Talking-points checklist

In order to provide the best possible medical care for you, your medical provider would like to improve your kidney health in addition to everything else. Listed below are the ten talking points for you and your provider put together by Arkansas state chronic kidney disease advisory committee.

What are my blood pressure goals?
Do I have protein in my urine?
If I have diabetes, what is my target HbA1c ?
What other complications could I have from kidney disease? Is there acid buildup?
When do I need to see a kidney doctor?
Did I get my age-appropriate vaccinations and cancer screening?*
What blood tests are needed to check my kidney function?
What are my diet goals? How much salt and protein can I eat?
If I smoke or use tobacco in any form how does that affect me?
Are my medications dosed correctly and am I on all the medications I should be on with kidney disease? What medications should I avoid? Are my medication lists updated?

*Getting vaccinations and cancer screening appropriate for your age are some of the easiest ways to ensure that you maintain long-term health.

CKD care checklist for Primary provider.

In order to provide the best possible medical care for a Chronic Kidney disease patient, the Arkansas Chronic Kidney Disease Advisory Committee developed key measures that can improve kidney health. The 10 steps for primary provider, listed below are to help in management of CKD patients. Rationale for these is given along with for your consideration.

Attain the blood pressure goal around 120/80. (In select patients with multiple medical conditions, a blood pressure tailored to the patient is best.)
Attaining proteinuria goal of <500 mg daily (RAAS: Renin Angiotensin Aldosterone System – blockade-: Ace Inhibitors, Angiotensin receptor blockers, (can also use non-dihydropyridine CCB Calcium channel blockers (Verapamil, Cardizem) MRA(mineralocorticoid receptor blockers)
Diabetes control to HbA1c of 7% (equivalent to an average blood glucose of 155 mg/dL) Consider SGLT2
Correction of metabolic acidosis to serum bicarb of about 22 (get a venous/arterial blood gas at least once prior to initiating therapy) in established CKD patients.
Referral to a nephrologist at CKD stage 3b (eGFR <45 mL/min/1.73m ²) or if proteinuria is >300mg daily, for co-managed care.
Age-appropriate vaccinations and cancer screening.
Have lab calculate eGFR for your patients and obtain a renal panel once a year.
Diet modifications for salt restriction 2gm daily, and based on kidney function by stage potassium and phosphorous restriction. In late stages of chronic kidney disease you consider protein restriction to 0.8 mg per kg per day.
Smoking cessation/tobacco advice and referral for management
Medication reconciliation for dose adjustment if needed based on kidney function and avoidance of medications such as NSAIDs that could cause further loss of kidney function and/or acute exacerbations of kidney injury. Include a statin if indicated. Consider SGLT2 inhibitor use early.

ICD 10 codes for Primary care

Chronic Kidney disease N18.1, CKD stage 1, • N18.2, CKD, stage 2 (mild), • N18.3, CKD, stage 3 (moderate), • N18.4, CKD, stage 4 (severe), • N18.5, CKD, stage 5, • N18.6, End-stage renal disease, • N18.9, CKD, unspecified
Hypertension: I12.9, BP >140/90 Hypertensive chronic kidney disease with stage 1 through 4 chronic kidney disease or unspecified chronic kidney disease. These two codes require an additional N18 code given above to identify the stage of kidney disease
Proteinuria R80.1 – persistent R80.8- DM type 2 with proteinuria R80.9-Protienuria,unspecified
Diabetic Nephropathy (DNP) E10.21- DM-type1 with DNP E11.22-DM-type 2 with DNP
Metabolic acidosis . E87.2 E87.8-Other disorders of electrolyte and fluid balance, not elsewhere classified
Referral- co-managed care: can put the appropriate CKD code, or N15.9
Vaccination and malignancy Vaccination schedule CDC guideline give in the next page Z 23 – encounter for vaccination (Procedure code required for the type of vaccination given) Z12.9- encounter for screening for malignant neoplasm, site unspecified
Anemia D 63.1-Anemia of chronic kidney disease D 50.9- Anemia -iron deficiency, unspecified
Dietary and exercise counselling Z 71.3- Dietary surveillance and counseling E66.9- Obesity -NOS Z 71.82- exercise counseling
Smoking cessation F 17.2- Nicotine dependence Z72.0- Tobacco use NOS Z 71.6- Tobacco abuse counseling
Medication reconciliation Z 76.89 -review of medications

CDC Guideline Vaccination Recommendations:

o https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html#notes

Over 350,000 adult Arkansans (15%) have Chronic Kidney Disease(CKD), but most are unaware. The majority are in CKD stage 3, and will die of cardiovascular ds before progressing to stage 4.

