic nephropathy or a more general feature of proteinuric disease.
**Aim:** To examine tubular albumin uptake and degradation in mouse models of acute and chronic proteinuric disease.
**Methods:** Models of acute proteinuria (24 hr LPS-induced albuminuria and 24 hr anti-GBM disease) and chronic diabetic nephropathy (streptozotocin-induced type 1 diabetes and db/db type 2 diabetes) were examined using fluorescent albumin probes. Mice were co-injected with Alexa-albumin and DQ-albumin 20 min before being killed and the kidney perfused.
**Results:** Total albumin uptake in proximal tubules was quantified by confocal immunofluorescence microscopy of Alexa-albumin (520 nm) in kidney sections. Albumin degradation was quantified in the same tubular cross-sections using DQ-albumin (622 nm) which only fluoresces following enzymic digestion. All four animal models showed a significant reduction in tubular albumin degradation compared to non-diseased controls. The fluorescence signal ratio for degraded/total albumin in tubules was significantly reduced in all four models, although this was not related to the degree of proteinuria. Only the LPS model showed a significant reduction in total albumin uptake in tubules, which probably reflects the reduced renal function in this model. Interestingly, there was no change in expression of the major lysosomal enzymes, cathepsin B and L, in kidney lysates from the four models.
**Conclusion:** We demonstrate that inhibition of tubular degradation of endocytosed albumin is a common feature in proteinuric disease. The molecular basis of this and how it contributes to albuminuria and the tubular response to injury requires further investigation.

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## THE ROLE OF TOLL-LIKE RECEPTOR PROTEINS (TLR) 2 AND 4 IN MEDIATING INFLAMMATION IN HUMAN MICROVASCULAR ENDOTHELIAL CELLS (HMEC-1)

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**Aim:** To determine the effect of varying glucose concentrations on TLR2 and 4 expression and their role in mediating inflammation in HMEC-1.
**Methods:** HMEC-1 cells (a human microvascular endothelial cell line) were exposed to control (5 mM), 30 mM (high), fluctuating (5/30 mM) and 11.2 mM (approximate clinical diabetic threshold) glucose limbs for 72 h. Cells were harvested for protein, mRNA and nuclear extract and assessed for TLR2, 4 and inflammatory markers. HMGB1 (High mobility group box protein 1) mediated NF-κB activation in HMEC-1 cells was assessed through western blot and electrophoretic mobility shift assay. TLR2 and 4 signalling was abrogated using a neutralizing antibody or inhibitor and the effect assessed on NF-κB activation.
**Results:** TLR2 and 4 are present in HMEC-1 cells and fluctuating glucose concentrations maximally increased TLR2, 4 transcription and protein expression. NF-κB activation was also induced with concomitant transcription of interleukin-8 (IL-8), vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) in the fluctuating glucose limb. Maximal HMGB1 protein expression was detected in the supernatant cultured with 30 mM glucose. Recombinant HMGB1 induced NF-κB binding which was prevented by TLR2 and 4 signalling inhibition. Additive effect of TLR2 and 4 signalling inhibitors further attenuated NF-κB activation.
**Conclusion:** Fluctuating glucose concentrations induced maximal TLR2 and 4 expression with an increase in NF-κB, inflammatory cytokines and vascular adhesion molecules suggesting that postprandial glucose fluctuations may be amplifying inflammatory responses in the human microvascular endothelium. The increase in HMGB1, an endogenous ligand to TLR2 and 4, with exposure to high glucose suggests that TLR2 and 4 may be regulated by HMGB1. Therefore, targeting their signalling pathways may be of therapeutic purpose in attenuating inflammation in the vascular bed.

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## THE PDE4 INHIBITOR ROFLUMILAST REDUCES TGF-β INDUCED PRO-FIBROTIC AND PROLIFERATIVE EFFECTS IN VITRO

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**Aim:** To evaluate the potential of the PDE4 inhibitor, roflumilast, in blocking TGF-β induced pro-fibrotic and cell proliferative effects in vitro.
**Background:** The prevalence of chronic kidney disease (CKD) is increasing globally from the rising incidence of hypertension and diabetes. The use of PDE inhibitors for treating CKD has garnered interest, especially with non-selective PDE inhibitor pentoxifylline, as it reduces renal inflammation and fibrosis, leading to its anti-proteinuric effect in animal models and human studies. Selective PDE4 inhibitors, like roflumilast, are more specific and potent, and may offer better renoprotection, as they possess both anti-inflammatory and anti-fibrotic properties.
**Methods:** Cultured rat mesangial cells (1097) were treated with increasing concentrations of roflumilast (1, 5, 10, 30 μM) and stimulated with 5 ng/ml TGF-β1 for 4 hours after drug treatment. Collagen formation and cell proliferation were determined using a 3H-proline incorporation assay and an MTT assay respectively. Mesangial cell activation was determined using western blotting for α-SMA expression.
**Results:** Roflumilast reduced TGF-β stimulated collagen formation in a dose response manner (DMSO: 9372 ± 1196; 5 μM: 6648 ± 561; 10 μM: 4815 ± 650, $P < 0.05$; 30 μM: 4130 ± 707 cpm/mg protein, $P < 0.01$). Similarly, TGF-β stimulated cell proliferation trended downwards with increasing roflumilast treatment (DMSO: 1.072 ± 0.042 VS 10 μM: 0.8768 ± 0.044 AU; $P < 0.05$). The drug also inhibited TGF-β induced mesangial cell activation by reducing α-SMA protein expression (DMSO: 1.588 ± 0.098 VS 10 μM: 1.045 ± 0.070 AU; $P < 0.01$).
**Conclusions:** Roflumilast has both anti-fibrotic and anti-proliferative properties in TGF-β stimulated mesangial cells. Therefore, the use of PDE4 inhibitors may be a potential therapeutic for the treatment of CKD. Future studies will evaluate the efficacy of roflumilast treatment in animal models of CKD.

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## URINARY BIOMARKER KIM-1 RISES EARLIER THAN NGAL IN EXPERIMENTAL ARISTOLOCHIC ACID NEPHROPATHY

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**Aim**: To investigate urinary and serum biomarker profiles in experimental Aristolochic-acid nephropathy (AAN).
**Background**: Aristolochic-acid (AA) is used in traditional medicine but is known to cause AAN, particulary its active ingredient, AA1. The urinary injury biomarkers neutrophil gelatinase-associated lipocalin ($_u$NGAL) and kidney injury molecule-1 ($_u$KIM-1) typically rise early in acute kidney injury but their expression profiles in AAN are unexplored.
**Methods**: Rats (n = 4/group) were administered AA1 (5, 10 or 20 mg/kg) ip for five days (d-5 to d0) and characterised for serum creatinine (SCr; μmol/L), $_u$KIM-1 (pg/ml) and $_u$NGAL (pg/ml) on the following days (d) d1, 3, 7, 14, 21, 28, and 35. Tubular interstitial (TID) and other damage was examined histologically on d7 and d35. Data are mean ± SD; *$P < 0.05$ was considered significant*.
**Results:** Rats treated with 20 mg/kg AA1 exhibited diffuse TID by d7, progressing to medullary disease by d35. These rats also showed persistent polyuria.

SCr increased in this group from d7 (42.8 ± 9.8* vs. baseline: 19.3 ± 3.3) until d35 (206.3 ± 0.9*) and increased later, and to lower levels, in 5 mg/kg (d21: 41.8 ± 4.8 vs. d35: 109.6 ± 2.3*) and 10 mg/kg (d21: 46.5 ± 17.5 vs. d35: 115.1 ± 3.0*) groups. The biomarker $_u$KIM-1 rose earlier than SCr on d-3 (28.1 ± 5.6* vs. baseline: 1.25 ± 0.1) until d7 (64.2 ± 12.7*) and fell gradually thereafter until d35 (11.2 ± 1.4*) in rats that received 20 mg/kg AA1. By contrast, $_u$NGAL increased later, on d14 (368.3 ± 31.6* vs. baseline: 228.7 ± 12.6) and continued to rise until d35 (1108.4 ± 95.9*) in rats that received 20 mg/kg AA1. $_u$KIM-1 and $_u$NGAL did not increase after lower doses of AA1.

**Conclusion:** In experimental AAN, $_u$KIM-1 increases before $_u$NGAL and SCr, and may allow early prediction of renal injury.

## POSTERS

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### CORRELATION OF SERUM CREATININE AT DAY 14 AND 180 POST RENAL TRANSPLANT WITH ALLOGRAFT KIDNEY VOLUME MEASURED RADIOLOGICALLY

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**Introduction:** Donor kidney weight has been shown to influence graft function. Recently, more accurate and informative radiological scans of donor renal vessels at our centre have been assessed using CT renal angiograms.

**Objective:** To determine the association between the donor renal volume and serum creatinine of the recipient at day 14 and 180 post transplantation.

**Methods:** This is a retrospective analysis of 19 donors who had a CT renal angiogram as part of their transplant work-up had their kidney volume calculated (in $cm^3$) by a single radiologist. Demographic and immunological risks of the recipients were also analyzed.

**Results:** The mean age of the recipients were 38 years (range 21–59 years), the mean BMI were 24 (range 16–38) and all had immediate graft function except one patient. There were no reported intraoperative adverse complications and all cases were performed by a single urologist and his team. Seven patients had borderline rejection, three patients developed acute rejections (AR) whilst the rest did not have any AR episodes. The mean donor kidney volume was 139 $cm^3$ (78 $cm^3$–185 $cm^3$) and a linear regression analysis performed showed that the larger the volume of the allograft received, the lower the serum creatinine of the recipient. The correlation between kidney volume and serum creatinine at day 14 and at day 180 were $r = -0.29$, $p$ NS and $r = -0.65$, $p < 0.008$ respectively.

**Conclusion:** Kidney volume calculated radiologically may influence the serum creatinine post transplantation especially at six months. A larger sample is needed to confirm our findings.

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### LOW TITRE DONOR SPECIFIC ANTIBODIES ARE ASSOCIATED WITH A HIGH RISK OF ANTIBODY MEDIATED REJECTION

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**Background:** Donor specific antibodies (DSAb) are associated with an increased risk of acute and chronic antibody mediated rejection (AMR) and graft failure. The mean fluorescence index (MFI) of DSAb in pre-transplant sera is used to stratify the potential risk of AMR. Whilst high MFI DSAb are likely to be associated with an increased risk of AMR we hypothesized that low MFI DSAb also carry a significant risk of AMR.

**Aim:** To define the rate of AMR, stratified by DSAb MFI, in the first 12 months after kidney transplantation in a real-world cohort of patients.

**Methods:** We undertook a retrospective cohort study of all patients transplanted at our institution during 2008–2009 (n = 134). DSAb, by Luminex, were considered positive at MFI > 500. All biopsies (protocol and indication) from the first 12 months post-transplant were reviewed for AMR. Transplants were divided into DSAb negative, weak positive (MFI < 5000) and strong positive (MFI > 5000)) and compared the rates of AMR.

**Results:** 25 patients (18.6%) had at least one DSAb. The rate of AMR during the first 12 months post-transplantation was 72% (n = 18) in patients with DSAb and 35% (n = 38) in patients without DSAb (RR 2.07, 95%CI 1.45–.2.94, p = 0.0013). There was no significant difference in the rate of AMR in patients who had weak DSAb and those who had strong DSAb, 63% (n = 10) vs 89% (n = 8), (RR 0.70, 95%CI 0.45–1.10, p = 0.35). Cell-mediated rejection rate was not different between those with and without DSAb, 28% vs 35%, (RR 0.78 95%CI 0.40–1.54, p = 0.48).

**Conclusion:** DSAb positive kidney transplants, even those with low level MFI are associated with a high incidence of AMR. Pre-emptive strategies to reduce the risk of AMR could be considered in such patients.

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### THE ASSOCIATIONS BETWEEN 25-OH VITAMIN D (25-OHD) AND CLINICAL OUTCOMES IN RENAL TRANSPLANT RECIPIENTS (RTR)

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**Background:** 25-OHD deficiency is associated with increased morbidity and mortality in CKD cohorts. Reported 25-OHD immuno-modulatory properties led to the hypothesis that deficiency may negatively influence renal transplant outcomes.

**Aim:** To examine the associations between 25-OHD levels, and renal allograft function and biopsy proven acute rejection (BPAR).

**Methods:** Incident RTRs (n = 195) at two transplant centres were followed for a median of 358 days (range 30–428). 25-OHD levels and renal function were measured at baseline and follow-up. A serum 25-OHD level of <50 nmol/L was considered deficient. Associations between 25-OHD levels, and BPAR and eGFR were assessed using Cox-regression analysis and panel data analysis adjusted for time, respectively.

**Results:** The median age of RTRs was 52 years, 60% were male, most (>95%) received IL2RA/Tac/MMF/PNL immunosuppression. 25-OHD deficiency was common, with a median level of 50 nmol/L. Individuals with and without rejection had similar baseline 25-OHD levels (54.2 vs. 57.2 nmol/L, p = 0.52). 25-OHD deficiency was not associated with rejection multivariate HR 1.31 (95% CI 0.79–2.20, p = 0.29). Interestingly, baseline calcitriol use was significantly associated with BPAR, multivariate HR 1.92 (95% CI 1.12–3.28, p = 0.02). Baseline 25-OHD levels did not predict eGFR at 12 months. 25-OHD levels were negatively associated with eGFR in the univariate (p = 0.01) but not the multivariate longitudinal models (p = 0.07). Baseline 25-OHD levels were not associated with BK viraemia.

**Conclusions:** Baseline 25-OHD deficiency was not associated with immune events (BPAR or BK viraemia) in this cohort, however higher 25-OHD levels were associated with lower eGFR over time. The use of vitamin D compounds in RTRs requires further evaluation before it can be widely recommended.

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### LATENT TUBERCULOSIS: TESTING AND RISK FACTOR ASSESSMENT IN POTENTIAL KIDNEY TRANSPLANT RECIPIENTS

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**Aim:** To determine (1) the prevalence of risk factors for latent tuberculosis (LTB), (2) the proportion of patients investigated for LTB, and (3) the results of LTB testing.

**Background:** Risk of active tuberculosis (TB) increases after kidney transplantation due to immunosuppression. Testing for LTB before transplantation can target post-transplant anti-TB prophylaxis to patients most at risk.

**Methods:** We included all patients who underwent transplant assessment between 2011–2012 in a single centre cohort. Using hospital records, clinical

notes and laboratory results, we collected data on patient characteristics, risk factors for LTB and results of LTB tests. Proportions were calculated with 95% confidence intervals (CI).
**Results:** 242 patients underwent kidney transplant assessment. We present preliminary data for 169 patients. Patients had a mean age of 50.0 years (range 19.7–71.8), 63.3% (CI 56.0–70.6) were male and 26.6% (CI 20.0–33.3) had received Bacillus Calmette-Guérin vaccination. Most frequent cause of kidney failure was diabetic nephropathy (26.0% [CI 19.4–32.7]). At least one risk factor for LTB other than chronic kidney disease was present in 65.1% (CI 57.9–72.3) of patients. Most prevalent risk factors for LTB were diabetes mellitus (31.4% [CI 24.4–38.4]), high-risk country of birth (27.8% [CI 21.1–34.6]) and prior immunosuppression (18.3% [CI 12.5–24.2]). Forty patients (23.7% [CI 17.3–30.1]) were tested for LTB. Fourteen patients tested positive for LTB, 20 tested negative and six were indeterminate or awaiting results. Of patients with at least one risk factor for LTB, only 31.8% (CI 23.1–40.5) were tested for LTB.
**Conclusion:** Data suggests that despite a high prevalence of risk factors for LTB in candidates for kidney transplantation, LTB may be missed in transplant work-up due to under use of available tests.

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## USE OF METFORMIN FOR TREATMENT OF NEW ONSET DIABETES AFTER TRANSPLANTATION (NODAT)

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Though metformin is the antiglycemic agent of choice in the general population, guidelines post-transplantation promote sulfonylureas and meglitinides rather than metformin for treatment of new onset diabetes after transplantation (NODAT).

Apart from the usual risk factors for diabetes, treatment with corticosteroids, calcineurin inhibitors and sirolimus are unique risk factors in the post-transplant group.

Despite the risk of lactic acidosis associated with metformin being very low, this concern denies transplant recipients of benefits attributed to metformin which include weight neutrality or improvement, improved pathophysiological components of the metabolic syndrome, lipid-lowering properties, and cardiovascular protection.

An observational study measured the plasma trough concentrations of metformin along with simultaneous lactate concentrations and eGFR in 12 post renal transplant patients who were started on metformin for NODAT. The serum metformin concentration ranged from 0.19 to 4.33 mg/L (0.4 to 1.5 mg/L) with a mean metformin concentration of 1.95 mg/L while lactate concentration ranged from 1.02 to 3.15 mmol/L (0.2 to 2 mmol/L) with a mean lactate concentration of 2.04 mmol/L. None of these patients were acidotic and serum bicarbonate concentration ranged from 21 to 31 mmol/L with a mean bicarbonate concentration of 25.4 mmol/L. Of the four patients who had lactate concentrations above 2.1 mmol/l, metformin concentration ranged from 1.23 to 2.48 mmol/L with a mean concentration of 1.85 mmol/L which was lesser than the entire group's mean metformin concentration.

The serum lactate levels did not correlate in a linear fashion with metformin concentration or eGFR. In conclusion, use of metformin for treatment of NODAT was not associated with increased incidence of lactic acidosis in this patient group.

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## OUTCOMES OF A UNIT-WIDE POLICY OF PROPHYLAXIS AGAINST PNEUMOCYSTIS JIROVECII PNEUMONIA (PCP) IN PREVALENT KIDNEY TRANSPLANT RECIPIENTS (KTR)

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**Aim**: To determine the effects of commencing low dose combination trimethoprim and sulfamethoxazole (co-trimoxazole) within a prevalent regional renal transplant population.
**Background**: PCP prophylaxis is universal in KTR for the first six months. Recent outbreaks of PCP prompted recommendations to nephrology units within Queensland to consider re-instituting PCP prophylaxis in all KTR in October 2011. Our unit elected to restart prophylaxis with co-trimoxazole as first line therapy.
**Methods**: A retrospective chart audit of KTR management between August 2011 and 2012 was undertaken. Exclusion criteria were patients already receiving co-trimoxazole, patients with unstable renal function prior to commencing treatment and patients who declined prophylaxis. Serum creatinine was recorded for three months before and after starting co-trimoxaxole. Information was recorded regarding stability of graft function, outpatient attendances, adverse events, prophylaxis cessation and transplant biopsy.
**Results**: Of 143 prevalent KTR, 70 were included in the analysis. The median increase in serum creatinine after starting co-trimoxazole was 12% (interquartile range 0%–20%), including 18 patients with creatinine rise >20%. 7 patients developed unstable graft function (creatinine variation over 3 tests >20%), of whom 2 underwent renal biopsies. No patients returned to dialysis. Adverse events included 1 allergic reaction and 4 patients with gastrointestinal side effects. 17.1% of patients ceased co-trimoxazole. No cases of PCP developed after prophylaxis was instituted.
**Conclusions**: Effective prophylaxis against PCP was able to be re-instituted in most patients in a prevalent KTR population. Although a small number of patients developed unstable graft function, there were no long term serious adverse outcomes.

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## CNI-TO-EVEROLIMUS CONVERSION IN RENAL TRANSPLANT RECIPIENTS WITH LOW IMMUNOLOGICAL RISK: IMPROVED OR MAINTAINED GFR AFTER 2.5 YEARS

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**Background & Aim:** Renal allografts decline in function over time, in part from CNI-toxicity. Indiscriminate conversion from CNI-to-mTOR based immunosuppression have either shown no benefit (ASCERTAIN) or unacceptable acute rejection risks (ZEUS). We describe our total collective experience of CNI-to-Everolimus conversion in established renal allografts from recipients with low-immunological risk or on low-levels of immunosuppression.
**Methods:** All transplant recipients to June 2011 converted from CNI-to-Everolimus (n = 22) were retrospectively reviewed. Two sub-groups were identified: Patients with low immunological risk by physician assessment (45.5%) and those with clinical issues prompting conversion (54.5%). Mean graft age at conversion was 4.6 years. Mean follow-up time points were at 1.6years ($T_1$) and 2.5years ($T_2$). At $T_2$ the mean graft age was 6.7 years.
**Results:** At $T_1$, mean creatinine decreased by 10.4 μmol/L ($p < 0.0019$) with corresponding significant GFR gains in both subgroups (6.8 *vs* 4.3 ml/min respectively). Graft age (>36 *vs* <36months) did not adversely affect GFR improvement (6.3 vs 4.8 ml/min, $p < 0.0189$ and 0.0053). However, patients with baseline GFR <50 ml/min made no gains ($p = 0.09$). At $T_2$, the overall gain in GFR was less pronounced but still better than baseline by 3.7 ml/min ($p = 0.0416$). Conversion within 36months of transplantation (n = 13) and females (n = 5) had the greatest improvements from baseline (4.8 ml/min, $p = 0.0053$ and 9.0 ml/min, $p = 0.0095$ respectively). There were two CNI reversions for rash and no acute rejection episodes. One second graft recipient developed transplant glomerulopathy >5 years post conversion. There was no significant increase in the frequency/degree of proteinuria.
**Conclusions:** CNI-to-Everolimus conversion is safe in low-risk renal transplant patients with good function. The place of mTOR inhibitors may be for patients with good expected outcomes to do better by avoiding CNI-toxicity and reducing vascular risks with better GFR.

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## MANAGEMENT OF KIDNEY TRANSPLANT RECIPIENTS (KTR) AT A SINGLE CENTRE IN THE CONTEXT OF RECENT GUIDELINE PUBLICATION

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**Aims**: In March 2012 the KHA-CARI adaptation of the KDIGO Clinical Practice Guideline for the Care of KTR was published. Few papers exist regarding success in achieving these recommended targets. This study compares the management of KTR at a single centre with the KHA-CARI recommendations.
**Methods**: A retrospective audit was performed of 130 KTR during 2011. Data collected included: transplant date; graft function; immunosuppression; vaccination status; skin examination; clinic blood pressure; lipid control; body mass index (BMI) and glucose tolerance testing.

