Chronic Kidney Disease – Tips for the Busy Family Physician

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CFPC Practical Talks for Family Docs, August 25, 2020, Noon EDT

Faculty/Presenter Disclosure

Faculty: **Dr. Allan Grill**

I have the following relevant financial relationships to disclose (past 2 years):

Relationships with financial sponsors:

- The Lung Association – Planning committee (COPD & Asthma CME program)
- CADTH – Member, Canadian Drug Expert Committee
- ON Ministry of Health – Chair, Committee to Evaluate Drugs
- CCO-ON Renal Network – Provincial Medical Lead (Primary Care)
- Conference speaker (OCFP ASA; Vital Family Medicine Update)
- CFPC - Physician Advisor, Dept. of Programs & Practice Support
- **All of the above organizations are not-for-profit**

- Relationships with commercial interests:
  - Not Applicable

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Learning Objectives

- To identify a practical clinical algorithm that can be implemented in primary care practice to help manage patients with Chronic Kidney Disease (CKD)
- To differentiate patients with increased risk of advanced CKD using the Kidney Failure Risk Equation
- To interpret blood pressure treatment targets and use of SGLT2 inhibitors for patients with CKD

Terminology

- Chronic Renal Failure is an outdated term
  - Replaced by Chronic Kidney Disease (CKD)
- Acute Renal Failure is also an outdated term
  - Replaced by Acute Kidney Injury (AKI)
- Isn't it better to focus on "Renal Suc

Prevalence of CKD

- 10% of North Americans have CKD
  - 26 million people
- 25% of North Americans > age 65 have CKD
- Only 3% of CKD patients progress to ESRD

Why Should CKD Be Important to Primary Care?

- ~ 90% of CKD cases are at low risk of progression and can be followed by a Primary Care Provider (e.g. family physician, nurse practitioner); 100% in LTC

– Early identification and treatment can prevent/delay End Stage Renal Disease (ESRD)

  - Medication reviews can prevent AKI in LTC

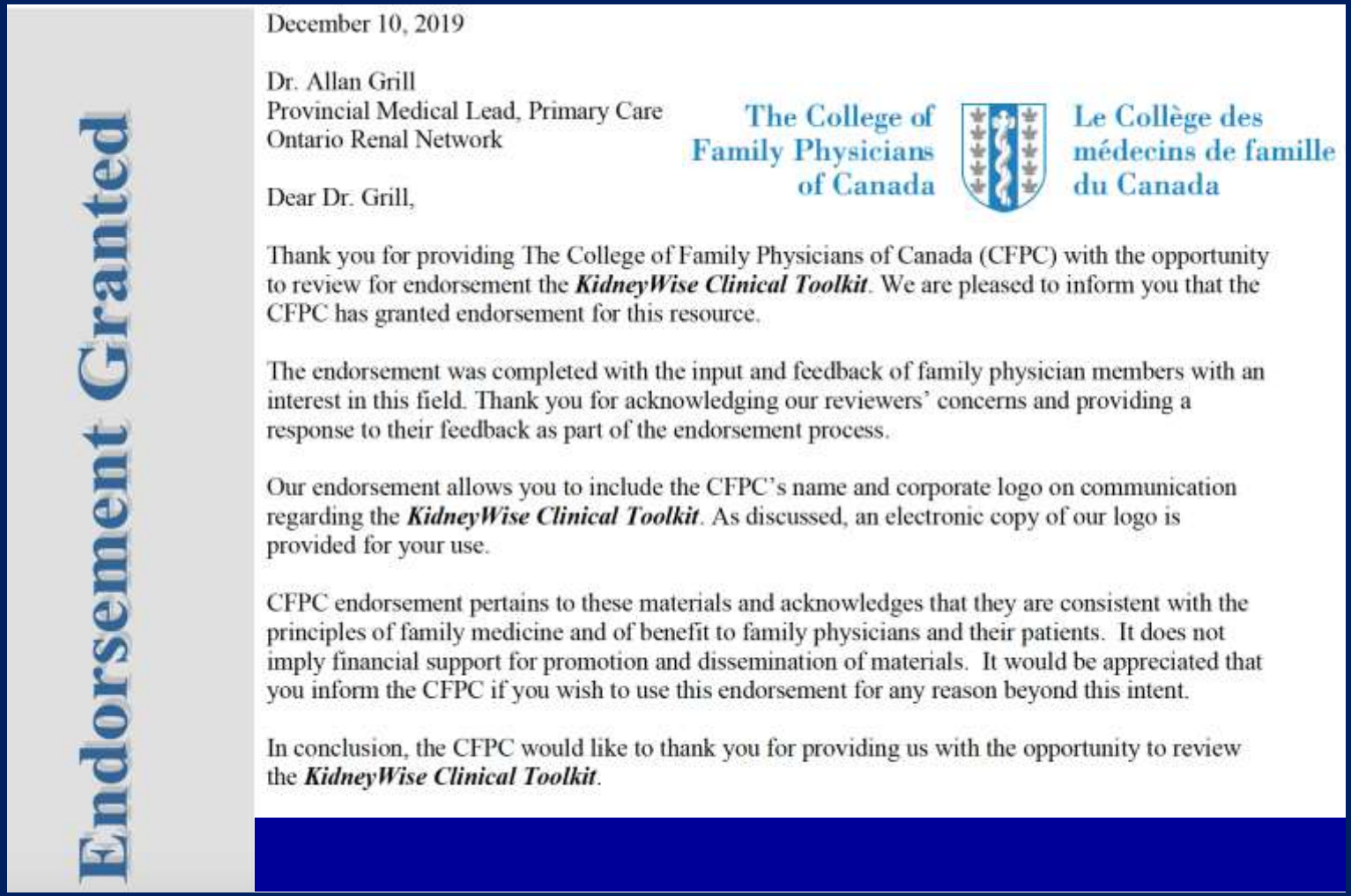
- Comorbid cardiovascular disease risk reduction/management (e.g. DM, CAD/CHF)
- Referral of patients at increased risk of progression to advanced stages of CKD to nephrology

