Notes

4/21/2015 ACE/ARB contraindications and bad drug partners highlighted in yellow were updated in the KB, but were not tested.

4/16/2015 A new December 2014 CKD Guidelines is now available, but has not been used for encoding.

?date? summing of doses is as described in this Rules document, but may not be correct; this is highlighted in yellow

**Rules Document for Chronic Kidney Disease (CKD)**

1. **Overview**

The recommendations included in this CDS are based upon the KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease [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.]. Only a subset of recommendations from this guideline was encoded, and these recommendations are listed in Appendix A. The identification of patients with CKD is done in SQL code, written by Marcos Lau, (modified by Dan Wang for this project) for the CKD dashboard, and is not part of the CDS. A summary of how the code classified patients into the different CKD stages is given in Appendix B. In the text that follows, “CKD stage N”, refers to that stage determined with the SQL code and provided by the SQL variable, “CKDflag.” A diagnosis of CKD is not used.

Because there is no Performance Measure for CKD, patients who have failed the performance measure for either Hypertension (Blood pressure >140/90), or Glycemic Control (HbA1c>9) or Hyperlipidemia (LDL-C>100 and not on a moderate dose statin) will receive CKD recommendations. This filter is performed in the SQL code.

A primary way to test the encoding of the KBs is by comparing its 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.

**Use of the Rules Document**

This Rules Document is a record of what is—or what should have been—encoded in the KB. This document is used by the DE in 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 KB will verify that what has been encoded (as described in this document) really is encoded
2. To identify gaps or extensions to the KB that become clear in the context of real patients.

Considerations when evaluating patients

The date of the KB’s and DE’s evaluation of the patients is referred to as the “session time”. When a time frame is given in the sections below, e.g. “with the past year”, this time frame is relative to this session time. Because the session time has been calculated, there are cases where the dates of lab values or blood pressures are AFTER the session time. Such lab values and blood pressures need to be ignored, because they are ignored by the CDS.

In the event that a patient has two different active prescriptions for the same drug, the dosages are summed, and a recommendation is made using this summed dosage. *From a discussion around 3/16/15, this summing –may- not be appropriate, but there has not been a decision as to what –is- the appropriate (Note also that we define ‘active prescriptions’ in SQL as ‘pills at hand’, that –could- make an inactive prescription active.)*

For this KB, warnings about a patient exceeding the maximum dose of a drug, has not been encoded and this item is part of a wish list.

**The following sections describe what has been encoded (or what should have been encoded, and has not been) in the Chronic Kidney Disease (CKD) KB**

1. **Eligibility, Exclusions, Goals**

**Eligibility**

* Patients with a non-null CKDflag

**Exclusions**

* Patients on hemodialysis (ICD9 codes see Appendix C)
* *Wish list; Patients who have had a kidney transplant should have been excluded, but were not. Need to identify appropriate ICD9 code, including V42.0 “Kidney replaced by transplant”*

**Goals**

* There are no goals

1. **Behavior of the CDS: Therapeutic Options**

Therapeutic recommendations are NOT provided

* if a patient’s Albuminuria to creatinine ratio (ACR) is older than 1 year or their eGFR is older than 1 year. Instead, a new ACR and/or a new eGFR are ordered.

Note: The SQL code uses, for Stages 1, 2, and 3, the presence of an ACR or PCR (protein creatinine ratio) of –any- time frame (see Appendix B). The KB requires that an ACR within the past year be present. Also, the KB does NOT use PCR. As a result, there can be many patients who have Stages 1,2, and 3 who will not have an ACR within the past year and will simply have the recommendation to “Order ACR” or “Order eGFR”.

* If a patient has CKD stage 4 or 5, that is, has CKDflag values of 4, 41, 5, or 51. Instead, the patient is considered out of scope and is referred to a nephrologist.

Therapeutic recommendations are provided if the ACR and eGFR are both within the past year and if the patient has CKD stage 1, 2 or 3; that is, has CKDflag values 1, 2, 3, or 31. The therapeutic recommendations can be divided into three groups

* Drug recommendations: Angiotensin Converting Enzyme Inhibitor (ACE-I) or Angiotensin Receptor Blocker (ARB)
* Messages, based upon various lab values and Orders
* Referral to nephrologist
  1. **Drug Recommendations**

Most CKD patients need to be on an ACE-I or an ARB. See Compelling Indication, below, for specific conditions..