**Results**: Mean time since transplantation was 9.4 ± 7.9 years and patient age was 55.2 ± 13.2 years. Serum creatinine was 140 ± 68.7 μmol/l. 69% of patients were vaccinated against influenza within 12 months while only 36% of patients had received the pneumococcal vaccine within 5 years. 79% of patients had had a documented skin examination within the last year. Although only 41% and 58% of patients achieved target systolic (<130 mmHg) and diastolic (<80 mmHg) blood pressure respectively, 80% of patients had a clinic systolic pressure <140 mmHg and 93% of patients had a diastolic pressure <90 mmHg. 98% of patients had total cholesterol measured (mean 4.69 ± 1.0 mmol/L), but HDL and LDL were measured in only 46%. Only 36% had a BMI between 20 and 25 (n = 50 as height was poorly documented). Assessment of diabetes status by formal glucose tolerance testing was poorly documented.
**Conclusions**: Although graft function was excellent overall, there are a number of areas in which kidney transplant patient care could be improved. These data provide a benchmark for other units.

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## HIGH-SENSITIVITY TROPONIN T AS A PREDICTOR OF CARDIOVASCULAR MORBIDITY IN RENAL TRANSPLANT RECEIPIENTS

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**Aim:** Determine if any significant change in High-sensitivity troponin T (hsTnT) occurs following renal transplantation.
**Background:** hsTnT is a biomarker for detecting myocardial injury. Its use as a predictor of cardiac events in stable dialysis patients has previously been investigated. It remains uncertain if pre-transplant hsTnT levels offer any predictive value in determining cardiac events post-transplant.
**Methods:** We designed a prospective cohort study in South West Sydney in a non-transplant centre. Serum hsTnT was analysed from 30 dialysis patients pre-transplant and post-transplant. Patients were then classified and analysed according to their pre-transplant hsTnT levels: normal (Group 1 – levels < 14 ng/L) and those with elevated hsTnT (Group 2). The difference in hsTnT in relation to transplantation and cardiac events following transplantation in a 2 year period was recorded. Data was analysed using SPSS software, $p < 0.05$ is significant. Data is expressed as median (Interquartile range).
**Results:** Only 8 of the 30 patients had data to date for hsTnT post-transplant. Group 1 (n = 5) had a hsTnT of 8.2 ± 4.27 ng/L which was lower compared to Group 2 (n = 25, 53.40 ± 36.85). Median ages in Group 1 were 43.39 ± 16.17 years and 52.45 ± 15.52 years in Group 2.
Group 2 hsTnT significantly decreased post transplant by 40.25 ± 40.14 ($p = 0.036$). Group 1 had no cardiac events post-transplant. However, 16% of Group 2 suffered a cardiac event in the post-transplant period.
**Conclusions:** Basally elevated hsTnT alters significantly following transplantation and possibly identifies patients at high risk for cardiovascular events following transplantation. Further investigation is warranted.

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## AN AUDIT OF PRE-TRANSPLANT CO-MORBITY AND SHORT-TERM OUTCOME IN DIABETIC KIDNEY TRANSPLANT RECIPIENTS AT A SINGLE TRANSPLANT CENTRE

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**Aim:** To audit pre-transplant co-morbidity and clinical outcomes in pre-transplant diabetic kidney transplant recipients at The Royal Melbourne Hospital from 2000–2010.
**Background:** Diabetes is the leading cause of kidney failure in Australia. Registry data indicate that pre-transplant diabetes is associated with worse outcomes, however there is limited knowledge of how the burden of disease brought to transplant modifies the risk of specific complications.
**Methods:** Individuals were identified in our departmental database and their chart reviewed. Audited characteristics included demographics, dialysis duration, diabetes duration, treatment and complications, transplant characteristics, peri-operative complications and graft/patient outcomes.
**Results:** 74 individuals with diabetes diagnosed prior to kidney transplantation were identified. 59 (79%) had diabetic nephropathy as cause of renal failure. 11 (15%) were pre-emptive transplants. Median duration of dialysis was 3 years. Median duration of diabetes was 20 years. 62 (83%) had at least one of: current or past smoking (38/74), ischaemic heart disease (32/74), peripheral vascular disease/diabetic foot disease (22/74) or cerebrovascular disease (7/74). Peri-operative complications included wound complications (22/74), infections (16/74), ileus (13/74), delayed graft function (11/74) and cardiac events (6/74). 1 graft failed immediately and 2 patients died within 3 months of transplant. 3/6 (50%) of the cardiac events (including the only 2 cardiac arrests) occurred in individuals with normal pre-transplant cardiac investigations.
**Conclusions:** Diabetic transplant recipients at our centre carried significant co-morbidity into transplant. Wound, ileus-related, infectious and cardiac complications were common. Despite long-standing diabetes and a high rate of co-morbidity, the peri-operative mortality was relatively low. Predicting outcome and cardiac risk at workup remains challenging. Interpretation of this data is limited by the lack of a matched cohort group.

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## RENOPROTECTION WITH SGLT2 INHIBITION

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**Aim:** To examine the renoprotective effects of a sodium glucose cotransporter 2 inhibitor (SGLT2i) using an *in vivo* model of diabetic nephropathy.
**Background:** A third of patients with diabetes suffer from diabetic nephropathy (DN) and current available management provides at best a 30% reduction in the decline of kidney function, revealing a significant treatment gap. SGLT2i are novel oral diabetic drugs, which block the reuptake of filtered glucose by inhibiting SGLT2, the primary glucose transporter in the kidney.
**Methods:** Diabetes was induced in 8 week old *enos -/-* mice using a low dose streptozotocin protocol. Animals were treated with Empagliflozin (SGLT2i) and Telmisartan (current best practice) for 20 weeks. Blood glucose levels in all the diabetic limbs were matched. Urinary albumin excretion and creatinine clearance was calculated preterminally. Kidney histology was assessed using Masson's trichrome and Periodic acid Schiff. Immunohistochemistry was performed for Fibronectin and F4/80 stain. Real time PCR on cortical tissue was done for fibronectin, transforming growth factor beta and collagen IV.
**Results:** Diabetic animals showed an increase in urinary albumin/creatinine, glomerulosclerosis and tubulointerstitial damage and a reduction in creatinine clearance compared to controls validating our model. Diabetic animals treated with empagliflozin showed a reduction in preterminal urinary albumin/creatinine ratio and an improvement in creatinine clearance. However they did not show any difference in the glomerulosclerotic index or macrophage infiltration. There was a nonsignificant trend towards a reduction in tubular atrophy and tubulointertitial fibrosis. There was significant improvement in diabetic animals treated with telmisartan.
**Conclusions:** Our preliminary results would suggest that although Empagliflozin improved renal function and reduced albuminuria, there was only a mild and nonsignificant histological improvement in our model.

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## OLIGOSACCHARYLTRANSFERASE-48 AS A NOVEL MEDIATOR OF CHRONIC KIDNEY DISEASE IN DIABETES

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**Aims:**
1. To characterise the physical and biochemical characteristics of the OST-48 transgenic knock-in model.
2. To investigate if changes in OST-48 expression in mice affects kidney function and insulin sensitivity in the presence or absence of diabetic kidney disease.

**Background:** Kidney disease affects up to one third of Australians with diabetes and is one of the most serious chronic complications. N-glycosylation, which is necessary for the correct folding and trafficking of many proteins, is controlled by a subunit called oligosaccharyltransferase-48 (OST-48) in mammals. Hence we have investigated the effects of modulating the expression of OST-48 globally on the development and progression of kidney disease in the presence and absence of diabetes.

**Methods:** Male heterozygous global OST-48 transgenic knock-in mice ($DDOST^{Tg/WT}$) and littermate controls (N = 8/group) were randomised to diabetes by low dose streptozotocin (50 mg/kg/day for 5 days) or no diabetes and followed for 24 weeks. Physical characteristics were measured throughout the study and biochemical properties were identified through metabolic caging. We then examined kidney function through the rate of albumin excretion measured by ELISA and the ratio of creatinine clearance by HPLC. Finally we investigated the insulin sensitivity of these mice through IPGTT and IPITT.
**Results:** $DDOST^{Tg/WT}$ mice had a significant decrease in insulin sensitivity and kidney function by the study completion and this was further exacerbated by diabetes.
**Conclusions:** This preliminary investigation has demonstrated that functional OST-48 may play a role in normal kidney function and insulin sensitivity, seen here as, impaired glomerular filtration rate and more pronounced insulin resistance. Therefore, we suggest that the alteration of functional OST-48 may play a role in kidney function which is further exacerbated by diabetes.

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## RENAL FIBROSIS FOLLOWING RENAL ISCHEMIA REPERFUSION INJURY (IRI) IS EXACERBATED IN THE PRESENCE OF A NORMAL KIDNEY

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**Background:** Renal ischemia is encountered frequently in the context of renal artery stenosis (RAS), which is associated with hypertension, ischemic nephropathy and chronic kidney disease (CKD). The pathological hallmark of CKD is parenchymal fibrosis.
**Aim:** To compare the fibrotic outcome of unilateral renal IRI in a mouse model with and without a normal contralateral kidney.
**Methods:** Mice were anesthetised and left renal pedicle was clamped for 23.5 mins before reperfusion. In the "IRI" model, the right kidney was left *in situ*. In the unilateral IRI ("UIRI") model, a right nephrectomy was performed before unilateral renal ischemia. Mice were then euthanised at week 4 and the kidneys were harvested for histological examination.
**Results:** Mice with the right kidney *in situ* had more fibrosis at week 4 compared to mice with unilateral nephrectomy. Fibrosis score was $0.3267 \pm 0.02963$ (n = 3) and $0.0602 \pm 0.006383$ (n = 5) respectively, p = <0.0001. The size of the left ischemic kidney was smaller if the right kidney was *in situ* compared to if it was removed; $107.0 \pm 7.550$ mg (n = 3) vs $181.8 \pm 6.931$ mg (n = 5), p = 0.0004.
**Conclusion:** The presence of a normal kidney exacerbates the development of fibrosis following hypoxic injury to the contralateral kidney. This may implications in the management of patients with unilateral RAS.

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## AMILORIDE MODIFIES RENAL FIBROSIS INDUCED BY LONG TERM LITHIUM TREATMENT

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**Aim:** To elucidate the long-term effect of amiloride on lithium-induced renal fibrosis.
**Background:** Chronic lithium administration has been reported to induce kidney fibrosis in some patients in addition to nephrogenic diabetes insipidus (NDI). We have previously demonstrated that long-term lithium administration in rats produces chronic interstitial fibrosis in the kidney along with cystic dilatation of the collecting ducts. Amiloride partially reverses lithium-induced NDI, however, the effects of long-term amiloride treatment on chronic lithium-induced interstitial fibrosis are unknown
**Methods:** 3 groups of male wistar rats, control, lithium alone and lithium plus amiloride, were studied. The rats were fed a diet containing lithium for 6 months (60 mmol $kg^{-1}$ food). Amiloride was added in the drinking water (0.2 mmol $L^{-1}$) after one-month of lithium treatment and continued for 5 months. After 6 months rats were euthanized, kidneys were processed for histology, immunohistochemistry and western blotting, focusing specifically on fibrotic markers.
**Results:** Masson's and Picro Sirius red staining demonstrated significant fibrosis in lithium treated group, which was attenuated with amiloride. Immunostaining revealed increased expression of, alpha-smooth muscle actin ($\alpha$-SMA) connective tissue growth factor (CTGF) and collagen III with lithium treatment that was substantially reduced with amiloride. The structural changes to the kidney such as the cystic dilatation of the collecting ducts and tubular atrophy was not modified with amiloride treatment.
**Conclusions:** Chronic amiloride treatment attenuates the lithium-induced fibrotic changes in the kidney without having any effect on the structural changes. Lithium inhibits intracellular cAMP pathways, which are compartmentalised within the cell. Thus lithium may have differing effects on these intracellular pathways involved in the maintenance of renal cell architecture. Further studies are underway to explore this.

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## MATERNAL OBESITY IS ASSOCIATED WITH CHANGES IN GENE EXPRESSION OF INFLAMMATORY CYTOKINES IN THE KIDNEY OF RAT OFFSPRING

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**Aim:** To determine the role of fetal metabolic programming in the development of chronic kidney disease (CKD). In particular, to determine whether the kidneys of offspring exposed to maternal obesity in utero display altered gene expression associated with CKD during postnatal life.
**Background:** Maternal obesity is associated with dyslipidemia, and constitutes an adverse intrauterine nutritional environment for embryo development. Maternal obesity may program a variety of lifelong metabolic abnormalities in offspring, such as obesity, dyslipidemia, diabetes and CKD.
**Methods:** Eight-week old rats were fed either standard or a high fat diet (HFD) for 5 weeks before mating and throughout pregnancy. On postnatal day 1, litter size was adjusted to 6 pups/mother. Mothers were fed the same diet postpartum. The pups' anthropometric measures, blood triglycerides and glucose/insulin levels were recorded at weaning (20 days). Their kidneys were weighed and snap frozen for protein and mRNA extraction. mRNA was extracted and gene expression of profibrotic factors (TGFbeta, CTGF, PAI-1), proinflammatory cytokines (TNFalpha, IL-6 and MCP-1), and metabolic markers (FXR, PPAR, SREBP) was measured by real time PCR.
**Results:** Offspring from obese rats displayed increased body weight, fat and kidney mass, blood triglycerides, and glucose intolerance compared with those from lean rats (N = 3). mRNA expression of proinflammatory cytokines was increased in offspring of obese mothers compared with lean controls and, in particular, TNFalpha and MCP-1 were significantly higher. There were no differences in profibrotic or metabolic genes.
**Conclusions:** Maternal obesity is associated with increased expression of proinflammatory cytokines in offspring's kidneys. Given the known role of inflammatory cytokines in CKD, these results support the role of epigenetic programming in utero to the development of CKD.

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## INTRAUTERINE HYPOXIA IMPAIRS KIDNEY DEVELOPMENT VIA DISRUPTION TO B-CATENIN ACTIVITY

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**Aim:** Kidney development can be affected by environmental stressors, with subsequent reductions in nephron number causing long term effects on renal function. As hypoxia is a common insult during pregnancy, we investigated the influence of oxygen tension on kidney development *in vivo* and *in vitro*.
**Methods:** Pregnant dams were subjected to midgestational (E12.5) moderate (12% O2) hypoxia for 48 hours after which kidneys were harvested from embryos. Embryonic kidneys at E12.5 were cultured in physiological hypoxia (1% $O_2$) for 40 hrs. Nephron number was quantitated and changes in gene and protein expression investigated in both models.
**Results:** E14.5 kidneys subjected to in utero hypoxia showed an immediate suppression of branching and nephron number that persisted into the postnatal period. Similarly, cultured E12.5 kidney explants showed reduced ureteric branching and a suppression of nephron induction in hypoxic conditions. QPCR and *in situ* hybridization confirmed this reduction in renal vesicles and showed a

loss of tip identity without significant loss of *Wnt9b* expression. The cap mesenchyme remained competent to respond to an exogenous canonical signal, however hypoxia resulted in reduced activated β-catenin within the ureteric tips. Inhibition of canonical Wnt signaling (IWR-1) mimicked this hypoxic phenotype whereas suppression of Wnt secretion (IWP-2) resulted in cap mesenchyme loss. Culture of UB2 cells in hypoxia confirmed a reduction in activated β-catenin.
**Conclusions:** We confirm an association between gestational hypoxia and inefficient canonical Wnt signaling and show this has affects final nephron number. Based on the diverse roles played by canonical Wnt signaling during kidney development, hypoxia may result in distinct renal developmental defects depending upon the timing, severity and duration of the hypoxic episode.

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## HUMAN KIDNEY PROXIMAL TUBULE EPITHELIAL CELLS (PTEC) MODULATE AUTOLOGOUS IMMUNE RESPONSES BY CONTACT DEPENDENT MECHANISMS

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**Aim:** To determine the affects of human proximal tubule epithelial cells (PTEC) on autologous B cell Ab production and to further characterise their mechanisms of T cell and dendritic cell (DC) down modulation.
**Background:** PTEC down modulate autologous human T/B cell and DC responses. (Wilkinson et al NDT 2011, 2012). We have extended this research by analyzing PTEC effects on B cell Ab production and culturing T cells and DC in the presence of autologous PTEC using contact dependent and independent culture systems in an effort to define the mechanisms of this modulation.
**Methods:** B cells, T cells and DC were cultured with or without PTEC in the presence of various stimuli. The numbers of B cells producing Ab was analysed using isotype specific ELISPOT, whilst readouts for T cells and DC included proliferation, Ag expression and cytokine secretion.
**Results:** PTEC significantly reduced the number of B cells that produced Ab in response to Toll-like receptor stimulation. PTEC also significantly down modulated T cell responses (n = 6) and this modulation was ablated when the cells were separated by a transwell membrane with 5 out of 6 donors demonstrating equivocal proliferation. Similarly, PTEC down modulation of DC differentiation was partially ablated when the DC and PTEC were separated by a transwell membrane resulting in mature MoDC development.
**Conclusions:** These results demonstrate for the first time that human autologous PTEC can regulate B cell Ab production and that their modulatory effects on T cells and DC are, at least in part, contact dependent. We will elucidate these mechanisms further in an effort to identify novel clinical targets for therapy in renal disease.

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## REDUCED NEPHRON NUMBER BUT HYPOTENSION IN MALE MOUSE OFFSPRING FOLLOWING PRENATAL CORTICOSTERONE EXPOSURE

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**Aims:** To investigate the effects of prenatal corticosterone (CORT) exposure on kidney structure and long-term cardiovascular and renal function.
**Background**: Exposure to synthetic glucocorticoids *in utero* has been associated with the development of hypertension in later life for both humans, and in animal models. The effects of natural glucocorticoids have been less well characterized. We used a mouse model of short-term prenatal exposure to excess CORT to investigate the long-term cardiovascular and renal outcomes.
**Methods**: C57/Bl6 mice received CORT (33 μg/kg/h) via osmotic mini pump from embryonic day 12.5–14.5. Controls remained untreated (UNTR). Dams littered-down naturally and male offspring were aged to 12 months to examine kidney function via metabolic cage studies and arterial pressure via radiotelemetry. A subset of animals was culled at postnatal (PN) day 30 for determination of nephron number and renal tubule lengths.
**Results:** Maternal CORT treated offspring had a 33% reduction in glomerular number at PN30 compared to UNTR (P = 0.0028). Lengths of renal proximal, distal, tubules, thin limb of loop of Henle and collecting ducts were similar between the CORT and UNTR offspring. At 12 months of age, urinary electrolyte and albumin excretion rates were significantly higher in male offspring from the CORT dams compared to UNTR (P < 0.05 for all). However, basal blood pressure (systolic, diastolic and mean) was significantly lower in the CORT offspring compared to UNTR.
**Conclusion:** Maternal CORT treatment result in a reduction in nephron number in male offspring. Despite this reduction in nephron number, aged offspring were hypotensive. Furthermore, while renal tubule lengths were similar at PN30, the increases in electrolyte excretion in older animals suggest renal tubular remodeling with ageing and needs to be further investigated.

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## CHRONIC MID-LATE GESTATIONAL HYPOXIA ALTERS RENAL STRUCTURE AND FUNCTION IN ADULT MALE MOUSE OFFSPRING

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**Aim:** This study examined the impact of chronic mid-late gestational hypoxia on renal structure and function in adult mouse offspring.
**Background:** The kidney is particularly susceptible to adverse in-utero environments. Fetal hypoxia is a common occurrence but the effects on the kidney are not well described. Alterations to the renal system during development may predispose offspring to diseases in adulthood.
**Methods:** Pregnant CD-1 mice were placed in a hypoxic (12.0% $O_2$; n = 11) or control (21% $O_2$; n = 11) environment from embryonic (E) day 14.5 to birth (E19.5). Offspring growth was monitored from postnatal day (P) 1 to adulthood. A subset of male and female offspring was culled at P21 for estimation of glomerular number using the physical disector/fractionator approach. Renal function under basal conditions and in response to 24 hours of water deprivation was assessed in 10-month (mth)-old animals.
**Results:** Hypoxia-exposed offspring were significantly lighter than controls at birth, and remained lighter until 1 mth. Absolute kidney weights were reduced in male and female hypoxia-exposed offspring compared to controls. Male hypoxia-exposed offspring had a 23% reduction in nephron number whereas females were unaffected. Urine flow and electrolyte excretion were similar in all groups under basal conditions at 10mth. However, male hypoxia-exposed offspring did not reduce urine flow and had increased urinary electrolyte excretion during water deprivation.
**Conclusions:** Maternal hypoxia led to growth restriction and subsequent catch-up growth. All offspring maintained basal renal function in adulthood, despite the nephron deficit in males. However, males challenged with water deprivation were unable to respond appropriately. This inability to adapt to additional stressors highlights the sex-specific effects of maternal hypoxia and suggests males may be more susceptible to adulthood disease.

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## PERICONCEPTIONAL ETHANOL EXPOSURE IN THE RAT ALTERS KIDNEY DEVELOPMENT WITH FUNCTIONAL CHANGES IN ADULT MALE OFFSPRING

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**Aim:** To investigate the effects of periconceptional ethanol exposure on the developing and adult kidney.
**Background:** The kidney is susceptible to perturbations at specific time points during development. Alcohol consumption during late pregnancy has been demonstrated to decrease nephron number and affect urine concentrating ability in offspring. While many women discontinue drinking after recognition of pregnancy, alcohol is frequently consumed around the time of conception. The effects of periconceptional alcohol on the developing kidney are yet to be characterised.
**Methods:** Female Sprague Dawley rats were placed on a liquid control diet or a diet containing a 12.5% v/v ethanol from 4 days before mating (E-4) until embryonic day four (E4). Tissues were collected at both embryonic day 20 (E20) and postnatal day 30 (PN30) and body weights measured. Renal function studies were performed over 24 hrs at six months of age.
**Results:** Ethanol exposure reduced body weight in both sexes at E20 (P < 0.05) although total kidney weight was not different. By PN30, body weight after exposure to ethanol was similar to control, but kidney weight was reduced and

nephron number was 10% lower ($P < 0.05$). At six months of age, urinary flow rate was significantly increased (by 23%) in male offspring exposed to ethanol ($P < 0.05$), although excretion of sodium, chloride and potassium remained unchanged.
**Conclusions:** This study shows that alcohol exposure around the time of conception can impair kidney development and influence renal function in adulthood. This occurs despite the alcohol exposure occurring prior to kidney development. Changes in kidney structure and function have been linked to adverse cardiovascular health. Our novel results highlight that women planning to become pregnant should avoid consumption of ethanol.

