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Chronic Kidney Disease in Adults – Identification, Evaluation and Management

Effective Date: October 30, 2019

Scope

This guideline provides recommendations for the investigation, evaluation, and management of adults at risk of or with known chronic kidney disease (CKD). These recommendations and treatment targets may not be appropriate in all cases because many patients with CKD are complex due to older age and comorbidities. Communication between primary care providers and specialists is strongly encouraged.

Key Recommendations

- Identify high-risk patient groups for evaluation of CKD: diabetes, hypertension, cardiovascular disease, family history, high risk ethnicity (Indigenous peoples, Pacific Islanders, African, Asian, and South Asian descent), history of acute kidney injury (AKI).
- Screen high-risk patients using eGFR and uACR. Confirm abnormal test results with a repeat measurement and obtain urinalysis.
- Determine likely cause of kidney disease where possible. The cause of CKD has important implications for the risk of end stage renal disease (ESRD) and other complications.
- The three dimensions of **C**ause, e**G**FR and **A**lbuminuria (CGA) are all important in developing a management plan.
- Prompt advice from local internists, local nephrologists or the RACE Line is available to assist in determining the need for and timing of referral.

Figure 1. Prognosis and recommendations for frequency of monitoring based on eGFR and uACR*

			Albuminuria (ACR) Categories		
			A1	A2	A3
			<3 mg/mmol	3-30 mg/mmol	>30 mg/mmol
eGFR Categories	G1	≥90			
	G2	60-89			
	G3a	45-59			
	G3b	30-44			
	G4	15-29			
	G5	<15			

Low risk

Moderate risk
Test annually

High risk
Test 2 times per year

Very high risk

Test 3 times per year

Test 4 times per year

* Adapted from ckdpathway.ca and Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney inter., Suppl*. 2013;3:1–150

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Background

CKD is associated with other common chronic diseases such as diabetes, hypertension, and cardiovascular disease (CVD)[1] and an estimated **1:10 British Columbians** has some form of significant kidney disease.[2]

CKD markedly increases the risk of: cardiovascular disease, adverse drug reactions, acute kidney injury and prolonged hospital admissions.[4–10, 13–14] Patients with CKD have a risk of progression to end stage renal disease (ESRD), often requiring dialysis or kidney transplantation.[6, 9, 11–14] Most patients with chronic kidney disease die from other comorbidities before they progress to kidney failure. The outcome of many patients who go on to dialysis remains poor with 10 percent annual mortality; the overall 5 year survival rate is worse than that of most cancers.[3]

Evidence clearly indicates that control of hypertension and proteinuria can prevent or postpone kidney function decline.[4–12] This underscores the importance of early detection, evaluation and management of individuals with kidney disease.

