Chronic Kidney Disease (CKD)

Case Definition

Chronic Kidney Disease (CKD) is either of the following, persisting for at least three months, repeated on at least two occasions:

1. Markers of kidney damage (e.g. proteinuria, haematuria or structural abnormalities on renal imaging) and / or:
2. GFR < 60 mL/min/1.73m^2.

Both eGFR and ACR are required to determine the stage and risk category of CKD as albuminuria is one of the biggest known risk factors for progression to End Stage Kidney Disease (ESKD).

Table 1: KDIGO staging of CKD

	ACR (MG/MMOL)		
eGFR	Normal <3.0	Micro-albuminuria 3.0-30	Macro-albuminuria >30
Stage 1 eGFR ≥90	**NO CKD** *(unless other markers of kidney damage detected)*	**MODERATE RISK CKD**	**HIGH RISK CKD**
Stage 2 eGFR 60-89			
Stage 3 eGFR 45-59	**MODERATE RISK CKD**	**HIGH RISK CKD**	**VERY HIGH RISK CKD**
Stage 3b eGFR 30-44	**HIGH RISK CKD**	**VERY HIGH RISK CKD**	
Stage 4 eGFR 15-29	**VERY HIGH RISK CKD**		
Stage 5 eGFR <15 or dialysis			

Screening

Up to 60% of adults in some Kimberley communities have markers of Chronic Kidney Disease (CKD). Increased creatinine occurs late in CKD and implies significant kidney damage.

Screen annually for patients with any of the following risk factors:

- Aboriginal or Torres Strait Islander person aged >= 15 yrs of age;
- Smoking;
- Obesity (BMI > 30kg/m^2);
- Family history of CKD;
- History of cardiovascular disease (e.g. stroke/CVA, heart attack/MI, peripheral vascular disease / PVD);
- Hypertension;
- Diabetes;
- Previous acute kidney injury (AKI);
- Use of nephrotoxic drugs (e.g. NSAIDS).

Patients assessed as not having risk factors should be regularly screened for the development of risk factors over time.

Screening for CKD requires:

- Blood pressure (BP) measurement;
- Blood test for urea, electrolytes and creatinine (UEC);
- Urine test for albumin:creatinine ratio (ACR):
  - ⇢ Dipstick prior to sending and document result;
  - ⇢ If leucocytes, blood and/or nitrates consider possible UTI / STI (see Table 2).

Table 2: Other causes of abnormal kidney screening tests and appropriate follow-up

ABNORMALITY	MANAGEMENT
Proteinuria with abnormal urine dipstick due to suspected urinary tract infection (UTI) or urethritis from sexually transmissible infection (STI).	Send urine for MCS and consider UTI treatment in discussion with GP. Follow appropriate STI guidelines for counselling, testing and treating possible STI (See RESOURCES). Repeat ACR with proof of cure of infection in three months or as clinically indicated.
Proteinuria / raised creatinine after vigorous exercise or heavy protein consumption.	Repeat screening when patient has not exercised in the previous 24 hours or fasting sample.
Isolated proteinuria in person without other risk factors for CKD aged less than 30 years (i.e. possible orthostatic proteinuria).	Recheck ACR on morning first void urine collected immediately on first standing
Increase in creatinine after commencement of ACE-inhibitor / ARB.	Creatinine rise to ≤25% acceptable – see management section. Monitor weekly until stable.

Considerations in interpreting screening results:

- Creatinine levels vary with muscle mass: eGFR on laboratory reports may under or overestimate renal function in people with extremes of body size, muscular diseases or amputations – calculators can be used to factors in body weight *(see Resources)*;
- Abnormalities persisting less than 3 months indicate acute kidney injury (AKI) which increases the risk of subsequent CKD;
- Episodes of AKI should be investigated for a cause and documented in the medical record;
- Newly abnormal eGFR should be repeated within a week to identify rapidly declining renal function.

Assessment

All patients with confirmed CKD require:

- BP, BMI, check for peripheral oedema;
- Renal tract ultrasound;
- FBP, CRP, iron studies, uric acid, LFT, calcium/ magnesium / phosphate, lipids, PTH (if calcium or phosphate are abnormal);
- Hepatitis B, hepatitis C, syphilis and HIV serology if not done within the last 12 months, with appropriate counselling as per Kimberley protocols;
- HbA1c:
  - ⇢ If diabetic and not done within the last 3 months;
  - ⇢ Otherwise, If not done within the last 12 months.
- If ACR > 30 and not previously done: Serum protein electrophoresis, urine protein electrophoresis, complements, ANA, ENA;
- If haematuria and not previously done: ANCA, anti-GBM;
- If haematuria and additional risk factors for malignancy (see Box 1): as above plus cystoscopy and / or urology referral, cytology x 3 (consider that transport delays may affect results).

