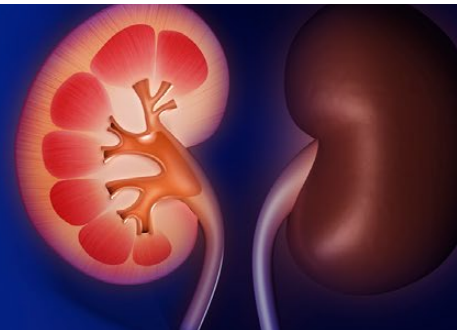
# Nephrology Practice Review™



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Issue 1 - 2018


## In this issue:



**Abbreviations used in this issue:**

**AVF** = arteriovenous fistulae; **AVG** = arteriovenous graft; **CKD-BMD** = Chronic Kidney Disease–Mineral and Bone Disorder; **KDIGO** = Kidney Disease: Improving Global Outcomes; **MBS** = Medicare Benefits Schedule; **NICE** = National Institute for Health and Care Excellence; **PBS** = Pharmaceutical Benefits Scheme; **PTH** = parathyroid hormone; **SWL** = shockwave lithotripsy; **TGA** = Therapeutic Goods Administration.

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# Welcome to the first issue of Nephrology Practice Review.

This new Review covers news and issues relevant to clinical practice in nephrology. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. And finally, on the back cover you will find a summary of upcoming local and international educational opportunities including workshops, webinars and conferences.

We hope you enjoy this new Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,


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## Clinical Practice

### New developments in KDIGO guidelines on chronic kidney disease–mineral and bone disorder

The Kidney Disease: Improving Global Outcomes (KDIGO) 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD–MBD) is a selective update of the prior CKD–MBD guideline published in 2009.

The update process resulted in the revision of 15 recommendations. This includes recommendations for diagnosis of CKD–MBD and treatment of CKD–MBD that emphasises decreasing phosphate levels, maintaining calcium levels, and addressing elevated parathyroid hormone (PTH) levels in adults with CKD G3a-G5 and those receiving dialysis. Key elements include basing treatment on trends in laboratory values rather than a single abnormal result and being cautious to avoid hypercalcaemia when treating secondary hyperparathyroidism.

#### Key recommendations

- Bone mineral density testing to assess fracture risk if results will impact treatment decisions in patients with CKD G3a–G5D. It is reasonable to perform a bone biopsy if knowledge of the type of renal osteodystrophy will impact treatment decisions.
- Basing CKD-MBD treatments for patients with CKD G3a–G5D on serial assessments of phosphate, calcium, and PTH levels, considered together.
- Lowering elevated phosphate levels toward the normal range in patients with CKD G3a–G5D.
- Avoiding hypercalcaemia in adult patients with CKD G3a–G5D.
- Using dialysate calcium concentration between 1.25 and 1.50 mmol/L in patients with CKD G5D.
- In patients with CKD G3a-G5D, decisions about phosphate-lowering treatment should be based on progressively or persistently elevated serum phosphate.
- In adult patients with CKD G3a-G5D receiving phosphate-lowering treatment, the guidelines suggest restricting the dose of calcium-based phosphate binders.

- In patients with CKD G3a-G5D, the guidelines suggest limiting dietary phosphate intake in the treatment of hyperphosphatemia alone or in combination with other treatments. It is reasonable to consider phosphate source (e.g., animal, vegetable, additives) in making dietary recommendations.
- Patients with CKD G3a–G5 not on dialysis who have levels of intact PTH progressively rising or persistently above the upper normal limit for the assay be evaluated for modifiable factors, including hyperphosphatemia, hypocalcaemia, high phosphate intake, and vitamin D deficiency.
- Calcitriol and vitamin D analogues should not be used routinely for adult patients with CKD G3a–G5. It is reasonable to reserve the use of calcitriol and vitamin D analogues for patients with CKD G4–G5 with severe and progressive hyperparathyroidism.
- Using calcimimetics, calcitriol, or vitamin D analogues, or a combination of calcimimetics with calcitriol or vitamin D analogues for patients with CKD G5D requiring PTH-lowering therapy.

