Early detection & management of Chronic Kidney Disease

Dr Balaji Hiremagalur (Nephrologist GCUH)

This workshop was conceived and developed by Kidney Health Australia’s Kidney Check Australia Taskforce with particular thanks to A/Prof Robyn Langham & A/Prof Timothy Mathew
Reviewed by A/Prof Craig Nelson & Dr Sheena Wilmot
V0715
What is CKD?

Chronic kidney disease is defined as:

Glomerular Filtration Rate (GFR) < 60 mL/min/1.73m² for ≥3 months with or without evidence of kidney damage.

OR

Evidence of kidney damage (with or without decreased GFR) for ≥3 months:

- albuminuria
- haematuria after exclusion of urological causes
- pathological abnormalities
- anatomical abnormalities.

CKD is a major public health problem

- 1 in 10 Australian adults has CKD\(^1\)
- Less than 10% of people with CKD are aware they have the condition\(^2\)
- You can lose up to 90% of your kidney function before experiencing any symptoms\(^2\)
- Major independent risk factor for cardiovascular disease\(^2\)
- Common, harmful & treatable

---
\(^2\)Chronic Kidney Disease (CKD) Management in General Practice, 3\(^{rd}\) edition. Kidney Health Australia: Melbourne, 2015
Kidney disease in Australia

Australians aged ≥ 18 years

5+ MILLION AT RISK

- Stage 1 - 2 CKD
- Stage 3 CKD
- Stage 4 - 5 CKD
- Dialysis or transplant

Less than 10% of these people are aware they have CKD

Hypertension / Diabetes

Australian Health Survey 2013; ABS population estimates June 2013; ANZDATA 2012 Report

CKD staging is according to the CKD-EPI equation
Age and ESKD
Relationship between age and treatment for ESKD

Number of dialysed and undialysed cases, by age group at kidney failure onset, 2003-2007.

- No dialysis or transplant
- Dialysis or transplant

The future

Growth in incidence rate of new treated ESKD and projections to 2020 (AIHW, 2011)

Note: The alternative projection results (lower dotted line) are derived by holding the average of incidence rates for years 2007–2009 for patients 70 years and over constant in projection years.

Source: Registered cases during 1996–2009 from ANZDATA.
Costs of treating current and new ESKD cases to 2020

- The cost of treating ESKD from 2009 to 2020 is estimated to be around $12 billion to the Australian government
- Kidney disease contributes approximately 15% of all hospitalisations in Australia

Cass et al, 2010, economic impact ESKD in Australia, KHA
What difference does a CKD diagnosis make if I already manage my patients well?
CKD diagnosis, management & patient outcomes

The diagnosis of CKD brings with it the need to identify risk reduction measures both for kidney and cardiovascular diseases.

- Treatment targets and therapy choices may differ with a CKD diagnosis.
- Early detection and management of CKD complications for better prognosis.
- Ensure dosages of all prescribed drugs are appropriate for kidney function and avoid nephrotoxic medications.
- Timely referral of CKD patients to a nephrologist.
Case study - Rita

Background
• 63 years old
• Accountant

Rita is a new patient to your practice
Case study - Rita

Past medical history

• Overweight (BMI 31kg/m^2)
• Mild intermittent asthma
• Chronic low back pain
• Mild hypertension

Family history

• Maternal grandmother died of a heart attack in her 60’s
• Mother has type 2 diabetes
• Father has angina and hypertension
Case study - Rita

<table>
<thead>
<tr>
<th></th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker:</td>
<td>20-25 cigarettes per day (25 pack-year history)</td>
</tr>
<tr>
<td>Alcohol:</td>
<td>1-2 glasses of wine 3-4 nights per week</td>
</tr>
<tr>
<td>Allergies:</td>
<td>Nil known</td>
</tr>
<tr>
<td>Medications:</td>
<td>Salbutamol 100mcg/dose as needed</td>
</tr>
</tbody>
</table>
Case study - Question