CKD AT-A-GLANCE: KIDNEYWISE

See tool at

www.kidneywise.ca

KidneyWise Clinical Toolkit



Endorsement Granted

December 10, 2019

Dr. Allan Grill
Provincial Medical Lead, Primary Care
Ontario Renal Network

The College of Family Physicians of Canada
Le Collège des médecins de famille du Canada

Dear Dr. Grill,

Thank you for providing The College of Family Physicians of Canada (CFPC) with the opportunity to review for endorsement the ***KidneyWise Clinical Toolkit***. We are pleased to inform you that the CFPC has granted endorsement for this resource.

The endorsement was completed with the input and feedback of family physician members with an interest in this field. Thank you for acknowledging our reviewers' concerns and providing a response to their feedback as part of the endorsement process.

Our endorsement allows you to include the CFPC's name and corporate logo on communication regarding the ***KidneyWise Clinical Toolkit***. As discussed, an electronic copy of our logo is provided for your use.

CFPC endorsement pertains to these materials and acknowledges that they are consistent with the principles of family medicine and of benefit to family physicians and their patients. It does not imply financial support for promotion and dissemination of materials. It would be appreciated that you inform the CFPC if you wish to use this endorsement for any reason beyond this intent.

In conclusion, the CFPC would like to thank you for providing us with the opportunity to review the ***KidneyWise Clinical Toolkit***.

KidneyWise Clinical Toolkit

- **Clinical Algorithm** that helps with identification, detection, and management of patients with CKD and guidance on which patients may benefit from referral to a nephrologist
- **Evidence Summary** that offers further clinical detail regarding the algorithm content, including references to clinical guidelines that were used in the development of the toolkit
- **Outpatient Nephrology Referral Form** that provides referral guidance by outlining clinical scenarios that would require consultation with a nephrologist along with the appropriate investigations that should accompany the referral

Guidelines Referenced

- Kidney Disease Improving Global Outcomes CKD Guidelines 2012
- Hypertension Canada Guidelines 2020
- Canadian Cardiovascular Society Dyslipidemia Guidelines 2012
- Diabetes Canada Clinical Practice Guidelines 2018
  - KidneyWise is referenced in CKD chapter

Clinical Algorithm – Identify

Hypertension
Diabetes
Cardiovascular Disease

Added FNIM (First Nations, Inuit, Metis) > 18 years old – 2018 update

Added First degree relative with CKD – 2020 update

Do not screen if life expectancy is less than 10 years (e.g. frail elderly population)

What Tests Should Be Ordered? - Detect

- Creatinine/ eGFR
  - **Measure of kidney function**
- Urine for ACR (albumin to creatinine ratio)
  - **Measure of kidney damage/injury (protein excreted in urine)**
  - **Do not order a 24hr. urine collection**
- Important Note: CKD detection should be done in the absence of acute inter-current illness
  - Low eGFR in such scenarios may reflect AKI (acute kidney injury) and require more rapid evaluation

If The Results Are Abnormal, When Should One Repeat The CKD Screening Tests? - Detect

Assuming no inter-current illness:

- If eGFR < 60, repeat in 3 months or sooner if clinical concern
- If urine ACR ≥ 3, repeat 1-2 more times over the next 3 months

One test result is not enough to make the diagnosis of CKD

CKD is defined as a persistent abnormality for at least 3 months

What if Initial Test Results Create Clinical Concern?

