Introduction to the KidneyWise Clinical Toolkit

The KidneyWise Clinical Toolkit is intended to provide guidance on the identification, detection, and management of chronic kidney disease (CKD) in primary care. The Toolkit also helps inform which individuals are likely to benefit from a referral to nephrology.

The Ontario Renal Network, a division of Cancer Care Ontario and an agency of the provincial government, is responsible for overseeing and funding the delivery of chronic kidney disease services across Ontario. By establishing consistent standards and guidelines, based on the best available evidence, along with information systems that measure performance, the ORN supports a continuously improving kidney care system in Ontario.

By using the Toolkit, Primary Care Providers (PCPs) can identify people at high risk of developing CKD, order the appropriate tests to confirm diagnosis, and best manage the disease to help prevent further progression and reduce cardiovascular risk.

The KidneyWise Clinical Toolkit has three components:

- **A Clinical Algorithm** that can be used at the point of care.
- **An Evidence Summary** offering PCPs further details regarding the Clinical Algorithm content including references that were used in the development of the Toolkit and;
- **An Outpatient Nephrology Referral Form** outlining appropriate clinical scenarios that may require PCPs to request consultation with a nephrologist, as well as the appropriate investigations that should accompany the referral.

Disclaimer

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KidneyWise
Identification, Detection, and Management of CKD in Primary Care

**IDENTIFY & EVALUATE**

Identify and evaluate people in your practice with elevated risk of CKD with any one of the following:
- Hypertension (HTN)
- Diabetes mellitus (DM)
- Age 60-75 with cardiovascular disease (CVD)
- First Nations, Inuit, or Metis people(s) ≥ 18 years of age

**DETECT**

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KD detection should be done in the absence of acute intercurrent illness. Low estimated glomerular filtration rate (eGFR) in such scenarios may reflect acute kidney injury (AKI) and require more rapid evaluation.

If a previous abnormal eGFR and/or urine albumin to creatinine ratio (ACR) result is available within the previous year of identifying a person with risk factors for CKD, then repeat the 2 tests to confirm diagnosis (the two sets of tests must be at least 3 months apart). If eGFR < 60 repeat measurement in 3 months, or sooner if clinical concern dictates (>2 rapid decline from previous eGFR result or very low eGFR).

If urine ACR ≥ 3 repeat measurement 1 or 2 more times over the next 3 months (at least 2 out of 3 random urine ACRs must be elevated ≥ 3) in order to be considered abnormal.

Always consider reversible causes prior to re-measuring (e.g. recent treatments with non-steroidal anti-inflammatory drugs (NSAIDs), recent use of contrast dye for diagnostic imaging, benign prostatic hyperplasia (BPH)/urinary retention).

**CONFIRM CKD DIAGNOSIS AFTER 3 MONTHS**

Box A: eGFR < 30 and/or ACR > 60
- Person has CKD
  - Based on above parameters, consider seeking consultation from nephrology
  - Work-Up
    - Urine R/M, electrolytes
    - Plus: CBC, Calcium, Phosphate, Albumin.

Box B: eGFR 30–59 and/or ACR 3–60
- Person has CKD
  - Monitor in Primary Care (see MANAGE box below)
  - Check urine R/M, electrolytes
  - Follow eGFR & urine ACR every 6 months

Box C: eGFR ≥ 60 and ACR < 3
- Person does not have CKD
  - Re-measure annually for people with DM, less frequently otherwise, unless clinical circumstances dictate more frequent measuring

If any of the following occur, consider referral to nephrology:
- eGFR < 30 or ACR > 60, or
- Rapid deterioration in kidney function: eGFR < 45 and decline of > 5 mL/min within 6 months in absence of self-limited illness; eGFR must be repeated in 2-4 weeks to confirm persistent decline, or
- 5-year Kidney Failure Risk Equation (KFRE) ≥ 3% (please refer to evidence summary for details on KFRE criteria), or
- Inability to achieve blood pressure (BP) targets, or
- Significant electrolyte disorder, or
- RBC casts or hematuria (≥ 20 RBC/hpf) suggestive of glomerulonephritis/renal vasculitis

**REFER TO NEPHROLOGIST; SEE MANAGE BOX BELOW WHILE WAITING FOR CONSULTATION**

**MANAGE**

Implement measures to reduce CV risk and/or slow CKD progression
- Lifestyle modification, smoking cessation
- Lipid management for people with CKD (see KDIGO guidelines for further details):
  - if with diabetes, age ≥ 18, or
  - if without diabetes, age ≥ 50, or
  - if age ≥ 18 with known coronary artery disease, prior stroke, or 10-year Framingham risk > 10%
  - For people with diabetes, target HbA1c to appropriate level using recommended therapies as per Diabetes Canada guidelines