Q1: Does Rita have an increased risk of CKD?
Risk factors for kidney disease

Eight major risk factors for CKD

✖ Diabetes
✓ Hypertension
✖ Established cardiovascular disease
✖ Family history of kidney failure (ESKD)
✓ Obesity, BMI >30kg/m²
✓ Smoker
✖ Aboriginal or Torres Strait Islander origin
✖ History of acute kidney injury

Rita has 3 of the 8 risk factors for CKD
Case study - Question

Q2: What would you do next?
Case study - Rita

You determine that Rita should have a kidney health check every year

Kidney Health Check

Blood Test
- eGFR calculated from serum creatinine

Urine Test
- Albumin / Creatinine Ratio (ACR) check for albuminuria

BP Check
- Blood pressure maintain consistently below BP goal

Case study - Rita

<table>
<thead>
<tr>
<th>Rita’s Kidney Health Check results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
</tr>
<tr>
<td>118 µmol/L</td>
</tr>
<tr>
<td>eGFR</td>
</tr>
<tr>
<td>55 mL/min/1.73m²</td>
</tr>
<tr>
<td>Urine ACR</td>
</tr>
<tr>
<td>5.7 mg/mmol</td>
</tr>
<tr>
<td>Blood pressure</td>
</tr>
<tr>
<td>155 / 95 mmHg</td>
</tr>
</tbody>
</table>
## Case study - Rita

### GFR Stage

<table>
<thead>
<tr>
<th>GFR Stage</th>
<th>GFR (mL/min/1.73m²)</th>
<th>Normal (urine ACR mg/mmol)</th>
<th>Microalbuminuria (urine ACR mg/mmol)</th>
<th>Macroalbuminuria (urine ACR mg/mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥90</td>
<td>Not CKD unless haematuria, structural or pathological abnormalities present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>45-59</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>30-44</td>
<td></td>
<td>RITA’S RESULTS PUT HER HERE</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>&lt;15 or on dialysis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Q3: Do Rita’s Kidney Health Check results mean she has Chronic Kidney Disease?

Not yet

To diagnose Rita with CKD, her urine ACR & eGFR needs to be repeated and results must be consistent over 3 months or more.
Case study - Rita

• If the first ACR is a random spot, then repeat tests should ideally be first morning void specimens

• CKD is present if at least 2 out of 3 ACR tests (including the initial test) in the next three months are positive

• When initial eGFR is <60 mL/min/1.73m² consider clinical situations where eGFR results may be unreliable/misleading

• To confirm CKD, the repeat eGFR in 3 months time should also be below 60mL/min/1.73m²
Repeating the urine ACR

Factors other than CKD known to increase urine albumin excretion...

- Urinary Tract Infection
- High dietary protein intake
- Congestive cardiac failure
- Acute febrile illness
- Heavy exercise within 24 hours
- Menstruation or vaginal discharge
- Drugs (especially NSAIDs)
Interpreting eGFR results
Clinical situations where eGFR results may be misleading

- acute changes in kidney function
- people on dialysis
- exceptional dietary intake (e.g. vegetarian diet, high protein diet, recent consumption of cooked meat, creatinine supplements)
- extremes of body size
- diseases of skeletal muscle, paraplegia or amputees (*may overestimate eGFR*) or high muscle mass (*may underestimate eGFR*)
- children under the age of 18 years
- severe liver disease present
- eGFR values above 90 mL/min/1.73m²
- drugs interacting with creatinine excretion (e.g. trimethoprim)

Source Australasian Creatinine Consensus Working Group (2012)
**Case study - Question**

*Rita comes back to see you three months later and you repeat her urine ACR, eGFR and blood pressure...*

<table>
<thead>
<tr>
<th>Test</th>
<th>1\textsuperscript{st} visit</th>
<th>This visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR</td>
<td>55 mL/min/1.73m\textsuperscript{2}</td>
<td>52 mL/min/1.73m\textsuperscript{2}</td>
</tr>
<tr>
<td>Urine ACR</td>
<td>5.7 mg/mmol</td>
<td>8.4 mg/mmol</td>
</tr>
<tr>
<td>BP</td>
<td>155/95 mmHg</td>
<td>160/95 mmHg</td>
</tr>
</tbody>
</table>

**Q4: What is your next step?**
### Case study - Rita

You can now diagnose Rita as having CKD stage 3a with microalbuminuria.