- **Clinical Concern** = rapid decline from previous eGFR or unexpected eGFR/urine ACR result
- Repeat eGFR & urine ACR sooner (e.g. 2 weeks)
- Always consider reversible causes prior to re-testing:
  - Recent treatments with NSAIDs
  - Herbal remedies
  - Use of contrast dye for diagnostic imaging
  - Obstruction (e.g. BPH/urinary retention)
  - Volume depletion (e.g. dehydration due to illness; diuretics)
  - Consider the above any time an eGFR/Cr is ordered and the result is unexpected (e.g. annual flu vaccine; medical w/u)
- Renal ultrasound not recommended as part of routine CKD screening, but can be ordered to rule out a cause of AKI!

Interpreting The Results Three Months Later - Detect

Box C **eGFR ≥ 60 and ACR < 3**

- Patient does **not** have CKD

Follow-Up Recommendations:

- Re-test annually for patients with diabetes, less frequently otherwise unless clinical circumstances dictate more frequent testing

- **Avoid labeling a patient with CKD unless confirmed**

Interpreting The Results Three Months Later - Detect

- Patient has CKD
- Refer patient to a nephrologist

<u>Work-Up Recommendations:</u>

- Consider ordering & sending the following with referral:
  - Urine R&M, electrolytes – update 2018
  - CBC, serum calcium, phosphate, albumin – update 2018

- Don’t lose relationship with your patient!

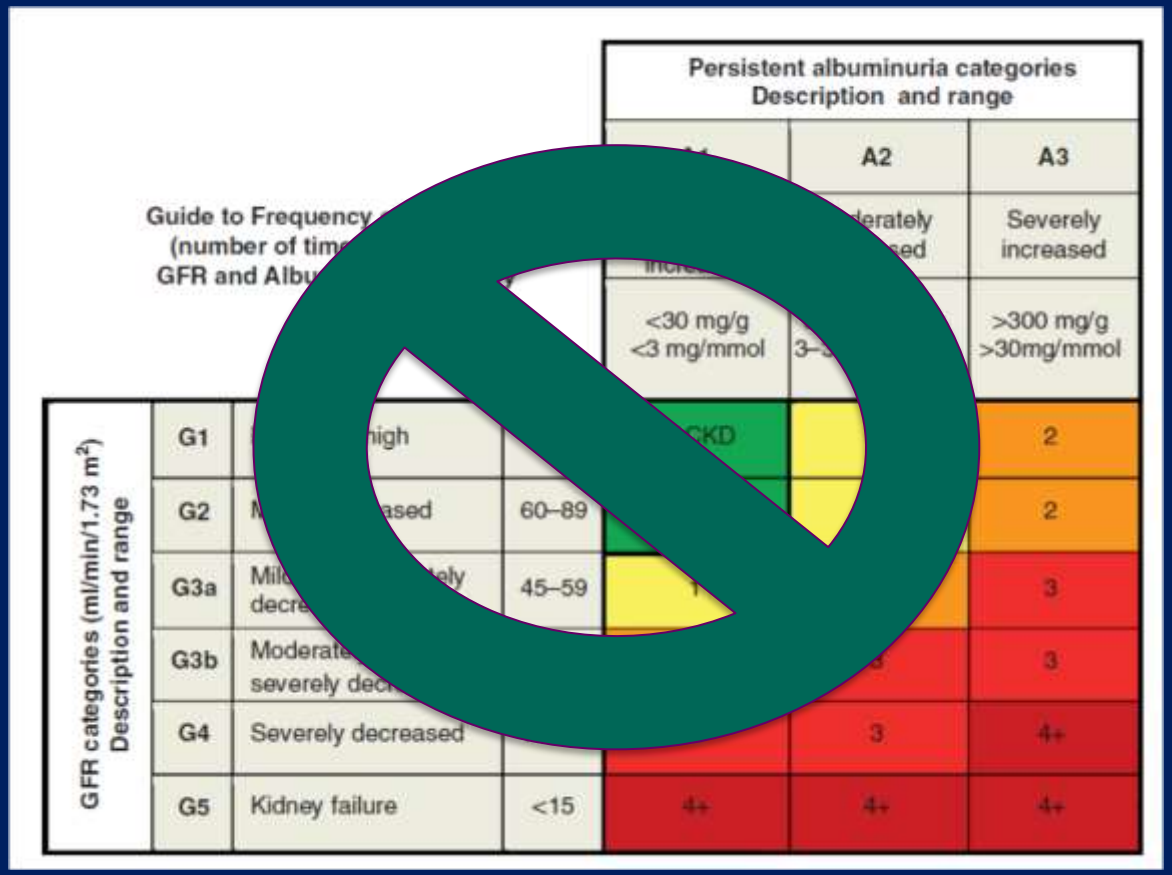
Interpreting The Results Three Months Later - Detect

- Patient has CKD
- Work-Up: Check urine R&M (inflammatory causes), electrolytes

Follow-Up Recommendations:

- How often do you follow-up?