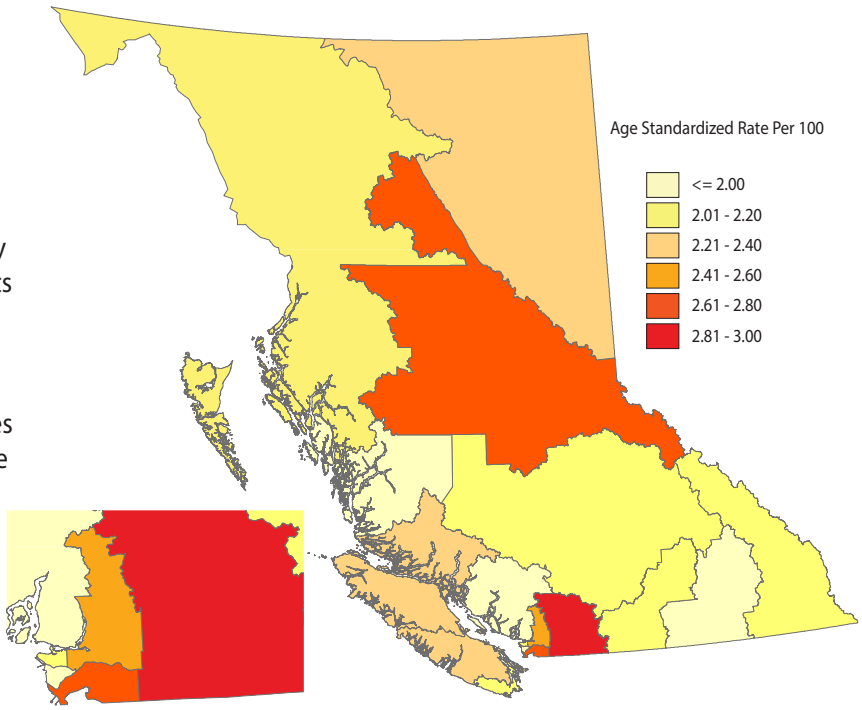

Figure 2. CKD prevalence by health service delivery area 2017/2018.

Definition

CKD is defined as an abnormality of kidney structure or function that is present for greater than 3 months.[13]

The two key parameters for classification are estimated glomerular filtration rate (eGFR) and urine albumin to creatinine ratio (uACR). eGFR is the best marker for kidney function and is calculated from creatinine. All labs in British Columbia (BC) automatically report eGFR when creatinine is ordered. **Note: the recommended equations for eGFR may change over time and are estimates only. Refer to page 3 for more information.**

For diagnostic purposes, other evidence of kidney damage includes: urine abnormalities such as hematuria; structural problems on imaging studies e.g., polycystic kidneys on ultrasound; histological findings on kidney biopsy.

Etiology

The two most common causes of CKD are hypertension and diabetes and they often co-exist.[13] Even if the cause seems obvious (e.g., diabetes), the possibility of a serious underlying primary renal disorder (e.g., glomerulonephritis) must be considered in patients with:

- Abnormal urinalysis, (e.g., proteinuria, hematuria, cellular casts). **Note: hyaline casts are normal.**
- Rapid sustained decline in kidney function (change in eGFR > 10-15%/year) despite remedy of reversible precipitants (e.g., volume contraction, febrile illness, medications).
- Constitutional symptoms suggesting systemic illness.
- Sudden or severe onset of symptoms (e.g., edema unrelated to heart or liver disease).

Risk Factors and Screening

The following populations are at increased risk for CKD and should be screened:	**At-risk populations should be screened every 1–2 years depending upon clinical circumstances (e.g., annually for individuals with diabetes) using:**
• Diabetes • Hypertension • Cardiovascular disease (CVD) • Prior acute kidney injury (AKI) • Family history of kidney disease (e.g., parent or sibling) • Specific high-risk ethnic groups: Indigenous peoples, Pacific Islanders, African Asian, and South Asian descent **Note: Older age alone is not a reason for screening.**	• eGFR • urinalysis (dipstick)* • urine ACR • review of risk factors ***Note: urine microscopy is not needed for screening.**

Diagnosis

CKD cannot be diagnosed with one isolated abnormal measurement of eGFR or urine ACR.

Estimated GFR (eGFR) Values and Interpretation

- Values of > 60 mL/min per 1.73m^2 without other markers of kidney disease (albuminuria, hematuria, structural abnormalities) **do not** indicate CKD.
- Values of < 60 mL/min per 1.73m^2 **which are persistent** (present for ≥ 3 months) are diagnostic of CKD.
- A single isolated measurement < 60 mL/min does not satisfy diagnostic criteria for CKD, but could reflect reduced kidney function and requires confirmatory testing.
- In patients with a **new unexpected finding of reduced eGFR**, the test should be repeated to establish stability or rapid deterioration.

Caveats of eGFR

- o eGFR is an estimated value that assumes a steady state of creatinine generation.
- o eGFR may be unreliable in extremes of muscle mass or with certain diets (e.g., very high or very low protein). Some medications can interfere with the excretion of creatinine (e.g., trimethoprim, fenofibrate).[14, 15]
- o In hospitalized patients or patients with AKI the fluctuations in creatinine make eGFR unreliable. In these circumstances, creatinine values should be used to guide management.
- o As a general rule, the eGFR can be used as a guide to outpatient drug dosing, even if the references use creatinine clearance (eCrCl). More caution is required for drugs with significant potential toxicity or a narrow therapeutic window (e.g., chemotherapy).

