

ISN Trial-List

June 2018



Once a month, the ISN-ACT (Advancing Clinical Trials) team collects and publishes a list of important nephrology trials from the latest medical literature. Each trial is reviewed in context and their risk of bias in seven key areas assessed.

Key to risk of bias assessment

- | | | |
|----|------------------------------------|-----------------------------|
| R | Random sequence generation | High risk |
| A | Allocation concealment | Uncertain risk / not stated |
| BP | Blinding of participants/personnel | Low risk |
| BO | Blinding of outcome assessment | |
| CD | Complete outcome data | |
| CR | Complete outcome reporting | |
| B | No other sources of bias | |

ISN Academy: [Chronic Kidney Disease](#), [Nutrition and Hydration](#)

Mediterranean diet may reduce uraemic metabolites in CKD

Nutritional therapy reduces protein carbamylation through urea lowering in chronic kidney disease

[Di Iorio, et al. Nephrol Dial Transplant. 2018;33\(5\):804-813](#)

Dietary approaches to reducing serum levels of uraemic toxins are gaining interest. Protein carbamylation is a detrimental chemical modification of serum proteins resulting from high levels of urea. Carbamylation of the amino acid lysine results in formation of homocitrulline – a marker carbamylation associated with adverse cardiovascular outcomes. Di Iorio, et al. randomised 60 participants with CKD stage 3b-4, in a cross-over design, to alternating 6 month periods of a low protein, vegetable rich ‘Mediterranean’ diet (MD) or a very low protein diet (VLPD) (with 3 months control period at the beginning of each phase). Compared with the control period, both diets resulted in lower levels of urea and homocitrulline, with significantly greater reductions in the VLPD group compared with those on MD (urea reduction: 20% versus 67%; [P<0.001]; homocitrulline reduction: 28% versus 41% [P<0.001]). While this study does not provide evidence for improvement in clinical outcomes or quality of life, it does suggest that the urea-lowering effects of low or very low protein diets do result in reductions in uraemic metabolites. The clinical implications of dietary therapies for chronic kidney disease may warrant further research.



ISN Academy: [Chronic Kidney Disease](#), [General Nephrology](#)

New trial could dampen enthusiasm for increased water intake in CKD

Effect of Coaching to Increase Water Intake on Kidney Function Decline in Adults With Chronic Kidney Disease: The CKD WIT Randomized Clinical Trial

[Clark, et al. JAMA. 2018;319\(18\):1870-1879](#)

If asked to name something ‘good for the kidneys’, most patients would probably say ‘drinking more water’. However, the evidence for this advice is limited to animal and observational studies and it is not known whether high fluid intake might preserve renal function in those with CKD. To answer this question, Clark, et al. randomised 661 participants with stage 3 CKD and albuminuria to regular coaching to target a fluid intake 1-1.5L higher than their baseline amount and provided with urine colour charts to encourage dilute urine. At the end of 12 months, compared to the control group, those in the water intake group increased their urine output by an average of 0.6L per day (95%CI 0.5-0.7; P<0.001), had a lower serum co-peptin level (-2.2pmol/l [95%CI -3.9 - -0.5; P =0.01) and higher urinary creatinine clearance (3.6ml/min [95%CI 0.8-6.4]; P=0.01). Despite this, there was no significant difference in change in eGFR (-0.3ml/min/1.73m² [95%CI -1.8-1.2]; P=0.74]). Accounting for the patients in the control group who also had an increase in urine volume in a per-protocol analysis produced a similar result. While disappointing, it may be that a greater separation in urine volume or a longer period of follow up is required for the benefits of increased fluid intake to become apparent. Further work is expected in this field and it may be premature to put aside the water bottles just yet.

