Product and Health Experience

August 2021

Chronic Kidney Disease (CKD) Screening, Referral, & Medication Management Toolkit

This Toolkit is intended to be a guide for practitioners to help with screening, referral, and medication management for patients that may be at risk for CKD or who are currently diagnosed with CKD. There are many risk factors that can contribute to CKD. Early detection, timely referral, and optimal medication management may reduce onset and delay progression of CKD.

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Overview

- This toolkit is intended to be a reference for practitioners looking for guidance on screening, referral, and medication management for patients who may be at risk for CKD, or who are currently diagnosed with CKD
- There are many risk factors that can contribute to CKD
- Early detection, timely referral, and optimal medication management may reduce onset and delay progression of CKD
- The intent of this guide is to aid in: (1) early identification of kidney function issues; (2) selecting a cadence for screening; (3) referring patients to nephrology; and (4) medication management considerations

Agenda

- CKD Risk Factors and Severity
- Screening Labs and Guidelines
- CKD Risk and Management Schedule
- Referral
- Medication Management Considerations
- Appendix

CKD Risk Factors and Severity

Screen Patients Who Have These Risk Factors

Chronic	Diabetes Type 2: screen at time of diagnosis then yearly Diabetes Type 1: screen 5 years after diagnosis then yearly Hypertension Systemic disease with renal implications (RA, HIV, lupus, vasculitis, hyperuricemia, multiple myeloma)
History	Family history (first degree relative) of kidney disease Personal history of Acute Kidney Failure
Urologic	Recurrent kidney stones Recurrent urinary tract infections (>3 / year) Other problems such as structural renal tract disease
Medications	High dose or chronic NSAIDs / Nephrotoxic agents

Serum creatinine: Classification by estimated Glomerular Filtration Rate (GFR)

Category (CKD stage)	GFR (mL/min/1.73 m^2)	Terms*
1	≥ 90	Normal or high
2	60-89	Mildly decreased
3a	45-59	Mildly to moderately decreased
3b	30-44	Moderately to severely decreased
4	15-29	Severely decreased
5	< 15	Kidney failure

Albuminuria: Classification by Albumin to Creatinine Ratio (ACR)

Category	ACR (mg/g)	Terms*
A1	< 30	Normal to mildly increased
A2	30-300	Moderately increased
A3	> 300	Severely increased**

* The Terms used for each category are relative to a young adult's level
** Including nephrotic syndrome (albumin excretion ACR > 2,220 mg/g)

Screening Labs and Guidelines

Screening Labs

Basic Metabolic Panel (BMP), Comprehensive Metabolic Panel (CMP), or Renal Function Panel (RFP)

- Check GFR
- If < 60, evaluate if urgent nephrology care is needed; if not, retest in 3 months – see Guidelines slide for more information
- Two tests are required to confirm CKD diagnosis
- For CKD management, see CKD Risk and Management Schedule slide for more information

Urinalysis for albuminuria (ACR)

- If after 1 test, ACR is greater than 300 mg/g, refer to nephrology
- If ACR is 30-300 mg/g, retest in 3 months – see Guidelines slide for more information
- Two abnormal test are required to confirm CKD
- For CKD management, see CKD Risk and Management Schedule slide for more information

It is recommended that CKD screening and risk stratification must consist of a dual assessment of GFR and ACR. A duration of 3 months between tests is required to confirm CKD diagnosis.

Guidelines: Screen At-risk Patients Annually

When you screen, order both:

- BMP/CMP/RFP to get GFR
- Urinalysis to get ACR

eGFR

- If > 60, continue to screen annually
- If < 60, suspect CKD and retest in 3 months
  - If confirmed and ≥ 45, begin CKD management per CKD Risk and Management Schedule slide
  - If confirmed and < 45, refer to Nephrology
  - If not confirmed (i.e. > 60), continue to screen annually

ACR

- If < 30 mg/g, continue to screen annually
- If > 300 mg/g, refer to Nephrology
- If between 30 - 300 mg/g, suspect CKD and retest in 3 months
  - If confirmed, diagnose as Probable CKD and order a BMP
    - If eGFR < 45, refer to Nephrology
    - If eGFR ≥ 45, begin CKD management per CKD Risk and Management Schedule slide
  - If not confirmed (i.e. ACR < 30 mg/g), continue to screen annually

modified from 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. The modification involves referring patients at Stage 3b vs the source material, which recommends at Stage 4.

