











The ISN-ACT (Advancing Clinical Trials) team presents this monthly round up of randomized trials in nephrology. Trials are selected not just for impact, but also to showcase the diversity of research produced by the global nephrology community. Each trial is reviewed in context and has a risk of bias assessment. We hope to drive improvement in trial quality and promote greater engagement in trial activity.

### Key to risk of bias assessment

-  Random sequence generation
-  Allocation concealment
-  Blinding of participants/personnel
-  Blinding of outcome assessment
-  Complete outcome data
-  Complete outcome reporting
-  No other sources of bias

High risk   
 Uncertain risk / not stated   
 Low risk 

Do you agree with our trial of the month? Tell us what you think!

@ISNeducation



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**ISN-ACT Clinical Trials Toolkit**  
[www.theisn.org/isn-act-toolkit](http://www.theisn.org/isn-act-toolkit)

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 Contact us at [research@theisn.org](mailto:research@theisn.org)

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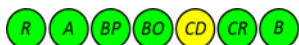
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ISN Academy: [Chronic Kidney Disease](#)

### Allopurinol does not slow the progression of chronic kidney disease

Effects of allopurinol on the progression of chronic kidney disease

[Badve et al. N Engl J Med 2020;382:2504-2513](#)

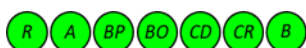


<p><b>About the study</b> 369 people with stage 3 or 4 chronic kidney disease, no history of gout, and declining renal function or albuminuria were randomised to receive allopurinol or placebo over 104 weeks.</p>	<p><b>Results</b> There was no difference in the change in eGFR (-3.33ml/min/1.73m<sup>2</sup>/year [95%CI -4.11 to -2.55] and -3.23ml/min/1.73m<sup>2</sup>/year [95% CI -3.98 to -2.47] for allopurinol and placebo groups respectively). There was no difference in adverse events.</p>
<p><b>Comment</b> This well conducted long-term RCT showed no benefit of allopurinol in patients without gout and CKD, to CKD progression, proteinuria or blood pressure. While there was incomplete enrolment and 30% discontinuation of the study drug, post hoc futility analyses identified a low probability of finding a significant effect of allopurinol. The trial does not support a causal role of urate in CKD progression.</p>	

ISN Academy: [Chronic Kidney Disease](#)

### Allopurinol does not slow the progression of kidney disease in patients with type 1 diabetes

[Doria A et al. N Engl J Med. 2020;382\(26\):2493-2503](#)



<p><b>About the study</b> 530 patients with type 1 diabetes, diabetic kidney disease (eGFR 40-99.9ml/min/1.73m<sup>2</sup> and albuminuria, or a</p>	<p><b>Results</b> After 3-year intervention and additional 2-month washout period, between-group difference of iothexol-based GFR was 0.001 ml/min/1.73m<sup>2</sup> (95% CI -1.9 to 1.9, P=0.99). Iothexol-based and</p>
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decline in eGFR $\geq$ 3ml/min/1.73m <sup>2</sup> in the previous 3-5 years), and serum urate $\geq$ 4.5mg/dl were randomised to allopurinol vs. placebo for 3 years.	serum creatinine-estimated GFR slope did not differ between two groups. Urinary albumin excretion rate after washout was 40% (95% CI 0 to 80) higher with allopurinol than with placebo.
<b>Comment</b> It was believed that urate-lowering agent would be a promising therapy for preservation of GFR, in light of the positive association between hyperuricemia and albuminuria in type 1 diabetic patients from observational studies. However, this trial, and the preceding CKD-FIX study, make it clear that urate reduction does not affect progression of CKD.	

