Chronic Kidney Disease Management

Chronic kidney disease (CKD) is estimated to affect between 1.9 million and 2.3 million Canadians. CKD is a chronic, progressive disease that often co-exists with cardiovascular disease and diabetes and is recognized as a risk factor that increases all-cause mortality and cardiovascular disease. (1) Most patients with CKD will die of events related to cardiovascular disease before end stage renal disease develops. Therefore, an important focus of care in CKD is the management of cardiovascular risk factors. Those who are most at risk of CKD include those who have diabetes, hypertension, smoking history, obesity, established cardiovascular disease, family history of CKD, and multisystem diseases with kidney involvement (eg. rheumatoid arthritis, systemic lupus erythematosus).

How do I assess for kidney disease?

Targeted testing for CKD in high risk groups includes:

- A blood test for serum creatinine to calculate an estimated glomerular filtration rate (eGFR),
- A urine albumin-creatinine ratio (ACR) for albuminuria quantification
- A urinalysis for presence of red blood cells

Serum creatinine alone is an insensitive measure of kidney function. CKD can be classified by the eGFR and/or ACR.

Table 1 Diagnostic criteria for CKD (present for more than 3 months) (3)

Decreased GFR	GFR less than 60 mL/min/1.73m^2 (category G3a-G5)
Markers of kidney damage	Albuminuria Urine sediment abnormalities Electrolyte and other abnormalities due to tubular disorders Abnormalities detected by kidney biopsy Structural abnormalities detected by imagine (ultrasound) History of kidney transplantation

The estimated GFR (eGFR) is calculated using prediction equations such as CKD-EPI that incorporate the serum creatinine (SCr) and it will be used for the purposes of this study. Once an initial measurement of

less than 60mL/min/1.73m^2 has been determined, a repeat test is to be done within 14 days to confirm the diagnosis of a "chronic" reduction in eGFR. (3)

eGFR can be unreliable and/or misleading in a number of situations including: (3)

- Acute changes in renal function
- Exceptional dietary intake (high protein, vegetarian, recent consumption of cooked meet)
- Extremes in body size
- Diseases affecting skeletal muscle, paraplegia, or amputees, or high muscle mass
- Severe liver disease
- Drugs interacting with creatinine excretion (fenofibrate, trimethoprim)
- Pregnancy

Table 2 GFR classification (3)

GFR category	**GFR** (mL/min/1.73 m^2)	**Description**
G1	>90	Normal or high*
G2	60-89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

*Relative to young adult level. In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD. ☐ Shaded area denotes CKD

Albuminuria refers to the abnormal loss of albumin in the urine. (3) Albumin is one type of plasma protein found in the urine of normal subjects but present in a larger quantity in those with some kidney diseases. (3) Albuminuria can be estimated using a random urine albumin-to-creatinine ratio (ACR). The primary advantage of using ACR is that it is a single sample taken preferably as the first early morning void spot specimen. An ACR between 3 and 30 mg/mmol is considered to be moderately increased and ACR greater than 30 mg/mmol is considered to be severely increased. (3)

Table 3 Albuminuria categories: Description and range (3)

Category	**AER** (mg/24hours)	**ACR** (mg/mmol)	**Description**
A1	<30 mg/24 hours	<3 mg/mmol	Normal to mildly increased
A2	30-300 mg/24 hours	3-30 mg/mmol	Moderately increased
A3	>300 mg/24 hours	>30 mg/mmol	Severely increased

The following table summarizes the amount of risk and recommended frequency of monitoring in patients with or at risk of CKD. (1)

Table 4 Prognosis of CKD and Recommended Frequency of Monitoring Per Year by GFR and Albuminuria Categories (3)

Prognosis of CKD and Recommended Frequency of Monitoring Per Year by GFR and Albuminuria Categories: KDIGO 2012			A1	A2	A3
			<3 mg/mmol	3-30 mg/mmol	>30 mg/mmol
			Normal to mildly increased	Moderately increased	Severely increased
G1	Normal or high	≥90	1 if CKD	1	1
G2	Mildly decreased	60-89	1 if CKD	1	2
G3a	Mildly to moderately decreased	45-59	1	2	3
G3b	Moderately to severely decreased	30-44	2	3	3
G4	Severely decreased	15-29	3	3	4+
G5	Kidney failure	<15	4+	4+	4+

Green: low risk (if no other markers, no CKD), Yellow: moderately increased risk, Orange: high risk, Red: very high risk

What are the targets for patients with CKD?