Urinalysis and ACR Values and Interpretation

- Significant abnormalities include persistent white blood cells or red blood cells in the absence of infection or instrumentation, and the presence of cellular casts.
- Urine ACR (uACR) is the preferred method to screen for protein in the urine.
  - o uACR quantifies albuminuria in a range which is not detected by dipstick urinalysis.
  - o The term **microalbumin** has historically been used. Recent guidelines and consensus from laboratories have recommended abandoning this term and to quote the uACR value instead.[13]
  - o uACR elevation (>3.0 mg/mmol) on serial testing is abnormal.
  - o In patients without diabetes, no specific treatment is recommended for isolated uACR values between 3 and 30 mg/mmol. These individuals remain at risk of CKD progression and cardiovascular disease, therefore surveillance is warranted.
  - o uACR may be unreliable in some patients due to acute illness, vigorous exercise, poorly controlled hypertension or poorly controlled blood glucose. Repeat testing should be done when in doubt.

- Urine test abnormalities, even with persistent eGFR values ≥ 60 mL/min per 1.73m^2 suggest kidney disease.
- 24-hour urine collections are not necessary in most cases.
- For equivalence of dipstick protein measurements, uACR and protein/creatinine ratios (PCR), see Appendix.

Renal Imaging

- Renal ultrasound should be undertaken to assess structural abnormalities and aid in diagnosis. Renal ultrasound should be performed in the following cases:
  - o Obstructive urinary symptoms
  - o Unexplained microscopic or macroscopic hematuria
  - o Unclear etiology of CKD, especially in young patients
  - o Patients with suspicion of benign prostatic hypertrophy (BPH)
  - o Family history of structural renal disease (e.g., cystic kidney disease)

Staging of CKD

Risk staging of kidney disease is important for care planning and patient management. Risk is determined based on **Cause**, e**GFR**, and u**ACR**, or **CGA**. Refer to Figure 1 (page 1). Further details on risk determination are available on the Kidney Disease Improving Global Outcomes (KDIGO) CKD management guideline at kdigo.org/home/guidelines.[13]

Risk Calculators

The Kidney Failure Risk Equation (KFRE) is an equation designed to estimate probability of requiring dialysis within 2 or 5 years. The equation is derived from 4 variables and can be calculated using QxMD: qxmd.com. Risks of > 10 – 20% indicate high risk (analogous to Framingham risk scores). The KFRE is a useful tool for prognostication, however its role has yet to be established in routine clinical practice.

Referral Recommendations

Indications for referral to specialist/nephrologist[22†]

Very high risk kidney disease (urgent communication needed)

- Presence of active urine sediments (red blood cell casts or cellular casts ± protein), especially when associated with reduced eGFR.
- AKI in absence of readily reversible cause (e.g., volume depletion, NSAIDs)
- Abrupt sustained fall in eGFR in a patient with known CKD.
- eGFR < 15
- Nephrotic syndrome

High risk kidney disease (patient to be seen within a timely fashion)

- GFR < 30†
- Unexplained persistent uACR >30 mg/mmol (regardless of eGFR) e.g., in absence of diabetes or HTN
- Progressive CKD, with eGFR decline > 5 ml/min/year†
- Diabetes and evidence of CKD with eGFR <45, urine ACR >30

Low to moderate risk kidney disease (patients that could be seen within a longer time interval, e.g., within 6 mos)

- Persistent abnormalities of serum potassium.
- Hereditary kidney disease.
- CKD, eGFR 30-45
- CKD and difficult to treat hypertension

† **Time to first consultation will vary based on individual circumstances.** Discussion with your local nephrologist as to timing of referral for specific individuals is encouraged if in doubt.

