Rules Document for Chronic Kidney Disease Management in VISN 21

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# Summary

This document describes the contents – the “encoding” – of the Protégé Chronic Kidney Disease (CKD) Management Knowledge Base (KB); that is, the patient characteristics, including diagnoses, conditions, laboratory values, and medications, that are used to evaluate each patient for management of CKD.

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# Overview

## Background

The CKD Management Protégé KB captures recommendations from the “VA/DoD Clinical Practice Guideline for the Management of Chronic Kidney Disease in Primary Care” (Version 3.0, 2014), a document jointly published by the U.S. Department of Veterans Affairs (VA) and the U.S. Department of Defense (DoD). These guidelines are to provide information and assist decision making, and they are not intended to define a standard of care.

This document has been created for the MedSafe Quality Enhancement Research Initiative (QUERI) Clinical Decision Support (CDS) project. The MedSafe CDS project is one of 3 projects in the VA Health Services Research and Development (HSR&D) MedSafe QUERI with Principal Investigators Paul Heidenreich, M.D. and Mary Goldstein, M.D.

Authors and contributors for this document are as listed on the title page. The project’s Principal Investigator is Mary Goldstein, M.D.

The CKD Management KB was created to encode the clinical knowledge for a CDS system intended to provide recommendations for routine CKD care to VA primary care professionals who are caring for patients with an estimated glomerular filtration rate (eGFR) from 30-59 mL/min/1.73m2 (see below for elaboration). These patients will be identified via the VISN 21 Pharmacy Benefits Management (PBM) Clinical Dashboard, a panel management tool. The VISN 21 Clinical Dashboard for patient aligned care team (PACT) teams draws on VA structured data to identify patients who are not meeting Healthcare Effectiveness Data and Information Set (HEDIS) performance measures for specific chronic diseases. The Clinical Dashboard displays the data used to determine whether or not the patient is meeting these measures. In the MedSafe QUERI project, we are linking the CDS system to the Clinical Dashboard to provide recommendations for patients who are not meeting their performance measures. Given the lack of HEDIS measures for CKD, these recommendations will be triggered by the HEDIS measures for hypertension initially, with possible expansion to HEDIS measures for diabetes mellitus. Patients who fail the performance measure for poor blood pressure control will be identified by the Clinical Dashboard and will be the starting set of patients who *could* receive CDS recommendations. Therefore, the CDS does not provide recommendations regarding care management for CKD when patients are already meeting measures for hypertension. The recommendations will be integrated with the VISN 21 Clinical Dashboard. A brief description of the Clinical Dashboard can be found in references (3) and (4) in [References](#_References) section.

The KB is only one part of an overall architecture for the CDS that also includes processes for extracting and preparing patient data, an execution engine (also known as a “guideline interpreter”) to process the patient data against the KB, generation of recommendations from the execution engine, and presentation of the recommendations in a user interface on the Clinical Dashboard. The overall structure follows the EON Model, a component-based approach to automation of protocol-directed therapy.

This Rules Document specifies the expected behavior of the CDS. It defines the clinical knowledge about CKD that is included in the CDS. This document is akin to the Requirements Document of Software Development. Unlike the Software Requirements Document, however, the Rules Document may change at any time before or after the deployment of the KB. Of note, this description of the behavior is specific to the CKD KB, and the behavior, including the terms and definitions, may not be exactly the same as in other disease KBs.

## Use of the Rules Document

The primary way to test the encoding of knowledge bases is to compare their output to the recommendations from a Domain Expert (DE) for real, de-identified patients. We refer to this process as “offline testing.” This Rules Document was created, in part, for this reason.

This Rules Document is a record of what clinical knowledge is – or what should have been – encoded in the KB. This document is used by the DE when offline testing in two ways:

* + 1. To provide recommendations consistent with the Rules Document. A comparison of the DE recommendations with the output of the CDS will verify that what was intended to be encoded has been encoded (recognizing that CDS output is determined not only by the KB encoding but also by patient data entered to the system, the execution engine, and the output display).
    2. To identify gaps in or extensions to the KB that become clear in the context of real patients.



# Eligibility, Exclusions, Scope, and Caveats



Here we identify criteria for inclusion and exclusion, as well as detail certain caveats for use of the CKD CDS. We will include messages displayed in their appropriate sections.

* 1. Eligibility and Exclusions

Eligible patients are those who *could* receive recommendations. They are defined as patients who meet all of the following criteria:

* + 1. Age ≥ 18 and ≤ 80
    2. Do NOT have a kidney transplant
    3. Are NOT undergoing hemodialysis or peritoneal dialysis
    4. Are NOT pregnant or planning to become pregnant
    5. Have urine albumin-to-creatinine ratio (UACR) < 600 mg/g or urine protein-to-creatinine-ratio (UPCR) < 1000 mg/g, or missing values in the past two years.
    6. Have an eGFR < 60 mL/min;

OR have a diagnosis of CKD stage 3;

OR have a diagnosis of hypertension, diabetes mellitus (type I or II), or ischemic heart disease (IHD; also referred to as coronary artery disease [CAD])

* + 1. Do NOT have a diagnosis of polycystic kidney disease (PCKD), congestive heart failure (CHF) or chronic liver disease (CLD) / cirrhosis.

