QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MANAGEMENT OF

CHRONIC KIDNEY DISEASE

(SECOND EDITION)
1. Targeted screening in high risk groups is necessary to detect chronic kidney disease (CKD) & early intervention is important to delay its progression. CKD management requires shared decision making & close collaboration between different levels of healthcare.

2. Screening for CKD includes assessment for proteinuria, haematuria & renal function [using estimated glomerular filtration rate (eGFR) based on CKD-epidemiology (CKD-EPI) creatinine equation].

3. Detection of CKD should be followed by staging using eGFR, risk stratification with albuminuria & determination of underlying cause. This is based on Kidney Disease Improving Global Outcomes (KDIGO) classification.

4. Target blood pressure (BP) & glycaemic control should be individualised according to co-morbidities & age.

5. Angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) should be used as first-line antihypertensive agent in diabetic kidney disease (DKD) with albuminuria & non-DKD with proteinuria ≥0.5 g/day.

6. Dual renin-angiotensin system blockade should only be used in carefully selected non-DKD patients with proteinuria under close supervision by nephrologists.

7. All cardiovascular (CV) risk factors should be addressed in patients with CKD to reduce CV events. Aspirin should only be used for secondary prevention of CV disease (CVD).

8. All female patients of reproductive age with CKD should receive pre-pregnancy care.

9. The optimal time of nephrology referral depends on the indications while the urgency is based on the trend of eGFR.

10. Screening for CKD-related complications is recommended at CKD stage 3 onwards.

This Quick Reference provides key messages & a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Chronic Kidney in Adults (Second Edition).

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

- Ministry of Health Malaysia: www.moh.gov.my
- Academy of Medicine Malaysia: www.acadmed.org.my
- Malaysian Society of Nephrology: www.msn.org.my

**CLINICAL PRACTICE GUIDELINES SECRETARIAT**

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SCREENING

- Patients with diabetes mellitus and/or hypertension should be screened at least yearly for CKD.
- Screening for CKD may be considered for patients with:
  - age >65 years old
  - obesity
  - CVD
  - metabolic syndrome
  - drugs e.g. nephrotoxic drugs, long-term use of proton-pump inhibitors or analgesics
  - family history of CKD or hereditary kidney disease
  - gout
  - multisystem diseases with potential kidney involvement e.g. systemic lupus erythematosus
  - structural renal tract disease, renal calculi or prostatic hypertrophy
  - opportunistic (incidental) detection of haematuria or proteinuria

KDIGO CLASSIFICATION

<table>
<thead>
<tr>
<th>Persistent albuminuria categories</th>
<th>Description and range</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>Normal to mildly increased</td>
</tr>
<tr>
<td>A2</td>
<td>Moderately increased</td>
</tr>
<tr>
<td>A3</td>
<td>Severely increased</td>
</tr>
<tr>
<td>&lt;30 mg/g &lt;3 mg/mmol</td>
<td>30 - 300 mg/g 3 - 30 mg/mmol</td>
</tr>
<tr>
<td>&gt;300 mg/g &gt;30 mg/mmol</td>
<td>G1 Normal or high ≥90</td>
</tr>
<tr>
<td>G2 Mildly decreased</td>
<td>60 - 89</td>
</tr>
<tr>
<td>G3a Mildly to moderately decreased</td>
<td>45 - 59</td>
</tr>
<tr>
<td>G3b Moderately to severely decreased</td>
<td>30 - 44</td>
</tr>
<tr>
<td>G4 severely decreased</td>
<td>15 - 29</td>
</tr>
<tr>
<td>G5 Renal failure</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

Green - low risk, Yellow - moderate risk, Orange - high risk, Red & Deep Red - very high risk

STRATEGIES IN DELAYING CKD PROGRESSION

1. Established strategies:
   a. Optimal BP control
   b. Optimal blood glucose control
   c. Proteinuria reduction
   d. Renin-angiotensin system blockers
2. Strategies requiring more evidence:
   a. Lifestyle modifications (smoking cessation, weight reduction, low salt diet & dietary protein restriction)
   b. Sodium-glucose co-transporter-2 (SGLT2) inhibitors
   c. Uric acid reduction
TARGETS OF CKD TREATMENT

- BP target for CKD should be aimed at:

<table>
<thead>
<tr>
<th>Cause</th>
<th>Proteinuria</th>
<th>≥1 g/day</th>
<th>&lt;1 g/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>DKD</td>
<td>≤130/80 mmHg</td>
<td>(SBP 120 to 130 mmHg)</td>
<td>≤130/80 mmHg (SBP 120 to 130 mmHg)</td>
</tr>
<tr>
<td>Non-DKD</td>
<td>≤130/80 mmHg</td>
<td>(SBP 120 to 130 mmHg)</td>
<td>≤140/90 mmHg* (SBP 120 to 140 mmHg)</td>
</tr>
</tbody>
</table>

SBP=systolic blood pressure
*BP targets should be individualised according to co-morbidities & age.