HTN treatment targets for people with CKD
Please refer to the 2018 HTN Canada Guidelines regarding proper BP measuring technique:
- if with diabetes, target BP < 130/80
- if without diabetes, target BP < 120/90.
  - Consider a higher target (<140/90) in frail individuals, long-term care residents, previous stroke, limited life expectancy (< 3 years), polypharmacy (> 5 meds), and standing systolic blood pressure (SBP) < 110
  - Use caution when treating systolic BP to target; risks may outweigh benefits when diastolic BP < 60

Minimize further kidney injury
- Avoid nephrotoxins such as non-steroidal anti-inflammatory drugs (NSAIDs), intravenous (IV) and intra-arterial contrast, etc. whenever possible (if eGFR < 60).
- If contrast necessary, consider oral hydration, withholding diuretics.
- Refer to Sick Day Medication List (see Evidence Summary).

Implement measures to slow CKD progression
Renin-angiotensin system (RAS) blockade:

- If with diabetes and with ACR > 3, use an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB) as first-line therapy. If BP already ≤ 130/80, use ACEI or ARB cautiously, monitoring for signs and symptoms of hypotension.

If without diabetes, ACR > 30 and BP not at target, use an ACEI or ARB as first-line therapy for HTN.

Repeat creatinine and potassium 2 weeks after initiation of ACEI, ARB or diuretic. (ACEIs, ARBs, and diuretics are safe and effective for treating CKD and decreasing proteinuria.)

*Medical conditions: active liver disease, high alcohol consumption or pregnancy. Women with childbearing potential should use a reliable contraceptive.

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The KidneyWise Clinical Algorithm was created as a resource for primary care providers (PCPs) to aid in the identification, detection, and management of chronic kidney disease (CKD), including referral.

**Note.** The Clinical Algorithm may not apply in the following situations:

- Frail and/or elderly people with a limited life expectancy
- When clinical circumstances warrant investigation for suspected acute kidney injury (i.e. volume depletion, urinary obstruction, etc.) or glomerulonephritis
- When an eGFR (estimated Glomerular Filtration Rate) is necessary for prescribing medications that require dose adjustment for reduced kidney function

Diabetes mellitus (DM) is the leading cause of CKD and end-stage renal disease (ESRD) in Canada. Hypertension (HTN) is an important risk factor for CKD and its progression, although it is uncommon as the sole cause if blood pressure is well controlled.

Most relevant guidelines, including Kidney Disease Improving Global Outcomes (KDIGO)34, recommend testing with both an eGFR and a urine albumin (Alb) to creatinine ratio (ACR) for the diagnosis of CRF. Both risk factors are independent of each other, and both are recommended for progression to ESRD. An eGFR with a value < 60 ml/min/1.73 m² should be repeated, as many people will have a value above 60 ml/min/1.73 m² on repeat testing. Consider the possibility of a reversible cause for a low eGFR, including volume depletion (i.e. recent gastrointestinal illness or excess diuretic use), or the concomitant use of Non-Steroideal Anti-Inflammatory Drugs (NSAIDs). Low eGFR in such scenarios may reflect an acute kidney injury (AKI) and require more rapid evaluation. The diagnosis of CKD requires evidence of chronicity (i.e. at least 3 months with an eGFR < 60). The urine ACR should be repeated if abnormal; confirmation requires at least 2 values to be elevated over a period of 3 months.

People with an eGFR > 60 ml/min/1.73 m² and an ACR < 3 cmol/g are re-evaluated in 1 year to monitor the underlying risk factor. Re-testing annually in people with DM is recommended. People with HTN may require less frequent testing, depending on the patient’s age, the presence of other co-morbidities, and the degree of blood pressure control. It is important to note that a substantial proportion of otherwise healthy elderly individuals will have an eGFR < 60 ml/min/1.73 m² due to normal aging (40% of women > 75 years of age and 30% of men > 80 years of age).1