Blood pressure:

CKD and diabetes: less than 130/80 mmHg

CKD no diabetes: less than 140/90 mmHg.

HgB A1C (for patients with diabetes): less than or equal to 7%

Body Mass Index: 18.5 – 24.9

Sodium intake: less than 1500 mg/day

How do I treat kidney disease?

The treatment of kidney disease involves reducing cardiovascular risk factors. This includes reducing albuminuria, improving modifiable lifestyle risk factors, reducing cholesterol, controlling blood pressure,

controlling diabetes, avoiding nephrotoxic medications and dose adjusting some medications for reduced kidney function.

Reduce albuminuria

Treatment usually involves a blockade of the renin-angiontensin-aldosteone system (RAAS) with ACEi or ARB's which have been shown to reduce urinary albumin. When an ACEi or ARB is initiated, it can cause a reversible reduction in GFR by 5-30% or an increase in serum potassium by 0.5 mmol/L. However, they can be prescribed safely in all stages of CKD and should not be avoided. (2) If potassium increases to 5.5-6.2 mmol/L, the patient should hold their ACEi or ARB, and re-check the potassium in 1-2 weeks, with consideration for use of calcium polystyrene and lactulose. If potassium normalizes the ACEi or ARB may be restarted at a reduced dose. If serum potassium is greater than 6.3 mmol/L, the patient should be referred to emergency for ECG and acute hyperkalemia management. (2)

Reduce modifiable lifestyle cardiovascular risk factors

All patients will benefit from reduction of modifiable cardiovascular risk factors. All patients should:

- Achieve a healthy body mass index (BMI) between 18.5 and 24.9
- Undertake at least 150 min of moderate-to-vigorous-intensity aerobic physical activity per week, in bouts of 10 min or more
- Cease use of tobacco products
- Maintain proper nutrition as symptoms of CKD may lead to malnutrition and low serum albumin. Low serum albumin may cause an increase in extracellular volume as the osmotic pressure over the blood vessel walls is decreased and fluid leaks into surrounding tissues making control of overall fluid status much more difficult.
- Maintain a low salt diet (less than 1.5 g of sodium/day); may require potassium and phosphate dietary restrictions as CKD progresses

For more information see lifestyle education material.

Antiplatelet therapy

Low dose ASA may be used for secondary prevention in patients with CKD and established coronary, cerebral or peripheral vascular disease (PVD). Coronary artery diseases include acute coronary syndrome (ACS), myocardial infarction, percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG). (7) Cerebrovascular diseases include stroke and transient ischemic attack. (7) Asymptomatic PVD patients may receive low dose ASA therapy if they are at high risk due of cardiovascular events, but have a low bleeding risk. (7) Symptomatic PVD patients should receive low dose ASA. (7)

Control cholesterol

Total, HDL and LDL cholesterol and triglyceride levels are used to decide on initiation of pharmacological cholesterol-lowering treatment. Routine monitoring of cholesterol levels is not necessary for most patients with CKD since the results will not alter management. Only regimens that included a statin (or statin/ezetimibe combination) have been convincingly shown to reduce the risk of adverse cardiovascular events in CKD populations. (6)

- Patients with CKD and diabetes or patients who have received a kidney transplant should receive a statin unless contraindicated
- Patients with CKD with or without diabetes and 50 years of age or older should receive a statin (statin/ezetimibe combination supported by the SHARP study)
- Patients with CKD, no diabetes and less than 50 years of age should receive a statin if they have:
    - coronary artery disease (myocardial infaction or revascularization)
    - ischemic stroke
    - estimated 10 year coronary event risk greater than 10% (ie. Framingham risk score greater than 10%)

Statins are contraindicated in patients who have active liver disease, high alcohol consumption or are pregnant.