Recommended history and tests to include in referral package:

- Comorbidities (especially cardiovascular)
- Medications
- Complete blood count (CBC)
- Electrolytes (Na, K, Cl, HCO3), calcium
- Creatinine/eGFR (include current value and any historical values available)
- Urinalysis (urine microscopy)
- Urine ACR
- If older than age 40: serum protein electrophoresis (SPEP), urine protein electrophoresis (UPEP)
- Renal ultrasound – not required prior to referral, but should be arranged with result sent to specialist when completed

Please use for referral:

- Use Pathways to see the list of specialists in your region and their wait times.
- Use the BC Renal website to locate nephrologist in your region: bcrenalagency.ca/kidney-services
- Real-time communication with local specialists (or RACE line if uncertain) can provide rapid advice for urgent cases and facilitate the most appropriate mechanism of referral.
- Patients benefit from inclusion in multidisciplinary clinics for prevention, education and management, including by telehealth.[16–18]

A urology consult is more appropriate than nephrology in the following scenarios:

- Renal mass, enlarged prostate, obstruction, and large symptomatic or obstructing kidney stone

Management

Refer to Figure 1 (page 1) for recommended follow-up intervals.

Customization of management plan

- Many patients with CKD have multiple comorbidities. In some situations, universal fixed targets may not be applicable and may even be harmful. Clinical judgment and individualized targets are recommended.
- Communication with specialists is encouraged if appropriateness of any of the targets is in question.

Table 2. Care objectives and targets for CKD

Domain	Recommendations	Comments
Avoidance of acute kidney injury	• Strongly consider holding ACEI, ARB, SGLT-2, and diuretics if patient receiving dye, has acute illness with dehydration, or is having surgery (see Table in Appendix) • If contrast dye (especially arterial) is required, the risk can be mitigated with pre-hydration, please talk to a nephrologist or use a published protocol. Creatinine should be measured pre and post procedure (within 3 days). The above medications can be restarted safely if there is no evidence of AKI.	AKI is defined as an increase in creatinine by >26 µmol/L or 1.5 times baseline Transient insults to the kidney may result in a change in trajectory of stable kidney function Risk of contrast-induced AKI is higher in people with volume depletion
Medications	• In CKD, some medications need to be used with caution or dose-adjusted for the level of eGFR (see Appendix) • Medication review is critical both during and after an episode of AKI. • If hospitalized or changing serum creatinine, seek additional advice re drug dosing • Refer to BC Renal Agency Pharmacy & Formulary information	Drug interactions are common in CKD and are avoidable
Kidney function measurements	• Refer to Figure 1 for frequency of eGFR and uACR measurements in specific risk categories. • Repeat eGFR sooner (within 10 days) after any change in medications (e.g., ACEi, ARB, or diuretics, SGLT2i), medical intervention, or hospitalization. • Check creatinine and potassium prior to starting ACEi, ARB, SGLT2i, MRA within 7–14 days of starting, and within 7–14 days after a dose increase. • Creatinine rise >20% after dose increase should be followed by further measurements within 7–14 days.	
Blood pressure	• ACE or ARB is generally first line therapy in proteinuric kidney disease • Measure and record BP at diagnosis and at every visit thereafter. See BC guideline: *Hypertension – Diagnosis and Management* • Ambulatory BP monitoring is encouraged • In general, a BP <140/90mmHg is appropriate. A lower target (< 130/80) should be sought in patients with diabetes or CKD with significant proteinuria • Consultation with a specialist colleague is recommended for complex patients, especially elderly patients with multiple comorbidities.	BP targets are continually changing. Use clinical judgment when interpreting BP targets. Consider comorbidities and prognosis.
CVD risk assessment	• Calculate & record CVD risk. See BC guideline: *Cardiovascular Disease – Primary Prevention* • Manage in accordance with relevant guidelines. See CCS Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. • Check lipids once to establish baseline and after therapy x 1. • Consider use of statins and lipid lowering strategies irrespective of LDL levels.	After LDL reduction achieved, regular monitoring of lipids may not be necessary
Diabetes	• ACE or ARB is generally first line therapy in proteinuric kidney disease • Long-acting sulfonylureas are associated with hypoglycemia and are not recommended • SGLT-2 inhibitors improve glycemic control and reduce the risks of CVD and CKD progression in patients with diabetes and chronic kidney disease[23] • In those with unstable eGFR or acute changes in clinical condition, metformin should be held, dose-reduced or avoided (see Table in Appendix)	HbA1C: ≤ 7.0% may not be appropriate for older frail patients See BC Guideline: *Diabetes Care* Risk/benefit of metformin can be challenging and requires discussion with a specialist
Conditions associated with CKD	• Measure at least annually: o CBC and iron profiles (percent iron saturation). o Mineral metabolism (calcium, phosphorus). o Albumin o If questions about any abnormalities feel free to contact specialist colleagues.	Target hemoglobin is lower than the normal range for patients on ESA therapy (95- 115 g/L) Iron saturation <20% indicates iron depletion. Ferritin is not a reliable test in CKD patients and should not be ordered to assess iron deficiency.
Vaccinations	• Influenza vaccine annually. • Pneumococcal and Hepatitis B vaccines recommended for adults at medically high risk. • Refer to immunizebc.ca for other recommended vaccines by age and risk profile	Patients with very advanced CKD are less likely to seroconvert after hepatitis B immunization. Confirmation of immunity is required after vaccination, which may need to be repeated (after consultation with specialist)