In patients with CKD G3a-G5D with biochemical abnormalities of CKD–MBD and low bone mineral density and/or fragility fractures, the guidelines suggest that treatment choices consider the magnitude and reversibility of the biochemical abnormalities and the progression of CKD, with consideration of a bone biopsy.

Download the guideline here.

## Recommendations for managing life-threatening bleeds from AV fistulae/grafts

The British Renal Society Vascular Access Special Interest Group and Vascular Access Society of Britain & Ireland have published new recommendations and resources to prevent a life-threatening bleed from dialysis access.

Life-threatening bleeds are those that do not resolve with normal pressure applied to the bleeding site. These recommendations are not related to minor bleeds from cannulation sites or venous needle dislodgement. Life-threatening bleeds can develop from cannulation sites or other areas on the arteriovenous fistulae (AVF) or graft (AVG) and can quickly become life threatening because of the volume of blood lost.

### Prevention

Avoid area puncture cannulation of AVFs / AVGs. Patients, carers and haemodialysis staff should be aware of warning signs of an increased risk of a life-threatening bleed from an AVF / AVG such as: any non-healing wound over the AVF / AVG; prolonged bleeding post haemodialysis or bleeding in between dialysis sessions; aneurysms that are increasing in size, either at cannulation sites or elsewhere; shiny, thin skin over the AVF / AVG, particularly over aneurysms; signs of infection – redness, swelling, pain, discharge or pus; other skin integrity issues near the AVF / AVG. All haemodialysis staff, patients and carers should know to report these warning signs urgently. Ensure there are clear and rapid referral pathways for patients with any warning signs of a potential life-threatening bleed from their AVF / AVG.

### Management

Patients, carers, emergency and transport staff should be educated about the steps to take in the event of a life-threatening bleed from an AVF / AVG. Patients should dial emergency services immediately for any bleeding which soaks through a dressing despite direct pressure. The priority is to stop the bleeding, not preserve AVF or AVG function. Once emergency services help has been initiated, patients should continue to apply direct pressure to the bleed. If easily available, a small, rigid object (e.g. large bottle top, hollow side down) can be used to apply pressure over the bleeding site. Do not use a large absorbent item, such as a towel, as this spreads pressure reducing its effectiveness. Tourniquets are not recommended to manage life-threatening bleeds.

Download the guidelines here.



## Safety profile of biosimilar epoetin alfa in nephrology

Italian researchers have published a post-marketing observational study that compared the efficacy and safety of two European biosimilars and the reference epoetin alfa in patients undergoing dialysis at 26 hospitals in Italy. The study concluded that the originator and biosimilar products have comparable safety profiles.

The study included all adult patients with chronic kidney disease who had haemodialysis at least twice weekly and who were treated with the innovator epoetin (Eprex) or a biosimilar (Binocrit or Retacrit). Each patient was followed for 12 months after the first visit. The study's outcomes included problems related to the dialysis device (such as complications or infections), cardiovascular or cerebrovascular events, and infections (such as pneumonia or sepsis). A total of 423 patients used the originator and 444 used one of the biosimilars (440 of the biosimilar users received Binocrit). Patients who took a biosimilar were older than those who took the reference, and were more frequently affected by arrhythmia and diabetes at baseline. Those who used the originator more frequently had arteriovenous fistula and previous renal transplant, and were more frequently on transplant wait lists and had received dialysis for a longer time.

A total of 274 patients (31.6%) experienced at least one of the safety outcomes; 123 events (29.1%) occurred in patients using the reference product and 151 (34.0%) occurred among the biosimilar users. The most common events were infections (11.5%), cardiovascular and cerebrovascular conditions (10.6%), and problems related to the dialysis device (9.8%). A total of 127 deaths occurred in the study population (14.6%) during the 12-month follow-up period.

After adjusting for confounding factors (such as age, vascular access, heart failure, and other conditions), Cox-regression analysis showed there was no increase in risk of safety outcomes in biosimilar users. Hazard ratio estimates were 1.0 (95% CI, 0.7-1.3) for any of the study outcomes, 0.9 (95% CI, 0.6–1.5) for infections, 0.9 (95% CI, 0.6-1.5) for cardiovascular and cerebrovascular conditions, and 1.1 (95% CI, 0.7-1.8) for dialysis device-related problems.