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## MIDKINE ANTIBODIES PREVENT RENAL INJURY IN ADRIAMYCIN NEPHROPATHY

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**Background:** Midkine (MK), a heparin-binding growth factor, regulates cell growth and survival in nephrogenesis and kidney development. It has been demonstrated that MK has a pathogenetic role in acute injury of renal ischaemia and in progression of diabetic nephropathy. However, the role of MK in chronic inflammatory kidney disease remains unclear.
**Methods:** AN was induced by Adriamycin in BALB/c mice. Two MK antibodies: IP-10 targeting the C terminal; and IP14 the N-terminal of MK were given at 25 mg/kg via peritoneum by 6 consecutive injections starting from one day before Adriamycin administration.
**Results:** Body weight loss was significantly less in AN mice injected with IP10 or IP14 in comparison to weight loss in AN control mice. AN mice administered with IP10 or IP14 had less glomerulosclerosis, tubular atrophy and interstitial expansion than that of control AN mice. AN mice infused with IP10 or IP14 also had significantly lower levels of proteinuria and serum creatinine than AN mice. Creatinine clearance was improved significantly in AN mice injected with anti-MKs compared to AN control mice. The possible mechanism underlying a protective effect of anti-MK may be related to reduction of inflammation by anti-MK. The number of inflammatory cells including macrophages, neutrophils and T cells was significantly reduced in AN with anti-MK compared to that of AN control mice. There was no significant difference between the effect of anti-MK targeting the C terminal versus N-terminal of MK in reduction of renal structural and functional injury in AN mice.
**Conclusion:** Anti-MK antibodies protected against renal injury in AN. The protective effect may be related to their ability to reduce renal inflammation.

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## THE ROLE OF β-CATENIN IN TGF-β1-INDUCED FOXP3 EXPRESSION AND TREG INDUCTION

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**Aim:** To examine the role of β-catenin in TGF-β1-induction of Tregs in vitro.
**Background:** TGF-β is known to play a key role in induction of $CD4^+CD25^+$ Foxp3 regulatory T (iTreg) cells. While Foxp3 has been proven to be a key transcription factor for iTreg induction, the transcription factor Foxo has been reported to enhance Foxp3 expression and iTreg induction. Recent studies have shown that β-catenin binding to Foxo can promote Foxo transcriptional activity in cancer cells. Inhibition of β-catenin interaction with the transcription factor TCF increased its binding to Foxo. Whether β-catenin can also play an active role in iTreg induction is unknown. This study investigated the role of β-catenin in TGF-β1-induced Foxp3 expression and iTreg induction by using a β-catenin protein degradation chimera F-Trcp-Ecad, and a β-catenin/TCF inhibitor ICG001.
**Methods:** Mouse $CD4^+CD25^-Foxp3^-$ T cells were treated with TGF-β1, IL-2 and anti-CD3/CD28 to induce $CD4^+CD25^+Foxp3^+$ iTregs. The role of β-catenin was examined by transfection of $CD4^+CD25^-Foxp3^-$ Tcells with F-TrCP-Ecad or wild type β-catenin, or by treatment with ICG001 during TGF-β1 induction of iTregs. Foxp3 and β-catenin expression was analysed by flow cytometry and Western blot. Topflash and Smad reporter assays were used to determine β-catenin/TCF and Smad transcriptional activity.
**Results:** TGF-β1 induced Foxp3 expression and conversion of $CD4^+$ $CD25^-Foxp3^-$ Tcells to iTregs. β-catenin expression was up-regulated in TGF-β1-induced Foxp3-expressing iTregs. Degradation of β-catenin by F-TrCP-Ecad prevented TGF-β1-induced Foxp3 expression and inhibited Foxo transcriptional activity. Overexpression of β-catenin or inhibition of β-catenin/TCF transcriptional activity by inhibitor ICG001 promoted TGF-β1-induced Foxp3 expression.
**Conclusion:** β-catenin upregulates TGF-β-induced Foxp3 expression, potentially through binding to Foxo.

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## MATERNAL HYPOMAGNESAEMIA CAUSES FOETAL GROWTH RESTRICTION BUT DOES NOT ALTER RENAL MORPHOLOGY OR MANGESIUM CHANNEL EXPRESSION IN OFFSPRING

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**Aim:** To investigate the impact of maternal magnesium deficiency on renal development, foetal growth, and the involvement of magnesium channels in these processes.
**Background:** Magnesium (Mg) is essential for the maintenance of normal cellular processes within the body. However, a large number of women are likely to be Mg deficient during pregnancy. Whilst Mg is recognised as being important in foetal development, how altered Mg levels during pregnancy may affect renal development remains unknown.
**Methods:** Hypomagnesaemia in female CD1 mice was induced using Mg-deficient diets (moderate deficiency 0.02% Mg; MMD, severe deficiency 0.005% Mg; SMD, vs. 0.2% control Mg diet, n = 12/group) for a period of four weeks prior to mating and throughout pregnancy. In late gestation (E18.5), dams were euthanized and embryos collected.
**Results:** Maternal plasma Mg levels in dams were significantly reduced ($0.49 \pm 0.029$ mmol/L; MMD and $0.34 \pm 0.036$ mmol/L; SMD) when compared to control ($0.81 \pm 0.035$ mmol/L). This was associated with reduced foetal plasma Mg in the SMD group. Foetal body weight was reduced in MMD ($1.21 \pm 0.03$ g) and SMD ($1.13 \pm 0.03$ g) groups when compared to control ($1.25 \pm 0.02$ g). Although brain and liver weights were reduced in Mg-deficient offspring, kidney weight was maintained ($9.81 \pm 0.31$ mg; MMD and $9.69 \pm 0.49$ mg; SMD) compared to control ($9.55 \pm 0.31$ mg). Interestingly, TRPM6 was modestly upregulated in male embryos, and TRPM7 upregulated in female embryos. No changes in MagT1 were seen between groups.
**Conclusions:** Despite maternal hypomagnesaemia causing foetal growth restriction, renal growth was not affected. However, further molecular and histological analyses are needed to elucidate the implications of maternal hypomagnesaemia on renal development.

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## ELEVATED CONCENTRATIONS OF INTERLEUKIN-12 AND 18 IN CHRONIC KIDNEY DISEASE PATIENTS SYNERGISTICALLY INDUCE T-CELL ACTIVATION AND PROLIFERATION *IN VITRO*

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**Aim:** To examine whether the elevated concentrations of interleukin (IL)-12 and 18 in chronic kidney disease (CKD) patients are capable of inducing T cell activation *in vitro*.
**Background:** CKD patients are at an increased risk of cardiovascular disease (CVD); possibly attributed to elevated pro-inflammatory cytokines IL-12 and 18 inducing aberrant T-cell activation.
**Methods:** Serum levels of IL-12 and 18 were quantified by ELISA in a cross-sectional cohort of 69 healthy controls and 139 stage 3–5 pre-dialysis CKD patients. Immunomagnetic-bead isolated CD3-positive T cells were cultured in complete medium (10% v/v fetal calf serum) in the presence of the average concentrations of IL-12/18 detected in CKD patients. T cell activation, proliferation and messenger ribonucleic acid (mRNA) expression of interferon-gamma receptor (IFN-γR), IL-12R and IL-18R were assessed.
**Results:** Serum concentrations of IL-12 (81 vs 30 pg/mL, $p < 0.01$) and 18 (455 vs 357 pg/mL, $p < 0.01$) were significantly higher in CKD patients. T cells stimulated with 100 pg/mL and 500 pg/mL of exogenous IL-12 and 18 respectively

produced over a 75-fold increase in IFN-γ and a 1.3-fold increase in bromodeoxyuridine incorporation into proliferating T cells compared to unstimulated cells ($p < 0.02$), which was suppressed by IL-12 and IL-18 blockers. Stimulation with IL-12 and 18 resulted in up to a 1.6-fold increase in mRNA expression of IFN-γR, IL-12R and IL-18R ($p < 0.05$). IL-12 or IL-18 alone in culture did not induce significant T cell activation and proliferation.
**Conclusions:** The elevated serum concentrations of IL-12 and 18 in CKD patients are capable of inducing a strong T cell response *in vitro*, which may contribute to the pathogenesis of CVD in this population.

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## ANALYSIS OF LINKAGE OF P2X7R TO BALB/C ASSOCIATED KIDNEY INJURY IN THE ADRIAMYCIN MURINE MODEL IN F2 MICE

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**Aims:** To assess whether the P451L functional polymorphism in P2X7R, a member of purinoceptors for ATP, is responsible for ATP-mediated injury associated with Adriamycin Nephropathy (AN).
**Background:** Prkdc mutations have been identified as risk factors for severity of AN in mice. Prkdc encodes a critical nuclear DNA double-stranded break repair protein and knockout produces the Severe Combined Immunodeficiency (SCID) mouse (BALB/c background). C57BL/6-SCID mice are susceptible to AN. Extracellular ATP and its major receptor P2X7R appear to be involved in early stages of damage in nephritis. A natural P451L mutation in C57BL/6 mice was reported to impair functions of the P2X7 receptor and accounts for differential strain responses to ATP in C57BL/6 (resistant) and BALB/c (susceptible) strains.
**Methods:** 50 F2 mice were generated from F1 (BALB/c x C57BL/6) mice and received Adriamycin (ADR) to induce AN. Four weeks after ADR, renal function and histology were assessed. The polymorphisms in Prkdc and P2X7 receptor (P451L) were studied by custom-single nucleotide polymorphism (SNP) platform.
**Results:** At week four post-Adriamycin, half of the F2 mice had increased urinary protein excretion and had a higher level of serum creatinine compared with normal BALB/c or C57BL/6 mice. Glomerular and tubular damage was observed in 11 out of 50 mice. Genotyping of mice demonstrated morphological damage in kidney after ADR was linked to a mutation in Prkdc gene as previously reported but not to the mutation in P2X7R gene.
**Conclusions:** While ATP can exacerbate renal injury its differential severity in BALB/c mice is not linked to mutations in the ATP sensitive P2X7R.

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## SURVEY OF CURRENT RENAL TRAINEE'S ATTITUDE TO INTERVENTIONAL NEPHROLOGY

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**Aim:** To determine attitude of renal trainees about current practices in interventional nephrology and utilise the information to allow ANZSIN to develop/improve training and certification in interventional nephrology.
**Background:** Currently there is no standards in training and accreditation in interventional nephrology among all Australian / New Zealand hospitals. This survey, the first from advanced renal trainees on interventional nephrology will provide information to identify training deficiencies and help develop standards in procedural nephrology.
**Methods:** A web based survey questionnaire on various aspects of interventional nephrology was sent out to trainees via Kidney School. A total of 17 out of 50 trainees responded.
**Results:** 100% of the trainees agreed that they should perform renal biopsies.82.3 % perform real time ultrasound guided renal biopsy while only 6% had performed CT guided renal biopsy. 88% thought renal trainees should place percutaneous dialysis catheters.70% had placed non cuffed HD catheter while only 41% had placed a cuffed HD catheter.93% can remove a cuffed HD catheter.

While only 11.7% had actually placed a PD catheter 70% of advanced renal trainees thought they should place peritoneal dialysis catheters.

58% thought they should be able to perform a fistuloplasty while only 5% had actually performed a fistula angioplasty. 52% were able to perform renal ultrasound while only 5% were able to perform fistula ultrasound with interpretation of results. 100% thought more ultrasound training would be useful.

Among all interventional procedures trainees thought the education given prior to performing procedures is inadequate (66–83%). Trainees found formal certification prior to any interventional procedure independently was needed, (76% for renal biopsy and 81% for dialysis catheter).
**Conclusions:** The survey found significant deficiencies in current procedural nephrology training from trainee perspective. The pre procedural theoretical training is thought to be inadequate and most trainees want a formal certification process.

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## COST EFFECTIVENESS OF URINE PROTEIN SCREENING ON DIFFERENT POPULATION

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**Aim:** To asses the cost effectiveness of urinary protein dipstick screening on different subgroups of the population.
**Background:** Performing a cost-effectiveness analysis on screening for proteinuria may help choose which population will yield higher number of proteinuria with the lowest cost.
**Methods:** Three population groups were screened using urinary dipsick test (Combur-10-Test™, Roche) to detect proteinuria on World Kidney Day event in 2011 and 2012 and cost-effectiveness analysis was performed for each group.
**Results:** The first group consisted of 444 soldiers and their families; the result were 15.20% with hypertension, 4.05% with diabetes and 40.1% overweight. Proteinuria was found in 25 participants (5.63%) and cost effectiveness in this group was $ 18.194 for each positive result. Group 2 were 100 employees of a manufacturing industry who visited the company clinic for various complaints; we found 32% with hypertension, 15% had diabetes, 66% overweight. Proteinuria was found in 6 participants (6%) and cost effectiveness was $ 9.76. Group 3 were 39 elderly people under supervision of a primary health care clinic, there were 51.3% with hypertension, 92.3% with diabetes, 35.90% overweight. Proteinuria was found in 6 partcipants (15.38%) and cost effectiveness was $ 2.65. After calculating the cost effectiveness ratio of each group, group 3 was the best comparator, resulting in higher CER of 3.67 in group 2 and 6.85 in group 1.
**Conclusion:** The highest number of participants with proteinuria was in group 3 (elderly population) (15.38%) and also the most cost effective. Compared to this group, performing screening was less cost effective in group 2 and the least cost effective in group 1.

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## CKD PATIENT PROFILES FROM A REGIONAL QUEENSLAND HEALTH RENAL CLINIC AND OUTCOMES AFTER ONE YEAR. CKD.QLD REGISTRY

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**Aim:** To profile CKD patients attending Queensland Health (QH) public renal clinics at the Mackay Base Hospital and assess longitudinal outcomes in a group followed for at least one-year.
**Background:** The CKD.QLD registry is addressing a significant evidence gap in CKD outcomes.
**Methods:** All CKD patients not requiring renal replacement therapy (RRT) attending Mackay Base Hospital renal clinics were offered entry into the CKD.QLD registry, based on written informed consent. Those enrolled were entered into a central database allowing analysis of patient outcomes.
**Results**: 225 patients were recruited, representing an estimated 90% of patients in the practice. Two patients declined. 111 were recruited more than a year ago. Of the 225, 56% were males, 44% females, with mean ages 65.6 yr for males and

61.7 yr for females. CKD stages represented were – 1: 14%, 2: 13.5%, 3A: 16%, 3B: 27.5%, 4: 30% and 5: 9%. Leading etiologies were hypertension 19.8%, diabetic nephropathy 16.8%, glomerulonephritis 13.9% and uncertain 18.8%. Over more than a year, 21 of the first 111 patients recruited became "inactive": 15 (13.5%) started RRT, 2 (2%) died cardiovascular deaths, 2 were discharged from care and 2 relocated. In the 87 followed for more than one year, mean rate of eGFR (CKD-epi) decline was 1.7 ml/min/1.73 $m^2$ eGFR declined by ≥5 ml/min in 15% (13/87); was approximately stable in 74% (64/87); and improved (by ≥5 ml/min) in 12% (10/87).
**Conclusions:** A comprehensive view in a regional QH renal clinic showed that most CKD patients were in stages 3B and 4; 28.5% lost renal function, including 13.5% who started RRT. There were fewer CV deaths than expected. Longer follow up of the larger cohort is underway.

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## THE LUPUS NEPHRITIS AUSTRALIAN REGISTRY (LUNAR)

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**Background:** Systemic lupus erythematosus (SLE) is a multisystem, autoimmune disease, characterised by frequent relapses and remissions. It generally affects females, particularly during childbearing years, and is almost 4 times more common in the Aboriginal population. Patients with kidney involvement, particularly WHO class III or IV lupus nephritis (LN), typically have poorer outcomes than those without. Until recently, the management of severe disease has involved corticosteroids and cyclophosphamide for both for induction and maintenance therapy. Cyclophosphamide has signficiant gonadal toxicity, is carcinogenic and recent studies have supported the use of alternative strategies involving mycophenolate for similar efficacy with reduced toxicity. In 2012 mycophenolate sodium was approved in Australia for induction and maintenance therapy in adult patients with WHO class III, IV or V LN.
**Aim:** To assess the safety, efficacy and outcomes of indigenous and non-indigenous patients treated for LN with Mycophenolate and other immunosuppressive agents within Australia.
**Methods:** This is an ongoing multicentre, non-interventional registry of patients treated for WHO class III, IV or V LN. Data is to be collected from approximately 250 patients taking mycophenolate sodium and other immunosuppressives over a 5 year period. Regular six-monthly observational data capture includes laboratory measures of disease (serum creatinine and complement levels, full blood count, ESR, CRP, anti-dsDNA and urinary estimations of erthrocytes and proteinuria), histopathology, and estimates of disease activity (SLE disease activity index (SLEDAI)).
**Results:** Six sites across different states of Australia are enrolled to participate in LUNAR.
**Conclusions:** LUNAR is the first study in Australia to examine outcomes in patients treated for WHO class III, IV or V LN with Mycophenolate and other immunosuppressive agents and may further inform therapeutic decisions regarding management of lupus nephritis.

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## ASSESSMENT OF CADMIUM LOAD IN RENAL BIOPSIES FROM SRI LANKAN PEOPLE WITH CHRONIC KIDNEY DISEASE OF UNKNOWN ORIGIN

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**Aim:** To determine cadmium levels in renal biopsy tissue from adults of North Central Province (NCP), Sri Lanka, who have unexplained nephropathy.
**Background:** There is a recognised epidemic of chronic kidney disease (CKD) of unknown aetiology in this region. The literature has reported cases from the year 2000 onwards. Sufferers, predominantly male agricultural workers, present with modest levels of albuminuria and experience a progressive loss of kidney function and premature mortality. One postulated explanation is chronic exposure to cadmium through environmental contamination. Cadmium levels in kidney tissue of these people are unreported.
**Methods**: In an opportunistic approach, using samples collected for another purpose, formalin-fixed, paraffin-embedded renal biopsy tissue from 14 Sri Lankan NCP males and 6 similarly-prepared samples from Australian males without CKD were compared. Mean ages were 47.9 and 42.3 years (P = 0.28) respectively. Ten μm thick sections were mounted on silicon nitride holders. Each was subjected to high-energy X-ray fluorescence synchrotron radiation at the Spring-8 Synchrotron, Japan. Bulk measurements of cadmium were followed by micro measurements of selected areas approximately 1 $\mu m^2$.
**Results**: Geometric mean cadmium was significantly lower in the Sri Lankan than Australian samples (52.48 and 134.90 ppm respectively, P = 0.0008). Cadmium mapping did not indicate localised distribution within any kidney structures, with mean cadmium values in the glomeruli or tubules not significantly different between the two groups (P = 0.77, P = 0.81).
**Conclusions**: Detectable cadmium is present in the Sri Lankan and Australian specimens. Lower levels in the Sri Lankan kidneys do not necessarily exclude a role for cadmium in the nephrotoxicity: without standards and samples from Sri Lankans without CKD from the same region, interpretation of any relationship between cadmium and CKD is not possible.

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## PREVALENCE AND COMPOSITION OF URINARY TRACT STONES FROM A TERTIARY CARE HOSPITAL, RIYADH

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**Aim:** The objective of the study was to study the Prevalence and Composition of Urinary Tract Stones in Saudi population.
**Background:** Urolithiasis is a common problem in elderly population of developed countries. Urinary stones formation is thought to be multi-factorial because of climatic conditions, eating habits, luxurious lifestyle.
**Methods:** A total of 332 urolithiasis patients of King Khalid University Hospital, of age ranging from 1–90 years (255 M & 77 F) were studied. Stone samples were obtained after surgery, for analysis. All stones were analyzed by spectroscopic semi quantitative method using Thermo Scientific analyzer with Thermo Electrons OMNIC spectroscopy software.
**Results:** In the present study 255 (76.8%) stone samples were obtained from male patients and 77 (23.1%) from female patients. Analysis according to age groups show high occurrence of urinary tract stones in males aged between 51–60 yrs (25.8%) and in females between the age of 41–50 yrs (23.3%). Anatomically, stones were found prevalent in kidneys (79.2%). Nephrolithiasis mainly affect females (88.3%). Calcium was the main constituent being seen in 316 (95.1%) stones, of these 178 (53.6%) stones show calcium as only cation with other anions and 138 (41.4%) stones show calcium with magnesium and other anions. Magnesium containing stones were profound in females (57.14%) than males (36.86%). Uric acid (28.1%) and cystine (12.9%) stones were least observed.
**Conclusions:** The current findings demonstrate an increased incidence of stone disease in males, but a shift is noticed in the prevalence by gender in nephrolithiasis in the population. In addition Calcium oxalate stones remain most frequent, with magnesium and uric acid.

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## RECOGNISING SALT WASTING NEPHROPATHY

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**Aims:** To increase awareness of tubular-interstitial pathology.
**Background:** Routine nephrological investigations only provide assessment of glomerular functions (i.e. e-GFR and proteinuria). When these are abnormal sodium retention is a frequent finding. My experience suggests that approximately 15% of patients seen in my clinic may have salt wasting. Recognition of this may well be indicative of renal tubular pathology and important in their care.
**Methods:** Retrospective study of case histories, for symptoms of salt depletion (thirst, postural dizziness, cramps), along with other associated symptoms, including nocturia, dysuria, alcohol sensitivity, headache, loin pain and enuresis. Alternative causes for salt wasting were excluded such as diuretic treatments and stoma losses.
**Results:** The presence of two or more of these symptoms in fifty patients identified by me as salt wasters gave best sensitivity and specificity ( 92% and 83%), compared to a group of 42 patients with biopsy proven GN (24 patients) and adult polycystic kidney disease (18 patients). Using three symptoms increased specificity to 90% but reduced sensitivity to 74%. Reliance on the presence of only one symptom increase sensitivity to 96% but reduced specificity to 60%.

**Conclusions:** Salt wasting nephropathy can be readily identified from the clinical history. This might provide valuable clinical insight and identify patients for further study.