CKD Risk and Management Schedule

CKD Risk and Management Schedule*

CKD Risk Map
Prognosis of CKD by GFR and Albuminuria Category

eGFR Category (GFR in mL/min/1.73 m²)				Albuminuria Category (ACR in mg/g) A1	A2	A3
				Normal to Mildly increased	Moderately increased	Severely increased
				< 30 mg/g	30-299 mg/g	> 300 mg/g
	G1	Normal or high	≥90	Monitor 1X yearly	Monitor 1X yearly	Refer
	G2	Mildly decreased	60-89	Monitor 1X yearly	Monitor 2X yearly	Refer
	G3a	Mildly to moderately decreased	45-59	Monitor 2X yearly	Monitor 2X yearly / Refer*	Refer
	G3b	Moderately to severely decreased	30-44	Refer	Refer	Refer
	G4	Severely decreased	15-29	Refer	Refer	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

Color key

	Low risk (if no other signs, no CKD)
	Moderately increased risk
	High risk
	Very High Risk
	Highest Risk

Source: *modified from* 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.

Monitor: Management in primary care could continue without referral to nephrology. Monitoring is suggested either 1X or 2X yearly per the table.
Refer*: Referral to nephrology should be *considered.* eConsult or other remote consultation may be appropriate prior to referring the patient.
Refer: Referral to nephrology is *recommended.*

*** These are general guidelines. Clinicians should use their discretion and individualize as needed for their patients.**

modified from 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. The modification involves referring patients at Stage 3b vs the source material, which recommends at Stage 4.

Referral

Refer to Nephrology

- Acute Kidney Infection or abrupt sustained fall in GFR;
- If eGFR <45 (stage 3b) per guidance on prior slides;
- A consistent finding of significant albuminuria (ACR > 300 mg/g or Albumin Excretion Rate > 300 mg/day; approximately equivalent to Protein to Creatinine Ration > 500 mg/g or Protein Excretion Rate > 500 mg/24 hours);
- Progression of CKD = Sustained decline in eGFR > 5 mL/min/1.73 m^2 per year;
- Urinary red cell casts, red blood cell > 20 per high power field sustained and not readily explained;
- CKD and hypertension refractory to treatment with 4 or more anti-hypertensive agents;
- Persistent abnormalities of serum potassium;
- Recurrent or extensive nephrolithiasis;
- Hereditary kidney disease

Additional Referral Resources

CKD patients often have comorbidities, such as hypertension and diabetes

If your patients have access to local chronic care clinics focused on these comorbidities, your patients might benefit from a referral to these clinics

Medication Management Considerations in CKD

Medications Matter: The Effect of Medications on the Kidneys

There is currently no cure for CKD, but treatment, and appropriate medication management can help slow progression

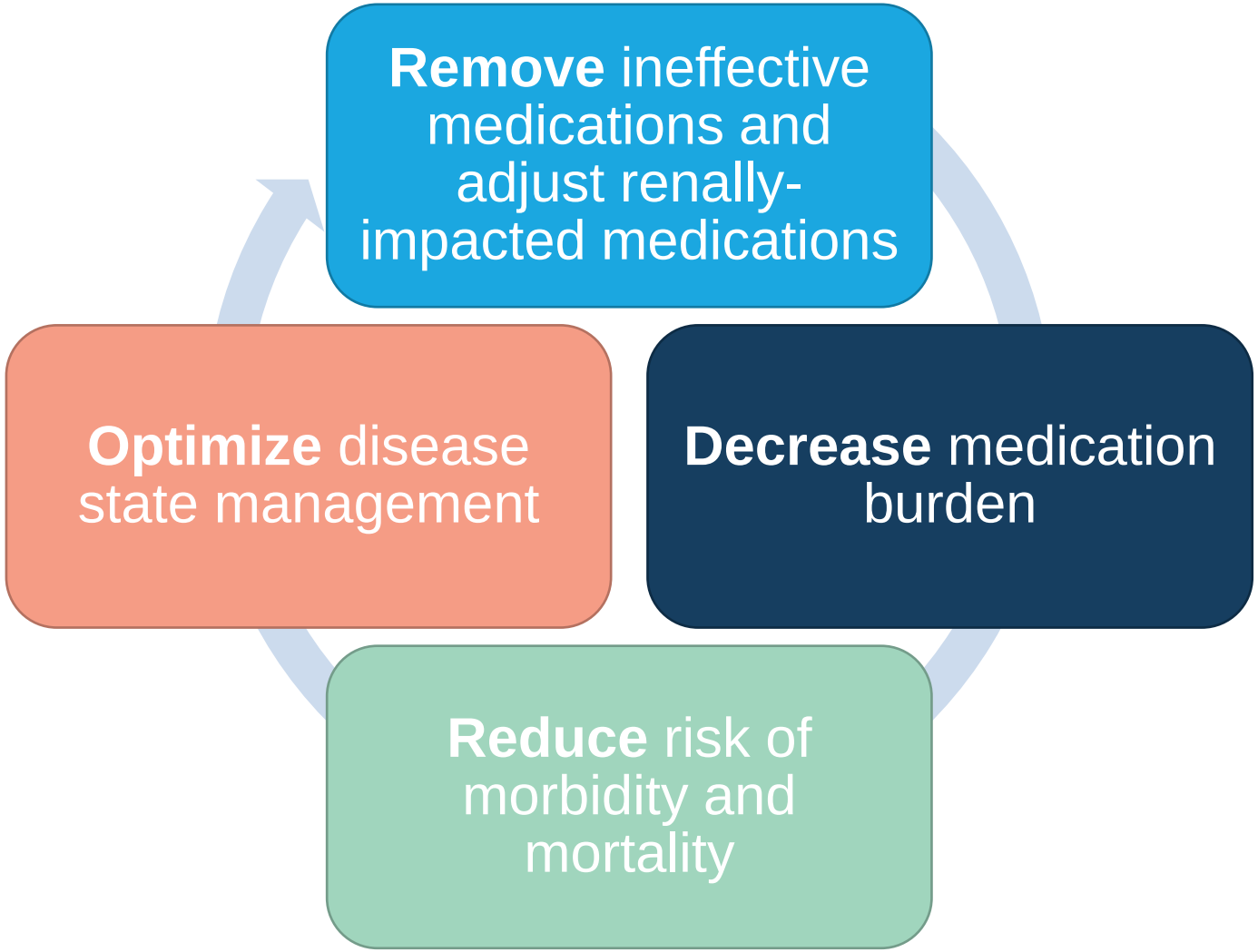
***Higher mortality rate**:* Due to inappropriate drug use, there is a 40% higher mortality rate in patients with CKD whose eGFR <60 mL/min/m^2 compared to patients without CKD