Lifestyle and Self-Management

Support patient self management with the means available in your community. Patients with CKD benefit from multidisciplinary renal teams who can support patients to make beneficial changes in diet, smoking and physical activity, and to understand medications, and the uncertainty and emotional distress that can be seen in those with chronic conditions. Denial, often associated with grief, is common in patients with chronic disease affecting a vital organ.

Encourage patients with CKD to consider advance care planning and their goals for future care, including for the end of life.

- Provincial advance care planning resources are available at gov.bc.ca/advancecare
- BC Guidelines on palliative care are available at bcguidelines.ca/submenu_palliative.html
- BC Renal Agency information about end of life care is available at bcrenalagency.ca/healthcare-professionals/end-life-resources

Complex Scenarios

The following common complex scenarios benefit from discussion with a specialist:

- Whether to change the approach to a patient when eGFR goes down to 30 or lower
  - *Example: A 60 year old woman with type 2 diabetes mellitus has a change in eGFR from 32 to 29. Should her metformin be stopped?*
- Deciding whether to stop diuretic therapy when the creatinine goes up or eGFR goes down
  - *Example: A 70 year old man with congestive heart failure requires escalation of diuretic therapy and experiences a deterioration in creatinine. Should his diuretics be discontinued?*
- Difficult-to-treat hypertension
- Anticoagulation in patients with CKD

Abbreviations

- AKI: acute kidney injury
- CKD: chronic kidney disease
- CVD: cardiovascular disease
- eGFR: estimated glomerular filtration rate
- ESRD: end stage renal disease
- uACR: urine albumin to creatinine ratio

Resources

Diagnostic code: 585 (chronic renal failure)

Associated Documents

- Chronic Kidney Disease Flow Sheet

Appendices

- Appendix A: Potential complications of CKD
- Appendix B: Interpretation of urine ACR values to assess albuminuria and proteinuria
- Appendix C: Recommended drug modifications in presence of acute kidney injury (AKI)

Practitioner Resources

- **BC Renal Agency –** bcrenalagency.ca
  Clinical resources for physicians, dieticians, pharmacists and information for patients.
- Chronic Kidney Disease Clinical Web/Mobile Tool: algorithm for CKD patient care

- **RACE: Rapid Access to Consultative Expertise Program** – raceconnect.ca

  A telephone consultation line for select specialty services for physicians, nurse practitioners and medical residents. **If the relevant specialty area is available through your local RACE line, please contact them first**. Contact your local RACE line for the list of available specialty areas. Currently in BC, regions providing Nephrology services include Vancouver (VCH/PHC), Fraser and Northern. Regions that don't currently have RACE support for Nephrology are Interior and South Island. If your local RACE line does not cover the relevant specialty service or there is no local RACE line in your area, please contact the Vancouver Coastal Health Region/Providence Health Care RACE line.