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## THE DEVELOPMENT AND GROWTH OF CKD.QLD: A FOUR YEAR JOURNEY

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**Aim:** To describe the development of CKD.QLD to this point.
**Case Report/Narrative**: The concept of CKD.QLD arose from an initiative, led by KHA, about a potential CRC in Chronic Kidney Disease (CKD) in Australia, which ultimately lacked an industry partner. It crystallised in Sept 2009 as a state-wide registry of all patients in public renal practices Queensland (QLD), to characterise CKD patients and follow their course longitudinally. QLD has great geographic variation, an area of 1,852,642 km$^2$, and a population of 4.6 million. The program is endorsed by service providers in all 12 QLD renal practice hubs and their satellites, with an estimated 11,700 patients. Data recording systems include Excel, Audit 4, and web-based programs, anticipating ultimate uniformity through e-health records. Patient recruitment, with informed consent, began in June 2011, and 4,300 patients are now enrolled, with few refusals. An application to change to waive of consent has been lodged.

CKD.QLD includes an interactive research platform, in which the patients and registry are central. Research themes include epidemiology and outcomes, practice improvement, clinical trials, and biomarker research. We are establishing a CKD.BioBank. We have four RHD students, and several participating renal trainees. Analyses now include CKD profiles of five sites and 2167 patients, and hospitalisations and longitudinal outcomes over more than one year on the first 1000 patients.
**Conclusion:** We hope to collaborate with other CKD surveillance programs nationwide, and are aligned with most major CKD surveillance systems globally. Supporters includes AMGEN, NHMRC (Hoy Fellowship), QLD.Health (in kind), Roche and Janssen. Continuation of CKD.QLD will depend on its demonstrated value to QLD.Health, in terms of potential for timely detection, predictions, service planning, cost-efficiencies and better outcomes.

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## TELE-VIDEO CONSULTATIONS: A USEFUL ADJUNCT FOR REGIONAL NEPHROLOGY?

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**Aim:** To explore feasibility and patient acceptance of nephrology consultations on video linkage using inexpensive technology.
**Background:** Fly in/fly-out nephrology clinics were established 10 years ago by a recently retired metropolitan-domiciled nephrologist. Clinics, initially in 4 towns around 500 km from metropolitan services , continued in 2 – on 3 days/month.The primary focus was CKD 3–4 with monitoring, medication adjustment, education and motivation. In 10 years no patients attending one clinic progressed to stage 5 and only 4 (of whom 1 was Caucasian) in the other, below anticipated requirements for end-stage CKD replacement therapy..
**Method:** A one day clinic was booked for video consultations only, with unselected patients (10 returns and 3 new) offered consultations by video link. All patients accepted. A standard Skype connection from the local Medical Centre to the metropolitan-based nephrologist at home was used. All patients rated the consultation as satisfactory or better and agreed that future consultations using video-link would be acceptable. Nephrologist and support staff found no significant limitations (as no patient had indications making examination mandatory). Time saved by nephrologist was 8 hours (travel time) and without a local service much patient travel would be needed.
**Conclusion:** Tele-video consulting could provide some aspects of nephrology care to regional locations and also enable more recently retired nephrologists to make contributions to minimizing workforce shortages. Sequential audits and validation of cost benefit will be essential.

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## IMMUNOFLUORESCENCE STUDY OF RENAL BIOPSIES IN NEPAL

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**Aim:** To evaluate importance of IF study in kidney pathology – A Superior additive tool.
**Background:** Kidney disease is significant health problem and Glomerulonephropathies are the third most common cause of end stage renal disease. Light microscopy, immunofluorescence studies or Electron microscopy are integral part of lab diagnosis of renal disease.
**Materials and method:** Present prospective study was conducted over a period of one year and 10 months. 85 patients of all age groups, presented with nephrotic syndrome, Proteneuric nephropathy, SLE, RPRF,acute nephritic syndrome,AKI,unexplained CKD and persistant hematuria were included in the study. Post renal transplant patients were excluded. Renal biopsies were performed according to standard protocol and transported to Religare Laboratory, Bombay India for Light microscopy and immunofluorescence studies.Data were recorded and analyzed.
**Results:** The patients presented with nephrotic syndrome (n = 30), proteinuric nephropathy (with sub nephrotic range proteinuria) (n = 17), AKI (n = 9), unexplained CKD (n = 9), acute nephritic syndrome (n = 7), SLE (n = 7), RPRF (n = 5), and persistant hematuria (n = 1). The most common finding under light microscopy were minimal change disease (n = 23) and mesangioproliferative GN (n = 12) followed by membranous GN (n = 9), Lupus nephritis. (n = 8). Nephrosclerosis with chronic tubulointerstitial nephritis (n = 4), IgA nephropathy (n = 3), nephrosclerosis with acute interstitial nephritis (n = 2) also observed. In addition to this 12 patients had dual pathology under LM study. The most common immuno reactant deposits were Complement-3, followed by IgG and IgM in our study. Fibrinogen deposit was negative in all biopsies.
**Conclusion:** Clinically, Nephrotic syndrome was the most common diagnosis and Minimal change disease and mesangioproliferative GN were common histological patterns seen. Additionally, IF study helped us to diagnose IgA nephropathy, MPGN Type I from Type II, differentiate early stage of membranous GN from MCD and Lupus nephritis Class IIa from IIb.

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## IS THE PRESENCE OF POSITIVE ANCA ASSAY SUFFICIENT TO PRECLUDE THE NEED FOR A RENAL BIOPSY?

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**Aim:** To see the atypical presentations of Antineutrophil cytoplasmic antibody (ANCA) associated vasculitides (AAV) along with emphasizing role of histopathology in establishing diagnosis and modifying nature of recommended therapy.
**Background:** A relationship among ANCA and renal limited vasculitis (pauci immune glomerulonephritis) has been well established. Two types of ANCA assays are used: Indirect immunofluoroscence and ELISA using specific antigens proteinase 3(PR3) and myeloperoxidase (MPO).Atypical ANCA patterns may be observed in patients with immune mediated conditions other than systemic vasculitis which are confusing. A negative ANCA assay doesn't rule out vasculitis. ANCA status may change with time and assays may not be accurate. A persistently ANCA negative status is no absolute proof of remission.
The issue whether treatment can be undertaken without tissue biopsy is debatable. It is reasonable to confirm clinical suspicion with histopathological proof before committing patients to life long treatment with toxic agents. Biopsy findings may reveal superimposed pathology on top of AAV. Therapy may need to be modified for better outcome.
**Methods:** We present retrospective analysis of a cohort (25) of patients with vasculitis. The end point was remission based on clinical grounds and serum creatinine.
**Results:** 4 out of 25(25%) had biopsy driven treatment modification. Two out of four had immune complex mediated glomerulonephritis consistent with IgA nephropathy with positive ANCA serology. Both responded very well to immunosuppressive therapy. The third and the fourth patient had pauci -immune GN with sclerosed glomeruli in which the biopsy directed discontinuation of therapy. The fourth one had associated Rheumatoid arthritis as well.
**Conclusion:** Confirmatory renal biopsy should be done in each patient of AAV due to varied presentations and doubtful utility of serology markers.

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## HISTOPATHOLOGY CLASSIFICATION OF LUPUS NEPHRITIS KIDNEY BIOPSY IN SEMARANG – INDONESIA

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**Aim:** Kidney biopsy in all glomerulonephritis was performed from 2007 to 2013, and collected in Lupus Nephritis patient to assess the classification of lupus nephritis.
**Background:** Systemic lupus erythematosus (SLE) is a systemic autoimmune disease caused by dysregulation of the immune system and affects many vital organs in the body. Approximately 50% of kidney disease more common in patients with SLE. Kidney biopsy in SLE is very important for the diagnosis and management. In addition to early diagnosis, a biopsy is also important in determining the level of activity, chronicity and severity of the disease. Initial biopsy also serve to compare to see the progression of the disease and further treatment.
**Methods:** To describe kidney biopsy in Lupus nephritis in Semarang – Indonesia from period 2007–2013.
**Results:** SLE was diagnosed in 65 patient, clinical Lupus Nephritis were diagnosed in 35 cases. 23 cases of biopsy results provide an overview of lupus nephritis Class I: 2 (8.7%), Class II: 7 (30.4%), Class III A: 11 (47.8%), Class III C: 2 (8.7%), Class IV: 1 (4.3%). Patients receive adequate treatment with Methylprednisolon and MMF/MMA. Biopsy were not perform in 13 patients because of their worsening conditions.
**Conclusions:** Kidney biopsy is very important in establishing the diagnosis and prognosis of lupus nephritis. By knowing the classification of lupus nephritis, appropriate treatment can be administered immediately to prevent any deterioration in the patient's condition.
**Key Word:** SLE, kidney biopsy, Classification of Lupus nephritis.

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## KIDNEY BIOPSY HISTOPATHOLOGY IN SEMARANG, INDONESIA

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**Aim:** To obtain the result of kidney histopathology performed in Semarang, Indonesia from March 2007-March 2013.
**Introduction:** Glomerular disease may vary in clinical manifestation. Many medical center in Indonesia, diagnose of glomerular disease still based on clinical manifestation which is nephritic syndrome and nephrotic syndrome. In Indonesia several medical center rarely perform kidney biopsy. Although clinical approach is important, Kidney biopsy is a gold standard for diagnosis in order to determine appropriate treatment and prevent from progression to end stage renal disease.
**Methods:** Total 140 kidney biopsy held in Dr.Kariadi Hospital and Telogorejo Hospital in Semarang, based on clinical diagnosis Nephrotic syndrome and Nephritic syndrome on March 2007-March 2013.
**Result:** Total 140 patients presumed glomerular disease, kidney biopsy which done on 2007 was (9), 2008 (6), 2009 (7), 2010 (17), 2011 (45), 2012 (46), 2013 (10). There were 49 man (35%) and 91 woman (65%). Results of kidney biopsy histopathology were MCD (20%), FSGS (35,7%), MN (4,3%), MPGN (4,3%), RPGN (5%), Lupus Nephritis (14,3%), IgA Nephropathy (3,5%), APSGN (2,8%), nephrosclerosis (1,4%), inconclusive (5,7%), diabetic nephropathy (2,1%), acute tubular necrosis (0,7%).
**Conclusion:** Epidemiology of glomerular disease may vary spectrum of morphological changes, depend on the variety of etiological factors. clinical approach gomerular disease is important, but Kidney biopsy is a gold standard for diagnosis in order to determine appropriate treatment and prevent from progression to end stage renal disease. All of 140 patient, most of them are FSGS (35,7%) consist of man (13,5%), woman (22,1%).
**Keyword:** Kidney biopsy, glomerular disease, histopathology.

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## HAEMOGLOBIN VARIABILITY AS A RESULT OF INFLAMMATION IN HAEMODIALYSIS PATIENTS

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**Aim:** A clinical audit tracking haemoglobin (Hb) variability over a 6-month period to ensure implementation of the latest Kidney Health Australia – Caring for Australasians with Renal Impairment (KHA-CARI) guidelines. Hb variability and anaemia was also assessed as a consequence of inflammation.
**Background:** Primary erythropoietin deficiency in haemodialysis (HD) patients is the most common cause of anaemia. Studies have shown that Hb < 100 g/L is strongly predictive of increased mortality. More recently, the CREATE and CHOIR trails concluded that Hb > 130 g/L didn't reduce the risk of adverse events and was associated with increased risk of stroke. The KHA-CARI guidelines (2011) recommend a Hb target of 100–115 g/L in patients using Erythropoiesis Stimulating Agents (ESA). It has also been documented that HD patients experience Hb variability with levels below and above the target range during a short follow-up period.
**Methods:** A retrospective analysis of 100 patients receiving outpatient HD in Central Australia. Patients were randomly-selected from the Renal Anaemia Management (RAM) database and data was collected for 6 months.
**Results:** Over the 6-month follow-up period, mean Hb was 108 ± 11.95 g/L with 36–44% of patients falling within recommended Hb target for each month. However, closer analysis showed inter-patient variability with only 6% of the patients maintaining Hb 100–115 g/L over the entire follow-up, while 82% fluctuated above and below the range. Elevated CRP predicted anaemia with a weak correlation ($r = 0.102$, $p = 0.01$) and contributed to variability.
**Conclusions:** With a narrow target of Hb for HD patients receiving ESA, there are difficulties maintaining patients within the recommended Hb range. Inflammation is one of multiple factors that contribute to Hb variability in the HD population of Central Australia.

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## MANAGEMENT OF HYPERPHOSPHATEMIA IN HAEMODIALYSIS PATIENTS IN AN OUTER METROPOLITAN DIALYSIS UNIT: THE OPERATION PHOSPHATE AGGRESSIVE LOWERING (OPAL) PROJECT

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**Background:** Hyperphosphatemia is now a recognised non-traditional risk factor for cardiovascular disease; as a key regulator of vascular calcification it triggers osteochondrogenic differentiation of vascular smooth muscle cells (VSMC), induces VSMC apoptosis, increases Fibroblast Growth Factor 23 levels and decreases Klotho expression. Management of hyperphosphatemia requires robust medication regimen, dietary education and patients' understanding and committed adherence.
**Aims:** To assess the impact of targeted management in patients with excessively high serum phosphate (>2.00 mmol/L).
**Methods:** A 6-month non-randomised observation study, involving 17 haemodialysis patients with serum phosphate > 2.00 mmol/L. Operation Phosphate Aggressive Lowering (OPAL) task force involved three-pronged approach comprising of Nurse Practitioner, dietician and dialysis nurses. A patients and staff survey was conducted on completion of the project.
**Results:** 13 patients completed the study. Mean (SD) of PO4 mmol/L and PTH pmol/L at entry was 2.38 (0.31) and 79.4 (42.6); at the end of study was 1.67 (0.4) and 58.19 (29.2), 2 patients remained with PO4 > 2.00.

Mean (SD) PO4 showed increasing trend [2.38, (0.31)] 3 months post study, reflecting education need for patients and staff. However, patients achieving stringent serum PO4 target (0.6–1.6) improved over time [Entry (nil); 6 months (7); and 9 months (5)] reflecting ongoing improvement in those compliant with intervention.

Survey returns were 100% (patients) and 68% (staff). Patients survey demonstrated lack of understanding of hyperphosphatemia, timing of binders but felt beneficial from the project. Nursing survey reflected need for improved understanding of hyperphosphatemia management.

**Conclusion:** An aggressive phosphate lowering task force addressing diet, medication and education delivered promising results in short term. On going sustained multidisciplinary input remains vital to overall hyperphosphatemia management.

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## EARLY EXPERIENCE WITH PLACEMENT OF TENCKHOFF PERITONEAL DIALYSIS CATHETERS USING THE MODIFIED SELDINGER TECHNIQUE

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**Background:** Placement of Tenckhoff catheters by surgeons either by open or laparoscopic techniques was the preferred technique till recently. Modified Seldinger technique for Tenckhoff catheter insertions has enabled nephrologists to perform this procedure under local anaesthesia and as a day procedure.
**Methods:** We performed a retrospective analysis of all the Tenckhoff catheter insertions using this technique from March 2009 to April 2013.
**Procedure:** The modified Seldinger technique was used to gain peritoneal access using a verrous needle. Intraperitoneal position of the needle was confirmed by instilling a small volume of radio-contrast. A 0.035 cm guide wire is inserted through the verrous needle under fluoroscopic guidance. A peel away sheath is introduced followed by the Tenckhoff catheter over a stylet, after removal of the verrous needle. The Inner cuff is buried in the rectus muscle. The catheter is exteriorised maintaining a short tunnel.
**Results:** A total of 8 catheters were inserted. The mean age of the patients was 44.75 years. There were 3 males and 5 females. 7 of the 8 patients were indigenous. Diabetic nephropathy was the aetiology in majority of patients. 6/8 patients were on haemodialysis prior to the procedure. Peritoneal dialysis was started after a mean of 44.2 days from insertion. There were no procedure related complications. One patient had prolonged bleeding through the exit site, which resolved without intervention. All procedures were performed as under local anaesthesia and the patients were sent home the same day.
**Conclusion:** The modified Seldinger technique was successful in inserting Tenckhoff catheters in this small cohort.

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## NUTRITIONAL STATUS AND ADEQUACY OF HAEMODIALYSIS

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**Aim:** Nutritive status has a significant role in improving the quality of life dialysis patients. The aim of this research was to evalute the impact of biochemical and anthropometrical markers of nutrition on the adequacy of hemodialysis.
**Methods:** The investigation was organized as a clinical study in the Abdul Moeloek General Hospital Bandarlampung, Indonesia. We evaluated demographic and anthropometric characteristics; co-morbid stages, smoking, duration of dialysis process and aterial pressure. Regarding biochemical markers of nutritive status, we determined the concentrations of protein, albumin, ferritin and blood-lipids and adequacy of hemodialysis. One third of our patients recieved the recommended dialysis dose and males were dominant. All tested anthropometric parameters showed statistically significant differences between the group with adequate versus non-adequate dialysis.
**Results:** Patients with adequate hemodialysis had been longer on dialysis. There were significant differences between the groups in number of leukocytes ($p = 0{,}027$), hemogoblin ($p = 0{,}047$), potassium ($p = 0{,}038$) and C-reactive protein concentrations ($p = 0{,}048$) as well as for serum total protein ($69 \pm 4{,}63$ vs. $65 \pm 5{,}74$ g/l; $p < 0{,}0001$) and albumin ($38 \pm 2{,}99$ vs. $29 \pm 4{,}4$ g/l; $p = 0{,}047$). Pearson's correlation of factors that may have impact on hemodialysis adequacy indicated a significant relation between serum protein concentrations and the index of hemodialysis adequacy $9r = 0{,}21$; $p = 0{,}0446$).
**Conclusion:** Biochemical markers of nutrition and anhtropometric characteristics for the patients involved in our study were impotant elements for evaluation of hemodialysis adequacy.

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## ANALYSIS OF THE COST-EFFECTIVENESS OF SWITCHING FROM SEVELAMER HYDROCHLORIDE TO LANTHANUM CARBONATE MONOTHERAPY: APPLICATIONS FOR AUSTRALIAN COSTS

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**Aim and background:** Recent US data demonstrate that the dose-relativity between sevelamer hydrochloride (SH) and lanthanum carbonate (LC) increases with the dose of SH required to control serum phosphate levels. Overall phosphate levels were similar when treated with LC or SH. This application aimed to calculate cost-effectiveness comparisons of switching Chronic Kidney Disease Stage 5D (CKD5D) patients from SH to LC monotherapy using Australian costs.
**Methods:** SH : LC dose-relativity was based on US real-world, phase 4 trial data evaluating the relative phosphate binder dosing levels required to maintain phosphate control in CKD5D patients. The overall dose-relativity in this US study (2.8) is similar to a meta analysis used for pricing and reimbursement in Australia (2.7). The relative costs of daily clinical monotherapy doses of SH and LC were calculated using Australian medicine prices (LC 1000 mg: $4.94; SH 800 mg: $1.72).
**Results:** Cost analysis of daily clinical doses, based on dosing levels required to treat phosphate levels to target from a US study, revealed LC 3000 mg/day ($14.82) is more cost-effective than SH ≥7200 mg/day ($15.48) but not lower SH doses (≤6400 mg/day; ≤$13.76). In the US study this accounted for >50% of patients. The annual cost saving of switching one patient from SH to LC 3000 mg/day ranges from $241/year (SH 7200 mg/day) to $2124/year (SH 9600 mg/day).
**Conclusions:** Our analyses indicate that LC 3000 mg/day is more cost-effective than SH ≥7200 mg/day. For these patients, switching phosphate binder therapy from SH to LC offers potential drug cost savings, a reduced daily tablet burden (3 vs ≥9 tablets/day), and effective serum phosphate control.

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## THE PLACEMENT OF TENCKHOFF CATHETER FOR CAPD WITH BANDUNG METHOD

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**Background:** The practice of placement Tenckhoff catheters by nephrologists remains uncommon in most countries, likewise in Indonesia.
**Methods:** We reported our single-center experience on placement of Tenckhoff catheter by nephrologists using the Bandung Method, a blind percutaneous placement of catheter modified from the Seldinger technique.
**Results:** In the period of May 2012 to March 2013, 20 ESRD patients (14 male, 6 female) were underwent placement of a Tenckhoff catheter by a nephrologist. Median age of the patients was 59 years old. Surgical dissection followed by exposure of the peritoneum under direct vision was performed under local anesthesia. An introducer needle was implanted toward the pelvis 0.5–1.0 cm beyond the abdominal wall. A guide-wire was inserted through the needle and into the deep pelvis. The needle was removed and a sheath and dilator were inserted through the guide-wire. The guide-wire and dilator were removed, leaving the sheath in place. The Tenckhoff catheter was threaded onto a stiffening stylet and advanced through the sheath into the deep pelvis while withdrawing the stiffening stylet until the deep cuff reached the peritoneum. Early postoperative complications were defined as those occurring during the procedure or within 30 days postoperatively. Within 1 month post-placement of catheter, complications appeared in 4 patients: 1 (5.0%) bleeding, 1 (5.0%) outflow failure, 1 (5.0%) mal-position, and 1 (5.0%) catheter infections; none of these complications led to catheter removal. Late postoperative complications were occurred in 1 (5.0%) patient with mal-position that could not be repositioned, led to catheter removal.
**Conclusions:** The Bandung method is a simple, inexpensive, and minimally invasive technique with reliably good outcomes and a low rate of complications compared to other techniques.
**Keywords:** CAPD; Seldinger technique; Bandung Method; Peritoneal Dialysis Catheter.

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## EVERY DAY IS A NEW DAY: THE CARDIOVASCULAR RESPONSE TO STANDARD IN-CENTRE HAEMODIALYSIS (HD) IS NOT CONSISTENT ACROSS SERIAL TREATMENTS

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We sought to characterize the nature and reproducibility of Systolic Blood Pressure (SBP) phenotype in an asymptomatic, nondiabetic HD outpatient cohort receiving stable HD prescriptions.

**Methods:** Six stable HD outpatients underwent multiple episodes of continuous, beat-to-beat SBP monitoring during 'short-break' HD within a period of 2 weeks. SBP profiles were compared for test/retest consistency between Start, End, Net treatment change directional slope, Peak, Trough, Mean, Variability (SD) and linear regression slope. Change in haematocrit/light-absorbtion blood volume was sampled at 30-minute intervals and compared by two-tail Kolmogorov-Smirnov comparison.