***Hospitalization**:* Higher rates and longer hospitalization durations have been shown in the absence of pharmacist-conducted drug therapy reviews

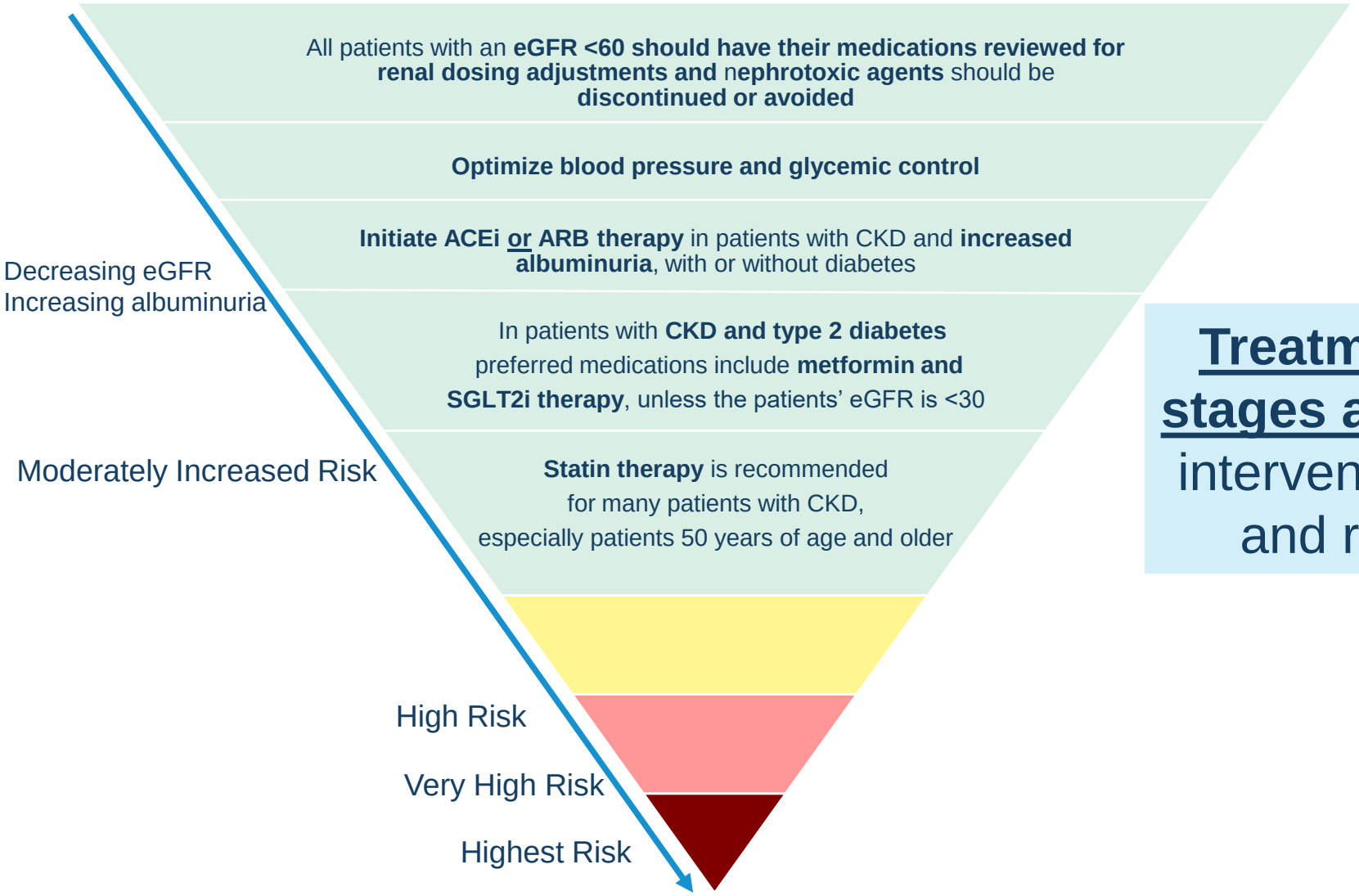
***Pain**:* High prevalence of pain in patients with CKD, which is associated with poor quality of life and poor survival