HAEMATURIA is:

- **Microscopic:** Hb on dipstick OR RBC detected on urine MCS, on two separate occasions at least a week apart, not associated with infection or menstruation, OR:
- **Macroscopic:** Red, brown or dark discoloration of urine observed by patient or staff. Confirm where possible by dipstick or urine MCS.

Macroscopic haematuria requires urgent urological follow-up to exclude malignancy, regardless of whether a urine MCS has bacterial growth, as malignancy predisposes to UTI.

BOX 1: RISK FACTORS FOR UROLOGICAL MALIGNANCY

- Age >35 years;
- Smoking history (risk correlates with the extent of exposure);
- History of macroscopic haematuria;
- History of other less common risk factors: chronic cystitis or irritative voiding symptoms; pelvic irradiation, exposure to cyclophosphamide; aristolochic acid; occupationally to chemicals or dyes (benzenes or aromatic amines), such as printers, painters, and chemical plant workers; chronic indwelling foreign body; previous analgesic abuse.

Microscopic haematuria is also a sign of glomerulonephritis. Document its presence on any referrals and investigate appropriately (see baseline assessment). Confirm haematuria when the patient is not menstruating if possible.

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Management

Prevent Progression

People with moderate or severe CKD (ACR › 30 mg/mmol or eGFR ‹45) are at the highest cardiovascular risk category, regardless of their score on absolute cardiovascular risk tools.

- Address all identified cardiovascular risk factors. Smoking cessation helps prevent progression to CKD. See SMOKING CESSATION and, HYPERLIPIDAEMIA protocols;
- Ensure immunisations up to date, HBV immune;
- Optimise control for patients with diabetes (see DIABETES protocol);
- Consider nephrotoxicity when prescribing and advise re: OTC medications such as NSAIDS;
- Appropriate early referral and management improves outcomes.

Manage proteinuria or hypertension with ACE/ARB:

For patients with proteinuria, ACE-Inhibitors (ACE-I) / Angiotension-II-Receptor Blockers (ARB) reduce overall mortality and progression to ESKD.

For all patients with proteinuria (ACR › 30 mg/mmol, or ›3 mg/mmol and DM, IHD or HTN):

- Prescribe an ACE-I **OR** ARB for all patients without contraindications, titrate to maximum dose tolerated without symptomatic hypotension. Monitor BP, UEC fortnightly during up-titration. Seek advice if:
  - Potassium ≥6.0 mmol/L – consider drug interactions e.g. spironolactone;
  - Creatinine rise › 20% - consider bilateral renal artery stenosis.
- **Do not combine ACE and ARB due to risk of acute kidney injury.**
- Once ACE-I or ARB maximised, use other agents as needed to control BP to goal of 130/80 unless other target specified by nephrologist / physician (see HYPERTENSION protocol).

For other patients with CKD, use ACE or ARB as the preferred first option for managing hypertension.

Prevent Acute Kidney Injury (AKI):

In acutely unwell patients with CKD:

- Check weight, BP, peripheral oedema, monitor UEC regularly;
- Consider temporarily ceasing ACE-I / ARB / diuretics in especially with hypotension / hypovolaemia (if unsure contact physician / nephrologist for advice);

Recheck UEC once acute illness has resolved to determine new baseline and ensure ceased medications are restarted.

TABLE 3: ACE-I and Angiotension-II-Receptor Blockers on the KSDL

	KSDL	SUPPLEMENTARY LIST
ACE Inhibitors	Quinapril: (5mg, 10mg, 20mg tab) Ramipril: (2.5mg, 5mg, 10mg tab)	Enalapril: (5mg, 10mg, 20mg tab) Quinapril / HCT: (20mg / 12.5mg tab)
ARB	Irbesartan: (75mg, 150mg, 300mg tab)	Irbesartan / HCT: (300mg/12.5mg tab)

Promote a Healthy Lifestyle

Achieving a healthy body weight and maintaining a healthy diet helps reduce progression to ESKD. See HEALTHY LIFESTYLE protocol. Additionally, If eGFR is ‹ 30 a dietician referral is recommended to manage weight, salt and phosphate intake and fluid.