This study confirms the comparable safety profiles of originator and biosimilar epoetin alfa drugs when used in patients with chronic kidney disease receiving dialysis. BioDrugs. 2018 Aug;32(4):367-375.

## Ciprofloxacin-associated acute kidney injury

The *Australian Prescriber* has detailed a case of ciprofloxacin-associated acute kidney injury. A 61-year-old man was prescribed ciprofloxacin for a urinary tract infection two weeks before presenting to a rural hospital, with advice to take ciprofloxacin 'on an empty stomach'. In response to this advice, the patient reduced his overall daily intake to small amounts of toast and 3–4 cans of beer. The patient developed twice-daily watery stools, but adhered to what he understood to be a fluid and food restriction and continued taking ciprofloxacin.

The patient presented to the rural hospital following a fall, complaining of abdominal swelling and diarrhoea. The patient was found to have acute kidney injury (serum creatinine > 500 µmol/L) and reduced urine output. The anuria persisted despite increased fluids so the patient was transferred to a specialist centre where his renal function slowly recovered.

The cause of acute kidney injury in this patient may have been due to dehydration, diarrhoea and ciprofloxacin-induced nephrotoxicity. Case reports of ciprofloxacin-induced acute kidney injury have suggested the cause may be interstitial nephritis, rhabdomyolysis or crystallisation within the renal tubules causing intra-renal obstruction.

A US study found that in men aged 40–85 years old current fluoroquinolone use had a 2.18-fold higher risk of acute kidney injury compared to patients taking amoxicillin and azithromycin.

Ciprofloxacin should be taken either one hour before or two hours after meals and patients should drink plenty of fluids. This is because the drug's absorption is decreased when it is taken with metallic compounds and due to reports of acute kidney injury from ciprofloxacin-induced crystalluria.

The patient remembered being told that ciprofloxacin should be taken on an empty stomach, but not about the timing of food intake or the importance of fluids. His decrease in food and water intake, together with diarrhoea, contributed to volume depletion and the onset of acute kidney injury.

In this case, clear communication may have reduced misunderstanding and confusion and improved adherence. An explanation of why ciprofloxacin is taken separately from food, but not water, may have helped.

Read the report here.

## Traditional Indian medicines can cause membranous nephropathy

An Indian working group has published five cases of nephrotic syndrome caused by membranous nephropathy with evidence of chronic mercury poisoning due to consumption of traditional Indian medicines such as Siddha and Ayurveda. The authors state that in the absence of strict quality controls for substances used in traditional medicine, patients should be warned that mercury poisoning can lead to membranous nephropathy as well other severe health issues affecting the brain, gut and kidneys.

Membranous nephropathy is a progressive kidney disease characterised by the buildup of immune complexes within the kidney. It often leads to nephrotic syndrome with proteinuria, hypoalbuminemia, and oedema, and may lead to kidney failure. Membranous nephropathy may have no known cause (primary membranous nephropathy), but can also be acquired via other diseases. Antibodies against phospholipase A2 receptor (PLA2R) are highly specific for the primary form of the disease, but do not occur in secondary forms.

This is the first report of its kind showing that traditional Indian medicines can cause membranous nephropathy, diagnosed by renal biopsy. All patients received such medicines and the index patients were seronegative for antibodies against PLA2R, showing they did not have the primary form of the disease.

Very few cases of mercury-induced membranous nephropathy have been reported in the literature and most known cases have been associated with traditional Chinese medicine, skin-lightening creams, inhalation containing mercury and hair dye containing mercury. Mercury is an ingredient in several traditional medicines such as Ayurveda, Unani, Siddha, Tibetan and Chinese medicines. Despite the widespread consumption of traditional Indian medicines, no renal toxicity has been reported so far. According to the authors, renal toxicity may be underreported because often patients do not mention they are taking traditional medicines in addition to prescription medicines. The authors say that mercury poisoning should be considered in patients with antiPLA2R antibody-negative membranous nephropathy, and that these patients should be asked if they have taken traditional Indian medicines.