***Cost**:* Treatment for kidney failure accounts for 6.7% of the total Medicare budget for <1% of the covered population

Goals of Medication Changes



Early Medication Management Matters



Treatments initiated during early stages are highly effective. Effective interventions delay CKD progression and reduce cardiovascular risk.

Medication Management in Patients with CKD

- Many medications and/or their metabolites are excreted by the kidneys
- Several medications can cause acute kidney injury or accelerate chronic kidney disease progression
- **Medications should be adjusted based renal function and nephrotoxic medications should be avoided**
- Below are common medication classes and agents that have renal considerations in patients with CKD

NSAIDs	**Lithium**	**Sulfonylureas**
Direct Oral Anticoagulants	**Bisphosphonates**	**Digoxin**
Antimicrobials & Antifungals	**Gabapentin & Pregabalin**	**Proton Pump Inhibitors**

The medications and medication classes listed are not comprehensive. Please refer to guidelines and drug references for more detail and information.

Medication Considerations in Patients with CKD

eGFR 45-60

- Review all medications for renal dosing adjustments
- Avoid prolonged NSAIDs
- Avoid codeine, hydrocodone, morphine, and tramadol extended release
- Continue metformin use
- Renally dose gabapentin and pregabalin
- Review dosing for direct oral anticoagulants (apixaban, dabigatran, edoxaban, rivaroxaban) as recommended dose varies by indication and level of kidney function

eGFR 30-45

- The above recommendations still apply as renal function declines and medications should continue to be reviewed for further renal dose adjustments
- Continue metformin use with close monitoring and at 50% dose

The medications and medication classes listed are not comprehensive. Please refer to guidelines and drug references for more detail and information.

Medication Considerations in Patients with CKD

eGFR <30

- Recommendations from the previous slide still apply as renal function declines and medications should continue to be evaluated for further renal dose adjustments, with further considerations below
- Avoid any NSAIDs
- Avoid bisphosphonates
- Avoid metformin and review all antihyperglycemic agents for dose reductions based on renal function and glycemic control to avoid hypoglycemia
- Do not initiate an SGLT2i, however, it is reasonable to continue an SGLT2i until renal replacement therapy due to continued renal and cardiovascular benefits
- Due to the cardiovascular benefits and potential protection of residual kidney function, do not routinely discontinue RAAS antagonists based solely on the eGFR and monitor serum potassium closely
- Sulfamethoxazole/trimethoprim should be used cautiously, even with reduced doses, due to risks of hyperkalemia; consider alternative therapy if possible

The medications and medication classes listed are not comprehensive. Please refer to guidelines and drug references for more detail and information.