Research has shown that kidney function can improve at any stage of CKD with positive changes.

Working together we can improve the outcomes of CKD patients.

CKD	CKD stage 1	CKD stage 2	CKD stage 3	CKD stage 4	CKD stage 5-	CKD,
stage					Not on dialysis	unspecified
ICD code	N18.1	N18.2	N18.3	N18.4	N18.5	N18.9

			Persistent albuminuria categories Description and range			
	Guide to frequency of monitoring (number of times per year) by GFR and albuminuria category			A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
²)	G1	Normal or high	≥90	1 if CKD	1	2
- 1.73 m ge	G2	Mildly decreased	60-89	1 if CKD	1	2
GFR categories (ml/min per 1.73 m ²) Description and range	G3a	Mildly to moderately decreased	45-59	1	2	3
ries (ml cription	G3b	Moderately to severely decreased	30-44	2	3	3
catego Desc	G4	Severely decreased	15-29	3	3	4+
GFR	G5	Kidney failure	<15	4+	4+	4+

GFR and albuminuria grid to reflect the risk of progression by intensity of coloring (green, yellow, orange, red, deep red). The numbers in the boxes are a guide to the frequency of monitoring (number of times per year).

Additional Information Regarding the CKD Checklist for providers.

Thank you for joining the effort to improve chronic kidney disease care. We appreciate your ongoing collaboration with nephrologists and we believe that with even better coordination, our state can achieve some of the best renal outcomes in the country. Below are the rationales for the ten interventions which we believe will have the largest impact on the renal health of your patients. The information below is designed to outline the supporting data which formed the recommendations.

Attain the blood pressure goal of around 120/80 -130/90 mmHg.

Controlling blood pressure to SBP <120 mmHg (referred to subsequently as intensive BP targets) as compared to <140/90 mmHg in patients with CKD provide two major benefits. This target reduces the risk of ESRD. This target reduces mortality whether or not the patient has proteinuria. These benefits are most evident on long-term follow up of patients.

There are three trials that inform this area – the MDRD study (1994), the AASK trial (2002), and the SPRINT trial (2015). The **MDRD** study showed that patients excreting more than 1 gram of protein daily had lower rates of CKD progression with an intensive BP target. Long-term follow up of MDRD participants echoed this finding. The original **AASK** trial showed no benefits to preservation of renal function in the original trial. On long term follow up of AASK trial participants, however, intensive BP targets slowed progression of CKD. The MDRD study and AASK trial show that long-term follow up is vital to seeing the benefit of intensive BP goals.

The **SPRINT** trial showed that aggressive BP targets reduce mortality regardless of the presence of proteinuria. No benefit was seen for preservation of renal function. Importantly, the risk of a 30% or greater decline in renal function was higher with intensive BP targets. This finding was recently examined in more detail in a study utilizing urinary proteomic biomarkers of kidney injury. It suggested that this 30% or greater decline of renal function in the intensive BP arm of the SPRINT trial was not due to actual damage of the renal parenchyma, but is instead attributable to hemodynamic effects of a lower BP. Thus, targeting an intensive BP target to lower mortality is reasonable.

In the most recent guidelines for management of hypertension in CKD (KDIGO 2021 Clinical Practice Guideline for Management of Blood Pressure in Chronic Kidney Disease) now recommended to use standardized office blood pressure readings rather than routine blood pressure readings. Standardized blood pressure readings refer to the protocol for blood pressure measurement rather than the device used to measure the blood pressure. Standardized blood pressure measurement can be performed with an oscillometric blood pressure cuff or manual blood pressure device. If standardized blood pressure measurement is performed, target a SBP of <120 as standardized readings are generally lower than routine office BP measurement. The large blood pressure trials used standardized measurements and therefore routine use of these measurements allows for better extrapolation of trial results to clinical care.