**Results:** Sixteen discrete intradialytic records were available for analysis (three sessions/individual in four patients and two sessions/individual in two patients.) Intraindividual ranges for each comparative SBP parameter were (expressed as Mean ± SEM, mmHg); Pre 28.5 ± 2.6, Post 23 ± 7.6, Intradialytic mean BP 23.2 ± 8.5, Peak 37.7 ± 9.3 and Trough 29.5 ± 6.2. The net direction of intradialytic BP was inconsistent in 2/6 (33%). The directional slope of first-order linear regression calculated from the continuous SBP record did not demonstrate intraindividual parallelism by beta-coefficient or 95% confidence bound overlap in any pair of HD treatments in any patient.

The only parameter to behave consistently across serial HD was circulating volume change. Trajectories were all qualitatively consistent with net volume reduction by ultrafiltration (mean 2.3 L ± 0.4 L). Paired-matrix testing of the intraindividual blood-volume series demonstrated consistency, with no statistically significant difference observed in any patient. Graphical representation confirmed congruity within all clinically acceptable limits.

**Conclusion:** By signaling that each discrete HD represents a unique proposition in terms of SBP response, this data suggests that a standardized, dialysis prescription may be inappropriate and supports a role for more rigorous clinical monitoring and tailored feedback-control HD strategies.

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## EMERGING PATTERNS IN BLOOD PRESSURE AND VOLUME IN THE INCIDENT DIALYSIS PERIOD: THE INFLUENCE OF PRIMARY RENAL DISEASE

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**Aim:** To assess changes in blood pressure and volume in incident haemodialysis patients.

**Background:** Incident haemodialysis patients have high mortality rates within the first 90 days. Hypertension may lead to adverse cardiac outcomes. Anecdotal evidence in our centre suggests BP is poorly controlled in the incident period, with unclear relationship to changes in dry weight.

**Methods:** Data was collected over 12 months (n = 79). Pre and postdialysis BP were recorded to 90 days, with ideal body weight (IBW) and medications. Changes in systolic blood pressure (SBP), diastolic blood pressure (DBP) and IBW were assessed by analysis of covariance.

**Results:** Mean age 61 years, 30% female, and 43% diabetes as primary disease. Baseline mean predialysis SBP was 152.5 mmHg, postdialysis SBP 151.87 mmHg. Predialysis SBP, DBP and postdialysis DBP were unchanged at 90 days, while postdialysis SBP fell 12.95 mmHg (95% CI 17.40, 8.50 $p < 0.001$)). Subjects with hypertensive renal disease or APCKD showed no significant reduction in postdialysis SBP, whilst those with diabetic renal disease (–19.46 mmHg, 95% CI –26.25, –12.66, $p < 0.001$) and glomerulonephritis (–12.61 mmHg 95% CI –24.75, –0.47, $p = 0.04$) fell significantly. Conversely, those with hypertension displayed the largest IBW reductions at 90 days (–6.07 kg, 95% CI –8.57, –3.56 $p < 0.001$), compared to diabetes (–5.06 kg 95% CI –6.29, –3.82, $p < 0.001$) and glomerulonephritis (–2.17 kg, 95% CI –4.03, –0.32 $p = 0.02$). Median antihypertensive tablet burden at baseline was 4, compared to 3 at 90 days ($p = 0.001$).

**Conclusions:** Decrease in BP in the incident haemodialysis period was limited to postdialysis SBP. The largest change was seen in those with diabetes as their primary disease, although the pathophysiology of this remains unclear. No correlation was seen between reduced postdialysis SBP and decreased IBW or medication burden.

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## INVESTIGATING BARRIERS TO EFFECTIVE PREDIALYSIS PLANNING OF PACIFIC ISLANDER PATIENTS IN WESTERN SYDNEY

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**Aim:** To investigate possible reasons behind high rates of unplanned dialysis commencement in patients from a Pacific Islander (PI) background in Western Sydney

**Background:** PI patients in Western Sydney are perceived to have high rates of unplanned dialysis initiation, which may be preventable through appropriate pre-dialysis care. This study aims to characterise PI patients commencing dialysis in Western Sydney in order to help to understand potential barriers to effective pre dialysis care.

**Methods:** PI patients commencing dialysis in Western Sydney between January 2011 and July 2012 were identified from ANZDATA and local databases. Demographic data and details of pre-dialysis care were collected and compared. Patient perceptions on their pre-dialysis care were also explored using a patient interview.

**Results:** 19 patients from a PI background commenced dialysis during this period; all commenced dialysis using a haemodialysis catheter. This group had high rates of diabetes (83%) and obesity (63%). 18 patients started dialysis in an emergency or unplanned fashion. Although 16 patients were known to a nephrologist, 75% were lost to follow-up and only 38% had engaged with recommendations for pre-dialysis education. Patient interviews identified themes of fear, low motivation and limited understanding as possible explanations for low rates of adherence with pre-dialysis care.

**Conclusions:** PI patients have high rates of unplanned dialysis initiation and low rates of adherence with pre-dialysis care in Western Sydney. Possible explanations for this include high rates of diabetes, cultural determinants of disease behaviour and deficiencies of existing models of care to address knowledge gaps and specific patient concerns in this group. Improved targeting of culturally relevant education may help to reduce incidence of poor dialysis-related outcomes in this patient group.

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## MICROBIOLOGICAL PROFILE OF BLOOD CULTURE POSITIVE BACTEREMIA IN CKD V PATIENTS UNDERGOING HAEMOADIALYSIS AND CLINICAL OUTCOMES

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**Background:** The Northern Territory of Australia has the highest national incidence of treated end-stage kidney disease in the country. Majority of these patients in central Australia are indigenous and haemodialysis is the preferred mode of renal replacement therapy. Infection is the second most common cause of hospital admission among patients undergoing hemodialysis.

**Methods:** A retrospective analysis of all positive blood cultures between January 2010 and January 2012, was performed in patients undergoing haemodialysis in Alice springs.

**Results:** A total of 187 patients were on haemodialysis. There were 46 positive blood cultures in 25 patients (indigenous n = 24, Caucasian n = 1) who presented with clinical evidence of infection. Incidence rate of bacteremia was 12.3 per 100 patient years. The vascular access was an arteriovenous fistula in 76% of patients with bacteraemia. Associated respiratory tract infections were seen in 45.7% and surgical related infections in 28.3%. The commonest microorganisms isolated were Streptococcus species 41% (n = 19), Staphylococcus aureus 23% (n = 11), E.coli 11% (n = 5), Enterococcus 6.5% (n = 3). Methicillin resistant Staphylococcus aureus were identified in 27.7% of cases with S.aureus bacteremia. Mean white cell count was 15.02(±6.08) and mean CRP was 135.2(±124.1). Intensive care treatment was required in 5 (10.9%) patients. There were no deaths.

**Conclusion:**

1. Bacteremia is commonly seen in patients undergoing maintenance hemodialysis, regardless of the type of vascular access.
2. 25 out of the 187 (13.4%) patients undergoing maintenance hemodialysis had one or more episodes of bacteremia with an incidence rate of 12.3 per 100 patient years.
3. Respiratory tract infection and wound/ soft tissue infections were the most common underlying source of bacteremia.
4. Antibiotic Therapy was empirical to start with and changed according to antibiotic sensitivity.

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## HAND GRIP STRENGTH AS A MARKER OF MALNUTRITION IN HAEMODIALYSIS PATIENTS

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**Aim:** This study aims to determine the clinical applicability of hand grip strength as a marker of nutritional status in haemodialysis patients by looking for the presence of a correlation between hand grip strength and Subjective Global Nutrition Assessment (SGA)
**Background:** Protein Energy Malnutrition (PEM), characterized by loss of body protein and fat mass stores, is reported in haemodialysis patients with an estimated prevalence between 20% and 50% in Australia. Evidence shows that malnutrition is associated with increased mortality and morbidity in patients on haemodialysis. There are few references available in the literature evaluating the correlation between hand grip strength and nutrition status according to SGA classification in patients on haemodialysis.
**Methods**: In this study, a convenient sample of 69 patients undergoing haemodialysis at the Royal North Shore Hospital, Sydney, was recruited. Subjective Global Nutrition Assessment was performed and hand grip strength was measured by a dynamometer.
**Results**: According to SGA Assessment classification, 44.9% of patients were classified as malnourished. The mean handgrip strength for all patients was 13.78 (10.47) kilogram. There was a significant difference in hand grip strength between well-nourished patients and patients with malnutrition. Multiple regression showed a negative relationship between Subjective Global Nutrition Assessment and hand grip strength after adjusting for gender and age ($R = 0.69$, $R^2 = 0.48$, $P = 0.047$).
**Conclusion:** A relatively high prevalence of protein energy malnutrition (44.9%) was identified in the study. Hand grip strength was negatively correlated with Subjective Global Nutrition Assessment with statistical significance. Hand grip strength should be considered as a marker of nutritional status in haemodialysis patients as part of a comprehensive nutritional assessment.

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## CONSIDER – CONSIDERATIONS OF NEPHROLOGISTS WHEN SUGGESTING DIALYSIS IN ELDERLY PATIENTS WITH RENAL FAILURE

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**Aims:**
1) To determine nephrologist preferences for recommending dialysis to elderly patients.
2) To determine the feasibility of a discrete choice experiment (DCE) to explore preferences.

**Background:** Recommending dialysis for elderly patients can be difficult in the context of factors such as comorbidity, cognitive impairment, expected quality of life and inclinations for treatment. Little is known about the trade-offs between patient attributes made by nephrologists when recommending dialysis.
**Methods:** A literature review identified patient attributes associated with readiness to recommend dialysis. These were presented to 10 nephrologists as a ranking exercise. Responses were used to design a pilot DCE. Patients were described using 12 attributes with various levels: age; gender; cognition; cancer history; number of comorbidities; quality of life; expected change in quality of life; life expectancy; family support; patient and family inclination for dialysis; and expected difficulties with dialysis. Each question consisted of two patient scenarios with the choice: "which patient would you prefer to recommend dialysis to: 'patient A' 'patient B' or 'neither' ". Demographic factors were also collected. Multinomial logit models were used to estimate choice models.
**Results:** The 12-choice survey was completed by 28 nephrologists. Most were 40 to 49 years old; 60% male and 64% Caucasian. Nephrologists considered most attributes germane to decision making, with several reaching statistical significance. In general, younger age; better cognitive function; and greater patient inclination toward dialysis all increased preferences for recommending dialysis.
**Conclusions:** This pilot demonstrated that nephrologists were able to express preferences for whom they would recommend dialysis when presented with scenarios combining patient attributes. The information on attribute importance and trade-offs will inform the design of a statistically efficient international survey.

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## BALLOON ASSISTED MATURATION (BAM) OF ARTERIOVENOUS ACCESS PERFORMED BY AUSTRALIAN NEPHROLOGISTS: A SINGLE CENTRE CASE SERIES

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**Aim:** To describe an Australian single centre experience of BAM performed by interventional nephrologists.
**Background:** BAM is a method of developing immature arteriovenous fistulae using angioplasty balloons in a graded and staged fashion to achieve sufficient dilation of the haemodialysis access to facilitate dialysis therapy. Therefore in reported series it is usual for more than one procedure to be required per patient.
**Methods:** All BAM cases between 2008 and 2013 in our unit were reviewed retrospectively.
**Results:** A total of 22 procedures were performed in 14 (12 patients) immature arteriovenous accesses. The mean age of patients at first procedure was 58 years. The majority (9/14, 64%) were radiocephalic fistulae, and only one (7%) was PTFE. BAM was successful in 11 (79%) cases and of these, 6 (55%) required one procedure to achieve maturation for dialysis use, 3 (27%) required 2 procedures, and 2 (18%) required 3 procedures. Fistuloplasty was used in all, except for one case requiring exclusion of accessory veins with a covered stent. Of the three unsuccessful cases, two required surgical conversion to forearm loop grafts (one autologous, one PTFE) which were again subjected to BAM. The third unsuccessful case continued on peritoneal dialysis. Only 4 of the 22 procedures (18%) resulted in lack of maturation. There were no complications. Six (50%) patients initiated dialysis with permanent access.
**Conclusions:** Balloon assisted maturation is a valuable addition to endovascular fistula therapy. The technique is safe, improves the rates of fistula use at first dialysis, decreases the rate of dialysis catheter use, and spares other potential access sites for future use.

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## FOODSERVICE SATISFACTION IN DIALYSIS PATIENTS ON RENAL DIETS DURING PREVIOUS HOSPITAL ADMISSIONS IS LOWER THAN GENERAL MEDICAL AND SURGICAL INPATIENTS

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**Aim:** To compare the level of foodservice satisfaction reported by maintenance haemodialysis or peritoneal dialysis patients who had been previously placed on renal-specific therapeutic diets with medical and surgical inpatients surveyed in 2012.
**Background:** Malnutrition is highly prevalent in dialysis patients who often have regular hospital admissions. However, dialysis inpatients have expressed dissatisfaction with being placed on therapeutic renal default diets as they may not receive what they ordered, may be capable of making suitable dietary choices and may have appropriate biochemistry.
**Methods:** Adult inpatients admitted to medical and surgical wards over 5 days in May 2012, and adult patients undergoing dialysis in 2013 who have previously been admitted to hospital within the past 12 months completed a validated foodservice satisfaction survey. Descriptive analyses, chi-squared and t-tests were conducted using SPSS to describe and compare patient demographics and foodservice satisfaction data in the dialysis group with medical and surgical patient groups.
**Results:** 23 patients on dialysis (D: 65%M, $62 \pm 13$ yrs, 50% had LOS > 1week, 39% of all patients on dialysis, 51% had no hospital admissions in last 12 months.) and 96 medical and surgical inpatients completed surveys (MSP: 41%M, $55 \pm 23$ yrs, 22% had LOS > 1week). Overall satisfaction (D: $3.7 \pm 1.1$, MSP: $4.2 \pm 0.9$) and food quality satisfaction (D: $3.5 \pm 0.9$, MSP: $4.0 \pm 0.9$) were significantly lower in dialysis patients retrospectively reporting their inpatient satisfaction than medical and surgical inpatients surveyed in 2012 ($p < 0.05$).

**Conclusion:** Patients on dialysis reported a significantly lower level of food-service satisfaction. Given that patients on dialysis may have regular hospital admissions and a longer length of stay, future research could investigate whether removing default renal diets provides more choice, improved satisfaction and similar or improved health outcomes in inpatients undergoing dialysis.

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## LINE USE AT FIRST DIALYSIS, IS THIS A VALID KEY PERFORMANCE INDICATOR?

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**Aim:** To determine if the high proportion of central venous catheter use in Western Renal Service (WRS) at incident dialysis is a patient level or system level problem.
**Background:** The WRS performs poorly in the chosen KPI of line use at first haemodialysis (HD), with 70% of new HD patients commencing with a haemodialysis catheter. Reasons behind this high proportion are unknown.
**Methods:** Data was collected on patients starting HD at the WRS over 12 months from July 2011 to June 2012. Reasons were elicited regarding why permanent access, in the form of peritoneal dialysis catheter or arteriovenous fistula, was not ready at the time of first dialysis.
**Results:** 56 patients in WRS initiated HD using a catheter during this period. Of this group, 11 patients were known to a nephrologist for less than 3 months, 4 patients were from outside this renal service prior to starting dialysis, 23 patients have been reviewed by a nephrologist but did not attend regular follow up, and 1 patient was originally planned for palliation. Only the remaining 17 patients were reviewed regularly by their nephrologist but did not have a permanent access ready at incident dialysis.
**Conclusion:** Only a minority of patients commencing HD with a venous catheter in Western Sydney were in regular contact with local nephrology services, making planning for permanent vascular access difficult. Although the external validity is uncertain, these data suggest that the chosen indicator does not accurately reflect system-level quality of care, but rather, reflect issues at the patient level. Further more detailed examination of patient level data and the details of predialysis care of this patient cohort will be presented.

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## MUCOCUTANEOUS MANIFESTATIONS OF CHRONIC KIDNEY DISEASE PATIENTS ON HEMODIALYSIS

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**Aim:** The aim of this study was to evaluate the frequency and relationship of dermatologic manifestations in CKD patients on haemodialysis.
**Background:** Chronic kidney Disease (CKD) invariably presents with an array of cutaneouse manifestations. Newer dermatosis are being described since the advent of hemodialysis..
**Materials and Methods:** 120 patients with CKD on hemodialysis along with Age & sex matched controls were enrolled. All patients were examined for skin, nail, hair and mucosal changes. Relevant diagnostic investigations performed when necessary. Patient data recorded as per Performa.
**Results:** A case control perspective study was carried out. Male predominance (M : F Ratio, 1.86: 1) was observed. Maximum number of Patient belong to age group 50–59 years. Majority of patients were having CKD less than 1 year (55%) and were on hemodialysis for variable period. Dermatologic manifestation were significantly associated with CKD patients ($p = 0.000$) but not with the duration of disease. Xerosis was the most common skin manifestation observed (48.3%) followed by Pruritus and hyperpigmentation (41.6%) and (22.5%) respectively. Nail, mucous membrane and hair changes were present in 45%, 25% & 29.16%. Furred tongue was the most common oral mucosal changes (58.33%) and Telogen effluvium was the commonest hair manifestation Specific cutaneous manifestations such as acquired perforating dermatosis, pseudoporphyria cutanea tarda, calciphylaxis, calcinosis cutis, and nephrogenic fibrosing dermopathy were not detected in any of our patients.
**Conclusion:** Dermatologic manifestations were significantly associated with CKD patients. The most common changes were xerosis and white nail.

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## INTERVENTIONAL NEPHROLOGY PROGRAM IN MAINTAINING PATENCY IN DYSFUNCTIONAL ACCESS IN REMOTE CENTRAL AUSTRALIAN RENAL PATIENTS

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**Aim and Background:** Central Australian renal service primarily deals with indigenous Australians and is situated thousands of kilometres away from the tertiary centres. Delays in maintaining patency meant a high rate of vascular access loss, hospitalisations for temporary access and creation of new AV fistula. Resident nephrologists undertook the responsibility of developing proficiency in percutaneous endovascular procedures.
**Method:** Retrospective study November 2009 until Dec 2012. Data collected from radiology, medical and dialysis records of patients (pts) who underwent fistulography, balloon angioplasty +/– Stent deployments. All procedures were performed by nephrologists on an outpatient basis in the digital subtraction angiography (DSA) suite, under local anaesthesia using standard endovascular equipment.
**Results:** 136 pts required interrogation of their dialysis access with fistulography for a variety of clinical reasons. 50 patients (37%) were noted to have significant stenotic lesions and required interventions at multiple time intervals. 44 had native AV fistulae and 6 AV grafts. Total of 115 venous angioplasties and a small number of Stent deployments were performed. Average of 2.3 procedures per pt, resulting in median survival of 558 days (range 1–1094 days). 12 pts presented with complete thrombosis. Of these, 7 underwent successful revascularization with routine endovascular pharmaco-mechanical measures, 3 had surgical thrombectomy and in 2, the access had to be abandoned. No significant complications.
**Conclusions:** Nephrologists have developed expertise in the endovascular management of dysfunctional accesses. The majority of access problems were successfully treated with good outcomes and very few complications.

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## CUFFED AND TUNNELLED VASCULAR ACCESS FOR HAEMODIALYSIS: A SINGLE CENTRE EXPERIENCE

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**Aim:** To determine the outcome of cuffed tunnelled access for haemodialysis.
**Background:** The incidence of patients requiring renal replacement therapy has increased in recent years. The native arteriovenous fistula (AVF), synthetic arteriovenous grafts (AVG) fistula and cuffed tunnelled line (permacath) are used for permanent vascular access. Despite the National Kidney Foundation Dialysis Outcomes Quality Improvement (NFK-KDOQI) and Caring for Australians with Renal Impairment (CARI) recommends AVF and AVG as first line permanent haemodialysis access, for various reasons, increasing numbers of end-stage renal disease patients are becoming dependent on cuffed haemodialysis catheters for chronic haemodialysis access.
**Methods:** We retrospectively analysed the outcome of all permacaths inserted and removed in John hunter Hospital during the period between 1st January 2012 and 21st December 2012 for haemodialysis.
**Results:** During study period 155 tunnelled lines was inserted on 135 patients. 61 (39%) was inserted as initiation of dialysis. The rest of them were due to primary access problem. Among the patients initiated on haemodialysis 14 (23%) had acute kidney injury and 47 (77%) had chronic kidney disease, waiting for renal replacement therapy. 24 (18%) patients still have permacath in situ. Mean survival of the permacath is 148.96 days (range 1 day to 1555 days) The most common cause for removal was complication 62 (42%) followed by available of more permanent access 31 (21%). The Most common complication was malfunction 22% followed by infection 19%.
**Conclusions:** Permacath is primarily used for temporary access. This study indicates that permacath may be a very useful alternative permanent vascular access for haemodialysis patients when other forms of access are not available or patients is haemodynamicaly unstable for having surgery for more permanent access.

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## ADEQUACY OF GLYCEMIC CONTROL IN DIABETIC DIALYSIS PATIENTS – A SINGLE CENTRE PROSPECTIVE OBSERVATIONAL STUDY USING CONTINUOUS GLUCOSE MONITORING

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**Aim:** To evaluate diabetic dialysis patients for periods of asymptomatic hypoglycaemia and to compare interstitial glucose readings with HbA1C levels in these individuals.
**Background:** Most international guidelines recommend targeting HbA1c of <7% irrespective of the presence of chronic kidney disease. However, the correlation of HbA1c with glycaemic control in dialysis patients is contentious due to shortened red cell survival, frequent blood transfusions, iron deficiency and use of erythropoietins. Paradoxically, a large retrospective analysis of diabetic dialysis patients has shown worse outcomes in dialysis patients with HbA1c <5%. Interstitial glucose measurements using Continuous Glucose Monitors (CGM) correlates well with blood glucose using a glucometer even in dialysis patients. Hence, Continuous Glucose Monitoring can identify periods of significant hypoglycaemia in dialysis patients.
**Method:** This is a single center observational study, conducted on all in-center diabetic dialysis patients. CGM was applied to each patient for a total of 6 days continuously. Patients underwent routine dialysis and kept a diary to record their food intake and episodes of hypoglycaemia. HbA1c was measured along with routine monthly dialysis bloods on each patient.
**Results:** There were no episodes of asymptomatic hypoglycemia in the study patients. There appeared to be better correlation between regular venous blood sugar reading than with HbA1C.
**Conclusion:** Asymptomatic hypoglycemia does not appear to be a factor in this small study. Regular blood sugar monitoring may be better marker for adequacy of glycemic control than HbA1C, in diabetic haemodialysis patients.