Proton Pump Inhibitors and CKD

- Proton Pump Inhibitors (PPIs) are available over the counter and by prescription for acid suppression therapy and often utilized in patients with CKD due to their nonrenal clearance and ease of dosing in this population, as opposed to histamine-2 receptor antagonists (H2RAs)

- While generally considered safe, PPI use has also been associated with an **increased risk of adverse effects** such as:
  - Increased risk of acute kidney injury
  - Incidence of CKD
  - CKD progression to end-stage renal disease

- In patients with or without CKD, **risks versus benefits of PPI therapy should be considered before prescribing or continuing long-term therapy**

- Certain conditions such as severe esophagitis, Barret's esophagus, previous GI ulcer bleed, chronic NSAID use, or Zollinger-Ellison Syndrome may warrant PPI continuation

Proton Pump Inhibitors and CKD

PPIs are one of the most common causes of acute interstitial nephritis and have been shown to have a greater risk of eGFR<60, doubling SCr, and AKI with longer duration of therapy compared to H2RAs

Review the EHR for previous AKI or PPI induced AKI before prescribing PPI therapy and monitor those who are on existing PPI therapy (SCr, urinalysis)

Because many PPIs are available without a prescription, it is vital to ask all patients with CKD or at risk for CKD if they are on OTC PPI therapy

Consider discontinuing PPI therapy if not clinically indicated or switching to an H2RA if possible

Hypertension Management in CKD

Hypertension

(Target SBP <120 mm Hg)

Preferred:

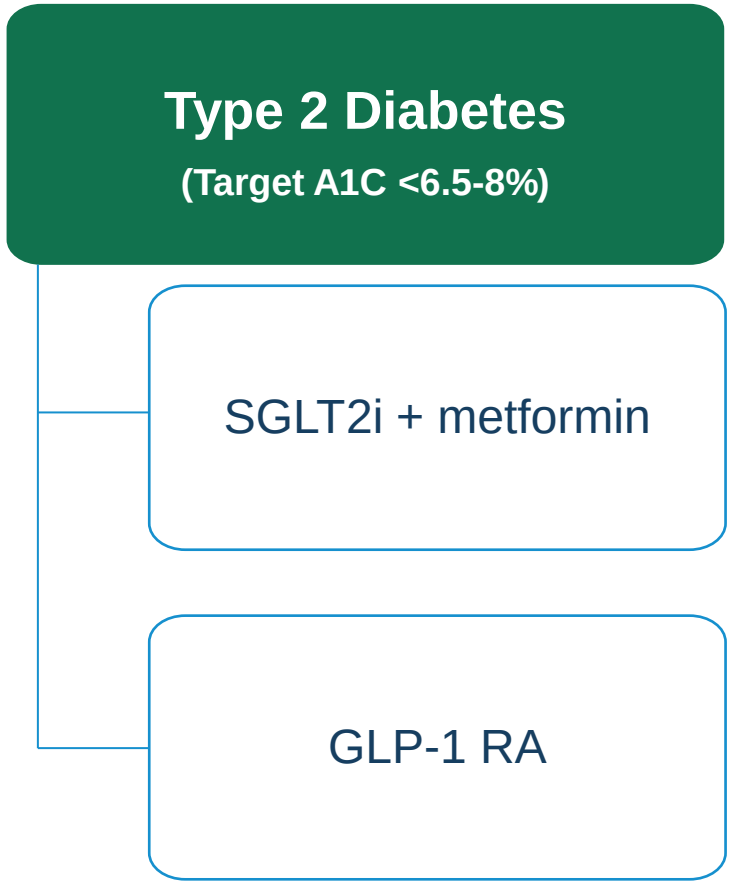
ACEi **or** ARB

CCB **and/or** thiazide-type diuretic

(loop diuretic if eGFR < 30)

- ACEi or ARB therapy is recommended in patients with CKD who have:
  - Severely increased albuminuria without diabetes (G1-G4, A3)
  - Moderately-to-severely increased albuminuria with diabetes (G1-G4, A2 and A3)
- ACEi or ARB therapy is suggested in patients with CKD who have moderately increased albuminuria without diabetes (G1-G4, A2)
- Use the highest approved ACEi **or** ARB dose that is tolerated
- Hyperkalemia often can be managed by measures to reduce serum potassium levels rather than decreasing the dose or stopping ACEi **or** ARB therapy
- Continue ACEi **or** ARB therapy unless SCr rises by more than 30% following initiation of treatment or an increase in dose
  - Blood pressure, SCr, and serum potassium should be checked within 2 weeks
- In trials that included participants with CKD, CV benefits have been most consistent with ACEi, ARBs, thiazide-like diuretics, and CCBs
- Non-dihydropyridine CCBs have additional benefit reducing proteinuria

Type 2 Diabetes (T2DM) Management in CKD



- First-line treatment for patients with CKD and T2DM should include metformin and an SGLT2i if eGFR ≥30
- The dose of metformin should be adjusted in patients with an eGFR <45
- Metformin should be discontinued in patients with an eGFR <30
- It is reasonable to continue an SGLT2i that has already been initiated if the eGFR falls below 30, unless it is not tolerated or until initiation of renal replacement therapy
  - Glucose-lowering effects of SGLT2i's are blunted with an eGFR <45, however, renal and cardiovascular benefits are still present
- In patients with CKD and T2DM who have not achieved glycemic targets despite use of metformin and SGLT2i therapy, or who are unable to use those medications, treatment with a GLP-1 RA is recommended