<table>
<thead>
<tr>
<th>GFR Stage</th>
<th>GFR (mL/min/1.73m²)</th>
<th>Albuminuria Stage</th>
<th>Normal (urine ACR mg/mmol)</th>
<th>Microalbuminuria (urine ACR mg/mmol)</th>
<th>Macroalbuminuria (urine ACR mg/mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
<td>≥90</td>
<td></td>
<td>Not CKD unless haematuria, structural or pathological abnormalities present</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2</strong></td>
<td>60-89</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3a</strong></td>
<td>45-59</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3b</strong></td>
<td>30-44</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>4</strong></td>
<td>15-29</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5</strong></td>
<td>&lt;15 or on dialysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Staging CKD

To stage CKD combine:

1. Kidney Function Stage \((eGFR)\) (stage 1-5)
2. Kidney Damage \((Albuminuria)\)
3. Clinical Diagnosis \((underlying\ cause\ of\ CKD)\)
**Orange Clinical Action Plan**

eGFR 30-59 mL/min/1.73m² with microalbuminuria OR

eGFR 30-44 mL/min/1.73m² with normoalbuminuria

**Goals of management**

- Investigations to determine underlying cause
- Reduce progression of kidney disease
- Assessment of Absolute Cardiovascular Risk
- Avoidance of nephrotoxic medications or volume depletion
- Early detection and management of complications
- Adjustment of medication doses to levels appropriate for kidney function
- Appropriate referral to a nephrologist when indicated
eGFR and drug dosing

Recommendation:

• Dose reduction of some drugs is recommended for patients with reduced kidney function

• Both eGFR (mL/min/1.73m²) and estimated CrCl (mL/min) provide an estimate of relative renal drug clearance

• If using eGFR for drug dosing, body size should be considered, in addition to referring to the approved Product Information

• For drugs with a narrow therapeutic index, therapeutic drug monitoring or a valid marker of drug effect should be used to individualise dosing
### Orange Clinical Action Plan

<table>
<thead>
<tr>
<th>Laboratory assessment</th>
<th>Frequency of monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR 30-59 mL/min/1.73m² with microalbuminuria OR eGFR 30-44 mL/min/1.73m² with normoalbuminuria</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 to 6 months</td>
</tr>
</tbody>
</table>

**Clinical assessment**
- Blood pressure
- Weight

**Laboratory assessment**
- Urine ACR
- eGFR
- Biochemical profile including urea, creatinine, electrolytes
- HbA1c (for people with diabetes)
- Fasting lipids
- Full blood count
- Calcium and phosphate
- Parathyroid hormone (6-12 monthly if eGFR <45 mL/min/1.73m²)

See CKD management handbook for other assessments for the Orange clinical action plan.
Orange Clinical Action Plan

eGFR 30-59 mL/min/1.73m² with microalbuminuria OR
eGFR 30-44 mL/min/1.73m² with normoalbuminuria

It is important to consider...

• Absolute Cardiovascular Risk Assessment
  (www.cvdcheck.org.au)
• Lifestyle modification
• Blood pressure reduction
• Lipid lowering treatments
• Glycaemic control
Case study - Question

Q5: As Rita’s general practitioner, how do you reduce her risks of cardiovascular disease?
Cardiovascular risk reduction in CKD

• CKD is one of the most potent known risk factors for cardiovascular disease

• It is essential to clinically determine the presence of CKD before using the Australian absolute cardiovascular risk tool (www.cvdcheck.org.au) to accurately calculate cardiovascular risk

• Individuals with CKD have a 2-3 fold greater risk of cardiac death than individuals without CKD

• People with CKD are at least 20 times more likely to die from cardiovascular disease than survive to need dialysis or transplant
CVD risk