This document is not intended to provide recommendations for care for more complex situations such as acute kidney injury, nephrotic syndrome, nephritic syndrome, PCKD, kidney transplant referral or aftercare, renal replacement therapy (dialysis), CKD in pregnancy, or CKD in patients with CHF and CLD. However, this information cannot reliably be algorithmically captured from VA electronic patient records. If these situations can be identified, the patients will not receive recommendations. Otherwise, the following messages will be displayed in the corresponding situations:

**Scenario: Patients *with* an out-of-scope condition**

**Action:** Display the following messages

**Message:** “*WARNING: This patient has a condition that is out of the scope of this system, and reliable recommendations cannot be provided. The following conditions preclude recommendation:*

* *Acute kidney injury*
* *Nephrotic/nephritic syndrome*
* *Kidney transplant recipients*
* *Congestive heart failure*
* *Chronic Liver Disease*
* *Dependence on dialysis (present or historical)”*

**Scenario: All patients *without* an out-of-scope condition**

**Action:** Display the following messages

**Message:** “*WARNING: This system cannot reliably process information regarding certain situations relevant to kidney disease care. The following recommendations should not be applied to patients with concerns for acute kidney injury or nephrotic/nephritic syndrome, patients who have undergone kidney transplantation, patients who are currently undergoing dialysis, or patients with congestive heart failure or cirrhosis/chronic liver disease.*”

**Scenario: Female patients, age 18-50 years, *without* an out-of-scope condition**

**Action:** Display the following message

**Message:** “*WARNING: These recommendations do not apply to woman who are currently or planning to become pregnant.*”

These messages are displayed first. Conditions that evaluate to “out-of-scope” for these messages include *only* those listed in 2.1.1 thru 2.1.6. There are further conditions that preclude recommendations listed in subsequent sections, but the messages in Section 2.1 will still be displayed in those situations. For example, if 2.1.1-2.1.6 evaluate to in-scope, but 2.2.1 evaluates to out-of-scope, the messages above will still be displayed.

* 1. Scope of Recommendations

This document is meant to guide routine chronic kidney disease ***outpatient*** care. The guidance is meant for primary care physicians. The target patient population is meant to be patients who suffer from CKD due to hypertension and/or diabetes. As such, attempts will be made to exclude patients who do not meet the eligibility criteria listed in “Eligibility and Exclusions,” with messages noting the system’s limitations. This system is primarily meant to focus on patients with CKD Stages 3a and 3b (CKD3a and CKD3b, collectively referred to as CKD3). In certain situations (specifically identifiable CKD1 or CKD2 in patients with diabetes), recommendations will be made with caveats.

However, therapeutic recommendations will still not be provided for some patients who meet the above eligibility criteria. Situations where full recommendations cannot be applied include:

* + 1. Latest eGFR more than 380 days old
    2. The latest eGFR is ≥ 60 mL/min and both the latest urine albumin measurement is < 30 mg/day (or < 30 mg/g Cr) AND the latest urine protein measurement is < 200 mg/day (or < 200 mg/g Cr)
    3. The latest measurement of urine albumin is ≥ 600 mg/day (or ≥ 600 mg/g Cr) OR the latest measurement of urine protein is ≥ 1000 mg/day (or ≥1000 mg/g Cr)

**Scenario: Latest eGFR is more than 380 days old**

**Action:** Display the following message, DO NOT proceed with further recommendations.

**Message:** “*The latest creatinine and eGFR measured are more than 380 days old, so the patient cannot be evaluated fully for recommendations. Recommend checking creatinine as part of the basic metabolic panel yearly.*”

**Scenario: The latest value of urine protein and urine albumin are more than 380 days old, there is a diagnosis of CKD stage 3 *without* a diagnosis of diabetes mellitus**

**Note:** This message specifically identifies labs “urine protein-to-creatinine ratio” and “urine albumin-to-creatinine ratio” (the second is also referred to as “urine microalbumin-to-creatinine ratio”)

**Action:** Display the following message. Proceed with further recommendations.

**Message:** “*Urine albumin-to-creatinine ratio has not been checked in the past year. Recommend screening for albuminuria periodically in CKD Stage 3.*”

**Scenario: The latest value of urine protein and urine albumin are more than 380 days old, and the patient has a diagnosis of diabetes mellitus (type I or II), with or without a diagnosis of CKD stage 3**

**Note:** This message specifically identifies labs “urine protein-to-creatinine ratio” and “urine albumin-to-creatinine ratio” (the second is also referred to as “urine microalbumin-to-creatinine ratio”). Compared to the previous message, regular urine albumin monitoring is more supported by studies.