# CASE REPORTS

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## BELATACEPT POST RENAL TRANSPLANTATION IN PATIENTS WITH CONTRAINDICATIONS TO CALCINEURIN INHIBITORS

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**Background:** Calcineurin inhibitors form the basis of immunosuppression for renal transplantation; however, they can be associated with significant side effects. In randomized controlled trials, conversion from CNI to belatacept (a costimulation blockade agent) may be associated with better graft and patient survival and was well tolerated.
**Case report:** We report the first use of belatacept in Australia for renal transplant recipients outside clinical trials. We have converted five patients (between March 2010 and April 2013, median time post renal transplant 8 months (0–26), median duration of therapy 22.5 months (8–38)) from a CNI to belatacept accessed on a compassionate basis. Replacement with mTOR inhibitors was contraindicated due to the presence of proteinuria or wound healing concerns. Each patient was treated with a low intensity belatacept regimen derived from the BENEFIT trials and maintained on prednisolone (5 mg) and mycophenolate (1–1.5 gm/day). All were EBV positive before transplantation. The reasons for conversion were: three cases of biopsy proven thrombotic microangiopathy (TMA) with no biopsy proven acute rejection (BPAR); one case of CNI sensitivity with red cell hypoplasia and BPAR following reduction of CNI and increase in mycophenolate dose; one case of CNI induced cortical blindness. One graft with TMA failed at one year with chronic glomerulopathy. There has been no BPAR post commencing belatacept and the remaining four patients have stable renal function (creatinine 150–250 micromol/L). None have developed diabetes post transplantation. Blood pressure has been controlled with one to three antihypertensive agents. There has been one case of CMV colitis and no cases of BK nephropathy or post-transplant lymphoproliferative disease.
**Conclusion:** Belatacept may be used in transplant patients in whom CNI and mTOR inhibitor may be deleterious.

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## RHABDOMYOLYSIS IN RENAL TRANSPLANT RECIPIENT ON STATIN THERAPHY POST INFLUENZA VACCINATION

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**Background:** Influenza virus infection causes significant morbidity and mortality in solid organ transplant recipients. Seasonal influenza vaccination is a public health measure considered safe and well tolerated by renal transplant recipients, with similar safety profile as healthy controls. However, there is one previously reported case of rhabdomyolysis causing acute renal failure following influenza vaccination in a renal transplant recipient.
**Case Report:** A 64-year Fiji Indian male presented with 2-week history of febrile illness and disabling muscle weakness with onset one day after influenza vaccination. His background history included insulin dependent diabetes mellitus, hypertension and dyslipidemia. He received cadaveric renal transplantation 8 years ago for diabetic nephropathy. His baseline creatinine was 120 μmol/L and medications included immunosuppression with tacrolimus, azathioprine, prednisolone, antihypertensives, ezetimibe/simvastatin (10/40 mg daily), aspirin and calcitriol. Examination revealed new onset proximal myopathy of both upper and lower limbs and clinical features suggestive of upper respiratory tract infection. He had an unremarkable examination of other organ systems including a non-tender transplant kidney.

Investigations revealed normal haematological profile, blood urea 14.7 mmoL/L, creatinine 161 μmoL/L, eGFR 40 ml/min/1.73 $m^2$, creatinine kinase (CK) 7,851U/L (38–174 U/L), LDH 1400 U/L, GGT 62U/L, ALT 319 U/L, AST 394 U/L, TSH 0.33 mIU/L, PTH 28.9 pmoL/L and proteinuria 1.8 g/day. Septic screen, including hepatitis screen, was negative. The Tacrolimus level was low at 1.2 ng/ml. The clinical diagnosis was influenza vaccination associated rhabdomyolysis. On ceasing statins, the myopathy gradually improved, CK reduced to 925 U/L and renal function returned to baseline after a week. He was discharged home after nine days following significant recovery.
**Conclusions:** This is the second only report of rhabdomyolysis following influenza vaccination in a renal transplant recipient on statin therapy.

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## APLASTIC ANAEMIA IN A KIDNEY-PANCREAS TRANSPLANT RECIPIENT

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**Background:** The introduction of more potent immunosuppression in solid organ transplantation has resulted in improvement in graft survival at the expense of higher risk of infection, cancer, cardiovascular and metabolic complications. Although bone marrow suppression is common with immunosuppression, the development of aplastic anaemia is rare.
**Case Report:** We report a case of a 56-year-old woman with type I diabetes and end-stage kidney disease who received a kidney-pancreas transplant in 2005 and was on tacrolimus, mycophenolic acid (MPA) and prednisolone as maintenance immunosuppression. In 2011, her renal allograft failed but pancreatic function remained normal. From 2009, she developed erythropoietin-resistant, transfusion-dependant anaemia. Over the subsequent 4 years, she became pancytopaenic despite tacrolimus dose reduction and cessation of MPA. With granulocyte colony-stimulating factor-unresponsive neutropaenia, she required frequent admissions for sepsis. Serial bone marrow aspirates performed between 2009 and 2013 demonstrated the evolution from normocellular marrow with erythroid hypoplasia to hypocellular marrow to aplastic anaemia. Viral infections, haemophagocytic lymphohistiocytosis and graft-versus-host-disease were excluded. Despite treatment with antithymocyte globulin and cyclosporine, she died after developing invasive pulmonary aspergillosis.
**Conclusion:** In conclusion, severe pancytopaenia following solid-organ transplantation is uncommon and patients must be aggressively investigated to exclude aplastic anaemia. This case illustrates the difficulties in balancing the need for adequate immunosuppression to reduce rejection risk in a dual organ transplant recipient, with the complications of chronic immunosuppression such as aplastic anaemia. Although complete withdrawal of immunosuppression in the presence of functioning allograft is undesirable, this case suggests that adopting a more aggressive approach in reducing the burden of immunosuppression in the presence of progressive bone marrow failure may be considered at an earlier stage.

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## A CASE OF ADENOVIRUS NEPHROPATHY IN A RENAL ALLOGRAFT

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**Background:** Adenovirus (ADV) infection in kidney transplant recipients is well recognized, and the spectrum of infection ranges from asymptomatic viraemia to clinically significant disease including allograft nephropathy. There is paucity of data on adenovirus allograft nephropathy and its optimal management.
**Case Report:** A 24 year old gentleman underwent renal transplantation for end stage renal failure secondary to presumed glomerulonephritis. The immediate post-transplant period was complicated by delayed graft function. Renal allograft biopsy on day 5 post transplant showed acute cell mediated rejection (Banff 1a) that was treated with pulse methylprednisolone and 10 doses of antithymocyte globulin. A week later, he was diagnosed with a culture-positive urinary tract infection (Enterobacter aerogenes & Escherichia coli) in presence of an indwelling urinary catheter. He remained pyrexial despite treatment with meropenem and removal of the catheter.

As he continued to require haemodialysis, a repeat graft biopsy on day 26 post transplant was performed. This showed widespread granulomatous tubulointerstitial nephritis with marked necrosis of tubules. Many tubular epithelial cells showed "smudgy" chromatin. These nuclei showed positive staining with ADV immunoperoxidase stain. These findings were consistent with ADV nephropathy. Whole blood as well as urinary adenovirus PCR was positive. He was treated with two doses of Cidofovir (0.6 mg/kg) and intravenous immunoglobulin (0.5 g/kg). The adenovirus PCR remained positive for 4 weeks following which it was undetectable.
**Conclusion:** ADV is increasingly being recognised as a pathogen that can affect renal allografts. It is important to consider this diagnosis in patients who present with suggestive clinicopathologic features. This case demonstrates successful treatment of ADV nephropathy with Cidofovir and IVIG.

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## INVASIVE PNEUMOCOCCAL DISEASE INVOLVING STERNO-CLAVICULAR JOINT SEPTIC ARTHRITIS AND OSTEOMYELITIS, IN THE LATE POST-RENAL TRANSPLANT PERIOD

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**Background:** Renal transplant recipients have greater risk of invasive pneumococcal disease than the general population, with higher rates of morbidity and mortality.
**Case Report:** A 42yo Caucasian male, with end-stage kidney disease due to tubulointerstitial nephritis treated with a renal transplant, presented with multifocal pneumococcal sepsis.

The deceased-donor renal transplant occurred 13 years prior to presentation, with 2/6 HLA mismatch. He received standard triple therapy induction-immune suppression but his course was complicated by delayed graft function, early borderline rejection and, later, chronic allograft nephropathy. Other complications included CMV infection, recurrent UTI, transplant ureteric stenosis and acne conglobata. Following the death of his father, he developed social isolation, decline in self-care and poor nutrition. Despite these challenges, he maintained stable graft function for some years, with creatinine 220 and eGFR 34, whilst receiving mycophenolate and prednisone.

He presented with 5 day history of being febrile and generally unwell. His examination was notable for a large phlegmon over his left sternoclavicular joint (SCJ), and large buttock abscesses. Imaging and aspiration of the lesions revealed invasive pneumococcal disease involving left SCJ septic arthritis with retrosternal extension and osteomyelitis, pneumonia and multiple large skin abscesses. Penicillin sensitive streptococcus pneumoniae was isolated from aspirates and blood culture. Following ICU admission, several weeks of penicillin and multiple abscess drainage procedures, he achieved full recovery. His pneumococcal vaccination status was unknown.
**Conclusion:** This is a rare case of invasive multifocal pneumococcal disease with osteomyelitis in late post-renal transplant period. This case illustrates many underlying risk factors for invasive infection. It emphasizes importance of pneumococcal vaccination in high risk population to minimise risk of developing potentially avoidable invasive infection.

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## RESISTANT HYPERTENSION WITH A CAROTID SPACE MASS: IS IT PARAGANGLIOMA? A CASE REPORT

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**Background:** Paragangliomas are neuroendocrine tumor derived from extra adrenal paraganglionic cells of autonomic nervous system with ability to secrete neuropeptides and catecholamines. We report a case of carotid space mass with features suggestive of paraganglioma in a patient with symptomatic and refractory hypertension without evidence of secretion of catecholamine raising the question if there is episodic hormone secretion by paraganglioma.
**Case Report:** A 75-year-old man with 8 months history of headache and 3 months of dizziness with refractory hypertension and recent episodic aggression with anxiety. CT of the head and neck showed a large carotid space lesion. Plasma metanephrines, normetanephrines were normal including 24-hour urine catecholamines. There was no adrenal enlargement on CT abdomen and renal artery stenosis was excluded. PET Octreotide and MIBG scan were suggestive of neuroendocrine mass.

Carotid space mass may be vascular, inflammatory, benign or malignant. Hallmarks of diagnosis of functional paraganglioma are plasma, urine metanephrines and their metabolites. Most patients with paraganglioma do not exhibit biochemical evidence of catecholamine hypersecretion, at least as assessed using measurements of urinary catecholamines and total metanephrines. Measurements of plasma-free methoxtyramine might be useful for identifying additional dopamine producing tumors. There can be temporal sampling errors caused by sampling when patients are asymptomatic or when paragangliomas are not hyper-secreting.
**Conclusions:** We describe a carotid space mass in the context of refractory hypertension and positive octreotide scan which points towards a paraganglioma. Tissue diagnosis or surgical removal was not an option due to potential complications including accelerated hypertension, autonomic instability and injury to neighboring structures.

There may be episodic secretion of paraganglioma. Sampling may be taken when patients are asymptomatic or when paragangliomas are not hyper-secreting.

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## LOCALISED CYSTIC DISEASE OF THE KIDNEY: CASE REPORT AND ANALYSIS OF LITERATURE

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**Background:** Localised cystic disease of the kidney is a benign and non-progressive renal anomaly that may be initially confused with autosomal dominant polycystic kidney disease or cystic neoplasms.
**Case Report:** We describe a 62-year-old male with a marked cystic abnormality of the right kidney, mild chronic kidney disease and hypertension who manifested many of the typical features of the condition. He was initially diagnosed with autosomal dominant polycystic kidney disease before further investigation and review suggested the most likely diagnosis.
**Conclusions:** We review all available published cases and the characteristic radiological abnormalities. The most common manner of presentation is incidental (40%), followed by flank pain (31%), haematuria (23%) and palpable abdominal mass (10%). Hypertension and renal impairment are uncommon. Awareness of this rare entity can avoid unnecessary investigations or nephrectomy.

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## ONE OF LOWEST EVER POTASSIUM TO HAVE SURVIVED

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**Background:** Ibuprofen misuse can lead to Renal Tubular Acidosis resulting in hypokalemia. We report a case of life threatening hypokalemia associated with excessive Ibuprofen use. This case sends a reminder to practitioners about serious complication of uncontrolled use of over the counter analgesics.
**Case report:** A 31 year old man was brought in by ambulance after being found on the floor with profound weakness and unable to move. He had a history of musculoskeletal back pain for which he was using up to 20 tablets of Ibuprofen a day for the last 12–15 years. On examination the patient had

epigastric tenderness and quadriparesis. Laboratory investigations were consistent with distal renal tubular acidosis (pH 7.3, $pCO_2$ 27, anion gap 15, $Na^+$ 143, $HCO_3^-$ 14, $Cl^-$ 124, urine anion gap 4) with profound hypokalemia 1.3. Electrocardiogram showed U waves and ultrasound of kidney demonstrated nephrocalcinosis. The ibuprofen was ceased and after initial management in intensive care for potassium replacement he returned to ward, his biochemical derangements normalised over the next few days with return of his muscle strength. He was discharged after a week on a pain management regimen with advice to avoid non steroidals and see his general practitioner should pain management needed escalation.
**Conclusion:** Profound hypokalemia due to renal tubular acidosis secondary to ibuprofen misuse could potentially be a fatal complication as this case illustrates and should be included in the differential diagnosis of patients presenting with hypokalemia. Careful literature search did not describe many cases having survived such hypokalemia.

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## AN UNUSUAL CASE OF DIETARY INDUCED SECONDARY OXALOSIS

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**Background:** We report the case of a 63 year old male with rapidly progressive renal failure (RPRF). This occurred on the background of previously normal renal function and a medical history of Type 2 diabetes mellitus (diet controlled), severe Obsessive Compulsive Disorder (OCD) and Depression.
**Case Report:** The patient presented with increased thirst and anorexia with a serum creatinine of 377 μmol/L. Eighteen months earlier it had been 120 μmol/L and more remotely, approximately 80 μmol/L and stable. Investigations revealed a benign urinary sediment, a negative autoimmune screen and normal renal arteries. There was no history of renal calculi, or intake of nephrotoxins on initial questioning. Renal biopsy demonstrated severe interstitial nephritis and acute tubular necrosis with normal glomeruli. There was marked tubular oxalate deposition, but of lesser density than expected for primary oxalosis. A 24 hr urine oxalate revealed excretion of 1.92 mmol/day (RR 0.0–0.5 mmol/day).

Despite initial treatment with 75 mg prednisone orally, the patient was readmitted 1 month later with worsening lethargy and a creatinine of 633 umol/L. Pulse intravenous Methylprednisolone and oral pyridoxine were commenced but over the next 4 days the patient progressed to end stage renal failure. Emergent haemodialysis was commenced and he remains dialysis dependent despite normalisation of urinary oxalate.

The patient initially denied a history of consumption of oxalate rich foods. However, subsequent questioning elicited a repetitive dietary regime comprising of up to 20 nut based health bars per day and high levels of Vitamin C supplementation (5–10 g/day).
**Conclusions:** This case report describes a rare, though potentially avoidable, case of secondary oxalosis, and highlights the importance of detailed and directed questioning to exclude secondary oxalosis as a cause of RPRF.

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## ATYPICAL HAEMOLYTIC URAEMIC SYNDROME WITH A NOVEL COMPLEMENT FACTOR H MUTATION

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**Background:** Atypical haemolytic uraemic syndrome is a rare, potentially devastating condition due to dysregulation of the alternative complement pathway. The majority of cases are now known to occur in individuals with mutations of key complement regulatory proteins such as complement factor H. Standard treatment is plasma exchange. Eculizumab, a monoclonal antibody to C5 has recently shown much promise.
**Case Report:** We describe the case of a 41-year-old female who presented with acute kidney injury and microangiopathic haemolytic anaemia following an upper respiratory tract infection. Prompt treatment with plasma exchange, corticosteroids and haemodialysis was begun. Subsequent investigation, including normal serum ADAMTS13 activity and the absence of evidence of Shiga-toxin producing E.Coli, led to a diagnosis of atypical haemolytic uraemic syndrome (aHUS). Four weeks after presentation she remained on daily plasma exchange and was dialysis dependent. A trial of eculizumab over the next four weeks did not lead to a response. Genetic analysis identified a novel mutation in the complement factor H gene (1106G > A) that introduces a stop codon.
**Conclusions:** This case adds to an evolving body of knowledge concerning the effect of various mutations in complement regulation on the natural history and response to therapy of aHUS. It also highlights the importance of a controlled trial in assessing the utility of novel therapeutics.

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## RENAL LIMITED TMA AND ACUTE INTERSTITIAL NEPHRITIS WITH SINGLE DOSE OF QUININE

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**Background:** Quinine, commonly used in over-the-counter preparations to treat muscle cramps, has been reported to cause HUS. Quinine is also present in beverages such as tonic water and bitter lemon. This case report highlights how a single tablet of Quinine can trigger HUS in susceptible individuals.
**Case:** A 66 year old lady presented with acute renal failure after taking a dose of 300 mg of Quinine 8 days ago for cramps. She has a past medical history of Rheumatoid arthritis. Her blood tests showed a Creatinine 1295 umol/L, Hb-80 g, Platelets – 173 /L, LDH-1014 U/L, AEC of 0.56 /L, Haptogloblin 0.46 g/L (0.50–2.50 g/L), dsDNA positive, ANA positive, RF positive. Quinine dependant antibodies were negative, and serum complements were normal. Peripheral smear showed no fragmented red cells. Stool microscopy and culture revealed no evidence of infection. Urine showed microscopic haematuria but no active sediments, proteinuria or eosinophils. Kidney biopsy revealed changes consistent with thrombotic microangiopathy, acute interstitial nephritis and acute tubular necrosis. Immunofluorescence was negative, including that for C1q. She required 5 sessions of haemodialysis. She was also treated with oral prednisolone, given the acute interstitial nephritis. She did not require plasma exchange because she improved once the offending agent was withdrawn. She was reviewed 3 weeks later and serum creatinine continues to improve (200 umol/L) and she maintains good urine output.
**Conclusion:** Although a rare entity, this case highlights that TMA and acute interstitial nephritis should be considered in patients who have taken even a single dose of quinine/tonic water.

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## AN UNUSUAL CASE OF ACUTE INTERSTITIAL NEPHRITIS

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**Background:** Fish oils are postulated to have various health benefits due to their antioxidant effects. These effects are attributed to the omega-3 long chain polyunsaturated fatty acids contained therein, particularly eicosapentanoic acid (EPA) and docosahexaenoic acid (DHA). Krill oil is derived from crustaceans and has a high content of EPA and DHA. In more recent years krill oil supplements have been investigated for use in various health conditions including dysmenorrhoea and premenstrual syndrome, dyslipidaemia and inflammation.

The majority of cases of acute interstitial nephritis (AIN) are drug-induced with common causative drugs being proton pump inhibitors, penicillins, cephalosporins and non-steroidal anti-inflammatory drugs[7]. We present a case of drug-induced acute interstitial nephritis (DIAIN) associated with krill oil.
**Case Report:** A 61 year old woman presented to the Emergency Department with a four day history of gastrointestinal symptoms which had begun when she commenced a krill oil tablet for management of osteoarthritic symptoms. She was in acute renal failure with severe metabolic acidosis and hyperkalaemia. The patient was initially dialysed due to the significant metabolic derangement and a subsequent renal biopsy confirmed the diagnosis of AIN. She was managed with a tapering dose of steroid therapy and now has chronic kidney disease as a complication of her DIAIN.
**Conclusion:** This is the first reported case of DIAIN associated with krill oil and highlights the importance of ongoing post-marketing surveillance of all pharmaceutical agents as well as the value of a detailed medication history in seeking to identify over the counter or complementary medicines as a cause for acute kidney disease.

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## RENAL THROMBOTIC MICROANGIOPATHY

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**Introduction:** Thrombotic microangiopathy (TMA) is characterized by occlusive thrombosis in the microvasculature. A variety of diseases are associated with TMA. This case is remarkable for a renal specific TMA without a clear cause.
**Case Description:** A 45-yr old Indian lady presented with a few weeks history of lethargy. Her background included Type II Diabetes Mellitus, Graves's disease and hypertension. Initial tests revealed severe iron deficiency anemia with hemoglobin 60 g/L and an acutely impaired renal function with creatinine 250 mcmol/L.

Physical examination showed an elevated blood pressure of 150/90 mmHg. Fundoscopy revealed small hard exudates reflective of her known hypertensive retinopathy. Remainder of examination was unremarkable and there were no skin changes suggestive of systemic sclerosis.

Investigations showed no hemolysis, thrombocytopenia or schistocytes and testing of ADAMTS-13 its inhibitors were unremarkable, excluding thrombotic thrombocytopenic purpura and hemolytic-uremic syndrome. Myeloma and immunology serology including antiphospholipid antibodies was unremarkable except for mild elevation of anti-nuclear antibody. Urine test showed microalbuminuria and no hematuria. Pregnancy test was negative. Renal biopsy showed glomerular mesangiolysis with dilatation of capillary loops filled with fragmented red cells and focal fibrin consistent with TMA; vessels appeared normal, lacking evidence of arteriolar hyalinosis and onion-skinning, making malignant hypertension and scleroderma less likely causes. Pan-endoscopy showed a bleeding area of gastric vascular ectasia treated with laser. Bone marrow biopsy was normal. Other causes of TMA include chemotherapy drugs, calcineurin-inhibitors and toxins of snake-venom, none of which were plausible in this case.
**Discussion:** This is a rare case that illustrates an unusual case of renal TMA with an unclear aetiology. Nevertheless, it is important to keep a close watch for other manifestations to surface and monitor for future autoimmune conditions.