In the section below, for both the ACE-I and ARB, we have the following:

* + Compelling indication (described above, also)
    - Drug with a compelling indication of a particular diagnostic condition will be recommended (if it is not contraindicated) and will be listed as a Therapeutic Options
  + Absolute contraindication
    - Drug will not be recommended if patient has this condition, and drug will be stopped if the patient is on the drug and this condition exists.
  + Relative contraindication
    - Drug is recommended and is listed as a Therapeutic Options, but lower in the list than those without the relative contraindication. If the patient is on the drug and this condition exists, drug will *not* be stopped.
  + Do not start conditions (blocked add drug)
    - Drug will be visible as a Therapeutic Option, but will be “blocked” because there are missing data. If a patient is on the drug, the do not start condition does *not* stop a drug (unlike an absolute contraindication).

* + Drug partner to avoid
    - Presence of a “drug partner to avoid” will stop recommendation

We would normally have a section entitled “Do not increase dose conditions” (below) but we do not recommend an increase dose, simply add or stop drug. Therefore this section is not included.

* + Do not increase dose conditions (blocked increase dose)
    - Patient is taking this drug and needs to have the dose increased, but the increase dose is “blocked” because there are missing data.

**Angiotensin Converting Enzyme Inhibitor (ACE-I) (benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril)**

* Compelling indication
* Absence of Diabetes and ACR>300 OR
* Presence of DM and ACR>=30
* Absolute contraindication
  + Pregnancy
  + Angioedema due to an ADR to ACE-I
  + ~~Presence of ARBs~~ updated; moved to “bad drug partner”
  + *K>5.5 in the past month <- updated*
* Relative contraindication
* ~~Angioedema due to ADR to ARB~~ removed
* *5.0<K<=5.5 in the past month <- updated*
* Renovascular Disease

ICDCode ICDDescription

403.01 HYPERTENSIVE CHRONIC KIDNEY DISEASE, MALIGNANT, WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

403.1 BENIGN HYPERTENSIVE RENAL DISEASE

403.11 HYPERTENSIVE CHRONIC KIDNEY DISEASE, BENIGN, WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

403.9 UNSPECIFIED HYPERTENSIVE RENAL DISEASE

403.91 HYPERTENSIVE CHRONIC KIDNEY DISEASE, UNSPECIFIED, WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

404.02 HYPERTENSIVE HEART AND CHRONIC KIDNEY DISEASE, MALIGNANT, WITHOUT HEART FAILURE AND WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

404.1 BENIGN HYPERTENSIVE HEART AND RENAL DISEASE

404.12 HYPERTENSIVE HEART AND CHRONIC KIDNEY DISEASE, BENIGN, WITHOUT HEART FAILURE AND WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

404.9 UNSPECIFIED HYPERTENSIVE HEART AND RENAL DISEASE

* Do not start conditions (blocked add drug), but do not stop if drug is present
  + Absence of K in the past month
  + ~~Most recent K>5~~ <- *updated*
  + Absence of SBP in the past month ~~year~~ <- *updated*
  + *Most recent SBP in past year <110 <- updateded*
* *Drug Partner to avoid*
  + - *ARB*
    - *Presence of Potassium sparing diuretics (amiloride, eplerenone, spironolactone, triamterene) <- updated*
* ~~Do not intensify conditions (blocked increase dose)~~  removed because we do not increase dose

**Angiotensin Receptor Blocker (ARB) (azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan)**

* Compelling indication
* Absence of Diabetes and ACR>300 OR
* Presence of DM and ACR>=30
* Absolute contraindication
  + Pregnancy
  + Angioedema due to an ADR to ARB
  + *Presence of K>5.5 in the past month<- updated*
  + ~~Presence of ACE-I~~ *updated* *moved to Bad drug partner*
* Relative contraindication
* ~~Angioedema due to ADR to ACE~~  *updated*
* *5.0<K<=5.5 in the past month <- updated*
* Renovascular Disease

ICDCode ICDDescription

403.01 HYPERTENSIVE CHRONIC KIDNEY DISEASE, MALIGNANT, WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

403.1 BENIGN HYPERTENSIVE RENAL DISEASE

403.11 HYPERTENSIVE CHRONIC KIDNEY DISEASE, BENIGN, WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

403.9 UNSPECIFIED HYPERTENSIVE RENAL DISEASE

403.91 HYPERTENSIVE CHRONIC KIDNEY DISEASE, UNSPECIFIED, WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

404.02 HYPERTENSIVE HEART AND CHRONIC KIDNEY DISEASE, MALIGNANT, WITHOUT HEART FAILURE AND WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

404.1 BENIGN HYPERTENSIVE HEART AND RENAL DISEASE

404.12 HYPERTENSIVE HEART AND CHRONIC KIDNEY DISEASE, BENIGN, WITHOUT HEART FAILURE AND WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE

404.9 UNSPECIFIED HYPERTENSIVE HEART AND RENAL DISEASE

* Do not start conditions (blocked add drug), but do not stop if drug is present
  + Absence of K in the past month
  + *~~Most recent K>5~~ <- updated*
  + Absence of SBP in the past month ~~year~~ <- updated
  + *Most recent SBP in past year <110 <- updated*
* ~~Do not intensify conditions (blocked increase dose)~~ removed because we do not increase dose
* *Drug Partner to avoid*
  + - *ACE*
    - *Presence of Potassium sparing diuretics (amiloride, eplerenone, spironolactone, triamterene) <- this has been encoded; differs from HTN where it is an exclusion criteria*
  1. **Messages and Orders**

The messages and orders listed here are part of offline testing **[confirm].** Additional messages can be found in Appendix C.

Blood pressure-related messages

*Note: a de-Identified patient may have multiple blood pressure (BP) measurements on the same day. If these BP are inconsistent, please ignore the patient as a test patient.*

If ACR>=30 and BP>130/80 in the past year, there will be a Primary Message: “We suggest that CKD patients with ACR>=30 have their blood pressure <=130/80.”

If ACR<30 and BP>140/90 in the past year, there will be a Primary Message: “We suggest that CKD patients with ACR<30 have their blood pressure <=140/90.”

If BP measurement within the past year is missing, there will be a a Primary Message: “Patient is missing BP measurement in past year. For CKD patients with ACR>=30, BP target is <=130/80. For CKD patients with ACR<30, BP target is <=140/90.”

eGFR<45

If a patient’s most recent eGFR<45, then the following laboratory values are expected to be present:

* + Calcium
  + Phosphate
  + Parathyroid Hormone (PTH)
  + Alkaline Phosphatase
  + Bicarbonate

If any of these laboratory values are missing (any time frame), then they will be ordered. In addition, there will be a Primary message: “CKD patients with eGFR<45 would normally have ?missingLab but this/these lab value(s) are missing.”

In addition, if any of the lab values are outside of their normal range (any time frame), then, there will be an Alert. There are separate messages for each lab value outside of normal range. [not for testing] *Ideally, there should be only one parameterized Alert, but I ran out of time; added to wish list.*

Normal ranges:

* + Calcium: 8.5<=Ca<=10.5
  + Phosphate: 2.5<=PO4<=4.5
  + Alkaline Phosphatase: 30<=Alk Phos <=115
  + Bicarbonate: 24<=bicarb<=32

eGFR<45 and PTH elevated

If a patient’s most recent eGFR<45 and PTH is elevated (>72), then, in addition to the labs listed above, the following laboratory values are expected to be present:

* + Vitamin D

If this lab is missing, then it will be ordered and there will be a Primary message: “PTH is elevated and vitamin D levels need to be assessed but lab is missing. Please order vitamin D lab.”

Note that the KDIGO recommendations state that, with “eGFR<45 and PTH elevated”, Calcium and phosphate values need to be measured. These missing labs will have been already identified under “eGFR<45”.

In addition, if Calcium or Phosphate or Vitamin D is outside of their normal range, there will be one message displayed: “PTH is elevated and Ca or phosphate or vitamin D labs are not within normal range. Please assess.” *Wish list: Ideally, there should be one parameterized message, with the specific lab listed, but I ran out of time.*

HGB (hemoglobin) checks

If 30<=eGFR<60 in the past year, then an HGB lab value within the past year is expected to be present. If not, then, HGB is ordered. And there is a message: “Patients with CKD and 30<=eGFR<60 are recommended to have their HGB checked annually.”

If eGFR>=60 in the past year and then an HGB lab value, any time frame, is expected to be present. If not, then there is a message: “Missing HGB lab. Order as clinically appropriate for CKD patients with eGFR>=60.” There is no order for HGB. [not for testing]

If a patient’s HGB<13 (male) or <12 (female), then there is a Primary message: “ALERT: Patient has anemia: HGB<13 (male) or HGB<12 (female).” [not for testing]

*The following –should- have been encoded, but was not encoded and therefore cannot be tested:*

*If eGFR<30 in the past year, then HGB labs need to be measured twice a year.*

Age>75 message

All patients with age>75 will receive the message: “Patient is over age 75; these patients need special attention in terms of drug dosing because of age related changes in pharmacodynamics and pharmacokinetics. Please use clinical judgment.”