- The target HbA1c should be ≤7% in DKD but this should be individualised according to co-morbidities & age.

**PREGNANCY IN CKD**

- Pregnancy may be considered in women with mild renal impairment (serum creatinine <124 µmol/L), well controlled BP & without significant proteinuria (<1 g/day).
- Pregnancy should be avoided in women with either:
  - moderate to severe renal impairment
  - poorly controlled hypertension
  - heavy proteinuria
  - active systemic disease
- All pregnant women with CKD should be co-managed by a multidisciplinary team.

**REFERRAL**

- A patient with CKD with any of the following criteria should be referred to a nephrologist/physician:
  - persistent heavy proteinuria [urine protein ≥1 g/day or urine protein: creatinine ratio (uPCR) ≥100 mg/mmol*] despite optimal treatment
  - persistent isolated microscopic haematuria after excluding urogynaecological cause
  - persistent haematuria with proteinuria (urine protein ≥0.5 g/day or uPCR ≥50 mg/mmol*)
  - rapidly declining renal function [loss of eGFR >5 ml/min/1.73 m² in 1 year or >10 ml/min/1.73 m² within 5 years]
  - eGFR <30 ml/min/1.73 m² (eGFR categories G4 - G5)
  - resistant hypertension (failure to achieve target BP despite 3 antihypertensive agents including a diuretic)
  - suspected renal artery stenosis
  - suspected hereditary kidney disease
  - pregnant or when pregnancy is planned
  - persistent abnormalities of serum potassium
  - unexplained cause of CKD

*This is an estimation for practical purpose. The actual conversion of urine protein 1 g/day=uPCR 113 mg/mmol.
TARGETS OF CKD TREATMENT

QUICK REFERENCE FOR HEALTHCARE PROVIDERS MANAGEMENT OF CHRONIC KIDNEY DISEASE IN ADULTS (SECOND EDITION)

- **BP target for CKD** should be aimed at:
  - ≤130/80 mmHg (SBP 120 to 130 mmHg)
  - ≤130/80 mmHg (SBP 120 to 130 mmHg)
  - ≤140/90 mmHg* (SBP 120 to 140 mmHg)

  - **DKD**
  - **Non-DKD**

  - **Cause Proteinuria**
    - ≥1 g/day <1 g/day

  - SBP = systolic blood pressure

  - *BP targets should be individualised according to co-morbidities & age.*

  - Based on SPRINT (Systolic Blood Pressure Intervention Trial) study (median follow-up of 3.3 years), lowering SBP towards 120 mmHg can be considered in non-DKD patients with high CV risk, in whom BP lowering is well-tolerated.

  - *This is an estimation for practical purpose. The actual conversion of urine protein 1 g/day = uPCR 113 mg/mmol.*

- The target HbA1c should be ≤7% in DKD but this should be individualised according to co-morbidities & age.

- Pregnancy may be considered in women with mild renal impairment (serum creatinine <124 µmol/L), well controlled BP & without significant proteinuria (<1 g/day).

- Pregnancy should be avoided in women with either:
  - moderate to severe renal impairment
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  - heavy proteinuria
  - active systemic disease

- All pregnant women with CKD should be co-managed by a multidisciplinary team.

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**ALGORITHM 1. SCREENING & INVESTIGATIONS FOR CKD IN ADULTS WITH DIABETES**

**Urine dipstick for protein**
- a) Type 1: After 5 years history of diabetes or earlier in the presence of other CV risk factors.
- b) Type 2: At time of diagnosis

**NEGATIVE**

**POSITIVE on 2 occasions**
(Urine protein >0.3 mg/mol) (exclude other causes e.g. urinary tract infection (UTI), congestive cardiac failure (CCF), others)

**POSITIVE**

- Screen for microalbuminuria on early morning spot urine

**NEGATIVE**

- Retest twice in 3 - 6 months (exclude other causes e.g. UTI, CCF, others)

- Yearly test for microalbuminuria & renal function

**POSITIVE on 2 occasions**
(Urine protein >0.3 mg/mol) (exclude other causes e.g. urinary tract infection (UTI), congestive cardiac failure (CCF), others)

- Quantify proteinuria

- Overt nephropathy

- Check renal function
- Exclude other nephropathies
- Perform renal ultrasound scan if indicated (refer to Section 3.3 in CPG)

- • If 2 of 3 tests are positive, diagnosis of DKD is established
  - • Quantify microalbuminuria
  - • 3- to 6-monthly follow-up of microalbuminuria

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  - • Quantify microalbuminuria
  - • 3- to 6-monthly follow-up of microalbuminuria
ALGORITHM 2. SCREENING & INVESTIGATIONS FOR CKD IN ADULTS WITHOUT DIABETES

Presence of risk factors for CKD

Check urine using dipstick (refer to Section 3.1 in CPG)