Treat complications of late CKD (STAGES 4 – 5)

[Note: Contact renal GP as needed for support with routine pathology].

PTH, phosphate and calcium: Usual pattern is progressively high phosphate and low calcium (Ca++) with compensatory secondary hyperparathyroidism. May require combination of calcitriol (titrated against PTH / serum Ca++) and phosphate binders (titrated against phosphate levels). General guidelines:

- **eGFR › 30 with normal Ca++ / phosphate and vitamin D levels ‹ 50 nmol/L:** Supplement with cholecalciferol;
- **Acceptable PTH (‹ 5 times upper limit of normal (ULN)) and normal adj. Ca++ (› 2.1 mmol/L) but high phosphate (› 1.6 mmol/L):** Dietary advice +/- phosphate binders (Caltrate / Cal-sup with meals, up to two TDS as needed). Review adherence and correct use. Can add second agent – discuss with renal GP;
- **Elevated PTH (›5 times ULN) and / or low adj. Ca++ (‹ 2.1 mmol/L):** Treat high phosphate first, unless symptomatic hypocalcaemia. Start calcitriol 0.25mcg daily, increase fortnightly up to 1mcg daily. Seek advice if adjusted Ca++ rise to ›2.4 mmol/L;
- Monitor serum Ca++ and phosphate fortnightly and PTH monthly whilst changing therapy.

Acidosis: If acidosis is persisting (serum bicarbonate ‹ 15 mmol/L) after correction of hypocalcaemia:

- Start sodium bicarbonate tablets (SodiBic 840mg) 1 BD, up to 2 tablets TDS to a target of 22 mmol/L. Monitor for exacerbation of HTN and heart failure (increased salt load).

Anaemia and iron deficiency: Anaemia occurs in late CKD due to both iron deficiency and reduced RBC production, and can be exacerbated by fluid overload. Exclude other causes of anaemia in early CKD, with absolute iron deficiency or in refractory anaemia. General guidelines:

- **TF saturation ‹ 20% and Hb ‹ 110:** Treat for iron deficiency, check B12 / folate. Oral iron is poorly absorbed in CKD. Refer for iron infusion if no improvement after one month or as first line in CKD 5;
- TF saturation › 20% and Hb ‹ 100: May require erythropoietin stimulating agent (ESA) (e.g. Mircera). Discuss with renal GP / nephrologist.

Symptoms of ESKD: Should be assessed for regularly:

- Ask about nausea, vomiting, anorexia, lethargy, SOB, leg swelling, restless leg symptoms and chest pain.
- Monitor for infections. Patients with CKD are immunosuppressed and vulnerable to infections. Severe infections may occur without prominent fever and dose adjustment of antibiotics may be needed. Contact renal GP, physician or nephrologist for advice as needed.

Initiate advanced care planning processes and refer to the pre-dialysis co-ordinator for support in counselling and renal pathway planning.

TABLE 4: Commonly prescribed drugs which require caution in CKD

DRUG	RISKS IN CKD / ACTION REQUIRED
Metformin	May increase risk of lactic acidosis, particularly when unwell. Withhold if unwell. Dose adjust: eGFR 30-45: Max 1g/day; eGFR ‹30: Cease, or discuss with nephrologist / on-call physician.
Diuretics	Volume depletion, contributing to AKI. Electrolyte disturbance. Withhold if unwell or dehydrated. Monitor UEC regularly.
Colchicine Digoxin Gentamicin Vancomycin	Accumulation, drug toxicity. Adjust dose according to eGFR (see Therapeutic guidelines) + / - monitor levels.
ACE-I, ARB	May increase risk of AKI during acute illness. Hyperkalaemia. Monitor K+. Withhold if unwell. Cease if eGFR ‹ 15 and not required for HTN.
NSAIDS	Increase risk of AKI. Avoid.
Gliclazide	Accumulation, Increased hypoglycaemia risk, Dose adjust: eGFR 45-60: Reduce dose, eGFR ‹ 45: Cease.
Insulin	Accumulation, Increased risk of hypoglycaemia Dose adjust based on BSL monitoring.
Sitagliptin	Accumulation, drug toxicity. Dose adjust: eGFR 30-50: 50mg daily, eGFR ‹ 30: 25mg daily.