Table 5 Recommended doses of statins in adults with CKD (6)

Statin	CKD stage G1-G2	CKD stage G3a-G5, including patients on dialysis or with a kidney transplant
Lovastatin	General population	Not studied
Fluvastatin	General population	80 mg*
Atorvastatin	General population	20 mg†
Rosuvastatin	General population	10 mg‡
Simvastatin/Ezetmibe	General population	20 mg/10 mg§
Pravastatin	General population	40 mg
Simvastatin	General population	40 mg

Data based on *ALERT, †4D, ‡AURORA, §SHARP.

Control blood pressure

The choice of initial therapy for treatment of hypertension in CKD depends on the presence of albuminuria and diabetes.

Table 6 Recommendations for blood pressure therapy in patients with CKD

Type of Patient with CKD	Recommended Blood Pressure Therapy
CKD with Diabetes	ACEi or ARB should be prescribed in all diabetics with CKD
	Add dihyrdropyridine calcium channel blocker for additive antihypertensive effect
	Add loop diuretic for volume control
CKD without Diabetes	ACEi or ARB should be prescribed if ACR is greater than 30 mg/mmol
	Add thiazide for additive antihypertensive effect
	Add loop diuretic for volume control

CKD- chronic kidney disease ACR-albumin to creatinine ratio ACEi –angiotensin converting enzyme inhibitor ARB-angiotensin receptor blocker PVD-peripheral vascular disease

The combination of an ACEi or ARB with a diuretic, NSAID or COX-2 inhibitor can increase the risk of clinically significant hyperkalemia and acute kidney injury. Many hypertensive CKD patients require using combinations of antihypertensives to reach targets. (2, 9) The combination of an ACEi and ARB is no longer recommended.

Control diabetes

Patients with CKD and diabetes should maintain a hemoglobin A1C less than or equal to 7%; a target hemoglobin A1C of 7-8.5% may be recommended for patients who have difficulty maintaining A1C less

than or equal to 7%, multiple co-morbitities, extensive coronary artery disease, limited life expectancy, high risk of hypoglycemia or hypoglycemia unawareness. (13) All patients with CKD and diabetes should receive an ACEi or ARB in order to reduce risk of macrovascular disease (coronary artery disease, cerebrovascular disease and peripheral vascular disease) and microvascular disease. (13) Patients with diabetes and CKD may be more susceptible to hypoglycemia due to impaired gluconeogenesis by the kidney and reduced clearance of insulin and other antidiabetic mediations, so close monitoring of blood glucose is recommended during dose titration or addition of new medications. (12, 13)

Metformin

- associated with increased risk of drug accumulation and lactic acidosis when used in patients with low kidney function
- use with caution in patients with eGFR less than 60mL/min and avoid in patients who have an eGFR less than 30mL/min
- Metformin may be used in certain circumstances if eGFR is 20-29 mL/min, but requires very close monitoring of serum bicarbonate levels to detect acidosis. Oral sodium bicarbonate may be prescribed to keep the level greater than 22mmol/L

Sulfonylureas: Glyburide, Gliclazide, Glimepiride

- reduced kidney function decreases clearances of the sulfonylureas or their active metabolites, necessitating a decrease in drug dosing to avoid hypoglycemia
- Glyburide may cause prolonged hypoglycemia due to accumulation when eGFR is less than 50 mL/min and product monographs suggest it is contraindicated when eGFR is less than 30 mL/min
- Gliclazide may also cause hypoglycemia, but is less affected by reduced kidney function than glyburide and is safe until eGFR is less than 15 mL/min

Repaglinide

- largely unaffected by reduced kidney function, but should be started at a lower dose and titrated cautiously when eGFR is less than 30 mL/min

Thiazolidinediones (TZD's): Pioglitazone, Rosiglitazone

- monotherapy with TZD's produces a long lasting glycemic control compared to metformin and glyburide
- dose adjusted when eGFR is less than 30 mL/min

- use is limited by side effects (edema, weight gain, risk of congestive heart failure (CHF), fracture risk, myocardial infarction risk)

Acarbose

- not recommended for use when eGFR is less than or equal to 25 mL/min
- not recommended as initial therapy in those with marked hyperglycemia