**Action:** Display the following message. Proceed with further recommendations.

**Message:** “*Urine albumin-to-creatinine ratio has not been checked in the past year. Recommend screening for albuminuria yearly in patients with diabetes.*

**Scenario: The latest value of eGFR is > 60 mL/min AND (the latest value of urine protein is ≥ 1000 mg/day (or ≥ 1000 mg/g Cr), OR the latest value of urine albumin is ≥ 600 mg/day (or ≥ 600 mg/g Cr)), AND the abnormal (UPCR or UACR) measurement is ≤ 380 days old.**

**Note:** This message specifically identifies labs “urine protein-to-creatinine ratio” and “urine albumin-to-creatinine ratio” (the second is also referred to as “urine microalbumin-to-creatinine ratio”). Compared to the previous message, regular urine albumin monitoring is more supported by studies.

**Action:** Display the following message, DO NOT proceed with further recommendations.

**Message:** “*The latest measurement of urine protein and/or albumin indicates a level of proteinuria that is beyond the scope of this system and may warrant extra care. Recommend referral to Nephrology if within the patients’ goals of care.*”

**Scenario: The latest measurement of eGFR is above 59 mL/min, (the latest value of urine protein is ≥ 200 mg/day [or ≥ 200 mg/g Cr], OR and the latest measurement of urine albumin is ≥ 30 mg/day [or ≥ 30 mg/g Cr]), and the abnormal measurement is ≤ 380 days old**

**Note:** This message specifically identifies labs “urine protein-to-creatinine ratio” and “urine albumin-to-creatinine ratio” (the second is also referred to as “urine microalbumin-to-creatinine ratio”). Compared to the previous message, regular urine albumin monitoring is more supported by studies.

**Action:** Display the following message, DO NOT proceed with further recommendations.

**Message:** “*The latest measurement of eGFR is above 59 mL/min, and the latest urine protein and/or albumin is elevated. This may occur in patients with diabetes who are developing nephropathy, patients with hypertensive nephropathy, or in more complex kidney disease. This work-up is beyond the scope of this system.*”

Due to the complexity of care, instructions to refer patients to a Nephrologist will be displayed in situations that may require elevation of care for diagnosis and management of CKD4, CKD5, and, in most cases, CKD1 and CKD2. There are likely situations where referral to a nephrologist is necessary that were not foreseen by the authors of this document. A high index of suspicion for severe or rapidly progressing disease must be maintained by the primary care physician.

Given its often urgent nature and laboratory situations causing inaccurately high levels, potassium management is not in the scope of this document. However, certain recommendations may be made with reference to potassium lab values.

## 2.3 Caveats

There may be alternative causes of elevated creatinine that are NOT the result of decreased glomerular filtration rate (GFR): drugs, large muscle mass, and certain diseases. These are not within the scope of this system. Alternatively, a patient may have inappropriately normal creatinine despite decreased GFR due to low muscle mass, extremity amputation, malnutrition, or older age. This system cannot distinguish those cases and may not give appropriate recommendations.

[There are other causes of proteinuria: fever, infection, exercise, heart failure, nonspecific joint inflammation, poor glycemic control, A1c > 8, BP > 160/100, LDL > 120](https://www.uptodate.com/contents/moderately-increased-albuminuria-microalbuminuria-and-cardiovascular-disease?topicRef=3101&source=see_link#H2) (see section labeled “Detection”). These causes are variable and sometimes difficult to capture, and they will not be included in the system.

Additionally, many kidney function laboratory tests fluctuate in acute illnesses that require hospitalization. These fluctuations are often not indicative of long-term disease. However, we may not be able to determine in-hospital vs outpatient laboratory values easily, and the CDS system will therefore use the latest measurements available.

# Possible Future Changes

1. Addition of drug dosing recommendations
2. Albumin-based CKD classification

# Data Required

**ALL MUST BE OUTPATIENT UNLESS OTHERWISE STATED**

* Chem-8: Sodium, potassium, chloride, serum bicarbonate/total CO2, BUN, creatinine, serum glucose
* Glomerular filtration rate (calculated)
* Serum Calcium, Magnesium, Phosphorus, Albumin, PTH, total protein
* Urine: Albumin (“microalbumin”), protein, and their ratios to urine creatinine.
* Urinalysis: Dipstick protein (1+, 2+, 3+, 4+?).
* Future possibilities: Urine specific gravity, granular casts, RBC casts, dysmorphic red cells?

# Algorithms

To be included in the following scenarios, the patient must meet the criteria for inclusion and NOT meet criteria for exclusion listed in Sections 2.1 and 2.2. Scenarios are listed as situations with a title relevant to the main parameter being evaluated, though at times there is crossover.