SGLT2 Inhibitors

- Canagliflozin
- Dapagliflozin
- Empagliflozin

- Patients with concurrent T2DM and CKD are at an increased risk of progression to kidney failure and cardiovascular events
  - In clinical trials SGLT2 inhibitors have demonstrated both renoprotective and cardioprotective effects in this patient population
- SGLT2i therapy has also been proven to be beneficial in patients with heart failure, regardless of T2DM diagnosis
  - Both dapagliflozin and empagliflozin have FDA approved indications to reduce the risk of CV death and hospitalization in adults with HFrEF
- **A transient decrease in eGFR may occur with initiation of SGLT2i treatment and is generally not an indication to discontinue therapy**
- It is reasonable to hold SGLT2i therapy during times of prolonged fasting, surgery, or critical medical illness in patients at risk for ketosis
- In patients at risk for hypovolemia, consider decreasing thiazide or loop diuretic dosages prior to initiating SGLT2i therapy
  - Counsel patients about symptoms of volume depletion and low blood pressure
  - Monitor volume status after SGLT2i initiation

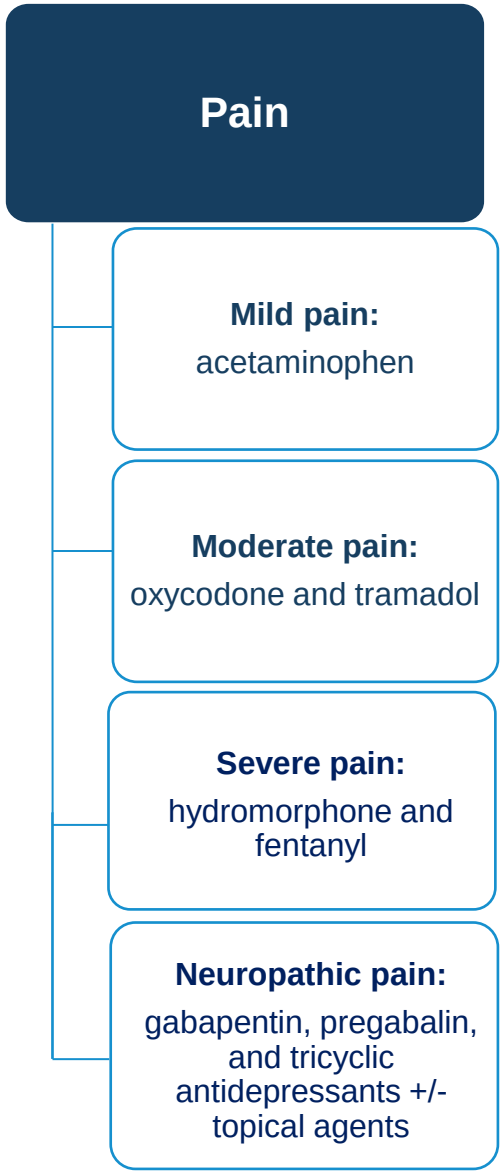
Cholesterol Management in CKD

Cholesterol-Lowering

Statin

- In adults ≥50 years of age with CKD, treatment with statin therapy is recommended, due to increased risk of future coronary events compared to those without CKD
- In adults 18-49 years of age with CKD, not treated with chronic dialysis or kidney transplantation, statin therapy is recommended in people with one or more of the following:
  - Coronary disease (myocardial infarction or coronary revascularization)
  - Diabetes mellitus
  - Prior ischemic stroke
  - Estimated 10-year incidence of coronary death or non-fatal myocardial infarction >10%
- Statin therapy should **not** be initiated in adults with dialysis-dependent CKD, however, patients receiving statin therapy at the time of dialysis initiation may continue statin treatment
- Reduced doses of statins are generally recommended for patients with CKD and an eGFR <60 (see Appendix for more details)
- Fibric acid derivatives are not recommended in patients with CKD

Pain Management in CKD



- Short-acting tramadol and oxycodone may be considered for mild pain not responsive to acetaminophen or pain rated as moderate
  - Renal dose adjustments required
- For severe pain, short-acting hydromorphone and long-acting fentanyl may be considered
  - Renal dose adjustments required
  - Transdermal fentanyl should not be prescribed to patients who are opioid naïve
- Methadone may be considered in patients with severe pain and CKD who are not opioid naïve, however, methadone requires referral to an experienced provider
- Serotonin and norepinephrine reuptake inhibitors, such as duloxetine and venlafaxine, may also be considered for neuropathic pain
  - While less effective than tricyclic antidepressants, they may be better tolerated due to less anticholinergic effects
  - Duloxetine should be avoided in patients with an eGFR <30
  - Venlafaxine requires renal dose adjustments
- The following medications should be **avoided** in patients with decreased kidney function:
  - Oral NSAIDs
  - Morphine
  - Codeine
  - Hydrocodone
  - Tramadol ER