Australian Absolute Cardiovascular Disease Risk Calculator

www.cvdcheck.org.au

If Rita stops smoking her CV risk is halved to 10%

• The tool is approved by NH&MRC

• If Rita had moderate to severe CKD defined as eGFR <45 mL/min/1.73m² or macroalbuminuria (ACR >25mg/mmol men; >35mg/mmol women) she would be at the highest CVD risk and in this case the tool should not be applied
Blood pressure reduction

- CKD can cause and aggravate hypertension and hypertension can contribute to the progression of CKD
- Reducing blood pressure to below target levels is one of the most important goals of CKD management
- ACE inhibitor or ARB is recommended first line therapy
- Combined therapy of ACE & ARB is not recommended
- Maximal tolerated doses of ACE inhibitor or ARB is recommended
- Hypertension may be difficult to control and multiple (3-4) medications are frequently required

Rita has stage 3a CKD with microalbuminuria so her blood pressure needs to be maintained consistently below 130/80 mmHg
Blood pressure reduction

Clinical tips

• ACE inhibitors and ARBs can cause a reversible reduction in GFR when treatment initiated.

• If the reduction is less than 25% and stabilises within two months of starting therapy...

  the ACE inhibitor or ARB should be continued

• If the reduction in GFR exceeds 25% below the baseline value...

  the ACE inhibitor or ARB should be ceased and consideration given to referral to a Nephrologist
Lifestyle approaches are essential in reducing the overall cardiovascular risk - the key elements are:

‘SNAP’ (smoking, nutrition, alcohol, physical activity)

- Stop smoking
- A low calorie diet to reduce BMI
- A low salt diet
- A reduction in alcohol intake
- Physical activity
- Weight reduction

Lifestyle modification presents an opportunity to engage the patient in self-management
## Lifestyle effects on BP

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>BMI 18-24.9 kg/m²</td>
<td>4.4mmHg (for 5.1kg weight lost)</td>
</tr>
<tr>
<td>Dietary sodium restriction</td>
<td>Reduce dietary sodium intake to no more than 2.4g sodium (or 6g salt)</td>
<td>4-7mmHg (for reduction by 6g in daily salt intake)</td>
</tr>
<tr>
<td>DASH diet</td>
<td>Fruit, vegies, low saturated and total fat</td>
<td>5.5-11.4mmHg (5.5 for normotensives 11.4 for hypertensives)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Aerobic activity for 30-60mins/day, 3-5 days/week</td>
<td>5mmHg</td>
</tr>
<tr>
<td>Moderate alcohol consumption only</td>
<td>No more than 2 drinks per day (men) or 1 drink per day (women)</td>
<td>3mmHg (for 67% reduction from baseline of 3-6 drinks per day)</td>
</tr>
</tbody>
</table>
Self management

Key self management principles include:

• Engaging the patient in decision making and management of their illness

• Allowing the patient to set appropriate and achievable goals

• Using evidence based, planned care

• Improving patient self management support (e.g. enlisting other health professionals and supports, and better linkages with community resources such as seniors centres, self help groups, skills and support programs)

• A team approach to managing care
Lipid lowering & glycaemic control

Lipids

• Rita’s lipids should be assessed
• Lipid-lowering treatment should be considered for CVD risk reduction

Glycaemic control

• For people with diabetes, blood glucose control significantly reduces the risk of developing CKD, and in those with CKD reduces the rate of progression
Case study - Question

Q6: Should Rita be referred to a nephrologist?
Referral is recommended if:

- eGFR <30mL/min/1.73m² (stage 4 or 5 CKD of any cause)
- Persistent significant albuminuria (urine ACR ≥ 30mg/mmol)
- A sustained decrease in eGFR of 25% or more with in 12 months OR a sustained decrease in eGFR of 15mL/min/1.73m² per year
- CKD with hypertension that is hard to get to target despite at least three anti-hypertensive agents