### 5.1 Evaluating CKD Stage

KDIGO defines CKD as abnormalities of kidney structure or function present for ≥ 3 months (here, using 90+ days). This Rules Document is intended to encompass care of CKD Stage 3a and 3b, with recommendations to refer to specialist care for other CKD Stages as appropriate. CKD Stage 3a includes patients with eGFR 45-59 mL/min, and Stage 3b includes patients with eGFR 30-44 mL/min.

**Notes:**

As a shorthand, ranges of the form “X-Y mL/min” (i.e., 30-59 mL/min) is meant to be “greater than or equal to X and less than Y + 1.” So, “30-59 mL/min” means “greater than or equal to 30 and less than 60.”

Picked 380 days to allow for the fact that some patients have scheduled yearly labs, and the labs may not be done exactly at one year – using a cutoff of 365 days could miss a significant number of patients.

**Scenario: Latest eGFR > 380 days old and the patient has a diagnosis of DM, HTN, or CKD.**

**Action:** Display the following message –

**Message:** “*Recommend checking creatinine as part of the basic metabolic panel yearly.”*

**Scenario: Latest eGFR < 60 mL/min, regardless of other lab values**

- The latest qualifying eGFR may be more than 1 year old

**Action:** Display the following message –

**Message:** “*Recommend counseling on reducing or eliminating NSAIDs such as ibuprofen (Advil, Motrin), naproxen (Naprosyn, Aleve), and celecoxib (Celebrex).”*

**Scenario: Latest eGFR 30-59 mL/min ≤ 380 days old, no other eGFR values available occurring 90+ days prior to the latest that are < 60 mL/min**

**Action:** Display the following message –

**Message:** “*This patient’s eGFR is in the range of CKD Stage 3, but there are no other recent labs available. Recommend repeating creatinine/eGFR measurement 90+ days after the latest measurement to confirm the diagnosis. Repeat sooner if concerned for acute kidney injury.*”

**Scenario: Latest eGFR 30-59 mL/min ≤ 380 days old, second latest eGFR ≥ 60 mL/min**

**Action:** Display the following message –

**Message:** “*This patient has a single eGFR reading in the range of CKD Stage 3, but previous measurements show higher kidney function. Recommend repeating creatinine/eGFR measurement 90+ days after the last measurement to confirm the diagnosis. Repeat sooner if concerned for acute kidney injury. Assess patient for volume depletion.*”

**Scenario: Latest eGFR 30-59 mL/min ≤ 380 days old, second latest eGFR < 30 mL/min**

**Action:** Display the following message –

**Message:** “*This patient has a single eGFR reading in the range of CKD Stage 3, but a previous measurement suggests a more advanced stage of CKD. Recommend assessing eGFR trend. If within goals of care, patients with eGFRs persistently below 30 mL/min should be seen by Nephrology.*”

**Scenario: Latest eGFR 45-59 mL/min ≤ 380 days old, and the most recent eGFR that is 90+ days older than the latest eGFR is 30-59 mL/min.** **The second latest eGFR is between 30-59 mL/min.**

**Action:** Display the following message –

**Message:** “*This patient meets criteria for CKD Stage 3a.”*

**Scenario: Latest eGFR 30-44 mL/min ≤ 380 days old, and the most recent eGFR that is 90+ days older than the latest eGFR is 30-59 mL/min. The second latest eGFR is between 30-59 mL/min. There has been a measurement of urine protein-to-creatinine ratio or urine albumin-to-creatinine ratio in the past 750 days.**

**Action:** Display the following message –

**Message:** “*This patient meets criteria for CKD Stage 3b.”*

**Scenario: Latest eGFR 30-59 mL/min ≤ 380 days old, and the most recent eGFR that is 90+ days older than the latest eGFR is 30-59 mL/min. The second latest eGFR is between 30-59 mL/min. No urine protein measurement in the past 750 days**

**Action:** Display the following message and make the following recommendation –

**Rec:** “*Check urine albumin-to-creatinine ratio (UACR) periodically. This patient has not had UACR checked in the past 2 years and is not on an ACE inhibitor or angiotensin receptor blocker. These medications are indicated for the treatment of hypertension in patients with CKD Stage 3 and UACR >= 30 mg/g.*”

**Scenario: Latest eGFR 30-44 mL/min ≤ 200 days old, the most recent eGFR that is 350 - 750 days older than latest eGFR is > 5 mL/min higher. The rate of decline of eGFR is > 5 mL/min/year from that previous eGFR to the latest.**

**Action:** Display the following message –

**Message:** “*This patient may have rapid progression of CKD, defined as a loss of eGFR of* ≥*5 mL/min/year. If the cause of this progression is not known, and it is within the patient’s goals of care, this patient may benefit from referral to Nephrology. Recommend checking urine protein-to-creatinine ratio (UPCR).*”

### 5.2 Evaluating proteinuria / albuminuria

Patients can be classified as having CKD by measurements of urine protein or urine albumin that persist for more than 3 months. This functionality will not be included at this time, but it may be added in the future. Patients with CKD should have UACR assessed yearly (KDIGO 2012 CKD guideline, “Not Graded”).