* 1. **Referrals**

The following patients will be evaluated for all drug recommendations (3.1) and messages (3.2), and will also receive a referral to a nephrologist:

* + Most recent ACR>300 OR
  + BP>140/90 in the past year and on 4 or more different block pressure medications

Reiterating what was said above, the following patients will be referred to a nephrologist, but will not get any recommendations, because they are out of scope:

* + CKDflag=4,41,5,51

**Appendix A: Recommendations from KDIGO that are included in the KB**

Strike-through text (e.g. ~~text~~) have not been encoded in the KB but have been included here for reference.

The following sentence was extracted from the Introduction, “General summary for the reader: what you will and will not find in this guideline”

The target population for the guideline is all people identified with CKD who are not on RRT (i.e., not on

dialysis or have not received a kidney transplant).

Recommendations

2.1.1: Assess GFR and albuminuria at least annually in people with CKD. ~~Assess GFR and albuminuria more often for individuals at higher risk of progression, and/or where measurement will impact therapeutic decisions (see figure below).~~ (Not Graded)

3.1.4: We recommend that in both diabetic and non-diabetic adults with CKD and urine albumin creatinine ratio <30 mg/g whose office BP is consistently >140mm Hg systolic or >90mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently <=140mm Hg systolic and <=90mm Hg

diastolic. (1B)

3.1.5: We suggest that in both diabetic and non-diabetic adults with CKD and with urine albumin creatinine ratio <30 mg/g whose office BP is consistently >130mm Hg systolic or >80mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤130mm Hg systolic and ≤80mm Hg diastolic. (2D)

3.1.6: We suggest that an ARB or ACE-I be used in diabetic adults with CKD and urine albumin creatinine ratio 30–300 mg/g (2D)

3.1.7: We recommend that an ARB or ACE-I be used in both diabetic and non-diabetic adults with CKD and urine albumin creatinine ratio >300 mg/g. (1B)

3.2.1: Diagnose anemia in adults and children >15 years with CKD when the Hb concentration is <13.0 g/dl in males and <12.0 g/dl in females. (Not Graded)

3.2.3: To identify anemia in people with CKD measure Hb concentration (Not Graded):

When clinically indicated in people with GFR ≥60 ml/min/1.73 m2 (GFR categories G1-G2); at least annually in people with GFR 30–59 ml/min/1.73 m2 (GFR categories G3a-G3b); at least twice per year in people with GFR<30 ml/min/1.73 m2 (GFR categories G4-G5).

3.3.1: We recommend measuring serum levels of calcium, phosphate, PTH, and alkaline phosphatase activity at least once in adults with GFR <45 ml/min/1.73 m2 (GFR categories G3b-G5) in order to determine baseline values and inform prediction equations if used. (1C)

3.3.3: In people with GFR <45 ml/min/1.73 m2 (GFR categories G3b-G5), we suggest maintaining serum phosphate concentrations in the normal range according to local laboratory reference values. (2C)

3.3.4: In people with GFR <45 ml/min/1.73 m2 (GFR categories G3b-G5) the optimal PTH level is not known. We suggest that people with levels of intact PTH above the upper normal limit of the assay are first evaluated for hyperphosphatemia, hypocalcemia, and vitamin D deficiency. (2C)

3.4.1: We suggest that in people with CKD and serum bicarbonate concentrations <22 mmol/l treatment with oral bicarbonate supplementation be given to maintain serum bicarbonate within the normal range, unless contraindicated. (2B)

5.1.1: We recommend referral to specialist kidney care services for people with CKD in the following circumstances (1B):

~~- AKI or abrupt sustained fall in GFR;~~

- GFR <30 ml/min/1.73 m2 (GFR categories G4-G5)\*; [notes: refer to nephrologist and out of scope]

- a consistent finding of significant albuminuria (ACR ≥300 mg/g [≥30 mg/mmol] ~~or AER ≥300 mg/24 hours, approximately equivalent to PCR ≥500 mg/g [≥50 mg/mmol] or PER ≥500 mg/24 hours);~~ [notes: refer to nephrologist but not out of scope]

- ~~Progression of CKD (see Recommendation 2.1.3 for definition);~~

~~- Urinary red cell casts, RBC >20 per high power field sustained and not readily explained;~~

- CKD and hypertension refractory to treatment with 4 or more antihypertensive agents [notes: refer to nephrologist but not out of scope]

- ~~Persistent abnormalities of serum potassium;~~

~~- Recurrent or extensive nephrolithiasis;~~

~~- Hereditary kidney disease.~~

**Appendix B: Different CKD stages, as defined by SQL code**

Reference: Marcos Lau email sent 10/27/14

Clarification regarding the CKDFlag:

* CKD Stages 1-5 = Value of 1-5
  + For Stages 1 & 2:  This is based only on the most recent eGFR & positive proteinuria/albuminuria lab
  + For Stages 3-5:  This is based on two eGFR readings (most recent + 3 months prior must be < 60) and does not depend on proteinuria/albuminuria labs
* CKDFlag 31, 41, 51
  + Most recent eGFR is within the Stage 3, 4, 5 range but the 3 month prior lab result is >= 60 or does not exist (query goes back for a 2 year time frame)
* CKDFlag 6
  + This identifies patients without CKD defined as: Negative or no proteinuria/albuminuria lab performed and most recent eGFR >= 60
    - CKDFlag = 7 was originally for the No proteinuria/albuminuria lab but has been removed
  + This would be equivalent to the CKDFlag = 11 or 21 that is mentioned in the email thread
    - These patients would not have CKD based on eGFR AND proteinuria/albuminuria.  However, the patient may still have a diagnosis of CKD based upon structural defects or other CKD defining conditions (code did not include these).  Or the patient may not have CKD.

**Appendix C: Additional messages, not for testing**

Presence of JNC8 BP meds: “Patients with CKD and on BP medications need to be aware of the possibility of postural hypotension.”

Presence of ASCVD: “Consider antiplatelet therapy for patients with CKD and atherosclerotic vascular disease.”

Presence of DM: “We suggest lowering protein intake to 0.8 g/kg/day in adults with diabetes.”

Messages to all patients:

“Patients with CKD need to be on a low salt diet; <2 gm Na per day or <5gm NaCl per day.”

“Consider immunizing patients againts the flu, pneumonia and hepatitis B.”

**Appendix D: Wish list (reviewed 9/22/2015 with Mike Ashcraft, Susana Martins, Geoff Tso)**

Items mentioned in text above:

* *Wish list; Patients who have had a kidney transplant should have been excluded, but were not. Need to identify appropriate ICD9 code, including V42.0 “Kidney replaced by transplant”*
* If a patient is taking a dose of a drug that exceeds the maximum dose, issue an ALERT.
* If the patient labs values for calcium, phosphate, alkaline phosphatase or bicarbonate are outside of their normal range, issue a parameterized message that those particular labs are outside their normal range. Right now, one message is issued, with all labs listed, any one of which can be outside their normal range. Similar situation for calcium, phosphate, vitamin d.
* Do not start conditions ACE/ARB K>5 vs K>5.5, need to be resolved
* Do not start conditions ACE-I and ARB:
  + *Most recent SBP in past year <110 <- this has not been encoded, wish list*

Item from autoPM meetings

* 11/14/2014 For identifying Stages 1 and 2, only the most recent eGFR and positive proteinuria or albuminuria labs are used. KDIGO guidelines recommend 2 measurements eGFR 3 months apart and ACR ratios. Improve SQL code by adding second lab (3 months earlier) according to KDIGO guideline. No mention of use of ACR
* 12/16/14 Query CDW for immunization status; issue message about need for immunization based upon this data
* 1/13/15 Renal dosing paper, from Noelle Hasson: ideally, issue message for each drug in paper about appropriate dosing; intermediate work, if patient is taking a drug listed in the paper, link to information for each drug. Currently, we do have not included any information from the paper.

Version control

Changes to v6

* Updating to clarify that for calcium, phosphorus, alk phosphatase, vit D, PTH and bicarb use the most recent value no matter how old.
* Typos correction

**WISH LIST (items from Geoff and Mike)**

* How is age computed in ATHENA? Does it round down? Does it use decimals. Clinically, we round down. Eg. Criteria age>75. We had test patient that was 75.2 years old (patient 501374)
* For criteria with “in past month” qualifier, how is this calculate? Does it use a certain number of days? Eg. Patient 501604 - (K was deemed old based on date, rather than actual calculating number of days (30)) - Criteria for old potassium in KB is "in past month". ATHENA recommended start of ACE/ARB with though last K 2/7/02 for session date 3/9/02
* **Bug: Patient 502609 - ATHENA recommended ACE/ARB with SBP 88 - need to figure out with Samson**
* For ACE - change do not start condition: Most Recent SBP in "past year" < 110 to "past month"
* For ARB - change do not start condition: Most Recent SBP in "past year" < 110 to "past month"
* For ACE - change potassium sparing diuretic from drug partner to avoid to relative contraindication
* For ARB - change potassium sparing diuretic from drug partner to avoid to relative contraindication
* Move “Refer to Nephrologist” check box to bottom of Access testing UI