**Purpose**

Review of the KDIGO Clinical Practice Guideline for Lipid Management in CKD53, Hypertension in Diabetes54 and Diabetes Canada55 clinical practice guidelines are recommended for detailed advice regarding hyperlipidaemia, hypertension (HTN), and glomerular control, respectively. These documents have been reviewed to ensure the recommendations have been incorporated and are consistent with the KidneyWise Clinical Toolkit. The blood pressure (BP) treatment targets for people with CKD and HTN have been updated to incorporate the results of the Systolic Blood Pressure Intervention Trial (SPRINT). People with CKD and HTN in Canada following proper blood pressure measurement technique “SPRINT” included people with CKD (but not DM) and found that an unattended systolic BP treatment target of < 120 mm Hg, measured with an automated oscillatory BP monitor (ACBP), reduced cardiovascular outcomes and mortality compared to a target of < 140 mm Hg.6 It is recommended that higher systolic BP targets are appropriate for people with CKD that were not well represented in the SPRINT trial and are at increased risk of adverse events; including those with a history of prior stroke, frailty, living in Long-Term Care, limited life expectancy (<1 year), or orthostatic hypotension (standing systolic BP < 110 mm Hg). It is also recommended that a cautious approach to treatment be taken for people who are on 5 or more medications (polypharmacy) and/or whose diastolic BP is ≤ 60 mm Hg as this may outweigh benefits (e.g. falls).6 SPRINT specifically excluded those with CKD who had a BP of the following: I. eGFR < 20 ml/min/1.73 m², II. polycystic kidney disease (i.e. urea ACR ≥ 60 U/mmol), III. glomerulonephritis, ≤ 58 years of age. Recognizing that most of these people are likely to be co-managed by a nephrologist and/or at higher risk of CKD progression and CV outcomes, the Ontario Renal Network chose not to exclude such individuals from the lowest systolic BP target of 120 mm Hg.

ACE inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), but not both, are recommended as outlined for most people with CKD who also have proteinuria, for normotensive people with DM as elevated ACR (> 35), an ACEI or ARB can be considered, although careful monitoring for signs or symptoms of hypertension is advised. Most people with DM and an elevated ACR will have hypertension in the absence of any anti-hypertensive therapy. The majority of people diagnosed with CKD can be managed by their primary care provider (PCP). Serial follow-up monitoring of eGFR and urine ACR is important to monitor for progression of CKD.

The KidneyWise Clinical Algorithm has updated the list of criteria when a referral to nephrology should be considered. The Kidney Failure Risk Equation (KFRE), calculated using the person’s age, sex, eGFR and urine ACR, provides a validated estimate of risk of progression to ESRD (treated kidney failure with dialysis or transplantation) in a 2 or 5 year period.15

As an example, an 80-year-old female with an eGFR of 35 ml/min and a urine ACR of 1.0 has a 5-year risk of eGFR of less than 2%. Alternatively, a 50-year-old woman with the same eGFR of 35 ml/min but a urine ACR of 30 ml/min has a 5-year risk of ESRD of about 14%.15

KFRE incorporates the important influences of age and urine ACR on the risk of CKD progression to kidney failure.15 We have selected a 5-year KFRE ≥ 5% to identify higher risk people who should be considered for referral, but might otherwise be missed by the existing KidneyWise criteria.15 The ORN is also working with community labs to provide KFRE results on lab reports when both the eGFR and urine ACR are ordered (KFRE calculator: https://qmdm.com/calculate/calculator_30b/kidney-failure-risk-equation-4-variable).

For people without DM with a blood pressure > 140/90 mm Hg and an ACR > 30, an ACEI or ARB should be used as first-line therapy for HTN.6 People with CKD who require statin therapy (i.e. those with diabetes) should be treated regardless of baseline lipid status and do not routinely require follow-up measurement of lipid levels. People with a non-renal indication for one of these agents (i.e. heart failure) should be treated accordingly.

It is recommended that a serum potassium and creatinine be repeated approximately 2 weeks after any initiation or dose increase of an ACEI, ARB, or diuretic to monitor for the development of a potassium disorder and/or a substantial decrease in eGFR.15 People with a substantial increase in creatinine (decline in eGFR after ACEI or ARB initiation may have underlying renovascular disease and/or be experiencing excessive diuretic use. This higher risk group requires careful monitoring and, in some cases, may require a reduction or discontinuation of the drug until further advice from nephrology is obtained.

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SICK DAY MEDICATION LIST

If people with CKD are unable to maintain adequate fluid intake during an illness, it is recommended that potentially nephrotoxic or renally excreted drugs should be withheld until the individual has recovered. As outlined in the Diabetes Canada guidelines,54 this can be recalled by referring to the acronym SADAM'S (Sulfonlureas, ACEi, Diuretics, Metformin, ARB, NSAIDs, SGLT-2 Inhibitors). Adapted from: Change in appropriate referrals to nephrologists after the introduction of automatic reporting of the estimated glomerular filtration rate. Askari A1, Ginmohamed I, Stacey D, et al. CJMMA 2012. DOI: 10.1503/cmj.1101685.