KDIGO CKD Follow-up Advice



Interpreting The Results Three Months Later - Detect

Follow-Up Recommendations:

- **Serial following of eGFR and urine ACR to monitor for progression**
- **Every 6 months once diagnosis made**
- **Annually once eGFR is stable for 2 years**

KFRE – Kidney Failure Risk Equation

- Uses demographic and lab information to calculate risk of kidney disease progression resulting in kidney failure and need for renal replacement therapy (e.g. dialysis or transplant) in patents with CKD stages 3-5.
- Abbreviated KFRE consists of 4 variables - age, sex, eGFR and urine ACR
- www.kidneyfailurerisk.com
- https://qxmd.com/calculate/calculator_308/kidney-failure-risk-equation-4-variable

CKD Criteria for Referral to Nephrology

Criteria	Status
eGFR < 30 ml/min/1.73m^2 on 2 occasions, at least 3 months apart	No change
Proteinuria (urine ACR > 60 mg/mmol on at least 2 of 3 occasions), present for > 3 months	No change
eGFR < 45 ml/min/1.75m^2 and decline ≥ 5ml/min within 6 months (confirmed on repeat testing within 2-4 wks)	Revised
eGFR <45 and urine ACR between 30 and 60 on 2 occasions, at least 3 months apart	Removed
5-year KFRE is ≥ 5%	New

Clinical Algorithm – 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%

  → **treat with a statin***
- For people with diabetes, target HbA1c to appropriate level using recommended therapies as per Diabetes Canada guidelines

Clinical Algorithm – Manage

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)

Sulfonylureas/**A**CEIs/**D**iuretics/**M**etformin/**A**RBs/**N**SAIDs/**S**GLT2s

Don't forget to adjust dose of renally excreted medications!

Cockcroft-Gault formula is validated for the purpose of drug adjustment, but studies show CKD-EPI formula just as accurate as a measure of eGFR

Summary of Proposed BP Treatment Targets - KidneyWise

Patient Population	Systolic BP Target	Diastolic BP Target
People with CKD (without DM)	**<120 mmHg**	**<90 mmHg**
People with CKD and DM	**<130 mmHg**	**<80 mmHg**
People with CKD that have any one of the following characteristics: • Frail Elderly • Resides in Long-Term Care/ Nursing Home • Polypharmacy (>5 medications)* • History of Stroke • Chronic illness likely to limit life expectancy to < 3 yrs.	**<140 mmHg**	**<90 mmHg**

Need to measure BP using an oscillatory automated cuff – otherwise not generalizable to the SPRINT study

Also applies to any 'high risk' patient

Summary of Proposed BP Treatment Targets – HTN Canada

*** Hypertension Canada *High-Risk* Patient**

Individuals ≥50y **AND** with SBP 130-180 mmHg **AND** with one or more of the following CV risk factors should be considered for intensive BP management:

- ✓ Clinical or sub-clinical cardiovascular disease

OR

- ✓ Chronic kidney disease (non-diabetic nephropathy, proteinuria <1g/d, *estimated glomerular filtration rate 20-59 mL/min/1.73m²)

OR

- ✓ Estimated 10-year global cardiovascular risk ≥15%

OR

- ✓ Age ≥75 years

Four variable Modification of Diet in Renal Disease (MDRD) equation

± Framingham Risk Score

Summary of Proposed BP Treatment Targets – HTN Canada

Patient population	BP threshold for initiation of antihypertensive therapy		BP treatment target	
	SBP mmHg	DBP mmHg	SBP mmHg	DBP mmHg
Hypertension Canada High-Risk Patient*	≥ 130	N/A	< 120	N/A
Diabetes mellitus**	≥ 130	≥ 80	< 130	< 80
Moderate-to-high Risk (TOD or CV risk factors)**	≥ 140	≥ 90	< 140	< 90
Low Risk (No TOD or CV risk factors)**	≥ 160	≥ 100	< 140	< 90

Go Slow or SPRINT? – you decide

Clinical Algorithm – CKD Management

	Blood Pressure	Urine ACR
CKD + DM	**If > 130/80 – treat HTN based on HTN Canada Guidelines**	**If > 3 - Treat with ACEI or ARB (but watch for hypotension)**
CKD (Non-DM)	If > 135/85 – treat HTN based on HTN Canada Guidelines	If > 30 AND BP > 135/85 – Treat HTN with ACEI or ARB (1st choice pharmacotherapy)

Lytes/Cr 2 weeks after starting ACEI or ARB

Expect up to 25% change in eGFR/Cr levels

CKD + DM – Role of SGLT-2 Inhibitors

Table 1: Summary of the major randomized controlled trials of sodium-glucose cotransporter-2 inhibitors