If a patient makes more than 30mg/day proteinuria, maximize ACE or ARB dosing to achieve a blood pressure <120 SBP

In addition to being a marker of kidney damage, proteinuria causes a slow inflammatory process in the kidney which leads to progressive real fibrosis and falling GFR. It is a fact that the degree of proteinuria is the best prognostic factor for future renal function. Targeting a certain reduction in proteinuria leads to future renal benefits is a point of contention in the nephrology community. In fact, it is falling out of favor. We know that ACE and ARB medications reduce proteinuria and area associated with renal benefits in those with proteinuria. What we do not know is that if this effect is due to a mechanism separate from proteinuria reduction. We are essentially at a point similar to the change in hyperlipidemia management where a proper dose of medication is prescribed based on the risk of the patient. We recommend that if a patient has any degree of proteinuria, Version 3 Grant #260118_Singh 6/29/2022 5

maximizing the dose of an ACE or an ARB to should take place (prior to addition of an additional medication) towards achievement of a goal BP of <120/90 mmHg. ACE and ARB medications work equally well, but an ACE and ARB should not be used simultaneously in a single patient.

If the patient has diabetes, target a HbA1c of 7.0%.

Achieving a HbA1c of 7.0% (referred to as an intensive target) has consistently been shown to provide large benefits in the CKD population and is one of the highest yield interventions for a patient. There have been multiple, high-quality studies on this. The **DCCT** and associated **EDIC** trials showed that on long-term follow up, this HbA1c goal resulted in a 50% risk reduction for development of an abnormal eGFR in patients with previous normal eGFR. The UKPDS study showed that an intensive target reduces diabetes-related death, allcause mortality, and the risk of diabetes-related complications (sudden death, death from hyperglycemia or hypoglycemia, myocardial infarction, angina, heart failure, stroke, renal failure, amputation, vitreous hemorrhage, retinal photocoagulation, blondness in one eye, or cataract extraction). The VA CSDM trial showed that this HbA1c target retards progression of microalbuminuria over a two-year period. The ADVANCE trial showed reductions in microvascular events with an intensive target. Lower HbA1c targets of <6% as compared to standard control with HbA1c of 7.0-7.9% increased mortality in the ACCORD trial, but did reduce the development of proteinuria. The ACCORD trial shows the dangers of blood glucose control that is too agaressive. but does add evidence to the general effect of reduced blood glucose on proteinuria development. Lastly, among the findings of the VADT trial were a reduction of albuminuria with intensive blood glucose targets. In summary, a multitude of trials show that there are renal benefits to a blood glucose control of a HbA1c of <7%.

If serum bicarbonate level is consistently below normal, check ABG or VBG and then correct this with sodium bicarbonate tablets to a serum bicarbonate level of 23 mmol/L.

Development of a non-anion gap metabolic acidosis in patients with chronic kidney disease is more prevalent in those with an eGFR <45 mL/min/1.73m². This occurs due to an increased loss of bicarbonate in the urine, increased production of non-volatile acids, and decreased renal excretion of acid due to nephron loss. The kidneys respond to this through increased ammonium excretion which causes tubulointerstitial inflammation and damage to the kidney over time. The result of this acidosis leads to decreased renal function. Secondly, as bones and amino acids serve as buffers for acidosis, ongoing acidosis leads osteoporosis and loss of muscle mass. Giving sodium bicarbonate to patients with consistent acidosis resolves these issues. In one study, patients with CKD4 with serum bicarb levels 16-20 mmol/L treated with sodium bicarbonate to achieve a sodium bicarbonate level of 23 mmol/L had a lower rate of renal decline (-1.88 versus -5.93 mL/min/1.73 m2 per year) and a lower risk of ESRD (6.5% vs 33%) at 2 years follow up. The differential diagnosis of a low serum bicarbonate is metabolic acidosis or respiratory alkalosis. Before sodium bicarbonate is given, it is important to get an ABG to ensure that the low serum bicarbonate is due to metabolic acidosis.

Referral to a nephrologist at CKD stage 3b (eGFR <45 mL/min/1.73m²) or if proteinuria is >300mg daily with any stage of CKD.

Those with an eGFR < 45 mL/min/1.73m² or those with more than 300mg/day proteinuria are at a high risk for further reductions in kidney function. Management of CKD until the eGFR is <45 mL/min/1.73m² typically only requires the measures noted on this checklist, however other issues typically arise when the eGFR is lower. Anemia is more likely to arise and we begin to provide more focused education on CKD. Patients with more than 300mg/day albuminuria are at a high risk of progression of CKD and may require further testing or management. We would enjoy taking a part in the patients care at this stage of CKD.