**Scenario: Latest eGFR 30-59 mL/min ≤ 380 days old, and the most recent eGFR that is 90+ days older than the latest eGFR is also within 30-59 mL/min. The second latest eGFR is between 30-59 mL/min. There is a urine protein-to-creatinine ratio > 150 mg protein/g of creatinine or a urine albumin-to-creatinine ratio > 30 mg albumin/g of creatinine in the past year. The patient is NOT prescribed an ACE-inhibitor or ARB. The patient’s latest systolic BP > 140 mmHg OR latest diastolic BP > 80 mmHg OR there is a diagnosis of HTN.**

- Patients with elevated proteinuria, as defined in Section 2.1, are already excluded from the CDS

**Action:** Display the following message –

**Message:** “*This patient has lab values consistent with proteinuria, defined as a urine protein-to-creatinine ratio > 200 mg protein/gram of creatinine or a urine albumin-to-creatinine ratio > 30 mg albumin/gram of creatinine. Patients with proteinuria benefit from use of ACE inhibitors (e.g lisinopril) and ARBs (e.g losartan) when balanced against the risk of hyperkalemia. Consider assessing alternative causes of proteinuria. Consider checking urine albumin-to-creatinine ratio yearly.”*

**Scenario: Latest eGFR 30-59 mL/min ≤ 380 days old, and the most recent eGFR that is 90+ days older than the latest eGFR is 30-59 mL/min. The second latest eGFR is between 30-59 mL/min. No urine protein/albumin measurement in the past 380 days, ON an ACE-inhibitor or ARB**

**Action:** Display the following message –

**Message:** “*If blood pressure and serum potassium allow, recommend maximizing dose of either an ACE-inhibitor/ARB. The maximum dose of lisinopril is 40 mg daily, and the maximum dose of losartan is 100mg daily. Consider checking UACR yearly to assess for progression of CKD.*”

See also Sections 2.1 and 5.1

### 5.3 Evaluation and treatment of metabolic acidosis

**Scenario: Latest eGFR 30-59 mL/min ≤ 380 days old, and the most recent eGFR that is 90+ days older than the latest eGFR is also within 30-59 mL/min. The second latest eGFR is between 30-59 mL/min. The patient’s serum bicarbonate (typically reported as Total CO2) is < 22 mEq/L.**

- Patients with elevated proteinuria, as defined in Section 2.1, are already excluded from the CDS

**Action:** Display the following message –

**Message:** “*This patient has lab values consistent with metabolic acidosis. Among other causes, this may be due to CKD. If the metabolic acidosis persists without another cause, treatment with sodium bicarbonate can be considered. The typical starting dose is sodium bicarbonate 650mg PO twice a day. CAUTION: Avoid sodium bicarbonate in patients with signs of volume overload such as peripheral edema and crackles on lung exam. Consider referral to Nephrology if severe.*

### 5.4 Evaluation and treatment anemia of CKD

**Scenario: Latest eGFR 30-59 mL/min ≤ 380 days old, and the most recent eGFR that is 90+ days older than the latest eGFR is also within 30-59 mL/min. The second latest eGFR is between 30-59 mL/min. The patient’s hemoglobin is (10.5-11.5 mg/dL). Missing EITHER ferritin or transferrin saturation in the past 380 days.**

**Action:** Display the following message –

**Message:** “*Anemia in the setting of chronic kidney disease is often related to depleted iron stores. Recommend checking an iron profile and repleting with PO iron if transferrin saturation is ≤ 30% and ferritin is ≤ 500 ng/mL.”*

**Scenario: Latest eGFR 30-59 mL/min ≤ 380 days old, and the most recent eGFR that is 90+ days older than the latest eGFR is also within 30-59 mL/min. The second latest eGFR is between 30-59 mL/min. The patient’s hemoglobin is (10.5-11.5 mg/dL). In the past 380 days, the latest value of transferrin saturation is ≤ 30% OR the latest ferritin is ≤ 500 ng/mL, but neither of them are above those thresholds (if any values available).**