Study characteristics	No. (%) of participants*			
	EMPA-REG OUTCOME[8] *n* = 7020	CANVAS program[9] *n* = 10 142	DECLARE-TIMI 58[10] *n* = 17 160	CREDENCE[11] *n* = 4401
Drug	Empagliflozin	Canagliflozin	Dapagliflozin	Canagliflozin
Dose, mg	10 or 25	100 or 300	10	100
Age, mean ± SD; yr	63.1 ± 8.7	63.3 ± 8.3	63.9 ± 6.8	63.0 ± 9.2
Sex, female	2004 (28.5)	3633 (35.8)	6422 (37.4)	1494 (33.9)
Follow-up time, median; yr	3.1	2.4	4.2	2.6
History of cardiovascular disease	7020 (100.0)	6656 (65.6)	6974 (40.6)	2220 (50.4)
History of heart failure	706 (10.1)	1461 (14.4)	1724 (10.0)	652 (14.8)
eGFR < 60 mL/min/1.73 m²†	1819 (25.9)	2039 (20.1)	1265 (7.4)	2631 (59.8)
Micro- or macroalbuminuria	2782 (39.6)	3026 (29.8)	5199 (30.3)	4370 (99.3)
Primary outcome(s)	MACE	MACE	MACE and admission to hospital for heart failure or CV death	Doubling of serum creatinine level, ESKD, or CV or renal death

Note: CKD-EPI = chronic kidney disease epidemiology collaboration equation, CV = cardiovascular, eGFR = estimate glomerular filtration rate, ESKD = end-stage kidney disease, MACE = major adverse cardiovascular events (defined as nonfatal myocardial infarction, nonfatal stroke or CV death), MDRD = modification of diet in renal disease equation.
*Unless specified otherwise.
†eGFR based on the MDRD equation in the EMPA-REG OUTCOME trial[8] and the CANVAS Program,[9] and the CKD-EPI equation in DECLARE-TIMI 58[10] and CREDENCE[11] trials.

CMAJ 2019 October 15;191:E1128-35

CKD + DM – Role of SGLT-2 Inhibitors

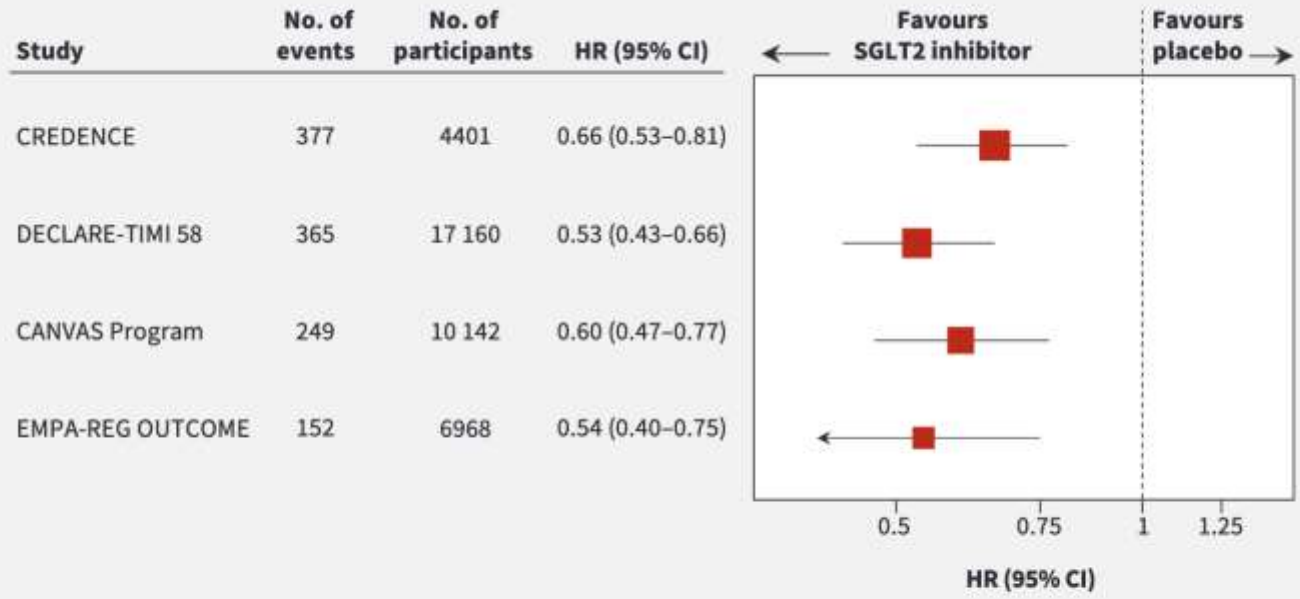


Figure 3: Substantial loss of kidney function, ESKD or death from kidney disease. Substantial loss of kidney function was defined as doubling of serum creatinine level in the CREDENCE[11] and EMPA-REG OUTCOME[8] trials and sustained 40% decline in estimated glomerular filtration rate in the CANVAS Program[9] and DECLARE-TIMI 58 trial.[10] The size of each box is weighted using the inverse variance method. Note: CI = confidence interval, ESKD = end-stage kidney disease, HR = hazard ratio, SGLT2 = sodium-glucose cotransporter-2.