ISN Academy: [Chronic Kidney Disease](#)

### Topical 6% gabapentin may be useful for uraemic pruritus

A randomized controlled study of 6% gabapentin topical formulation for chronic kidney disease-associated pruritus

[Monette et al. Int J Dermatol. 2020;59\(8\):955-961](#)



<b>About the study:</b> Double-blind study in 30 patients on maintenance haemodialysis with a baseline visual analog scale pruritus score $\geq$ 5, randomised to topical 6% gabapentin or placebo. The primary outcome was the mean change in pruritus scores from baseline after 1 and 2 weeks of once daily application.	<b>Results:</b> Treatment with topical 6% gabapentin resulted in significantly decreased mean pruritus scores at 1 week (mean score 2.7; p <0.001) and 2 weeks (1.3, p<0.001), compared to baseline (5.9). The mean change in pruritus scores from baseline to week 2 was significantly higher in the gabapentin group compared to control (-4.6 vs -2.6, p<0.01). There were no reported treatment-related adverse events in the two groups.
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**Comment:** Oral gabapentin is commonly used in the management of neuropathic pain and uraemic pruritus, but is associated with higher risk of toxicity in patients with chronic kidney disease. This study suggests the potential role of topical gabapentin in treating uraemic pruritus with fewer adverse events. Further studies with a larger sample size and longer treatment duration should be considered.

ISN Academy: [Acute Kidney Injury](#)

### No benefit to early Renal-Replacement Therapy in AKI

Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury

[Bagshaw et al. N Engl J Med. 2020;383\(3\):240-251](#)



<b>About the study</b> 3019 participants with acute kidney injury across 168 hospitals, in 15 countries, were randomised to an accelerated strategy (n = 1512) versus a standard strategy (n = 1507) for initiation of renal-replacement therapy.	<b>Results</b> There was no difference in the primary outcome of death at 90 days (RR 1.00; 95% CI 0.93 to 1.09) or in the secondary composite outcome (death, dependence on RRT, major adverse kidney events, death in ICU, or length of hospitalisation) between the two groups. There was an increased risk of dialysis-dependence (RR 1.74, 95% CI 1.24-2.43) and adverse events (RR 1.40; 95% CI 1.21 to 1.62; p<0.001) in the accelerated-strategy group when compared to the standard-start group.
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**Comment** Despite previous observational studies suggesting a benefit from early initiation of renal replacement therapy in acute kidney injury, this study marks the third randomised control trial which has not found any mortality benefit from an accelerated-start strategy. Additionally, it highlights that an early start is associated with more people remaining on dialysis, and more adverse outcomes as a consequence of an early start to therapy.

ISN Academy: [Peritoneal Dialysis](#)

### Low-sodium solution in hypertensive peritoneal dialysis patients

Single-dwell treatment with a low-sodium solution in hypertensive peritoneal dialysis patients

[Davies et al. Perit Dial Int. 2020 May 19;896860820924136](#)



<p><b>About the study</b></p> <p>123 hypertensive PD patients were randomised to change one of their daytime PD fluid exchanges to either a low-Na PD solution (112 mmol/L Na and 2% glucose) or a standard-Na solution (133 mmol/L Na and 1.5% glucose) for 8 weeks to assess efficacy of blood pressure (BP) lowering, continued for 4 months to assess the safety of the intervention.</p>	<p><b>Results</b></p> <p>At 8 weeks, 20 patients (34.5%) in the intervention group met the blood pressure efficacy outcome of either a 6mmHg reduction in systolic BP or a fall in BP requiring a medical intervention, compared to 16 patients (29.1%) in the control group. The difference between the groups for this outcome was not significant (rate difference 5.4%, 95% CI -11.6% to 21.9%). 9 patients in the low-Na group required medical intervention for hypotension compared to 0 patients in the control group. There was no overall difference seen on 24-hour ambulatory BP measurement (ABPM) or office readings. Hypotension and dizziness occurred in 17 (27%) and 7 (11.1%) patients in the intervention group, and in 11 (16.9%) and 3 patients (4.6%) in the control group. Hyponatraemia occurred in 4.8% of those with the low-Na dialysate compared with 1.5% in the control group.</p>
<p><b>Comment</b></p> <p>The superiority of low-Na solution over standard-Na solution was not established in the trial. Adding a daily exchange of a low sodium PD dialysate does appear to affect blood pressure, as demonstrated by the differences in acute hypotension, but the benefit may not be sustained, however, or may not be consistent across a 24-hour period. There were higher rates of several adverse effects with the intervention. The lack of blinding may introduce bias, and the small numbers and 28% loss to follow-up may have resulted in insufficient power to detect a meaningful treatment difference. At this point, such a hyponatremic dialysate cannot be recommended.</p>	

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