Proteinuria on 2 out of 3 occasions

No

Yes

Yearly urine test & renal function test (refer to Section 3.2 in CPG)

• Quantify proteinuria
• Check renal function (refer to Section 3.2 in CPG)
• Perform renal ultrasound scan if indicated (refer to Section 3.3 in CPG)

QUICK REFERENCE FOR HEALTHCARE PROVIDERS MANAGEMENT OF CHRONIC KIDNEY DISEASE IN ADULTS (SECOND EDITION)

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• Screening for CKD may be considered for patients with:
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   obesity
   CVD
   metabolic syndrome
   drugs e.g. nephrotoxic drugs, long-term use of proton-pump inhibitors or analgesics
   family history of CKD or hereditary kidney disease
   gout
   multisystem diseases with potential kidney involvement e.g. systemic lupus erythematosus
   structural renal tract disease, renal calculi or prostatic hypertrophy
   opportunistic (incidental) detection of haematuria or proteinuria

SCREENING STRATEGIES IN DELAYING CKD PROGRESSION

1. Established strategies:
   a. Optimal BP control
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   c. Proteinuria reduction
   d. Renin-angiotensin system blockers

2. Strategies requiring more evidence:
   a. Lifestyle modifications (smoking cessation, weight reduction, low salt diet & dietary protein restriction)
   b. Sodium-glucose co-transporter-2 (SGLT2) inhibitors
   c. Uric acid reduction

DIAGNOSIS OF ABNORMAL PROTEIN OR ALBUMIN EXCRETION

<table>
<thead>
<tr>
<th>Class</th>
<th>Urine dipstick reading</th>
<th>Urine ACR in mg/mmol</th>
<th>Urine total protein excretion in g/24 hour</th>
<th>Urine ACR in mg/mmol</th>
<th>Urine albumin excretion in µg/min (mg/24 hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Negative</td>
<td>&lt;15</td>
<td>&lt;0.15</td>
<td>&lt;2.5 (male) &lt;3.5 (female)</td>
<td>&lt;20 (&lt;30)</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>Negative</td>
<td>&lt;15</td>
<td>&lt;0.15</td>
<td>≥2.5 to 30 (male) ≥3.5 to 30 (female)</td>
<td>20 - 200 (30 - 300)</td>
</tr>
<tr>
<td></td>
<td>Trace</td>
<td>15 - 44</td>
<td>0.15 - 0.44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>1+</td>
<td>45 - 149</td>
<td>0.45 - 1.49</td>
<td>&gt;30</td>
<td>&gt;200 (&gt;300)</td>
</tr>
<tr>
<td></td>
<td>2+</td>
<td>150 - 449</td>
<td>1.50 - 4.49</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3+</td>
<td>≥450</td>
<td>≥4.50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Presence of risk factors

Check urine using dipstick (refer to Section 3.1 in CPG)

Proteinuria on 2 out of 3 occasions

No

Yes

Yearly urine test & renal function test (refer to Section 3.2 in CPG)

• Quantify proteinuria
• Check renal function (refer to Section 3.2 in CPG)
• Perform renal ultrasound scan if indicated (refer to Section 3.3 in CPG)
ALGORITHM 3. EVALUATION OF HAEMATURIA IN CKD IN ADULTS

Presence of microscopic haematuria

- Treat infection
- Confirm resolution of microscopic haematuria with follow-up urinalysis after 6 weeks completion of therapy

Signs & symptoms of UTI

- Yes
- No

Other aetiologies*

- Yes
- No

Stop contributing factors

Re-test for microscopic haematuria

Presence of haematuria

- Yes
- No

Evidence of glomerular disease**

- Yes
- No

Refer to nephrologist

Refer to urologist

Discharge

*Vigorous exercise, trauma to urethra, menstruation, medications

**Proteinuria, red cell casts, dysmorphic red blood cells, elevated creatinine
Diagnosis of CKD

- Non-Diabetic Kidney Disease

  - Hypertension (BP >140/90 mmHg)
    - Yes ⇒ Proteinuria (≥1.0 g/day)
      - Yes ⇒ ACEi/ARB (preferred)
      - No ⇒ Non-dihydropyridine calcium channel blockers
    - No ⇒ Any antihypertensive to achieve target BP

- Diabetic Kidney Disease

  - Optimisation of glycaemic control
  - Strict BP control
  - ACEi/ARB

General measures in the management of CKD

- Encourage exercise, weight reduction & smoking cessation
- Manage CV risks including dyslipidaemia
- Monitor renal function according to individual patient’s characteristics (baseline renal function, risk factors for CKD progression & specific treatment given)

Restrict sodium intake to <2,400 mg/day (1 teaspoon of table salt)
Avoid excessive protein intake
Identify other end-organ damage of diabetes & hypertension

ALGORITHM 4. TREATMENT FOR CKD IN ADULTS