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## MYELOMA CELLS CAUSING CORONARY OSSIFICATION

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**Background:** Multiple myeloma (MM) is characterized by the neoplastic proliferation of immunoglobulin-producing plasma cells. Most patients with MM present with signs or symptoms related to the infiltration of plasma cells into the bone or other organs or with renal injury from excess light chains. These presentations include anaemia, bone pain, elevated creatinine or serum protein, fatigue, and hypercalcemia.

Infiltration of the pericardium and myocardium by myeloma cells has been reported. Patients typically suffer from cardiac tamponade as a result of massive pericardial effusion. There have been rare cases of plasmacytomas formed in the cardiac chambers. Our case puts forth the probability of ossification of the coronary vessels caused by infiltrating myeloma cells which has not previously been described.
**Case Report:** This is a case of a 75 year old female who was seen by our department for Acute Kidney Injury (AKI). Her past medical history consisted of hypertension and Type 2 Diabetes Mellitus. She underwent a renal biopsy after an ultrasound scan of her renal tract ruled out obstruction. During this admission, she deteriorated very quickly after a cardiac ischaemic event and died in intensive care. Her autopsy revealed interesting pathology slides of myeloma cells infiltrating the myocardium and coronary arteries and causing ossification of the vessel. Post mortem did not suggest that there was significant pericardial effusion or infiltration of the pericardium by myeloma cells. Her renal biopsy was consistent with myeloma kidney.
**Conclusion:** The post mortem finding in this case describes the infiltration of the coronary vessels by myeloma cells with evidence of ossification of the coronary arteries. We postulate that this ossification is caused by the myeloma cells.

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## LERCANIDIPINE INDUCED ACUTE INTERSTITIAL NEPHRITIS, NEVER REPORTED BEFORE

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**Background:** Acute interstitial nephritis (AIN) is characterized by inflammatory infiltrate in the kidney interstitium often induced by drug therapy, autoimmune or systemic disease, infections and TINU syndrome. Calcium channel blockers like Amlodipine and Diltiazem have been associated with AIN but Lercanidipine has never ever been reported which we hereby report.
**Case report:** A 60 year old man was seen in the outpatients for assessment of hypercalcaemia (3.80 mmole/l) and acute renal failure (creatinine 270 μmole/l) and eosinophilia ($2.11 \times 10^9$ /l) after a brief admission in hospital for worsening shortness of breath related to longstanding obstructive sleep apnoea. He had a history of hypertension for which he was on Lercanidipine. He denied being on any other drug and never took over the counter medications or herbal supplements. Physical examination was non contributory. Extensive laboratory and radiological investigations were undertaken to find the cause. Results came back negative for any malignancy, multiple myeloma or parathyroid disease. Renal biopsy was performed which showed acute interstitial nephritis and tubulointerstitial scarring. Bone marrow biopsy was undertaken which did not show any granuloma. A final diagnosis of AIN was made which was probably due to Lercanidipine. Cessation of the offending drug and a short course of steroids returned the biochemical parameters to normal.
**Conclusion:** Any drug can cause AIN with any frequency. In the case described renal failure and eosinophils are expected in AIN but hypercalcaemia can be attributed to PTH independent production of calcitriol from activated mononuclear cells. Lercanidipine has never been reported to date on extensive literature review to cause AIN but should be added on to the growing list.

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## HEMOPHAGOCYTOSIS CAUSING ACUTE TUBULAR NECROSIS, A CASE REPORT

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**Background:** Hemophagocytic syndrome (HPs) is a rare but distinct condition caused by inappropriate and dysregulated activation of the immune system. Primary HPs is linked to inherited immune dysregulation, whereas secondary HPs tends to be triggered by an infectious or neoplastic disease. Multiorgan failure can occur in this condition and renal failure has been reported, acute kidney injury due to acute tubular necrosis (ATN) and nephrotic syndromes being the commonest presentation. We hereby report a case of ATN due to HPs.
**Case report:** A 69 year old man with stable long standing chronic lymphocytic leukemia (CLL) was admitted to hospital with non-specific symptoms two weeks after treatment with chlorambucil. He had been on Prednisolone and Valacyclovir (Cytomegalovirus prophylaxis). He was febrile, tachycardic on presentation with hepatosplenomegaly on examination. Initial laboratory results were consistent with acute kidney injury (creatinine 187 μmole/l), acute liver injury (total bilirubin 45 μmole/l, alkaline phophatase 141 U/L, gamma glutamyl transferase 139 U/L, ALT 111 U/L, AST 138 U/L), thrombocytopenia ($50 \times 10^9$/l), CRP 140 mg/l and ferritin of 58900 μg/l. Search for possible infection was noncontributory. His renal function went on to deteriorate further requiring haemodialysis. Tazosin was empirically initiated. Renal biopsy was conducted with platelet cover which showed features of acute tubular necrosis with no CLL cells. A bone marrow biopsy was done which was consistent with hemophagocytosis. As his condition improved he became dialysis independent, biochemical parameters returned to normal and was discharged with further plans for CLL treatment to be discussed in the haematology outpatients.
**Conclusion:** We speculate that the HPs in our patient was due to unidentified infection as there was no evidence of active CLL and the condition went into remission with empirical antibiotic. The notable aspect of this case for practicing Nephrologist was the ATN due to HPs which is due to interstitial inflammation. Treatment for HPs is suppression of triggering factor. Although rare, Nephrologists should be aware of this condition and include in the list of differential diagnosis for AKI.

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## RENAL SCLEROSING PERITUBULAR NODULE-HOW RARE IS IT?

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**Introduction:** Neurofibromatosis type 2 (NF2) is a rare autosomal dominant disorder. It affects about 1 in 25,000 people. Kidney involvement in NF2 has not been studied extensively. A relatively rare lesion, the renal sclerosing peritubular nodule (RSPN), was first described in a mother and 2 sons with NF2 who died and underwent autopsy in 1981.

**Case report:** A 53-year-old man with neurofibromatosis type II was referred for investigation and management of his deteriorating renal function. Physical examination revealed cutaneous manifestations of NF2. Serial blood tests showed declining renal function. Urine showed microscopic hematuria with no proteinuria. An ultrasound showed normal size kidneys and renal tract.A renal biopsy was performed.
**Results:** Light microscopy showed 3 out of 9 glomeruli globally sclerosed. Within the interstitium were paucicellular nodules, adjacent to tubules . The nodules were lightly eosinophilic on H&E, PAS negative and argyrophilic on PASM.The nodules stained blue with Masson trichrome, resembling collagen. In the context of the clinical history, the morphology of the collagenous nodules was consistent with RSPN.
**Conclusion:** Our case represents a rare form of a hereditary renal abnormality in NF2. There are only two previous case reports. It has been thought that these nodules do not alter normal kidney function, even when they are extensive, however none of the previous patients survived into their fifth decade. With increasing frequency of NF2 patients surviving with advanced medical care, RSPN like lesions are more likely to be seen on their renal biopsy. Since these histologic lesions appear morphologically progressive early recognition, careful monitoring of the renal function and avoidance of potentially nephrotoxic agents is prudent.

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## ATYPICAL HEMOLYTIC SYNDROME AND POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

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**Introduction:** Atypical Hemolytic Uremic Syndrome (aHUS) is a life threatening and progressive disease due to uncontrolled complement activation.We describe a case of aHUS on Eculizumab and co-existing malignant hypertension
**Case:** A 24 year Gentleman presented to the Emergency Department with 5 day history of nausea and vomiting.He was hemodynamically stable with no significant examination findings.His investigations showed microangiopathic hemolytic anemia, thrombocytopenia, fragmented red blood cells on peripheral smear, elevated LDH and acute renal failure.A diagnosis of HUS was made which was later confirmed on renal biopsy.
**Follow up:** He was commenced on daily plasma exchange (PE) with fresh frozen plasma. On days 3&4 his PE was continued and initiated on haemodialysis due to worsening renal function. He however continued to have ongoing thrombotic microangiopathy and was initiated on Eculizumab. On day 6 his PE was ceased. His dialysis was stopped after 3 weeks due to progressive improvement of his renal functions.He was hypertensive managed on a single antihypertensive medication. After discharge he had an episode of accelerated hypertension with seizures with MRI confirming posterior reversible encephalopathy syndrome. His hemolytic screen showed no recurrence. His seizures were managed with antiepileptics and tight blood pressure control. He is currently well, off antiepileptics with ongoing fortnightly course of Eculizumab.
**Conclusion:** Neurological involvement in the acute phase of HUS occurs in 17–52%. The pathogenesis of CNS involvement in aHUS is multifactorial secondary to metabolic abnormalities, uraemia,electrolyte imbalance and hypertension.Seizure usually are early in the course of the disease.This case report describes the uncommon finding of late onset seizures. This case provides an example of aHUS coexisting with malignant hypertension and requires both complement mediated TMA and hypertension to be controlled.

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## PARANEOPLASTIC ANCA NEGATIVE PAUCI-IMMUNE CRESCENTIC GLOMERULONEPHRITIS WITH RENAL LIMITED THROMBOTIC MICROANGIOPATHY IN A PATIENT WITH METASTATIC BREAST CANCER – A CASE REPORT

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**Background:** Glomerular disease occurring in association with a malignancy remains rare. The most common paraneoplastic glomerulopathy is membranous nephropathy. Minimal change disease and membrano-proliferative nephropathy is associated with Hodgkin's lymphoma and chronic lymphocytic leukaemia respectively. Paraneoplastic ANCA positive pauci-immune glomerulonephritis (GN) has also been reported.
**Case Report:** We present a 65 year old, Caucasian, Australian female who presented to her ophthalmologist with sudden onset of deterioration in vision since four weeks and increasing generalised body oedema and shortness of breath since three weeks. She was diagnosed with bilateral exudative retinal detachments and right superior hemi-branch retinal vein occlusion and referred for further evaluation. On examination she was hypertensive with anasarca and bilateral pleural effusions. Vision was restricted to finger counting at one metre. She was also found to have a large upper outer quadrant breast mass with multiple right axillary lymph nodes. She had nephrotic range proteinuria with hematuria and renal 'failure' as per RIFLE criteria. Ultrasound of renal tract was normal. Renal biopsy was done which demonstrated crescentic GN with most glomeruli showing severe focal and segmental damage. Fibrin thrombi were seen in some arterioles with no evidence of vasculitis. Immunofluorescence was consistent with pauci-immune crescentic glomerulonephritis (CGN). ANA was positive 1:320 with negative dsDNA. ANCA returned negative. Complement levels were normal. CT-guided core biopsies of breast lesion showed invasive ductal carcinoma. Nodal and bony metastases were detected on further scans.
**Conclusions:** To our knowledge, paraneoplastic ANCA negative pauci-immune GN with renal limited thrombotic micro-angiopathy in metastatic breast cancer has not been reported previously in medical literature.

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## DIFFUSE ALVEOLAR HAEMORRHAGE – IS IT LUPUS? OR IS IT CMV?

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**Background:** Diffuse alveolar haemorrhage in systemic lupus erythematosus (SLE) could be due to the disease itself, or may be related to concomitant infection with CMV. We report a case of CMV infection in a patient with SLE who presented with severe lupus nephritis & diffuse alveolar haemorrhage.
**Case report:** A 24 year old indigenous lady with known SLE presented with respiratory distress and nephrotic syndrome with renal insufficiency. Investigations demonstrated haemoglobin of 28 g/L and diffuse alveolar haemorrhage. She had been recently prescribed Mycophenolate mofetil and prednisolone.

Her clinical condition rapidly deteriorated and she required invasive ventilation. She was started on pulse methylprednisolone, plasmapheresis, a single dose of intravenous cyclophosphamide and continuous veno-venous haemodiafiltration. She developed profound pancytopenia, and was therefore treated with two doses of Rituximab (1 g) and intravenous immunoglobulin.

CMV DNA was detected in serum and bronchoalveolar lavage with a significantly high viral load. Gastroscopy showed multiple erosions in the oesophagus, gastric antrum & duodenum, the appearance of which was consistent with CMV infection. She was treated with intravenous gancyclovir and CMV immunoglobulin. Lung biopsy was not performed due to ongoing haemorrhage and respiratory instability.

Following stabilization of clinical condition, a renal biopsy was performed. This showed Lupus nephritis class III & V with severe scarring. She made a remarkable recovery, and remains dialysis independent with complete resolution of pulmonary disease.
**Conclusion:** CMV infection should always be suspected early and treated promptly in patients with SLE who present with diffuse pulmonary haemorrhage.

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## A CASE OF LARGE IVC AND BILATERAL RENAL VEIN THROMBOSIS IN AN ADULT WITH MEMBRANOUS NEPHROPATHY PRESENTING AS A LEFT TESTICULAR VARICOCELE

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**Background:** Nephrotic syndrome predisposes to venous thromboembolism. We report an unusual presentation as a testicular varicocele, of renal vein thrombosis in a patient with nephrotic syndrome.
**Case Report:** A 40 yr old road layer was referred by his General Practitioner to the Renal unit for investigation of his recently diagnosed nephrotic syndrome, which was made when he presented with new onset bilateral pitting odema of his legs. Investigations revealed nephrotic range protienuria, hypo-albuminaemia and hyperlipidaemia, confirming the diagnosis.

During the admission for a renal biopsy, patient complained of a swelling in his scrotum for the last 2 weeks. Genital examination revealed a boggy swelling along the spermatic cord on the left side consistent with a varicocele. This raised the suspicion of a left renal vein thrombus, given that the left testicular vein joins the left renal vein.

Renal biopsy of the right kidney was performed which showed membranous nephropathy. It also included a section of a renal vein showing complete occlusion of lumen due to a fibrin thrombus.

Patient was commenced on therapeutic anti-coagulation. CT-angiogram showed large thrombus in the inferior venacava, extending to both renal veins.
**Conclusions:** Renal Vein thrombosis has been noted in patients with idiopathic membranous nephropathy and nephrotic syndrome. It is usually asymptomatic and diagnosed incidentally, although patients can present acutely with flank pain and macroscopic hematuria. While it is known that renal cell cancer invasion into the renal vein can present as an acute varicocele, this is an unusual presentation of renal vein thrombus secondary to nephrotic syndrome.

Ours is only the third reported case of a person with nephrotic syndrome presenting with a left varicocele secondary to renal vein thrombosis.

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## ANCA NEGATIVE PAUCI-IMMUNE CRESCENTIC GLOMERULONEPHRITIS FOLLOWING TWO EPISODES OF SEPSIS

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**Background:** ANCA negative pauci-immune glomerulonephritis (GN) is rare cause of Acute Kidney injury (AKI). We describe the first published case of ANCA negative pauci-immune crescentic GN, following 2 episodes of sepsis, who responded well to immunosuppression.
**Case report:** A 34 yr old male presented with fever and AKI. He was found to have staph aureus bacteremia and AKI improved initially with treatment of sepsis. After 3 weeks, he developed pseudomonas urosepsis with worsening AKI. AKI worsened in spite of treatment of sepsis. Differential diagnosis was post-infectious glomerulonephritis, acute interstitial nephritis or acute tubular necrosis. He was found to have hematuria with isomorphic and dysmorphic cells in the ratio of 20:1. He had proteinuria of 2.3 g/day. Ultrasound revealed large kidneys suggestive of pyelonephritis. All autoimmune and viral serology were negative and complement levels were normal. He underwent a renal biopsy, which surprisingly showed acute crescentic pauci-immune GN, even though ANCA was repeatedly negative. 14 out of the 17 glomeruli in the specimen had cellular or fibrocellular crescents. Immunofluorescence was negative indicating pauci-immune GN. He was commenced on treatment with Corticosteroids and Cyclophosphamide while continuing antibiotics. Renal function dramatically improved from eGFR of 13 mls/min to 60 mls/min and remains stable on maintenance therapy.
**Conclusion:** ANCA negative pauci-immune GN is rare and has been described to occur after episodes of sepsis with certain gram-negative organisms due to molecular mimicry. The renal survival is usually poor, but our patient responded well to treatment with immunosuppression perhaps due to early diagnosis and treatment. This also highlights the importance of renal biopsy in acute kidney injury after sepsis as most of the time AKI is attributed to sepsis.

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## OVARIES IN DISGUISE: A PRIMARY GRANULOSA CELL TUMOUR MIMICS A PHEOCHROMOCYTOMA

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**Background:** Given their common embryological origin in the urogenital ridge it is not surprising that ovarian tissue can be identified within adrenal glands. Several cases have been reported of granulosa cell tumours developing within adrenal glands & elsewhere within the abdominal cavity. Several cases report resistant hypertension associated with renin-producing ovarian tumors. Here we report the case of drug resistant hypertension in an individual with a primary adrenal granulosa cell tumor.
**Case Report:** A 67-year-old female with 20-year history of resistant hypertension, chronic kidney disease and hypokalaemia has adrenal mass incidentally discovered on imaging, with normal renal and renal artery anatomy. MIBG scan revealed no tracer accumulation within the left adrenal gland. Renin and aldosterone levels could not be checked as she was on multiple antihypertensive that would interfere with the assessment of the RAAS.

Unilateral adrenalectomy for a suspected pheochromocytoma is curative of resistant hypertension, however pathology of adrenalectomy specimen excludes pheochromocytoma and is suggestive of a granulosa cell tumour. Repeat abdominal and pelvic imaging is unable to detect a primary site.

Blood pressure control post surgery maintained initially with a single agent, ceased 6 months post surgery.

**Conclusions:** We postulate that the case described here represents a renin secreting primary adrenal granulosa cell tumor, unusual in that its location and proposed impact on the patients blood pressure effectively mimicked a pheochromocytoma. Cases like these highlight the potential importance of extra-renal, and especially ovarian, sources of renin in those patients presenting with hypertension and hypokalaemia and normal renal function.

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## SUCCESSFUL PARATHYROID ETHANOL INJECTION THERAPY FOR PERSISTANT SECONDARY HYPERPARATHYROIDISM

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**Background:** Parathyroid ethanol injection therapy (PEIT) as an alternative for treatment of secondary hyperparathyroidism has been described in the literature. Japanese guidelines are available, and most success comes from targeting large (>0.5 $cm^3$), single glands. Dysphonia is a known side effect, reported in up to 6% of cases, and is usually temporary.
**Case Report:** A 55 year old male home haemodialysis patient with ESKD on dialysis due to type 2 diabetes mellitus underwent two attempts at total parathyroidectomy after failing calcimimetic therapy. Due to persistent elevation in parathormone level (151 pmol/L), a sestamibi parathyroid fused SPECT-CT was performed and revealed a right inferior parathyroid adenoma or hyperplastic gland. USS defined the size of this parathyroid tissue as 12x19x24 mm (2.85 $cm^3$). Under USS visualisation, 3.5 mL of absolute alcohol was injected into the centre of the parathyroid using a 22 gauge needle. The patient developed dysphonia immediately. Seven days later the parathormone level was 31 pmol/L and plateaued at 75 pmol/L by four months. The dysphonia remained for three months and resolved completely.
**Conclusions:** PEIT can be an effective alternative to pharmacological and surgical treatment of secondary hyperparathyroidism in selected patients with appropriate glandular enlargement. Dysphonia is an unusual complication, which is usually temporary as in this case, and is likely due to the alcohol injection causing a neuropraxia, due to spilling, or impinging due to volume effect on the recurrent laryngeal nerve.

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## RHIZOBIUM RADIOBACTER ASSOCIATED PERITONAL DIALYSIS PERITONITIS – A CASE REPORT WITH LITERATURE REVIEW

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**Background:** The plant pathogen *Rhizobium radiobacter* is a gram negative bacillus found in the soil. Opportunistic infections with *R.radiobacter* in humans are rare and are usually associated with indwelling catheters. There have been eleven case reports on *R.radiobacter* associated Peritoneal Dialysis (PD) peritonitis since 1991 and more than half of them required PD catheter removal. This finding reflects the impact of *R.radiobacter* infection on PD technique survival. Feasibility of returning to PD after a severe *R.radiobacter* peritonitis remains unknown with limited published case reports.
**Case Report:** We present the first case from Australia; namely, a 37-year old Caucasian lady who had recently undergone modality change to Automated PD for End-Stage Renal Disease secondary to Polycystic Kidney Disease. She presented with clinical features of peritonitis, not supported by laboratory analysis or culture of the effluent (WCC-93 × $10^6$; N-15 × $10^6$; no growth). She was given a dose of empiric intraperitoneal (IP) Cefazolin and Gentamicin. Four days later, she represented with worsening symptoms and effluent analysis confirmed peritonitis (WCC-4895 × $10^6$; N-4552 × $10^6$) and a slow growth of Gram-negative bacilli later confirmed as *R.radiobacter*. She failed to respond despite appropriate treatment with IP Gentamicin. This necessitated PD catheter removal on Day 6. We present a literature review of similar cases with *R.radiobacter* peritonitis.
**Conclusion:** *R.radiobacter* associated PD peritonitis has shown variable outcome with technique survival. The factors that may negatively influence the outcome include inherent antibiotic resistance of the organism by production of antibiotic-inactivating enzymes, delay in obtaining the antibiotic sensitivity due to its slow growth and unstandardized antibiotic reference breakpoints, relapsing infection with colonization of catheters, ignoring the culture result as environmental contaminant and immunosuppressed state. The rarity of the infection necessitates the formation of a global PD registry to study the patterns of outcome.