Clinical tip
Anyone with rapidly declining eGFR and/or signs of acute nephritis (oliguria, haematuria, acute hypertension and oedema) should be regarded as a medical emergency and referred with out delay

Recommended tests prior to referral
Current blood chemistry and haematology
Urine ACR and urine microscopy for red cell morphology and casts
Current and historical blood pressure
Urinary tract ultrasound
Referral is NOT usually necessary if:

- Stable eGFR ≥30 mL/min/1.73m²
- Urine ACR < 30mg/mmol (with no haematuria)
- Controlled blood pressure

The decision to refer or not must always be individualised, and particularly in younger individuals the indications for referral may be less stringent.

Useful tips

✓ Pay attention to CVD risk reduction
✓ Consider discussing management issues with a nephrologist in cases where uncertainty regarding referral exists.
✗ Don’t refer to a nephrologist if targets of therapy are achieved
✗ Spiral CT angiogram for hypertension is not recommended without specialty advice
‘Orange’ clinical action plan for Rita
(found in ‘CKD management in General Practice’ 3rd ed)

- Cardiovascular risk reduction
- Blood pressure should be consistently below 130/80 mmHg – use of ACE or ARB as appropriate
- Lifestyle modification
- Avoid nephrotoxic medications
- Adjust dose of other medications to levels appropriate for her kidney function
- No need for Nephrology referral at this stage
- Continue to monitor 3-6 monthly

Orange Clinical Action Plan

eGFR 30-59 mL/min/1.73m² with microalbuminuria OR
eGFR 30-44 mL/min/1.73m² with normoalbuminuria
## Treatment targets for people with CKD

### Clinical factors

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Target</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood pressure</strong></td>
<td>( \leq 140/90 \text{ mmHg} ) or ( \leq 130/80 \text{ mmHg} ) if albuminuria is present (ACR &gt; 2.5 mg/mmol males; &gt;3.5 mg/mmol females)</td>
<td>Lifestyle modification ACE inhibitor or ARB</td>
</tr>
<tr>
<td><strong>Albuminuria</strong></td>
<td>( \geq 50% ) reduction of baseline value</td>
<td>ACE inhibitor or ARB</td>
</tr>
<tr>
<td><strong>Cholesterol</strong></td>
<td>Total &lt; 4.0 mmol/L ( \text{ LDL} &lt; 2.0 \text{ mmol/L} )</td>
<td>Dietary advice statins</td>
</tr>
<tr>
<td><strong>Blood glucose</strong> (for people with diabetes)</td>
<td>( \text{HbA1c} &lt; 7.0% / 53 \text{ mmol/mol} )</td>
<td>Lifestyle modification Oral hypoglycaemic Insulin</td>
</tr>
</tbody>
</table>

*Clinical guidelines now advise all people with CKD, over the age of 50 years to be prescribed a statin regardless of cholesterol level.*
Summary

• CKD is common, harmful and treatable
• Early detection is beneficial
• Systematically identify patients at high risk of CKD (the 8 risk factors)
• Perform a Kidney Health Check (urine ACR, eGFR, blood pressure) for at risk patients
• Maintain blood pressure consistently below the relevant threshold
• Refer to the CKD staging table and clinical action plans in ‘CKD Management in General Practice’ booklet
• Most CKD patients can be managed in general practice
‘do not miss forest for trees’

Box 1: Problems with applying population based evidence to individuals

- Randomised trials often exclude patients with comorbidities
- Guidelines describe the evidence for single conditions; real patients often have several comorbidities
- Individual patients may have different values and preferences from their clinician and the people creating the evidence
- Guidelines may not cover aspects of care important to patients
- Guidelines may make recommendations, quite often based solely on expert opinion, when individual patients would make a different choice; this perpetuates the power imbalance between patients and clinicians
- Risks, benefits, and downsides of management options may be viewed differently at the level of the population than from the perspective of an individual
- Shared decision making is not clearly enabled in contemporary practice

BMJ 2016;353:i2452 doi: 10.1136/bmj.i2452 (Published 16 May 2016)