CMAJ 2019 October 15;191:E1128-35

CKD + DM – Role of SGLT-2 Inhibitors

- Side effects:
  - Mycotic genital infections
  - DKA (rare)
  - Caution if using in combination with loop diuretics → AKI secondary to volume depletion.
  - Lower limb amputation (CANVAS trial – Canagliflozin)
- When do we use these?:
  - Poor glycemic control for patients with DM and CVD (2nd line)
  - **Poor glycemic control for patients with DM & CKD (elevated urine ACR)??**

- Don't forget:
  - Dose adjustment – e.g. Empagliflozin can be given until eGFR 30
  - SADMANS

CMAJ 2019 October 15;191:E1128-35

CKD + DM – Role of SGLT-2 Inhibitors

- Diabetes Canada 2018
  - adults with type 2 DM
  - **Known CVD**
  - Poorly controlled HbA1c target on existing antihyperglycemic medication(s) – eg Metformin
  - eGFR >30 mL/min/1.73 m2
  - Consider an SGLT2 inhibitor to reduce the risk of progression of nephropathy [Grade B, Level 2 for empagliflozin; Grade C, Level 3 for canagliflozin]

CKD + DM – Role of SGLT-2 Inhibitors

- European Renal Association
  - Poorly controlled HbA1c target on existing antihyperglycemic medication(s) – eg Metformin
  - Plus:
  - Patients achieving HbA1c targets on more than 1 anti-hyperglycemic medication should switch one of the additional agents to an SGLT-2 inhibitor
- American Diabetes Association
  - Consider adding SGLT-2 inhibitor independent of HbA1c level

CKD + DM – Role of SGLT-2 Inhibitors

- More trial data to follow
  - DAPA-CKD & EMPA-Kidney looking at primary renal outcomes
  - Composite of ESRD, doubling of sCR, CV or renal death

Outpatient Nephrology Referral Form

Ontario Renal Network

Patient Information (please fill in or affix label):

NAME: _____ DOB: ____/____/____ (DD MM YY)

ADDRESS: _____

PHONE #: _____ HEALTH CARD #: _____

ALT. CONTACT INFO: _____

Outpatient Nephrology Referral Form

Date of referral: ____/____/____ (DD MM YY) Is this a re-referral? ☐ Yes ☐ No

Name of nephrologist seen previously: _____

Recommended Reason for Referral:

Indications for referral for chronic kidney disease (CKD), including proteinuria:

- ◯ eGFR < 30 on 2 occasions, at least 3 months apart, *or*
- ◯ Rapid deterioration in kidney function: eGFR < 45 and decline of > 5 within 6 months in absence of self-limited illness; eGFR must be repeated in 2-4 weeks to confirm persistent decline, *or*
- ◯ Proteinuria: urine ACR > 60 mg/mmol on at least 2 of 3 occasions, *or*
- ◯ 5-year KFRE ≥ 5%

Other indications for referral to nephrology:

- ◯ Resistant or suspected secondary hypertension
- ◯ Suspected glomerulonephritis/renal vasculitis, including RBC casts or hematuria (> 20 RBC/hpf)
- ◯ Metabolic work-up for recurrent renal stones
- ◯ Clinically important electrolyte disorder
- ◯ Other (have you considered utilizing the provincial eConsult service?): _____

Additional Comments:

Co-morbid Conditions:

◯ Diabetes mellitus ◯ Coronary artery disease ◯ Hypertension ◯ Frailty ◯ Peripheral vascular disease

◯ Previous stroke ◯ Cognitive impairment ◯ Connective tissue disease (*eg SLE, RA, vasculitis*)

Lab Values:
Please fill out below if applicable; refer to the ORN KidneyWise Clinical Algorithm for suggested investigations

Date #1: (DD/MM/YY)	eGFR:	Creatinine:	Urine ACR:
Date #2: (DD/MM/YY)	eGFR:	Creatinine:	Urine ACR:
HbA1c:	Hgb:	K^+:	Ca^{2+}:
PO_4^{3-}:	Albumin:	PTH:	Hematuria (dipstick):
Other (or attach):			

Current Medications: (please attach separately)

Referring Practitioner/Address/Phone/Fax:	**Referring Billing #:**
	Signature:

Recommended Reasons for Referral

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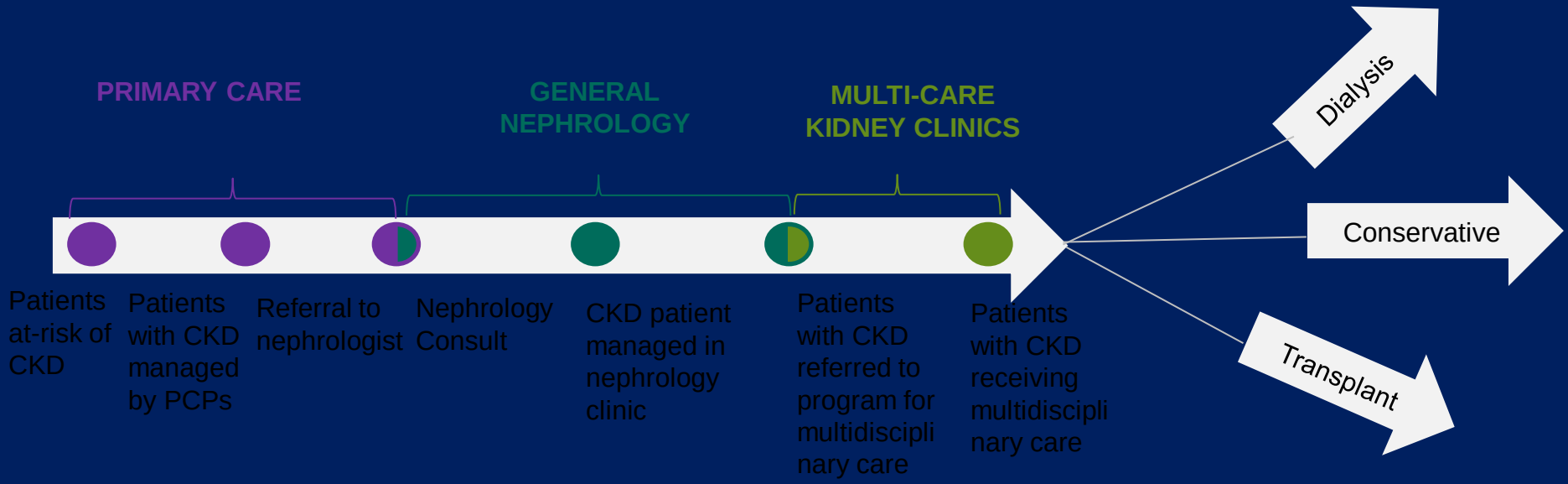
- ◯ Clinically important electrolyte disorder
- ◯ Other (have you considered utilizing the provincial eConsult service?): _____

_____

Most patients with non-progressive/ low-risk CKD can be managed by primary care providers!

Simplified CKD Patient Pathway



Primary Care management of CKD doesn't stop after referral!

CFP – Oct. 2018 – pg. 728-735

CLINICAL REVIEW

Approach to the detection and management of chronic kidney disease

What primary care providers need to know

Allan K. Grill MD CCFP(COE) MPH FCFP Scott Brimble MD MSc FRCPC

Abstract

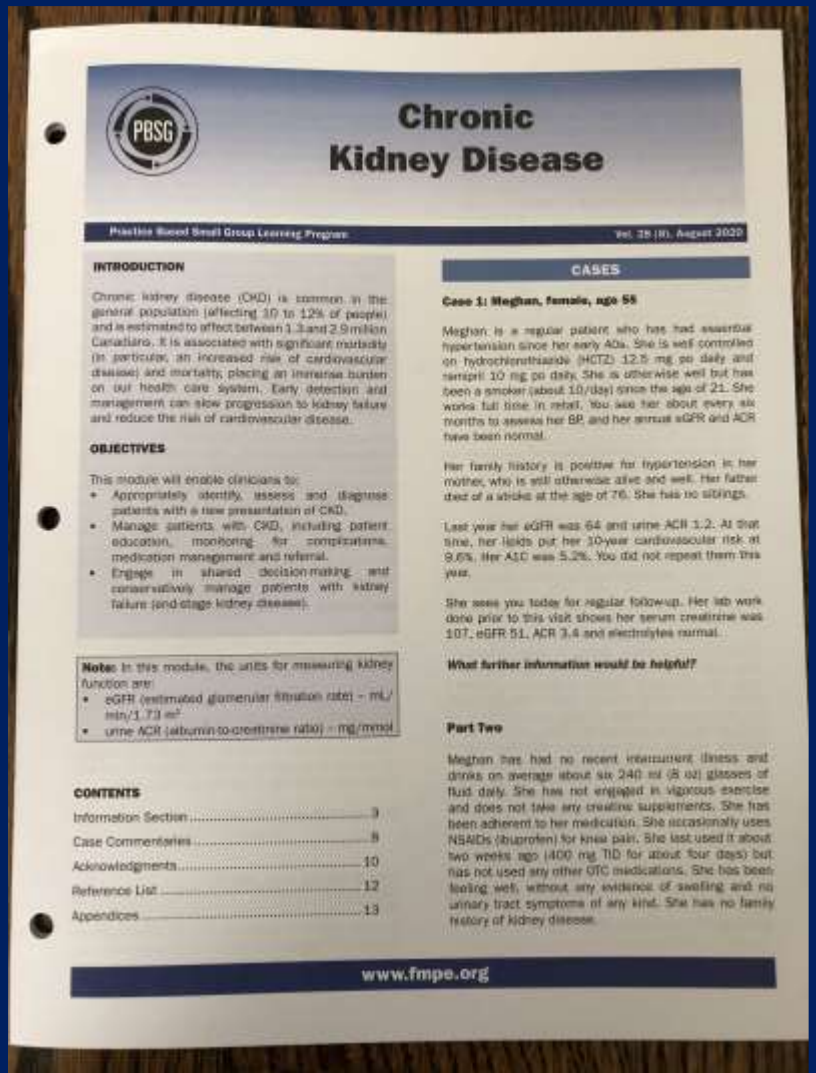
Objective To help primary care providers, both family physicians and nurse practitioners, identify, detect, and manage patients with and at risk of chronic kidney disease (CKD), as well as outline criteria for appropriate referral to nephrology.