Read the report here.

## NICE draft guideline for assessment and management of renal and ureteric stones

Patients with nephrolithiasis should have greater access to non-invasive procedures, according to the National Institute for Health and Care Excellence (NICE). Their draft guidance for managing renal and ureteric stones states a priority is to improve the detection, clearance and prevention of stones to reduce patients' pain and anxiety.

The guidance recommends greater use of shockwave lithotripsy (SWL), a procedure that directs high-energy shock waves that break down kidney stones into small crystals so they can be passed in urine. SWL is non-invasive and avoids the need to undergo surgery. Patients eligible for this treatment should be offered the procedure within 48-hours of a medical assessment.

More resources may be needed to increase the use of SWL, including extra mobile lithotripters, more fixed-site machines or better organised referral systems. However, one benefit would be that more patients could be seen as day cases, reducing theatre time and hospital stays.

Another recommendation is that patients should be given a CT scan within 24 hours of an initial medical assessment if they are experiencing severe abdominal pain, thought to be suspected renal colic. Current practise in the UK is to investigate renal colic using ultrasound or plain abdominal radiographs. However, NICE said that while a CT scan was more expensive, it lessened the likelihood of needing follow-up investigations. This recommendation had been made because renal function can decline quickly when stones are present.

Find out more here and here.





## Regulatory News

### Changes to Medicare-funded renal medicine items

The Government is making changes to Medicare-funded renal medicine items to address recommendations from the Medicare Benefits Schedule (MBS) Review Taskforce.

To improve access to renal dialysis in remote areas a new MBS item will be introduced from 1 November 2018 to provide funding for the delivery of dialysis by nurses, Aboriginal and Torres Strait Islander health practitioners and Aboriginal healthcare workers in primary care. There is also a change to the item descriptor for the removal of an indwelling Tenckhoff peritoneal catheter (item 13110) to bring into line with the item descriptor for the insertion of a Tenckhoff peritoneal catheter (item 13109). This will increase consistency across the MBS and clarify the service for providers. Item 13112 for the insertion of a temporary catheter for peritoneal dialysis will be removed; this will not affect patients as the procedure is no longer part of current clinical practice.

Find out more here.

### PBS listings

**Cabozantinib** (Cabometyx®), has been listed on the PBS for the treatment of patients with stage IV clear cell variant renal cell carcinoma who are not responding well to existing first-line treatments.

Read more here.

### TGA – new or extended registrations

**Nivolumab** (Opdivo®), in combination **ipilimumab** (Yervoy®), is now also indicated for the treatment of patients with intermediate/poor-risk, previously untreated advanced renal cell carcinoma. Nivolumab, as monotherapy, is now also indicated for the treatment of patients with locally advanced unresectable or metastatic urothelial carcinoma after prior platinum-containing therapy.

**Pembrolizumab** (Keytruda®) is now also indicated as monotherapy for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing therapy, or have received platinum-containing chemotherapy.

Read more here.

### FDA approves first oral treatment for Fabry disease

The US Food and Drug Administration (FDA) has approved **migalastat** (Galafold®), the first oral medication for the treatment of adults with Fabry disease. Migalastat is indicated for adults with Fabry disease who have a genetic mutation determined to be responsive to treatment with the drug based on laboratory data. Fabry disease is a rare and serious genetic disease that results from build-up of globotriaosylceramide (GL-3) in blood vessels, the kidneys, the heart, the nerves and other organs.

Read more here.

## News in Brief

### Higher amputation rate amongst Indigenous Australians

A North Queensland study has found that Indigenous Australians are more likely than non-Indigenous Australians to require lower limb amputations as a result of chronic diseases, such as diabetes. Between 2000 and 2015 the rates of major amputations in Indigenous and non-Indigenous patients with diabetes were 291.9 and 70.1 per 100,000 population respectively. Indigenous patients with diabetes were almost seventeen times more likely to undergo a major amputation compared to those Indigenous patients without diabetes.

Download the abstract here and read the media release here.