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## A CASE SERIES OF SUSPECTED LERCANIDIPINE INDUCED CHYLOPERITONEUM IN A PERITONEAL DIALYSIS POPULATION

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**Background:** Benign chyloperitoneum, that is macroscopically indistinguishable from infective peritonitis, is acknowledged as a known consequence of calcium channel blocker (CCB) use. Its incidence seems to have been increasing though with the more widespread use of dihydropyridine based CCBs and in particular, lercanidipine. This may be related to its lipophilic properties although the exact mechanism by which this occurs still remains unclear.
**Case Report:** We report a series of 4 patients with suspected benign chyloperitoneum following a retrospective review of our peritoneal dialysis population from the last 5 years. All patients had had exposure to lercanidipine at a dose of at least 20 mg daily. There were three male patients and one female patient with ages ranging between 40 and 73. Three were on \automated peritoneal dialysis, the other on continuous ambulatory peritoneal dialysis. All patients have had recurrent episodes of cloudy peritoneal fluid, several of which were associated with mild abdominal pain – none however had microbiological proven peritonitis. Many episodes were managed with empirical intra-peritoneal antibiotics and hospital admission. Three of these patients had triglyceride analysis of the peritoneal fluid, with the mean triglyceride level being 1.0 ± 0.62 mmol/L suggesting the alternative diagnosis of benign chyloperitoneum.
**Conclusions:** Cloudy peritoneal effluent always needs to be considered as being infective but benign chyloperitoneum represents an increasing mimic in those on a CCB and, in particular, lercanidipine. The elevated peritoneal triglyceride content in the right clinical context may aid in the diagnosis and possibly avoid prolonged unnecessary antibiotic administration and hospital admission.

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## THE FIRST CASE OF PARACOCCUS YEEII SPECIES INFECTION IN AUSTRALIA CAUSING PERITONITIS IN AN APD PATIENT

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**Background:** Peritonitis is the most serious infectious complication associated with Peritoneal dialysis (PD). In Australia, the rate of PD peritonitis is about 0.60 episodes per patient year. 53.4% of cases are due to gram positive organisms (most commonly Staphylococcus Epidermidis), 5.3% due to pseudomonas and 23.3% are due to other gram negative organisms.
**Case Report:** A 72 indigenous male, on automated peritoneal dialysis (APD) for diabetic nephropathy, presented to our unit with a 24 hour history of abdominal pain. On examination he was afebrile and hemodynamically stable. PD fluid was cloudy and microscopy showed total white cell count of $350 \times 10^6$ (only 32% polymorphs). Empiric treatment with intraperitoneal (IP) vancomycin (patient colonized with methicillin resistant Staph. Aureus) and gentamicin was commenced. 48 hrs elapsed before the organism was identified as a gram-negative bacillus and a further 2 weeks before formal identification as paracoccus yeei. The patient made an uneventful recovery after 3 weeks of IP gentamicin.
**Conclusions:** Paracoccus yeei is a nonfermenting, non-motile, non-spore forming bacterium that exist in a vacuolated or O shaped diplococcoid or coccobacillary forms. The organism is difficult to isolate using standard microbiological techniques and usually requires 16S rRNA gene sequencing. The 4 documented cases are bacteremia secondary to infected bullous skin lesions, another case of PD peritonitis in a young male with IgA nephropathy, corneal graft infection and myocarditis in heart transplant patient. Paracoccus Yeei probably causes opportunistic infections although cases may simply not be identified due to suboptimal identification techniques. Furthermore, even if identification is delayed, the organism is readily susceptible to commonly used anti-microbials.

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## A GRAM-NEGATIVE RAMPAGE IN A FLEDGLING PD PROGAMME

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**Background:** In the past 3 years the Fraser Coast Service has worked hard to expand the number of patients on the home therapies programme. With an increase in patients on Peritoneal Dialysis (PD), there has been an expected increase in peritonitis episodes. However, we report an unusually high proportion of gram-negative organisms, including a number of less common species.
**Case Report:** Currently PD patients account for 24% of our total dialysis population and 65% of the home therapies population. Since our peritonitis register was commenced in 2010, we have recorded a median peritonitis rate of 17.62 months to first episode, with 9/17 prevalent patients not having had peritonitis to date.

12 patients in our programme have had peritonitis, with a total of 14 episodes. 3 patients required catheter removal, 2 patients had a second episode with the same organism, and 2 patients had polymicrobial infection. Interestingly, and in stark contrast to national and international data, 10/13 (77%) identified organisms were gram-negative pathogens, with only 1 episode coagulase-negative staphylococcus, 1 episode Methicillin-resistant Staphylococcus aureus and 1 episode culture-negative. Furthermore, only half of the gram-negative pathogens were in the top 5 reported organisms in Australia (1 Escherichia coli, 1 Pseudomonas, 3 Enterobacter species). Other organisms identified include less commonly reported Pantoea species (2), Achromobacter xylosoxidans (1), Acinetobacter baumanii (1) and Citrobacter koseri (1).
**Conclusion:** A disproportionately high number of peritonitis episodes in our population are caused by gram-negative organisms, including some rarer unusual pathogens. Whilst the low number of gram-positive infections gives us confidence in our patient training programme, the poorer outcomes associated with gram-negative peritonitis give cause for concern.

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## SUCCESSFUL TREATMENT OF MYELOMA CAST NEPHROPATHY WITH THE NEW HIGH-CUTOFF ULTRAFLUX EMiC2 DIALYSER

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**Background:** Cast nephropathy is the most common diagnosis in patients with multiple myeloma and clinical renal dysfunction, and is associated with poor outcomes. Accumulation of high serum concentrations of monoclonal free light chains (FLC) leads to intratubular cast formation and direct tubular toxicity but early, aggressive treatment to achieve a sustained reduction in FLC is effective. We describe a patient treated with the Ultraflux EMiC2 dialyser, combined with bortezomib-based chemotherapy. The use of this filter has not previously been described in this setting.
**Case Report:** A 50 year old Caucasian man presented with dialysis-dependent, acute kidney injury. Blood tests revealed normal serum calcium, elevated urate 0.60 mmol/L, 39 g/L IgG kappa paraprotein, and markedly elevated serum FLC > 4000 mg/L and kappa : lambda ratio of 778. Bone marrow biopsy confirmed multiple myeloma, and kidney biopsy demonstrated cast nephropathy, with no significant chronic interstitial damage. The patient was switched from conventional to extended haemodialysis with the EMiC2 dialyser, and commenced on chemotherapy with bortezomib, cyclophosphamide and dexamethasone. After 2 weeks, there was a rapid reduction in serum FLC, improved renal function and dialysis independence. Mild hypoalbuminaemia occurred but no replacement was required. After 2 months, the patient remained dialysis independent and in stable clinical remission. Comparisons are made with 5 other patients at our centre treated with high-cutoff dialysis with the Theralite HCO 1100 dialyser.
**Conclusions:** In our patient, the use of the new Ultraflux EMiC2 dialyser, combined with chemotherapy, was effective in a sustained reduction in serum kappa FLC and resolution of acute kidney injury, with minimal albumin loss. Further studies are required to determine its efficacy in the long term and in patients with elevated serum lambda FLC.

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## HEPATITIS C VIRUS INFECTION DURING HAEMODIALYSIS ON VACATION: A SERIES OF 3 CASES

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**Background:** Analysis of recent Australian registry data suggests that the overall prevalence of Hepatitis C virus (HCV) in haemodialysis patients remains low, 1.6%, compared to the rest of world. It is well established that the incidence of HCV increases with the time on haemodialysis, as patient to patient spread is the most common mode of transmission in renal units. An

emerging risk factor for the acquisition of HCV is vacation haemodialysis in resource poor countries where the prevalence of HCV is much higher and standards of infection control are often inadequate. This risk factor has come to light at a time where accumulating evidence has demonstrated an adverse impact of HCV infection on survival outcomes in both the dialysis and renal transplant population.
**Case Report:** We present a series of three cases from our Satellite haemodialysis unit who acquired Hepatitis C during vacation haemodialysis to the Indian subcontinent in the 2012 calendar year. These patients constituted 37.5% of the total HCV positive patients in our dialysis unit (3/8). The new diagnoses were detected on antibody seroconversion on return from travel and confirmation was with HCV PCR and genotyping for the purpose of treatment. For 2/3 patients the seroconversion was only noted at the time of routine annual screening. For all 3 patients there were immediate adverse consequences relating to their candidacy for transplantation keeping them off the transplant waiting list.
**Conclusions:** These cases highlight the need to advise our incident haemodialysis patients, particularly those who are potential renal transplant recipients, against travel to resource poor countries. We also propose that units should reassess their surveillance and infection control procedures for patients returning after vacation dialysis.

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## A CASE REPORT OF CALCIPHYLAXIS: SEQUENTIAL CALCIPHYLAXIS AND WARFARIN INDUCED SKIN NECROSIS

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**Introduction:** Calciphylaxis(CPX) a potentially life-threatening condition seen in chronic kidney disease and some other conditions. The cause of CPX is multifactorial, but its precise mechanisms are unclear. Some patients who are at risk of developing CPX may require warfarin therapy for thromboembolic disease.
**Case report:** A 61 year old female with near ESRD secondary to diabetic nephropathy presented with a 4 weeks of nodulo-papular rash to the arms, trunk and face and a 2 weeks of bilateral painful ulceration in calves. The pain associated with the ulcers was disproportionate to the lesions. Her comorbid conditions included type 2 diabetes mellitus, hypertension, obesity and hypercholesterolemia. On examination, there was typical CPX ulceration with surrounding erythema in both calves, and nodulo-papular rash to the arms, shoulder and face. Her creatinine, eGFR, corrected calcium, phosphate and parathyroid hormone were 663 micromol/L, 6 ml/min, 2.41 mmol/L, 2.77 mmol/L and 565 pg/ml respectively. Haemodialysis and phosphate binder were commenced. Doppler ultrasound revealed right below knee deep vein thrombosis, complicated by pulmonary embolism and new onset atrial flutter. The patient received heparin infusion initially and then was commenced on warfarin with a two day cross-over period. On the sixth day of warfarin therapy the patient developed bilateral skin necrosis and extension of the lower limb ulcers. Right leg ulcer biopsy showed microvascular thrombosis with probable early infarction. Warfarin was ceased and enoxaparin commenced with anti-Xa level monitoring. Unfortunately, our patient died of bilateral cerebral infarct whilst awaiting sodium thiosulphate supply for her ulcers.
**Conclusion:** Calciphylaxis and warfarin induced skin necrosis in practice may be difficult to distinguish. Warfarin use may precipitate or exacerbate calciphylaxis and ischaemic stroke by accelerating vascular calcification via inhibition of Matrix GIa protein and Gas-6.

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## 14 YEARS OF HAEMODIALYSIS WITH IMPOSSIBLE VASCULAR ACCESS: TRANSLUMBAR INFERIOR VENA CAVA CATHERISATION AS SALVAGE THERAPY

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**Background:** Vascular access in haemodialysis is often referred to as a patient's "lifeline". Central venous catheters (CVCs) for long-term dialysis are not the preferred mode of access because of their associated complications (including infections and stenoses), and increased morbidity and mortality. However, when all conventional access fails, CVCs have been used as salvage therapy. Traditional sites for catheter placement include the internal jugular and subclavian veins, and less frequently the femoral veins. We present a patient whose entire 14 year-long haemodialysis career has been enabled solely by CVCs, the most recent 7 years via a translumbar inferior vena cava (IVC) catheter.
**Case report:** VH is a 62 year female who commenced haemodialysis in1999 secondary to obstructive nephropathy from malacoplakia and a horseshoe kidney. Multiple attempts to create a permanent haemodialysis access never resulted in a functioning fistula or graft due to thromboses and infection. The patient also suffered from endometriosis, resulting in severe intra-peritoneal scarring which precluded her from peritoneal dialysis. An urgent renal transplantation from her son was unsuccessful due to failure of the renal vessel arterial anastamosis. No primary thrombophilic state has been identified but she has been managed with lifelong warfarin until recurrent GI bleeding precluded this. VH has dialysed via a CVC from the very beginning, and after exhausting all central and peripheral options, a translumbar IVC catheter was placed in 2006 and replaced on regular occasion. Complications include occlusion of both the IVC and SVC with extensive collateral formation and also hepatosplenomegaly.
**Conclusions:** This case demonstrates the feasibility of long-term survival on haemodialysis with central venous access alone.

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## RENAL ALLOGRAFT AND BLADDER MALAKOPLAKIA IN A RENAL TRANSPLANT RECIPIENT: A CLINICAL DILEMMA

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**Background:** Malakoplakia is an unusual granulomatous inflammatory disorder associated with diminished bactericidal action of leucocytes, often in the context of host immunosuppression.
**Case Report:** We present the case of a 56 year old female cadaveric transplant recipient (surgical date 2010). She was highly sensitised with 96% PRA, moderate DSA (DR8, DR11) and 6/6 mismatch. Borderline vascular rejection was treated with steroids, intravenous immunoglobulin and plasma exchange in the first post-transplant month, with improvement in allograft function to baseline. Maintenance triple immunosuppression included tacrolimus, mycophenolate and steroids. Recurrent urinary tract infections followed from March 2011, with development of a large perinephric collection aspirated in July 2011. This cultured Escherichia coli, treated with intravenous therapy followed by prolonged course of quinolones. Subsequent infections demonstrated progressive resistance to oral therapy. Following this, ultrasound imaging detected a large mass in the graft, and a biopsy diagnosis of renal malakoplakia was made. She was treated with protracted courses of intravenous antibiotics along with mycophenolate discontinuation and dose reduction of tacrolimus and prednisolone. Multiple cystoscopies with biopsy confirmed bladder involvement, with growth of Klebsiella pneumoniae from cultured tissue.

Effective control of bacteriuria was achieved with weekly oral fosfomycin (3000 mg) and oral faropenam 150 mg TDS with stable allograft function and reduction in size of the renal lesion. Transplant nephrectomy or withdrawal of immunosuppression was not pursed due to limited options of renal replacement therapy.
**Conclusion:** Contrary to historical prejudice, renal parenchymal malakoplakia in the transplant recipient may not associate with poor outcomes, if diagnosed and treated aggressively and promptly.

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## CEREBRAL SINUS VENOUS THROMBOSIS TEMPORALLY ASSOCIATED WITH COMBINATION TACROLIMUS/SIROLIMUS IMMUNOSUPPRESSION

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**Background:** Cerebral sinus venous thrombosis (CSVT) is a rare, but potentially fatal cause of stroke. Established risk factors include inherited and acquired thrombophillic tendencies. The thrombophillic potential of sirolimus can be inferred from excess rates of stent thrombosis with sirolimus drug eluting stents (DES), vessel thrombosis in neoplastic lesions, and occurrence of de novo

thrombotic microangiopathies (TMAs) in patients co-administered sirolimus and calcineurin inhibitors (CNIs) or on sirolimus monotherapy.
**Case Report:** We present the case of a 67 year old male, who received a living unrelated renal transplant in August 2007 (3/6 HLA mismatch) for IgA nephropathy. Early post transplant course was complicated by biopsy proven BK virus associated nephropathy (2008) and multiple non-melanoma skin cancers. Tacrolimus was continued due to borderline rejection after its withdrawal in 2009. Myfortic was replaced with azathioprine in Feb 2012 for diarrhoea. Azathioprine was changed to sirolimus in January 2013 due to recurrent skin cancers and cytopathic changes of BK virus on urine analysis.

The patient presented with a generalised seizure followed by right hemiparesis secondary to imaging confirmed transverse sinus thrombosis in February 2013, with no prior history of thrombosis. He was treated with levetiracetam and anticoagulation, and sirolimus was replaced by azathioprine. Allograft function did not deteriorate, nor did he demonstrate any significant proteinuria or post-transplant erythrocytosis. The patient achieved a good functional outcome without residual neurological deficits.
**Conclusion:** Sirolimus induced thrombophilia should be considered in transplant patients presenting with CSVT, and use of this agent should be cautioned in patients with pre-existing thrombophillic tendencies.

CONFLICTS OF INTEREST

**A PRAGMATIC TRIAL OF A POLYPILL-BASED STRATEGY TO IMPROVE ADHERENCE TO INDICATED PREVENTIVE TREATMENTS AMONG PEOPLE AT HIGH CARDIOVASCULAR DISEASE RISK**
A Cass, A Patel, A Rodgers
The polypill formulations used in this study have been developed and provided free of charge by Dr Reddy's Laboratories, Hyderabad, India.
**A RANDOMISED, CONTROLLED TRIAL OF EXIT SITE APPLICATION OF MEDIHONEY FOR THE PREVENTION OF CATHETER-ASSOCIATED INFECTIONS IN PD PATIENTS – HONEYPOT STUDY**
D Johnson, S Badve, E Pascoe, E Beller, A Cass, C Clark, J de Zoysa, S McTaggart, N Isbel, A Morrish
DJ is a consultant for Baxter Healthcare Pty Ltd and has previously received research funds from this company. He has also received speakers' honoraria and research grants from Fresenius Medical Care. He has previously been a consultant to Gambro Pty Ltd and was the recipient of a Gambro Research Grant which partly funded the HONEYPOT trial. NI, CC, and DJ received a Baxter Healthcare Renal Discoveries Extramural Program Grant which partly funded the HONEYPOT trial. DJ is an International Society of Peritoneal Dialysis Councillor and is a current recipient of a Queensland Government Health Research Fellowship.
**ACUTE KIDNEY INJURY, ANALGESIC NEPHROPATHY AND TOXIN-MEDIATED KIDNEY INJURY IN AN AUSTRALIAN CHRONIC KIDNEY DISEASE (CKD) COHORT**
A Mallett, A Salisbury, Z Wang, HG Healy, WE Hoy
AM as supported by a RBWH Foundation scholarship and Queensland Health. CKD.QLD is supported by Amgen, NHMRC Australia (Australian Fellowship: Hoy), the Colonial Foundation of Australia, Queensland Health (in kind) and Roche.
**ALPORT SYNDROME AND THIN BASEMENT MEMBRANE NEPHROPATHY IN THE QUEENSLAND CHRONIC KIDNEY DISEASE (CKD) REGISTRY**
A Mallett, A Salisbury, Z Wang, HG Healy, WE Hoy
AM as supported by a RBWH Foundation scholarship and Queensland Health. CKD.QLD is supported by Amgen, NHMRC Australia (Australian Fellowship: Hoy), the Colonial Foundation of Australia, Queensland Health (in kind) and Roche.
**ANALYSIS OF THE COST-EFFECTIVENESS OF SWITCHING FROM SEVELAMER HYDROCHLORIDE TO LANTHANUM CARBONATE MONOTHERAPY: APPLICATIONS FOR AUSTRALIAN COSTS**
R Agnew, R Wilson, M Keith, J Brian Copely
RA is an employee of Shire Australia and stockholder of Shire Development LLC.
**APOPTOSIS SIGNAL-REGULATING KINASE 1 (ASK1) PROMOTES RENAL FIBROSIS AND APOPTOSIS IN THE OBSTRUCTED KIDNEY**
F Y Ma, D Breckenridge, D Nikolic-Paterson
DB is an employee of Gilead Science. Gilead provided financial support for this study. DN-P is a consultant for Gilead.
**AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE IN AN AUSTRALIAN CHRONIC KIDNEY DISEASE (CKD) POPULATION**
A Mallett, A Salisbury, Z Wang, HG Healy, A Salisbury, WE Hoy
AM is supported by a RBWH Foundation scholarship and Queensland Health. CKD.QLD is supported by Amgen, NHMRC Australia (Australian Fellowship: Hoy), the Colonial Foundation of Australia, Queensland Health (in kind) and Roche.
**BLOCKING THE NADPH OXIDASE NOX4 ACTIVITY PROVIDES RENOPROTECTION IN LONG TERM DIABETIC NEPHROPATHY**
J Jha, SP Gray, K Wingler, C Szyndralewiez, F Heitz, ME Cooper, H HHW Schmidt, KA Jandeleit-Dahm
CS and FH are paid employees and own shares of GenKyoTex SA, Geneva, Switzerland. All remaining authors report no conflicts.
**BLOCKADE OF SPLEEN TYROSINE KINASE (SYK) INHIBITS ANTIBODY-MEDIATED REJECTION IN RAT RENAL ALLOGRAFTS**
S Ramessur, F Ma, G Tesch, N Woodman, Y Han, K Blease, W Mulley, J Kanellis, D Nikolic-Paterson
KB and D N-P are employees of Celgene
**CALCIPROTEIN-ASSOCIATED FETUIN-A CONCENTRATION IS ASSOCIATED WITH ALL-CAUSE MORTALITY IN PATIENTS WITH PRE-DIALYSIS CKD**
E Smith, L Tomlinson, M Ford, E Bodenham, L McMahon, Ci Rajkumar, S Holt
ES, LM and SH have received research funding from Amgen and Baxter. ES has received honoraria from Shire. SH has received honoraria from Amgen, Baxter, Gilead and Shire.
**CHRONIC KIDNEY DISEASE (CKD) IS NOT RENAL REPLACEMENT THERAPY (RRT): THE CKD.QLD REGISTRY DATASET**
H Healy, A Salisbury, Z Wang, A Mallett, S Huynh, A Salsbury, T Mohandas, P Sanghi, D Heffernan, R Fassett, W Hoy
CKD.QLD is supported by Amgen, NHMRC Australia (Australian Fellowship: Hoy), the Colonial Foundation of Australia, Queensland Health (in kind) and Roche.
**CHRONIC KIDNEY DISEASE (CKD) PATIENT OUTCOMES: A LONGITUDINAL REPORT FROM THE CKD.QLD REGISTRY**
A Salisbury, A Mallett, Z Wang, H G Healy, S Huynh, S Smith, D Heffernan, W E Hoy
CKD.QLD is supported by Amgen, NHMRC Australia (Australian Fellowship: Hoy), the Colonial Foundation of Australia, Queensland Health (in kind) and Roche.
**CKD PATIENT PROFILES FROM A REGIONAL QUEENSLAND HEALTH RENAL CLINIC AND OUTCOMES AFTER ONE YEAR. CKD.QLD REGISTRY**
R Fassett, A Salisbury, C Banney, R Cherian, ASalisbury, Z Wang, W Hoy
RF is supported by Queensland Health, and via CKD.QLD, by Amgen, NHMRC Australia (Australian Fellowship: Hoy), the Colonial Foundation of Australia, Queensland Health and Roche.
**CNI-TO-EVEROLIMUS CONVERSION IN RENAL TRANSPLANT RECIPIENTS WITH LOW IMMUNOLOGICAL RISK: IMPROVED OR MAINTAINED GFR AFTER 2.5 YEARS**
H Gock, M Mathew
HG has received honoraria from Novartis in 2012 and 2013 for presentations at sponsored meetings.
**END-STAGE KIDNEY DISEASE – SUPPORTING THE TREATMENT OPTION DECISION MAKING PROCESS**
D Fortnum, T Smolonogov, L Kairaitis
Decision aid meetings were funded by Baxter with an unrestricted educational grant