Sources of information Published guidelines on the topic of CKD and its comorbidities were reviewed. A MEDLINE search was conducted using the MeSH terms *chronic renal insufficiency, family practice, and primary health care.* The search was limited to reviews and articles in English. The search covered all relevant articles from 2006 to the present.

Main message The KidneyWise clinical tool kit, created by the Ontario Renal Network and available at **www.kidneywise.ca**, provides evidence-informed, practical guidance to primary care providers on the diagnosis and management of CKD. A component of this tool is an algorithm that offers a step-by-step approach to diagnosing and managing CKD. This resource will help empower providers to identify those at high risk of this condition, order appropriate diagnostic tests, help prevent further disease progression, and reduce comorbid cardiovascular risk in patients with CKD.

Conclusion Most patients with CKD can be managed in primary care. Serial follow-up is essential to identify patients at high risk of progression to advanced stages of CKD, including end-stage renal disease. Primary care providers must continue to work together with local nephrologists to improve the lives of those living with CKD.

FMPE - PBSG



PBSG

Chronic Kidney Disease

Practice Based Small Group Learning Program Vol. 28 (8), August 2020

INTRODUCTION

Chronic kidney disease (CKD) is common in the general population (affecting 10 to 12% of people) and is estimated to affect between 1.3 and 2.9 million Canadians. It is associated with significant morbidity (in particular, an increased risk of cardiovascular disease) and mortality, placing an immense burden on our health care system. Early detection and management can slow progression to kidney failure and reduce the risk of cardiovascular disease.

OBJECTIVES

This module will enable clinicians to:

- Appropriately identify, assess and diagnose patients with a new presentation of CKD.
- Manage patients with CKD, including patient education, monitoring for complications, medication management and referral.
- Engage in shared decision-making and conservatively manage patients with kidney failure (end-stage kidney disease).

Note: In this module, the units for measuring kidney function are:

- eGFR (estimated glomerular filtration rate) – mL/min/1.73 m²
- urine ACR (albumin-to-creatinine ratio) – mg/mmol

CONTENTS

CASES

Case 1: Meghan, female, age 55

Meghan is a regular patient who has had essential hypertension since her early 40s. She is well controlled on hydrochlorothiazide (HCTZ) 12.5 mg po daily and ramipril 10 mg po daily. She is otherwise well but has been a smoker (about 10/day) since the age of 21. She works full time in retail. You see her about every six months to assess her BP, and her annual eGFR and ACR have been normal.

Her family history is positive for hypertension in her mother, who is still otherwise alive and well. Her father died of a stroke at the age of 76. She has no siblings.

Last year her eGFR was 64 and urine ACR 1.2. At that time, her lipids put her 10-year cardiovascular risk at 9.6%. Her A1C was 5.2%. You did not repeat them this year.

She sees you today for regular follow-up. Her lab work done prior to this visit shows her serum creatinine was 107, eGFR 51, ACR 3.4 and electrolytes normal.

What further information would be helpful?

Part Two

Meghan has had no recent intercurrent illness and drinks on average about six 240 ml (8 oz) glasses of fluid daily. She has not engaged in vigorous exercise and does not take any creatine supplements. She has been adherent to her medication. She occasionally uses NSAIDs (ibuprofen) for knee pain. She last used it about two weeks ago (400 mg TID for about four days) but has not used any other OTC medications. She has been feeling well, without any evidence of swelling and no urinary tract symptoms of any kind. She has no family history of kidney disease.

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Take Home Points

- CKD testing should only be applied to patients at high risk of CKD and in the absence of acute intercurrent illness; avoid in elderly patients with limited life expectancy – **Identification**
- eGFR and urine ACR are the tests of choice - **Detection**
  - eGFR should be done at least annually in some situations (e.g. med reviews; flu season - LTC)
- Most cases of CKD in primary care are low-risk and can be managed by PCPs – **Management**
  - Refer to nephrology as appropriate
- The KidneyWise Clinical Toolkit will make CKD care easier for PCPs and empower us to improve patient outcomes
- The 2 major updates to the KW Toolkit (2018) were BP treatment targets and addition of KFRE (5-year ≥ 5%) as a referral criteria to nephrology

Questions?

kidneywise@renalnetwork.on.ca;
www.kidneywise.ca

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Forum en médecine familiale

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