Administer age-appropriate vaccinations and cancer screening.

We also encourage these measures and note the utility of the USPSTF AHRQ ePSS smartphone app or web app. (https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html)

Ensure that your laboratory or medical provider calculates your estimated glomerular filtration rate (eGFR). Obtain a renal panel and complete blood count with iron panel once a year.

The eGFR is the best way to follow renal function in stable CKD patients over time. There are several GFR estimating equations currently available. The currently recommended equation is the CKD-EPI equation. It Version 3 Grant #260118_Singh 6/29/2022

gives the most accurate estimation of true GFR and this is the eGFR equation used by most large laboratories. The predecessor to the CKD-EPI equation was the MDRD equation which also gives a reasonable estimate of the GFR. We are making a concerted effort for Arkansan CKD patients to know their "kidney number" which is their eGFR. Ensuring that the patients know this lab on each visit provides very important information to the patient. Checking a CBC yearly and iron panel, if indicated, is recommended.

Dietary modification: Reduce salt intake to 2300mg daily. Reduce protein intake to <0.8 mg/kg/day if you have an eGFR <30 mL/min/1.73m² or if you have diabetes with any degree of CKD.

Reducing sodium intake to 2300mg/day helps lower blood pressure, improves the effectiveness of ACE and ARB medications, and reduces proteinuria. Excessive protein intake is thought to cause renal damage as it transiently increases GFR, leading to hyperfiltration which can lead to glomerular damage. The Modification of Diet in Renal Disease (MDRD) study showed a small benefit in reductions in protein intake for preservation in renal function. Although the data supporting a reduction in protein is nowhere near as robust as that for blood pressure and glucose management, reducing protein intake to 0.8 grams/kg body mass is a recommendation by governing bodies in nephrology and is one which is followed by nephrologists.

Address smoking and use of other tobacco products.

Tobacco smoking damage the kidneys in addition to its other well-known effects. We appreciate your efforts for improving patient's health in this regard.

Adjust medications for renal function. Avoid non-steroidal anti-inflammatory drugs (NSAIDs). Start taking a statin if indicated. Consider SGLT2 inhibitor use early.

In patients with CKD, NSAIDs worsen renal function, with the exception of daily aspirin (81mg or 325mg daily). In patients without CKD, the data does not support the idea that NSAIDs cause CKD. The combination of volume depletion and heavy NSAID use is the main situation during which we see AKI in those with previously normal renal function. Statin or a combination statin/ezetamibe medication use is recommended for CKD patients that are older than 50 years old or who are <50yo with CKD with DM, CAD, stroke, or 10yr cardiovascular risk of >10%. The SHARP trial showed that patients with CKD similar to these above reduced their risk of major atherosclerotic events by 17% through use of these medications.

Consider starting an SGLT2 inhibitor

SGLT2 inhibitors are medications that have gained increased attention over the past few years. Initially trialed as antihyperglycemic agents, they were found to have more robust effects for improved renal and cardiovascular outcomes. Multiple randomized controlled trials have shown renoprotective effects for SGLT2 inhibitors. EMPA-REG showed a reduced risk of doubling of creatinine with empagliflozin. The CANVAS trial showed a reduced risk of sustained major kidney outcomes with canagliflozin. The CREEDENCE Trial showed a 34% lower risk of the primary outcome of end-stage kidney disease, a doubling of creatinine, or death from renal or cardiovascular outcomes. EMPA-REG, CANVAS, and CREEDENCE were all done in patients with diabetes mellitus and showed cardiovascular benefits and the renal benefits mentioned above. More recently though, the DAPA-CKD Trial included patients with proteinuric CKD (with and without diabetes) and showed roughly a 50% reduction in the primary composite outcome of a sustained decline in GFR by 50%, end-stage kidney disease, or death from renal or cardiovascular causes. Additionally, it showed around a 30% reduction in a composite outcome of death from cardiovascular causes or hospitalization for heart failure. Taken as a whole, SGLT2 inhibitors reduce CKD progression with proteinuric CKD in patients with or without diabetes. The SGLT2 inhibitors have been associated with an increased risk for genitourinary infection, Fournier's gangrene, DKA, and amputations, and fractures. In addition, SGLT2 inhibitors can cause hypotension and can cause AKI, especially when combined with diuretics. These risks should be discussed with patients and proper vigilance undertaken to assess for these adverse effects.