DPP-4 Inhibitors: Sitagliptin, Saxagliptin, Linagliptin

- all are renally excreted to some extent and require dose adjustments and/or discontinuation at reduced eGFR
- lack long term efficacy and safety data

GLP-1 receptor agonists: Exenatide, Liraglutide

- are renally excreted and require dose adjustment and/or discontinuation at eGFR less than or equal to 50 mL/min
- effective in promoting glycemic control and weight reduction
- lack long term efficacy and safety data

When deciding which agent to add to metformin, consideration should be given to a number of factors including effectiveness in blood glucose lowering, degree of hyperglycemia, kidney function, and risk of hypoglycemia.

Insulin

- long-acting insulin may be added to metformin therapy in patients with type 2 diabetes and if mealtime bolus insulin is required, other oral antidiabetic agents should be stopped
- during periods of acute illness accompanied by dehydration, vomiting or diarrhea, metformin and sulfonylureas should be held and patients should increase frequency of blood glucose monitoring and adjust dose of insulin as required

See the diabetes education module for further details

Renal dose adjustments

Clinical judgment is vital when making drug dosing decisions in patients with low kidney function.

The evaluation of a patient's medication list is best performed using a stepwise approach.

1. Obtain all relevant information
    a. Ensure that all patient information is gathered to determine that the best drug is chosen for the patient
    b. Are there other therapeutic alternatives to the drug in question that may be less nephrotoxic?
2. Estimate the GFR
    a. Calculate CrCl using Cockcroff-Gault and/or reported eGFR
    b. The CKD-EPI equation is the equation used by most laboratories to report estimated GFR
    c. Most references have drug dosing information derived from the Cockcroft-Gault equation; therefore, it should be used when determining dosing regimes
3. Review Medication list
    a. Identify medications that may require renal dosage adjustment (see Table 7)
    b. Drugs that have a narrow therapeutic index or are primarily renally eliminated are easy targets for renal dose adjustments
4. Determine the most appropriate dosing regime
    a. Consult references to determine the appropriate dosage adjustment
    b. Drugs may need adjustment in either in dose or interval or both
    c. The risk of toxicity potential should be balanced against the risk of inadequate drug response
5. Monitor for response and adverse effects
    a. Patients should be monitored for drug response and appearance of any adverse side effects that may indicating toxicity
6. Reassess and adjust dosing regimen as needed
    a. As health status may change over time, reassess the renal function and modify the drug dosing regimen as needed

See appendix 1 and 2 for examples of this process.

Table 7 Common medications requiring renal dose adjustments

Antimicrobials	• Beta-lactam antibiotics • Intravenous Vancomycin • Macrolides • Ciprofloxacin, levofloxacin • Fluconazole (prolonged therapy) • Antivirals
Cardiac drugs	• Beta blockers • Digoxin • Spironolactone • Fenofibrate
Antidiabetic drugs	• Sulfonylureas • Metformin (monitor closely when GFR less than 30mL/min) • Insulin (more susceptible to hypoglycemia)
Centrally acting drugs	• Benzodiazepines • Opioids • Gabapentin
Anticoagulants	• Low molecular weight heparins • Oral anticoagulants (dabigatran, rivaroxaban, apixaban)
Miscellaneous	• Allopurinol, colchicine • Methotrexate

Warfarin use in patients with GFR less than 30mL/min is associated with a higher risk of bleeding so lower doses and close monitoring of INR is recommended. (3)

Avoid nephrotoxic medications

There are medications and combinations of medications that can that can cause damage to the kidney. Refer to Table 8 for specific medications and their reported effects.

Table 8 Potentially nephrotoxic medications relevant to primary care

Nephrotoxic Medication	**Effects of Medication**
NSAID's & COX-2 Inhibitors	Interstitial nephritis, papillary necrosis
Combination ACEi/ARB, NSAID plus diuretic	Increased risk of acute kidney injury due to changes in blood supply to kidney
Lithium	Renal tubule damage leading to impairment in renal concentrating ability
Tacrolimus, cyclosporine	Acute or chronic changes in renal function primarily due to afferent and efferent arteriolar vasoconstriction
Radio Contrast dye	Risk of acute kidney injury (0-11%), some populations more at risk*
Aminoglycosides	Damage to proximal tubule and secondary injury to the glomerulus
Bisphosphonates	Renal toxicity reported

*GFR < 60 mL/min, > 70 years old, diabetes, dehydration, CHF, large doses of contrast, use of high osmolality agents

What should I tell the patient?