**Action:** Display the following message –

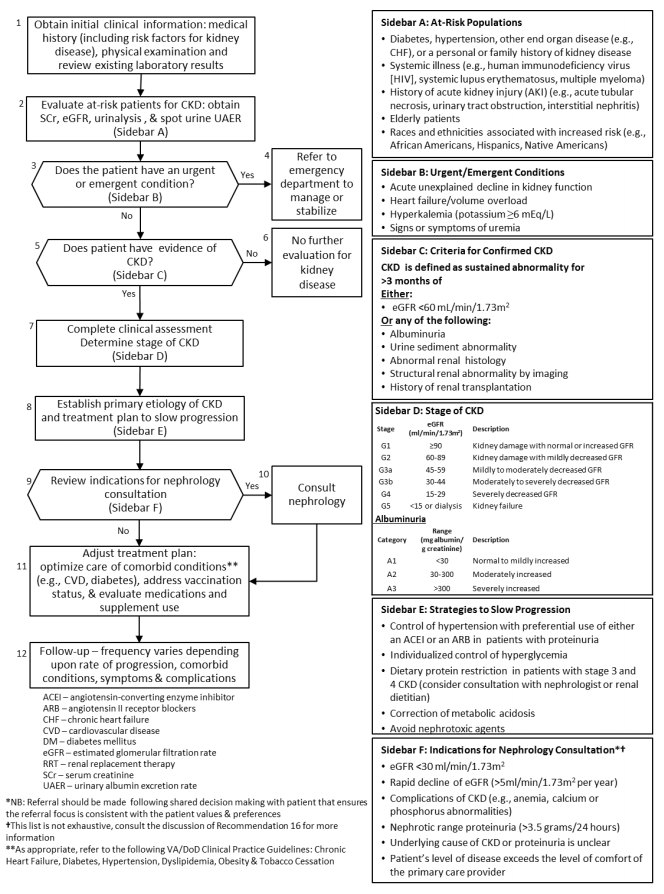
**Message:** “*Anemia in the setting of chronic kidney disease is often related to depleted iron stores. Recommend checking an iron profile and repleting with PO iron if transferrin saturation is ≤ 30% and ferritin is ≤ 500 ng/mL.”*

### 5.5 Administration of Immunizations

Currently, additional vaccination is only recommended for patients with eGFR < 30 mL/min. Notably, Hepatitis B and PCV13/PPSV23 (earlier than age 65) are recommended. These will not be included at this time, but they may be added in the future.

# FOR REFERENCE

The following sections are not part of the CKD Rules Document. These are summaries of sections of the VA/DoD CKD guideline for the management of CKD.



# Indications for referral to Nephrology

* CKD4, CKD 5 (eGFR < 30 mL/min)
* Rapid decline in GFR (decline >5 mL/min per year) – need a time minimum for this calculation of this cutoff (1 year?).
* Complications of CKD:
  + Anemia
  + Secondary hyperparathyroidism: Calcium and/or phosphorus abnormalities
* (KDIGO) Consistent finding of UACR >= 300 mg/g (PCR >=500 mg/g) or urine albumin excretion of >= 300mg/24hrs (protein >= 500mg/24hrs)
* AKI or abrupt/sustained fall in GFR (define by RIFLE?)
* Progression of CKD (from CKD3a to 3b?, etc?)
* Red cell casts, RBC > 20/hpf sustained and not readily explained
* CKD and HTN refractory to treatment with 4+ antihypertensives
* Persistent abnormalities of serum potassium
* Nephrotic range proteinuria (>3.5 g/24hr) (should really not be this strict)
* Underlying cause of CKD or proteinuria is unclear
* Nephrolithiasis
* Patient’s level of disease exceeds the comfort level of the PCP

# Acute Kidney Injury Avoidance / Contrast Management

* This system cannot predict administration of contrast. A blanket set of recommendations for contrast management that is always present may not be helpful, so this will not be addressed in this document.

# Management of CKD

* Weak: sodium restriction, protein diet 0.6-0.8 g/kg/day, weight loss in obese patients
* Weak: multidisciplinary care
* Weak: bicarb
* Strong: <140/90 (change?)
* Strong: non-DM CKD + HTN + albuminuria 🡪 ACE-inhibitor, ARB substitution okay if cough
* Strong: DM + HTN + Albuminuria 🡪 ACE-inhibitor or ARB
* Strong: AGAINST combo ACE-inhibitor/ARB, or either one with direct renin inhibitor
* Strong: 10-year CVD risk, recommend statin per VA/DoD dyslipidemia guidelines
* Weak: *against* statin *for preservation of kidney function*
* Strong: *against* intensive glycemic control in CKD3 or worse
* Weak: oral iron rather than parenteral in CKD 3 and 4
* Strong: *against* ESA for Hgb goal >11.5 (i.e., keep it below 11.5) (stroke, HTN)
* Weak: Vitamin D (not specific regarding 1,25-OH or 25-OH); call nephrology
* Weak: *against* Vit D or calcitriol for CKD 3 and 4 with elevated PTH due to lack of known benefit
* Weak: *against* phosphate binders in CKD 3 and 4
* Weak: *against* calcimimetic in CKD 3-4

# Screening

* Do not encourage screening due to lack of evidence.

# Military Occupational Risk

There is no known environmental or occupational exposure uniquely associated to military service. There is insufficient evidence to associate exposure to depleted uranium and solvents such as hydrocarbons.