  - **VCH Region/Providence Health Care:** ☎ 604-696-2131 or 1-877-696-2131 (toll free)
  - **Northern RACE:** ☎ 1-877-605-7223 (toll free)
  - **Fraser Valley RACE:** raceapp.ca

- **Pathways** – PathwaysBC.ca

  An online resource that allows GPs and nurse practitioners and their office staff to quickly access current and accurate referral information, including wait times and areas of expertise, for specialists and specialty clinics. In addition, Pathways makes available hundreds of patient and provider resources that are categorized and searchable.

- **HealthLink BC:** healthlinkbc.ca

  HealthLink BC provides reliable non-emergency health information and advice to patients in BC. Information and advice on managing chronic kidney disease in several languages is available by telephone, website, a mobile app and a collection of print resources. Patients can speak to a health services navigator, registered dietitian, registered nurse, qualified exercise professional, or a pharmacist.

  Patients may call 8-1-1 toll-free in B.C., or for the deaf and the hard of hearing, call 7-1-1.

- **Health Data Coalition:** hdcbc.ca

  An online, physician-led data sharing platform that can assist you in assessing your own practice in areas such as chronic disease management or medication prescribing. HDC data can graphically represent patients in your practice with chronic kidney disease in a clear and simple fashion, allowing for reflection on practice and tracking improvements over time.

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This guideline is based on scientific evidence current as of the effective date.

The guideline was developed by the Guidelines and Protocols Advisory Committee in collaboration and adopted by the Medical Services Commission.

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Appendix A: Potential Complications of CKD*

Potential Complications of CKD[1] (listed alphabetically)	
• Acute Kidney Injury (e.g., dehydration, contrast dye, drugs) • Anemia • Hypertension • Calcium absorption decreases • Drug toxicity • Dyslipidemia • Heart failure/volume overload	• Hyperkalemia • Hyperparathyroidism • Hyperphosphatemia • Hyperuricemia • Left ventricular hypertrophy • Malnutrition potential (late) • Metabolic acidosis

* Listed complications are not specific to CKD but tend to occur with increasing frequency and are more directly attributable to more severe reduction in kidney function. If complications are noted at an early stage of CKD, investigation of alternative causes is recommended (e.g., profound anemia at eGFR of 55 mLl/min is likely not attributable to low kidney function alone). Kidney damage is defined as pathological abnormalities (e.g., kidney biopsy results) or markers of damage including abnormalities in blood or urine tests (e.g., protein/albumin in the urine, red blood cells, white blood cells or casts) or imaging studies.[13]

Appendix B: Interpretation of urine ACR values to assess albuminuria and proteinuria

Categories	uACR (mg/mmol)	Protein reagent strip	PCR (mg/mmol)
Normal to mildly increased	< 3.0	Negative to trace	< 15.0
Moderately increased	3.0 – 30.0	Trace to +	15.0 – 50.0
Severely increased	> 30.0	+ or greater	> 50.0

Appendix C: Recommended drug modifications in presence of CKD and in acute kidney injury (AKI)*

This list is not inclusive and only provides some examples of drugs that require adjustment in CKD and AKI. Primary care practitioners should consult a specialist or pharmacist for more information about specific medication questions.