Many patients do not "feel" any symptoms of chronic kidney disease until function is severely impaired and eGFR is less than 15 mL/min. Most patients think immediately of hemodialysis when they hear about kidney disease. Approximately 1 mL/min of renal function is lost each year after the age of 40 as a part of normal aging. Conditions such as uncontrolled diabetes, hypertension or vascular disease can speed the decline up to 10-15 mL/min per year. (29) In practice many health care professionals equate eGFR to a percentage in order to make it more understandable for patients. Although a normal eGFR is approximately 120 mL/min (or 100%), an eGFR of 40mL/min is referred to as 40% of normal function. The goal of controlling blood glucose, blood pressure and reducing cardiovascular risk is to reduce the rate of decline in kidney function. Renal replacement therapy options such as hemodialysis, peritoneal dialysis or transplant are used when patients start to have symptoms of end stage kidney disease and typically have an eGFR less than 10%.

References

1. Levin A, Hemmelgarn B, Culleton B, Tobe S, McFarlane P, Ruzicka M, et al. Guidelines for the management of chronic kidney disease. Can Med Assoc J. 2008;179(11):1154-62.

2. Chronic kidney disease (CKD) management in general practice. 2nd ed. Melbourne, Australia: Kidney Health Australia; 2012.

3. 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 print;3(1):1-150.

4. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. Kidney inter , Suppl. 2012 print;2(5):341-414.

5. Tobe SW, Stone JA, Brouwers M, Bhattacharyya O, Walker KM, Dawes M, et al. Harmonization of guidelines for the prevention and treatment of cardiovascular disease: The C-CHANGE initiative. Can Med Assoc J. 2011;183(15):E1135-50.

6. Kidney Disease: Improving Global Outcomes (KDIGO) Lipid Work Group. KDIGO clinical practice guideline for lipid management in chronic kidney disease. 2013 July 15, 2013 manuscript, not yet printed.

7. Bell AD, Roussin A, Cartier R, Chan WS, Douketis JD, Gupta A, et al. The use of antiplatelet therapy in the outpatient setting: Canadian cardiovascular society guidelines. Can J Cardiol. 2011;27(3, Supplement):S1-S59.

8. Volpe M, Savoia C, De Paolis P, Ostrowska B, Tarasi D, Rubattu S. The renin-angiotensin system as a risk factor and therapeutic target for cardiovascular and renal disease. Journal of the American Society of Nephrology. 2002 November 01;13(suppl 3):S173-8.

9. Hackam DG, Quinn RR, Ravani P, Rabi DM, Dasgupta K, Daskalopoulou SS, et al. The 2013 canadian hypertension education program recommendations for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. Can J Cardiol. 2013 5;29(5):528-42.

10. National Collaborating Centre for Chronic Conditions. Chronic kidney disease: National clinical guideline for earlyidentification and management in adults in primary and secondary care. London, UK: Royal College of Physicians; 2008.

11. Gilbert RE, Rabi D, LaRochelle P, Leiter LA, Jones C, Ogilvie R, et al. Treatment of hypertension. Canadian Journal of Diabetes. 2013;37(Supplement 1):S117-8.

12. Rocco MV, Berns JS. KDOQI clinical practice guideline for diabetes and CKD: 2012 update. American Journal of Kidney Diseases. 2012;60(5):850-86.

13. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian diabetes association 2013 clinical practice guidelines for the prevention and management of diabetes in canada. Canadian Journal of Diabetes. 2013;37(Supplement 1):S1-S212.

14. Matzke GR, Aronoff GR, Atkinson AJ, Bennett WM, Decker BS, Eckardt K, et al. Drug dosing consideration in patients with acute and chronic kidney disease—a clinical update from kidney disease: Improving global outcomes (KDIGO). Kidney Int. 2011;80(11):1122-37.