# Periodic Evaluation

* DM, HTN, CHF, other end-organ disease, personal/family history of kidney disease
* Systemic illness (HIV, SLE, MM)
* History of AKI, including obstruction or interstitial nephritis
* Elderly
* African American, Hispanic, Native American (increased risk)
* Elderly patients at increased risk for CKD: [O’Hare](https://www.ncbi.nlm.nih.gov/pubmed/16452492)
* “In addition, medications should be reviewed to identify those that may be contributing to kidney impairment including: non-steroidal anti-inflammatory drugs (NSAIDs), other analgesics, diuretics, lithium, cyclosporine, tacrolimus, antiviral agents, chemotherapeutic agents, antibiotics, allopurinol, and dietary and herbal supplements.”
* Large kidneys (>13 cm): DM, amyloid, infiltrative, HIVAN
* Small kidneys (<8 cm): irreversible disease
* Asymmetry

# Acute Kidney Injury Avoidance

Mainly avoid CIN. Risk factors:

* CKD: Cr >1.5, eGFR < 60
* DM, HF, age > 75, >100mL contrast, high-osmolality contrast
* Consider recommendation for saline?

# Self-Management Strategies

* Sodium intake reduction
* CKD 3-4: Limitation of dietary protein to 0.6-0.8 g/kg/day

# Immunization

For patients with CKD:

* Influenza\*
* Tdap
* PCV13 and PPSV23 (even if under age 65)
* Hepatitis B
* Zoster / shingles\*
* Varicella\*
* MMR\*
* \*Some of these are available only or optionally as live-virus formulations. Caution with immunodeficiency.

# Medication Dose Adjustments/Avoidance

Do not include for now. Common options to possibly address in the future:

* NSAIDs
* Lithium
* Zoledronic Acid
* Metformin
* Gabapentin
* Allopurinol
* Spironolactone
* Thiazide

# Metabolic Acidosis

Stage 1-4 CKD: Bicarb

* Look at other guidelines, no dosing or target mentioned. Tentative 650mg PO BID for goal 22+

# Blood Pressure

Defer to HTN knowledge base. Check for:

* RAAS blockade: CKD, HTN, albuminuria: ACE-inhibitor or ARB
* Reason: “Slow progression”
* Avoid: any combination ACE-inhibitor, ARB, and direct renin inhibitor (aliskiren)
* Up to 30% increase in SCr within the first 2 weeks is acceptable
* Dose reduction for hyperkalemia or low-potassium diet or addition of diuretic

# Cardiovascular Risk Reduction

Recommend all CKD patients NOT on dialysis with 10-year CVD risk use at least a low-dose statin. REFER TO LIPID TOOL

# Glycemic Control

Recommend AGAINST intensive control in patients with CKD3-5 due to lack of benefit on renal/CV outcomes, along with potential for harm

# Anemia

* Initiation of oral iron therapy in CKD 3-4 (consult with nephrologist if Hgb <10). No iron targets recommended
* Recommend AGAINST ESAs to patients with CKD for target 11.5 g/dL or higher (contact pharmacist if Hgb 11.5 or higher)
* Recommend AGAINST initiating ESAs at hemoglobin level >= 10 g/dL. (Bring this up with Hgb 10-11 or 10-12? Need male/female here)
* Anemia of CKD is usually normochromic and normocytic
* Consider iron deficiency. Check iron profile (iron profile and Hgb within 3 months of CKD?)
* Referral to nephrology

# Calcium and Phosphorus Homeostasis

* Supplemental vitamin D for CKD 3 or 4 *for* *deficiency only*
* Do not offer Vitamin D analogs or calcitriol to patients with CKD 3 or 4 with elevated PTH
* Refer to nephrology for Vitamin D analog use
* Do not offer phosphate binders for those with CKD 3 or 4 with normal serum phosphorus. They may be considered in those with elevated phosphorus, being managed by a nephrologist.
* Suggest not offering calcimimetics for CKD 3 or 4
* Hypocalcemia and/or hyperphosphatemia in patients with CKD are indications for nephrology referral

# Definitions

1. Moderately increased albuminuria (“moderate albuminuria”)
   1. Note: “Microalbumin” is the same thing as “albumin” in the urine, though can be identified differently in VA records/labs.
   2. Defines CKD *Category* A2
   3. Defined as:
      1. Urine albumin/Cr ratio ≥ 30 mg/g but ≤ 300 mg/g (spot urine test)

OR

Urine albumin ≥ 30 mg/24hr but ≤ 300 mg/24hr (usually from a specimen collected from a longer duration than a “spot” urine test)

* 1. Should be repeated to confirm that it remains 30 mg/g or above. Encoded definition should require two consecutive measurements meeting criteria.

1. Severely increased albuminuria (“severe albuminuria”)
   1. Note: “Microalbumin” is the same thing as “albumin” in the urine, though can be identified differently in VA records/labs.
   2. Defines CKD *Category* A3
   3. Defined as:
      1. Urine albumin/Cr ratio > 300 mg/g (spot urine test)

OR

Urine albumin > 300 mg/24hr (usually from a specimen collected from a longer duration than a “spot” urine test)

* 1. Should be repeated to confirm that it remains 300 mg/g or above. Encoded definition should require two consecutive measurements meeting criteria.