Women of Child Bearing Age

- Encourage use of reliable contraception, pre-pregnancy counselling and early antenatal care;
- Stop ACE-I / ARBs as soon as pregnancy planned or suspected. If pregnant, discuss with obstetrician / physician promptly and consider early referral to high risk pregnancy clinic;
- If breastfeeding, use enalapril as preferred ACE/ARB.

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Refer/ Discuss

TO NEPHROLOGIST:

- Persistent haematuria plus proteinuria;
- Proteinuria › 1g/day (ACR › 70, PCR › 100);
- Patients with proteinuria not tolerating ACE/ARB;
- Patients with very high risk CKD;
- CKD and difficult to manage HTN on three agents;
- Persisting anaemia despite iron therapy;

Urgent discussion required:

- Abnormal eGFR / ACR and suspected connective tissue disease (e.g. facial rash, polyarthritis, lethargy, abnormal investigations);
- Heavy proteinuria (ACR›220) and possible nephrotic syndrome (oedema, hypoalbuminaemia, hyperlipidaemia);
- Rapidly declining renal function (eGFR decline by 15min/min within 12 months).

TO OBSTETRICIAN if planning pregnancy or early pregnancy.

TO ALLIED HEALTH as needed, and particularly:

- Dietician: CKD and high BMI or any BMI and eGFR ‹ 30;
- Diabetes educator: CKD with insulin therapy and / or sub-optimal diabetic control.

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TO PRE-DIALYSIS CO-ORDINATOR if eGFR‹30.

TO RENAL GP: CKD patients of any stage. Referral of patients high / very high risk assists with care coordination.

CALL YOUR LOCAL RENAL HEALTH CENTRE FOR SUPPORT REGARDING THE CARE OF PATIENTS WITH CKD IN THE KIMBERLEY REGION.

Routine schedule of care for stable CKD patients by risk category*

CKD STAGES	CKD RISK CATEGORY			
	MODERATE RISK:	**HIGH RISK:**	**VERY HIGH RISK (NOT YET ESKD)**	**ESKD**
CKD STAGE 1 AND 2	eGFR › 60 + Microalbuminuria	eGFR › 60 + Macroalbuminuria		
CKD STAGE 3	eGFR 45-60 + Normal ACR	eGFR 45 – 60 +Microalbuminuria	eGFR 45 – 60 + Macroalbuminuria	
CKD STAGE 3B		eGFR 30 – 45 + Normal ACR	eGFR 30 – 45 + Microalbuminuria	
CKD STAGE 4			eGFR 15 – 30	
CKD STAGE 5				eGFR ‹ 15
PATHOLOGY:				
UEC, ACR, LFT, FBP, CRP, Ca++, Mg++, phosphate	12 monthly.	3 – 6 monthly.	1 – 3 monthly.	Monthly.
HbA1c, lipids	12 monthly, more often for other conditions as needed (e.g. diabetes).			
PTH				Every three months.
Iron studies	As needed for the investigation and management of anaemia.		Monthly if Hb ‹ 100, otherwise 3 monthly.	Monthly.
CLINICAL REVIEW:				
BP, weight, assess smoking, diet, exercise	12 monthly.	3 – 6 monthly.	1 – 3 monthly.	Monthly.
Symptoms of ESKD			1 – 3 monthly.	Monthly.
Review by renal GP	At any stage, on referral from primary provider.			
Review by nephrologist	On referral from primary provider.		3 – 6 monthly.	Each opportunity.
Review by pre-dialysis coordinator				

**Does not apply to patients who are unstable or who have rapidly changing renal function.*

Resources

Chronic Kidney Disease (CKD) Management in GP, Kidney Health Australia: http://kidney.org.au/cms_uploads/docs/ckd-management-in-gp-handbook-3rd-edition.pdf

Caring for Australasians with Renal Impairment Guidelines, Kidney Health Australia: http://www.cari.org.au/

KRS Contact list: See https://kams.org.au/kamsc-services/kimberley-renal-services/

Creatinine clearance calculators: https://www.ebmconsult.com/app/medical-calculators/glomerular-filtration-rate-gfr-calculator

Other chronic disease and STI protocols for the Kimberley region: http://kams.org.au/resources/clinical-protocols-guidelines/