15. Verbeeck RK, Musuamba FT. Pharmacokinetics and dosage adjustment in patients with renal dysfunction. Eur J Clin Pharmacol. 2009;65(8):757-73.

16. Rifkin DE, Winkelmayer WC. Medication issues in older individuals with CKD. Advances in chronic kidney disease. 2010;17(4):320-8.

17. McLean AJ, Le Couteur DG. Aging biology and geriatric clinical pharmacology. Pharmacol Rev. 2004;56(2):163-84.

18. Van Spall H, Toren A, Kiss A, Fowler R. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: A systematic sampling review. JAMA: the journal of the American Medical Association. 2007;297(11):1233-40.

19. Hubbard RE, O'Mahony MS, Woodhouse KW. Medication prescribing in frail older people. Eur J Clin Pharmacol. 2013;69(3):319-26.

20. Mangoni AA, Jackson SHD. Age-related changes in pharmacokinetics and pharmacodynamics: Basic principles and practical applications. Br J Clin Pharmacol. 2004;57(1):6-14.

21. Nobili A, Garattini S, Mannucci PM. Multiple diseases and polypharmacy in the elderly: Challenges for the internist of the third millennium. Journal of Comorbidity. 2011;1(1):28–44.

22. The American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American geriatrics society updated beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;60(4):616-31.

23. Barry PJ, Gallagher P, Ryan C, O'mahony D. START (screening tool to alert doctors to the right treatment)—an evidence-based screening tool to detect prescribing omissions in elderly patients. Age and Ageing. 2007 November 01;36(6):632-8.

24. Gallagher P, O'Mahony D. STOPP (screening tool of older persons' potentially inappropriate prescriptions): Application to acutely ill elderly patients and comparison with beers' criteria. Age and Ageing. 2008 November 01;37(6):673-9.

25. Pannu N, Nadim MK. An overview of drug-induced acute kidney injury. Crit Care Med. 2008;36(4):S216-23.

26. Munar MY, Singh H. Drug dosing adjustments in patients with chronic kidney disease. Am Fam Physician. 2007 May 15;75(10):1487-96.

27. Gitlin M. Lithium and the kidney. Drug Safety. 1999;20(3):231-43.

28. Kidney Disease: Improving Global Outcomes (KDIGO) AKI Work Group. Work group: KDIGO clinical practice guideline for acute kidney injury. Kidney inter , Suppl. 2012;2(1):1-138.

29. Furth SL, Abraham AG, Jerry-Fluker J, Schwartz GJ, Benfield M, Kaskel F, et al. Metabolic abnormalities, cardiovascular disease risk factors, and GFR decline in children with chronic kidney disease. Clinical Journal of the American Society of Nephrology. 2011;6(9):2132-40.

APPENDIX 1: Case study in renal dose adjustment

A physician Dr. T calls your pharmacy. He has a female patient AA who chronically has a high serum creatinine and requires treatment with ciprofloxacin. Dr. T normally uses ciprofloxacin 500mg PO BID for his patients, but since he knows ciprofloxacin is eliminated by the kidneys, he wants your recommendation on what dosing regimen he should use.

1. Do you have all of the information you need?
Consider: how sick is AA, allergy status, is AA's renal function stable, what is the indication/site of infection, culture and sensitivity results, are there any other options, concomitant drug therapy, pharmacokinetics and pharmacodynamics of ciprofloxacin, cost, potential side effects

***2. Determine the estimated GFR** (CKD-EPI reported by most laboratories)*
The best practice is to use the Cockcroft-Gault formula since it is used in all pharmacokinetic studies. However, in practice the Cockroft-Gault and CKD-EPI formulas should give similar estimations of renal function and therefore, the reported eGFR may be used for the purposes of this study.
Cockcroft-Gault formula: $CrCl = \frac{[(140-age) \times weight\ in\ kg\ ] \times 1.23}{SCr\ in\ mcmol/L} \times (0.85\ if\ female)$
For obese patients, may use ideal body weight, but this has not been validated in the literature
$Males: IBW = 50\ kg + 2.3\ kg\ for\ each\ inch\ over\ 5\ feet.$
$Females: IBW = 45.5\ kg + 2.3\ kg\ for\ each\ inch\ over\ 5\ feet.$

3. Review medication list for drugs that might require renal dose adjustments

4. Calculating treatment regime
You look in three references and find the following information:
One reference suggests modifying the dose to 250mg PO BID, another suggests 500mg PO every 18 hours and a third reference recommends 500mg PO daily.