### New program for young Australians with kidney disease

Kidney Health Australia is establishing a new social and educational support program for young people aged 15 to 24 with advanced kidney disease who have received a kidney transplant. These patients face the transition from paediatric to adult healthcare around the age of 18 and must begin managing complex treatment and medication requirements associated with kidney transplantation or dialysis. The program includes an online forum, face-to-face activities to bring affected young people together, a new helpline support service, and new educational resources. Read more here.

### Donor family and transplant recipient correspondence SOP

The Australia Transplant Nurses' Association, in collaboration with Organ and Tissue Authority, the DonateLife Network, and the Australian Transplant Coordinators Association, have published a standard operating procedure (SOP) for donor family and transplant recipient correspondence. The SOP has been developed to allow consistency in communication by DonateLife Agencies and Transplant Coordinators, and details how communication between donor families and transplant recipients should be managed.

Access the SOP here.

### ANN UK – new association

The British Renal Society has announced the formation of a new organisation: The Association of Nephrology Nurses (ANN UK). ANN UK is a non-profit organisation that endeavours to provide support for nurses through education, research, evidence-based practice and by setting national standards for nurses working in renal care.

More details here.

## Conferences, Workshops, and CPD

Please click on the links below for upcoming local and international nephrology meetings, workshops and CPD.

ANZSN - Upcoming Conferences and Meetings

Renal Society of Australasia - Events

TheConferenceWebsite – Renal Medicine Conferences

Conferenceseries.com – Nephrology Conferences

Conference Management Software – Nephrology

## Research Review Publications

### Nephrology Research Review

**with Professor Vlado Perkovic**

https://tinyurl.com/y8tuowwg

### ERA-EDTA 2018 Conference Review

https://tinyurl.com/yap2u5u5



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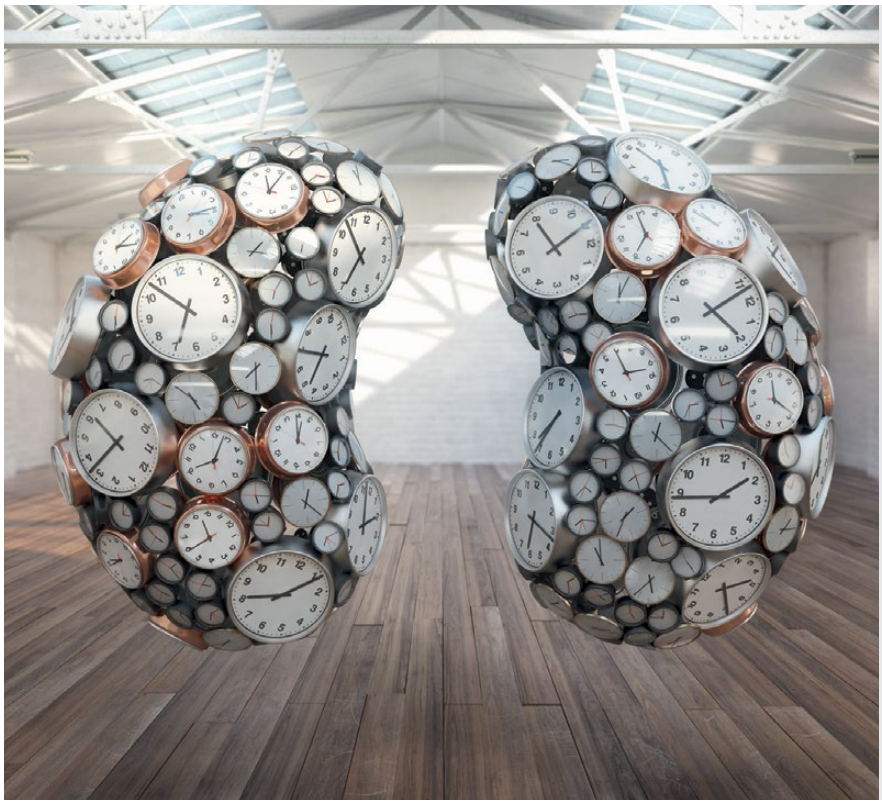



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