Managing Hyperkalemia

- **Hyperkalemia** associated with ACEi or ARB therapy **can often be managed** by measures to reduce potassium levels, **rather than decreasing the dose or stopping ACEi or ARB therapy**
- Improvement in potassium control can lead to continued use of ACEi or ARB therapy in patients with a clinical indication
- Multiple measures, such as the ones listed below, can be taken to avoid discontinuation of ACEi or ARB therapy

Restrict dietary potassium and certain salt substitutes

Rule out pseudo-hyperkalemia and discontinue other medications that can induce hyperkalemia (e.g. aldosterone antagonists)

Add potassium-wasting diuretics and/or oral potassium binders

Oral Potassium Binders

- Patients on ACEi or ARB therapy who develop hyperkalemia can often be controlled with newer oral potassium binders, allowing for ACEi or ARB therapy to be continued at the recommended dose

Patiromer (Veltassa®)

- **Powder packets for oral administration**
  - Specific preparation instructions come with packets
  - Mix with water only
  - Packets should be refrigerated, but packets may be stored, as needed, at room temperature for up to 3 months
- **Recommended starting dose is 8.4 grams once daily**
  - May be titrated at weekly intervals of 1-week or longer by increments of 8.4 g/day up to a maximum of 25.2 g/day
    - Dose adjusted based on serum potassium and the desired target range
- **Administer other oral medications at least 3 hours before or after patiromer administration**
- **Common Adverse effects:**
  - Constipation (7.2%), hypomagnesemia (5.3%), diarrhea (4.8%), nausea (2.3%), abdominal discomfort (2%), and flatulence (2%)

Sodium zirconium cyclosilicate (Lokelma®)

- **Powder packets for oral administration**
  - Mixed with at least 3 tablespoons of water or more if desired
  - Mix with water only
  - Packets do not require refrigeration
- **Dosing for patients not on dialysis**
  - For initial treatment, 10 g three times a day up to 48 hours
  - For maintenance treatment, 10 g once daily
    - May be dose adjusted by increments of 5 g at weekly intervals of 1-week or longer based on serum potassium and the desired target range
    - The recommended maintenance dose range is from 5 g every other day to 15 g daily
- **Administer other oral medications at least 2 hours before or after sodium zirconium cyclosilicate administration**
- **Common adverse effects:**
  - Edema (5 g daily: 4.4%, 10 g daily: 5.9%, 15 g daily: 16.1%)

Oral potassium binders should not be used as an emergency treatment for life-threatening hyperkalemia