1. Moderately increased proteinuria (“moderate proteinuria”)
   1. Defines CKD *Category* A2
   2. Defined as:
      1. Urine protein/Cr ratio ≥ 150 mg/g but ≤ 500 mg/g (“spot” urine test)

OR

Urine protein ≥ 150 mg/24hr but ≤ 500 mg/24hr (usually from a specimen collected from a longer duration than a “spot” urine test)

* 1. Should recommend assessment of albuminuria

1. Severely increased proteinuria (“severe proteinuria”)
   1. Defines CKD *Category* A3
   2. Defined as:
      1. Urine protein/Cr ratio ≥ 500 mg/g (“spot” urine test)

OR

Urine protein ≥ 500 mg/24hr (usually from a specimen collected from a longer duration than a “spot” urine test)

* 1. Should recommend assessment of albuminuria

1. Nephrotic range proteinuria
   1. These patients should already be excluded from the CDS recommendations
   2. Typically defined by total protein, but can be defined by heavy albuminuria (lesser known)
   3. Defined as:
      1. Urine protein/Cr ratio ≥ 3500 mg/g (“spot” urine test)

OR

Urine protein ≥ 3500 mg/24hr (usually from a specimen collected from a longer duration than a “spot” urine test)

* + 1. Urine albumin/Cr ratio ≥ 2200 mg/g (“spot” urine test)

OR

Urine albumin ≥ 2200 mg/24hr (usually from a specimen collected from a longer duration than a “spot” urine test)

Glomerular Filtration Rate (GFR)

Surrogate measurement for overall kidney function, used in staging of kidney disease

Units: mL/min per 1.73 m2. However, in this document the units will be left off completely or stated as “mL/min”

Difficult and impractical to measure correctly

Unless explicitly stated, assume “GFR” means “eGFR” (See “Estimated Glomerular Filtration Rate”)

Estimated Glomerular Filtration Rate (eGFR)

Estimate of GFR based on empirically derived equations

In CPRS, calculated using the CKD-EPI equation. Unless otherwise stated, “eGFR” refers to a calculation using this equation.

Often used interchangeably with CrCl (see “Creatinine Clearance”)

Creatinine Clearance (“CrCl”)

Previously used estimate of GFR before eGFR equations created. Now typically a calculation using the Cockcroft-Gault equation. Unless otherwise stated, “CrCl” refers to a calculation using this equation.

Occasionally, nephrologists will calculate creatinine clearance based on serum and urine lab tests.

Confirmed CKD

Sustained abnormality for ≥ 3 months of EITHER eGFR < 60 mL/min (meaning 2 measurements of eGFR < 60 that were taken 90+ days apart) OR any of the following:

(Moderately or severely increased) Albuminuria

Urine sediment abnormality (out of scope of this system)

Abnormal renal histology (out of scope of this system)

Structural renal abnormality by imaging (out of scope of this system)

History of renal transplantation

CKD Stage 1 (CKD1) or Stage 2 (CKD2):

eGFR ≥ 60 with:

Moderately or severely increased albuminuria (should be repeated for confirmation)

Albuminuria or proteinuria (with repeated measurement for confirmation)

Refer to [NKF guidelines](https://www.kidney.org/professionals/explore-your-knowledge/how-to-classify-ckd), which is adapted from [KDIGO 2012 Supplement 3](https://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf). Note: GFR >=60 without other evidence of kidney damage does not meet criteria for “Chronic Kidney Disease” as referenced in the remainder of this document.

And what about known diabetics with new albuminuria/proteinuria after regular checks showing normal urine protein levels?

CKD Stage 3a (CKD3a)

eGFR < 60 but ≥ 45 on two consecutive measurements separated by at least 90 days

OR

eGFR < 60 but ≥ 45 on one measurement, but also has moderate albuminuria, severe albuminuria, or proteinuria

**Check urine albumin-to-creatinine ratio at least annually**

**Check UACR upon change to this CKD Stage**

CKD Stage 3b (CKD3b)

eGFR < 45 but ≥ 30 on two separate measurements separated by at 90 days

OR

eGFR < 45 but ≥ 30 on one measurement, but also has moderate albuminuria, severe albuminuria, or proteinuria

**Check urine albumin-to-creatinine ratio at least annually**

CKD Stage 4 (CKD4)

eGFR < 30 but > 15 on two separate measurements separated by at least 90 days

**Check urine albumin-to-creatinine ratio at least annually**

Refer to Nephrology

CKD Stage 5 (CKD5)

eGFR < 15 on two separate measurements

**Check urine albumin-to-creatinine ratio at least annually**

Refer to Nephrology

“Heavy proteinuria”: Not perfect definitions

UPCR > 1500 mg/g? or UACR > 1000 mg/g

Urine protein > 1500 mg? or Urine albumin > 1500 mg

Nephrotic: ACR >2200 mg/g

# References