Medication	Pathophysiology	Recommendation in CKD	Hold in AKI?
NSAIDS	Decreases renal perfusion, Interstitial nephritis	Use with caution in CKD.	Yes
ACEI, **ARB**, or any medication containing those compounds	Protective in proteinuric CKD, diabetes, and heart failure but can cause decreased renal perfusion and hyperkalemia	ACEI or ARB should be held in hypovolemia, and if receiving IV contrast.	Yes
Potassium sparing diuretics (**spironolactone**, **eplerenone**, and **amiloride**)	Volume depletion and hyperkalemia	In CKD (other than in AKI), dose and frequent monitoring is essential if eGFR < 50 mL/min.	Yes
Metformin	Increased risk of metformin associated lactic acidosis (MALA)	Avoid if GFR <30	Yes
SGLT-2 Inhibitors	Protective in diabetic nephropathy and cardiovascular disease but can cause decreased renal perfusion in the setting of volume depletion	Hold temporarily in the setting of volume depletion, or prior to administering contrast dye.	Yes
Diuretics: furosemide and **thiazides**	Volume depletion and electrolyte abnormalities	N/A	Yes, unless volume overloaded
Opioids (e.g., **hydromorphone**, **fentanyl**, **methadone** (for pain), **oxycodone**)	Metabolites can accumulate	Reduce dose in CKD For opioids that are considered safer in CKD, and opioids to avoid in CKD, consult: bcrenalagency.ca/resource-gallery/Documents/Preferred-Medications.pdf	Consider dose reduction
Pregabalin and **gabapentin**	Accumulation	Reduce dose and monitor for adverse effects In severe renal failure, dose should not exceed 300 mg gabapentin per day.	Consider dose reduction
Digoxin	Hyperkalemia Accumulation with side effects (bradycardia, confusion)	Reduce dose in CKD and monitor potassium and drug levels. Consider alternative therapy in the setting of renal failure.	Adjust dose
Acyclovir	Risk of crystal nephropathy Drug accumulation and side effects (risk of seizures/confusion)	Encourage hydration. Dose adjust for GFR	No. Ensure hydration.
Statins	Risk of rhabdomyolysis	Consider dose reduction in CKD. Hold if rhabdomyolysis or unexplained/persistent muscle pain.	No
Phenytoin	Risk of accumulation and toxicity	Monitor levels and also adjust level for serum albumin	No
Lithium	Accumulation and increased risk of side effects Risk of nephrogenic diabetes insipidus Risk of chronic interstitial nephritis	Monitor lithium and electrolyte levels Encourage hydration Refer to a nephrologist if eGFR declines.	No
Hypoglycemics (sulfonylureas, insulin, meglitinides, thiazolidinediones)	Accumulation can increase risk of hypoglycaemia	Avoid long acting preparations in moderate-severe CKD. May require dose adjustments.	No
Trimethoprim and **co-trimoxazole**	Risk of hyperkalemia Reduces tubular secretion of creatinine so leads to a rise in serum creatinine without renal injury	Reduce dose when eGFR <30 mL/min, monitor GFR and potassium	No
Colchicine	Risk of accumulation and serious toxicity (GI, CNS)	Use lower dose and consider other agents (e.g., Steroids)	No
Proton pump inhibitors	Risk of interstitial nephritis	Clarify indication and consider other agent (e.g., H2 blocker)	No

For more information on dosing of DOACs in kidney disease please visit the 2018 European Heart Rhythm Association Guidelines (Figure 4). Available from academic.oup.com/eurheartj/article/39/16/1330/4942493

For more information on common prescribing questions for patients with CKD, consult:
bcrenalagency.ca/resource-gallery/Documents/CKD-Common_Prescribing_Qs_CKD_Patients_not_on_Dialysis.pdf

bcrenalagency.ca/health-professionals/clinical-resources/symptom-assessment-and-management

Further information about drug dosage adjustments in chronic kidney disease is available from:
rxfiles.ca/rxfiles/uploads/documents/ltc/HCPs/CKD/SDIS.Renal_newsletter.pdf

* Adapted from: *Acute Kidney Injury – potentially problematic drugs and actions to take in primary care*. "Think Kidneys" initiative by the UK Renal Registry in partnership with NHS England. Available from: thinkkidneys.nhs.uk/aki/wp-content/uploads/sites/2/2016/07/Primary-Care-Advice-for-medication-review-in-AKI-.pdf