Appendix

The following contents are available to all Providers

- Kidney Smart
- Palliative Care Resources

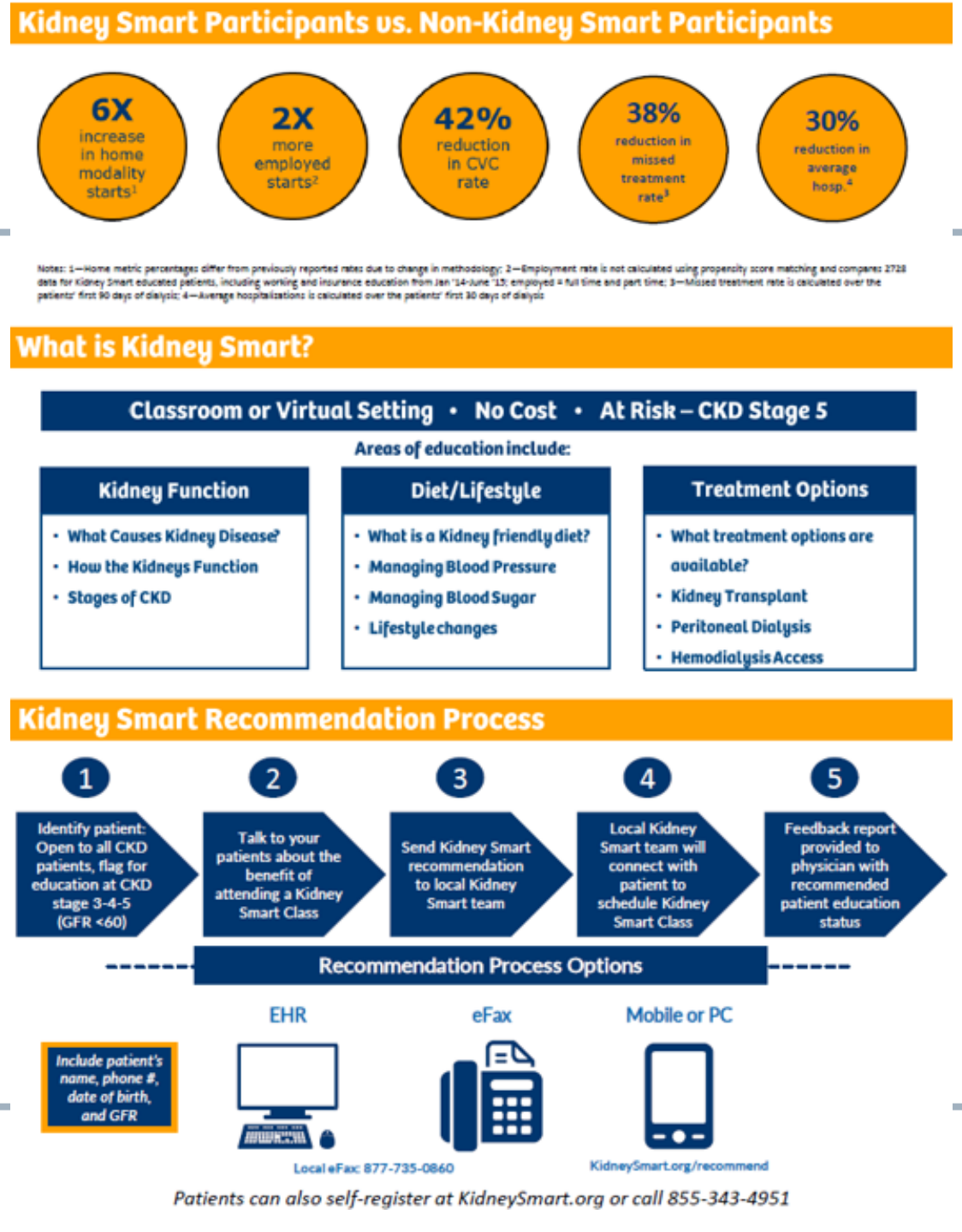
Kidney Smart

Kidney Smart is a non-branded CKD education class that anyone can sign up for and take for **free**

Participants will learn about:

- Causes of kidney disease
- CKD basics and lifestyle choices
- Basic diet and nutrition information
- Insurance and employment options
- Treatment options

A Kidney Smart 1-page flyer is to the right:



Palliative Care Resources

- What is Palliative Care? (www.getpalliativecare.org - with links to handouts for patients and families)
- General Palliative Care criteria - www.getpalliativecare.org/resources/clinicians/
- UCSF prognosis calculator - https://eprognosis.ucsf.edu/calculators/#/
- PA POLST - https://www.papolst.org/
- Center to Advance Palliative Care (CAPC) - https://www.capc.org/
- VITAL Talk – Clinician Communication - https://www.vitaltalk.org/
- Palliative Care Fast Facts - https://www.mypcnow.org/fast-facts/
- Advance Care Planning Billing Codes and Guide - https://respectingchoices.org/wp-content/uploads/2018/09/RC_5009_ACP_Billing_Resource_Guide_09.19.18.pdf

Statin Dosing

- KDIGO suggests that statin doses in people with an eGFR <60 be based on regimens and doses that have been shown to be beneficial in randomized trials done specifically in this population
- Patients with progressive renal dysfunction who are tolerating a current statin regimen do not necessarily need to be switched to a recommended regimen
- Dose modifications based on manufacturer recommendations may conflict with KDIGO recommendations

Statin	KDIGO Recommended Doses in Adults with CKD and eGFR <60 (G3a-G5)	Dose Modifications Based on Manufacturer Recommendations
Atorvastatin	20 mg/day	No dosage adjustment necessary
Fluvastatin	80 mg/day	No dosage adjustment necessary for mild to moderate renal impairment. Has not been studied at doses greater than 40 mg in patients with severe renal impairment, use with caution
Lovastatin	Not studied	CrCl <30: Dosage increases above 20 mg/day should be carefully considered
Pitavastatin	2 mg/day	CrCl <60:1-2 mg/day
Pravastatin	40 mg/day	In patients with significant renal impairment, a starting dose of 10 mg daily is recommended
Rosuvastatin	10 mg/day	CrCl <30: 5-10 mg/day
Simvastatin	40 mg/day	No dosage adjustment necessary for mild to moderate renal impairment. Caution should be exercised when initiated in patients with severe renal impairment, such patients should be started on 5 mg/day and closely monitored

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