Assuming ciprofloxacin is the best antibiotic for this patient, which of the three dosing regimes do you choose?
Consider: Dosing a medication every 18 hours is not likely a good choice since patient compliance may be affected. Ciprofloxacin is a concentration-dependent killing antibacterial meaning it requires high concentrations of drug at the site of infection (up to 10 times the MIC of the particular bacteria) and then exhibits a prolonged post-antibiotic effect that continues to kill bacteria even though the concentration is lower than the MIC of the bacteria. Therefore, maintaining high peaks is more important than maintaining a trough concentration above the MIC. In this case, ciprofloxacin should be dosed as 500mg PO daily to maintain the high peak concentration.

5. What monitoring would you recommend?
Consider: how do you know the patient is improving or getting worse, what are the potential adverse/toxic effects, do you expect any other changes in the patient's medical status

Three days later, AA visits Dr. T again because he is feeling worse. Dr. T calls for your advice. AA has now developed a fever and culture and sensitivity reveal that the bacteria is sensitive only to ciprofloxacin. Dr. T wants to know if he can safely increase the dose of ciprofloxacin.

6. Revising the regime based on drug response or change in patient status

Would you suggest increasing the dose? What are the risks and benefits of your decision?

APPENDIX 2: Case study of a diabetic patient with CKD

Patient DG is a 75 year old, 70 kg female with type 2 diabetes who has been a patient at your pharmacy for many years. She also has a history of GERD, hypertension and peripheral vascular disease. She was diagnosed with having CKD five years ago when she had an eGFR of 50 ml/min (baseline serum creatinine of 100 umol/L). Over the past couple months her health has deteriorated after three hospital admissions for recurrent infections. She arrives at your pharmacy after a recent discharge. You check Netcare for her recent labs you note that her serum creatinine is stable over the past 2 weeks at 155 umol/L, eGFR 40 mL/min, blood glucose random – 17.1 mmol/L, potassium 4.2mmol/L, her urinalysis from 3 days ago is positive for Enterococcus which is sensitive to Amoxicillin.

She has been prescribed the following:

Amlodipine 5 mg po daily-increased from 2.5 mg daily
Pantoprazole 40 mg po daily-as prior to admission
Metformin 1000 mg po tid-as prior to admission
Gliclazide 10 mg po bid-increased from 5 mg po bid
ASA EC 81 mg po daily-as prior to admission
Amoxicillin 500mg po tid x 7 days for Enterococcus UTI

1. Do you have all of the information you need?
Consider: Is DG on all the appropriate therapy for her medical conditions? Are there any further labs you would like to evaluate? Should any medications be initiated/discontinued/dose adjusted?
You recheck her Netcare after realizing that she is diabetic to see if she has had an ACR done. She did on her last admission 2 weeks ago and it is 10mg/mmol. Should any changes be made to her medication?

2. Determine the estimated GFR using serum creatinine (eGFR on lab report form)

3. Review medication list for drugs that might require renal dose adjustments
Indication
- ***What is the indication and duration of treatment?***
- ***Does the patient require this agent? Alternatives available?***

Effectiveness
- ***Does the patient require this dose?***
- ***Is there an objective monitoring parameter to follow?***

Safety
- ***Is the patient's renal function at 'steady state'?***
- ***What percentage of drug elimination is via the renal route?***
- ***What are the consequences of not adjusting the dose?***
- ***What is the clinical status of the patient?***

4. Changes to Treatment regimen
Consider: frequency of dosing, dose recommended for renal function, addition of other non-renally cleared agents, addition/substitution of more appropriate therapy?

5. What monitoring would you recommend?
Consider: how do you know the patient is improving or getting worse, what are the potential adverse/toxic effects, and labs that may reflect these effects. Do you expect any other changes in the patient's medical status?