Ontario Renal Network

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.

Ontario
Cancer Care Ontario

Ontario Renal Network

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 (CV)
- ○ First Nations, Inuit, or Metis people(s) ≥ 18 years of age

DETECT

CKD 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)

Measure eGFR and urine ACR

Note: eGFR calculation needs to be adjusted for black people (multiply eGFR by 1.16)

→ **If eGFR < 60** repeat measurement in 3 months, or sooner if clinical concern dictates (i.e. 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 → If eGFR remains stable for 2 years, follow eGFR and urine ACR every 12 months

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) ≥ 5% (please refer to evidence summary for details on KFRE criterion), *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

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

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* → **treat with a statin***
  - If without diabetes, age ≥ 50, *or* → **treat with a statin***
  - If age ≥18 with known coronary artery disease, prior stroke, or 10-year Framingham risk > 10% → **treat with a statin***
- 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

KidneyWise.ca

*Contraindications: active liver disease, high alcohol consumption or pregnancy. Women with childbearing potential should use a statin only if they are using reliable contraception.

Ontario Renal Network

Evidence Summary for the KidneyWise Clinical Algorithm

PURPOSE

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

IDENTIFY & EVALUATE

Diabetes mellitus (DM)[1] is the leading cause of CKD and end-stage renal disease (ESRD) in Canada. Hypertension (HTN)[1] is an important risk factor for CKD and its progression, although it is uncommon as the sole cause if blood pressure is well controlled.

Other risk factors listed for CKD are based on epidemiologic findings (e.g. age 60–75 with cardiovascular disease).[2] First Nations, Inuit, or Métis people(s) are also at higher risk of developing ESRD.[3]

DETECT

Most relevant guidelines, including Kidney Disease Improving Global Outcomes (KDIGO)[4], recommend testing with both an eGFR and a urine ACR (Albumin to Creatinine Ratio), as both measures are independent risk factors for progression to ESRD. An eGFR with a value < 60[a] should be repeated, as many people will have a value above 60[a] 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-Steroidal 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[a]). The urine ACR should be repeated if abnormal; confirmation requires at least 2 of 3 values to be elevated over a period of 3 months.

People with an eGFR ≥ 60[a] and an ACR < 3[b] can be re-screened at an interval commensurate with the underlying risk factor. Re-testing annually in people with DM is recommended. People with HTN may require less frequent testing, depending on the person'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[a] due to normal aging (40% of women > 75 years of age and 30% of men > 80 years of age).[5]

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.[6]

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

KFRE incorporates the important influences of age and urine ACR on the risk of CKD progression to kidney failure.[6] **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**.[7] 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://qxmd.com/calculate/calculator_308/kidney-failure-risk-equation-4-variable).

MANAGE

Review of the KDIGO Clinical Practice Guideline for Lipid Management in CKD[8], Hypertension Canada[9] and Diabetes Canada[10] clinical practice guidelines is recommended for detailed advice regarding hyperlipidemia, hypertension (HTN), and glycemic 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). Please refer to HTN Canada regarding proper blood pressure measurement technique.[9] SPRINT[11] 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 (AOBP), reduced cardiovascular outcomes and mortality compared to a target of < 140 mm Hg.[11] 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 (<3 years), 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)[12] and/or whose diastolic BP is < 60 mm Hg as risks may outweigh benefits (e.g. Falls).[13] SPRINT specifically excluded those with CKD who had any of the following: i) eGFR < 20 ml/min/1.73m^2; ii) polycystic kidney disease; iii) urine ACR ≥ 60; iv) glomerulonephritis; v) < 50 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 lower systolic BP target of 120 mm Hg.[9]

ACE inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), but not both, are recommended as outlined for most people with CKD who also have proteinuria[4]; for normotensive individuals with DM with an elevated ACR (> 3[b]), an ACEI or ARB can be considered, although careful monitoring for signs or symptoms of hypotension is advised. Most people with DM and an elevated ACR will have hypertension in the absence of any anti-hypertensive therapy.

For people without DM with a blood pressure > 140/90 mm Hg and an ACR > 30[b], an ACEI or ARB should be used as first-line therapy for HTN.[4] 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.[8] 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.[4] 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.

> Note: given the high risk of influenza-related complications among people with CKD, PCPs should recommend they receive the seasonal influenza vaccine on an annual basis.[14]

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[10], this can be recalled by referring to the acronym SADMANS (Sulfonylureas, 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. Akbari A., Grimshaw J., Stacey D, et al. CMAJ 2012. DOI: 10.1503/cmaj.110678

a units for eGFR are ml/min/1.73m^2
b units for ACR are mg/mmol
c units for Blood Pressure are mm Hg

1 Levin A, et al. Guidelines for the Management of Chronic Kidney Disease. CMAJ. 2008; 179(11): 1154-1162. http://www.cmaj.ca/content/179/11/1154
2 Collins A, et al. Who Should Be Targeted for CKD Screening? Impact of Diabetes, Hypertension, and Cardiovascular Disease. Am J Kidney Dis. 2009; 53(S3): S71-S77
3 Gao S, et al. Prevalence of chronic kidney disease and survival among aboriginal people. J Am Soc Nephrol. 2007; 18(11): 2953- 9. http://jasn.asnjournals.org/content/18/11/2953.long
4 Kidney Disease Improving Global Outcomes CKD Guidelines. http://kdigo.org/home/guidelines/ckd-evaluation-management/
5 Wetzels JFM et al. Age-and gender specific reference values of estimated GFR in Caucasians: The Nijegen Biomedical Study. International Society of Nephrology. 2007; 72: 632-637. https://www.kidney international.org/article/S0085-2538(15)52697-5/pdf
6 Tangri N, et al. A Predictive Model for Progression of Chronic Kidney Disease to Kidney Failure. JAMA. 2012; 305(15): 1553-9. https://jamanetwork.com/ journals/jama/fullarticle/897102
7 Acedillo RR, Tangri N, Garg AX. The Kidney failure risk equation: on the road to being clinically useful? Nephrology Dialysis Transplantation. 2013; 28(7):1623-4. https://academic.oup.com/ndt/article/28/7/1623/1858713
8 Kidney Disease Improving Global Outcomes Clinical Practice Guideline for Lipid Management in CKD. 2013. http://kdigo.org/guidelines/lipids-in-ckd/
9 Nerenberg KA, Zarnke KB, Leung AA, et al. Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. Canadian Journal of Cardiology. 2018. http://www.onlinecjc.ca/article/S0828-282X(18)30183-1/abstract
10 Canadian Diabetes Association Clinical Practice Guidelines. 2018. http://guidelines.diabetes.ca/Browse.aspx
11 The SPRINT Research Group. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med. 2015; 373: 2103-2116
12 Zia A, Kamaruzzaman SB, & Tan MP. Polypharmacy and falls in older people: Balancing evidence-based medicine against falls risk. Postgraduate Medicine. 2014; 127:3, 330-337.
13 Ruzicka M, et al. Thus Far and No Further: Should Diastolic Hypotension Limit Intensive Blood Pressure Lowering? Curr Treat Options Cardio Med. 2017; 19:80
14 Public Health Agency of Canada: For Health Professional Flu (Influenza). 2018. https://www.canada.ca/en/public-health/services/diseases/-fu-influenza/health-professionals-flu-influenza.html

KidneyWise Clinical Toolkit Version 2.0 Updated August 2018 ORN4005

Ontario
Cancer Care Ontario