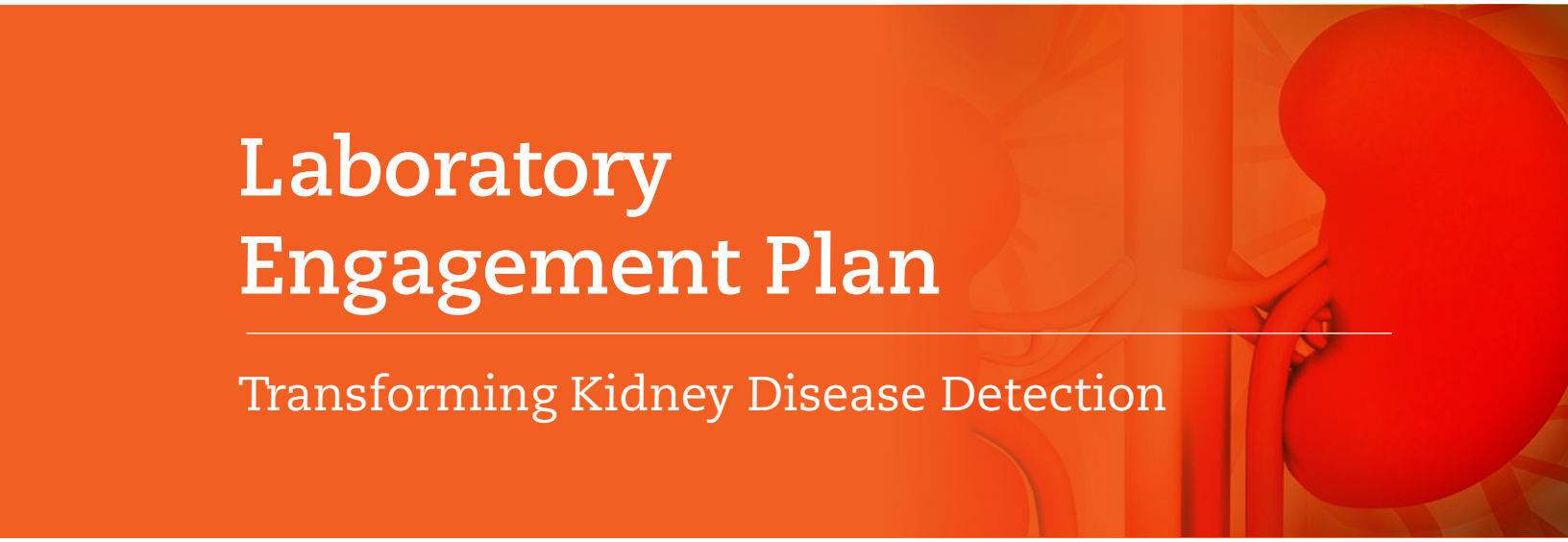
CKD intercept

Laboratory Engagement Plan

Transforming Kidney Disease Detection



February 2018
National Kidney Foundation
Laboratory Engagement Advisory Group

National Kidney Foundation®

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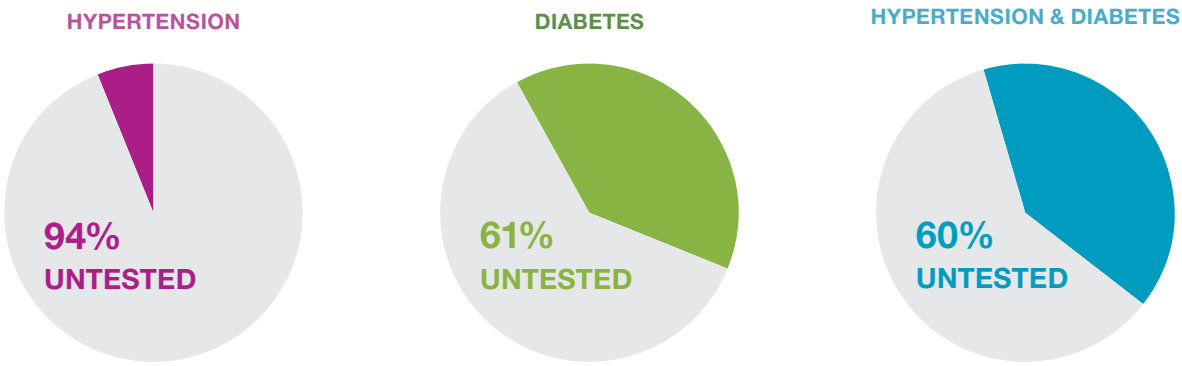
GAP ANALYSIS

Thirty million American adults are estimated by the Centers for Disease Control to be living with chronic kidney disease (CKD) today, with over 80% unaware of the condition that puts them at increased risk for cardiovascular events and progression to kidney failure and death.[1] Almost 90% of adults with type-2 diabetes and CKD are not currently diagnosed, and as many as 50% of patients with advanced CKD (Stage G4) remain undiagnosed in primary care populations.[2] Several national surveys have shown only 10 to 20% of Americans who have laboratory evidence of CKD are aware that they have the condition.[2,3] While current clinical practice guidelines for CKD assessment recommend that adults with diabetes and/or hypertension be tested annually for albuminuria, there is underutilization of yearly urinary albumin-creatinine ratio testing in people at risk for CKD. Less than 10% of those with hypertension and less than 40% of those with diabetes are appropriately assessed.[4,5]

LOW RATES OF ALBUMIN-CREATININE RATIO TESTING FOR CHRONIC KIDNEY DISEASE (CKD)

Hypertension and diabetes are the top two risk factors for developing CKD, but many people with these conditions are not receiving recommended testing.



Source: United States Renal Data System. 2016 USRDS annual data report: epidemiology of kidney disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2016.

Chronic kidney disease is diagnosed using two, simple, widely available laboratory tests. One is the estimated glomerular filtration rate (eGFR) or a test of kidney function, while the second is the urine albumin-creatinine ratio (ACR) or a test of kidney damage. Early recognition and management of CKD allows clinicians more opportunities to protect kidney health. As CKD progresses, the risk for cardiovascular events, mortality, and kidney failure dramatically increases.

Two large studies have shown that people with both low eGFR and high ACR have increased risk of cardiovascular events and death.[6,7] The age-standardized rates of cardiovascular events per 100 person-years increases dramatically with lower levels of kidney function in the population, as shown.[6]

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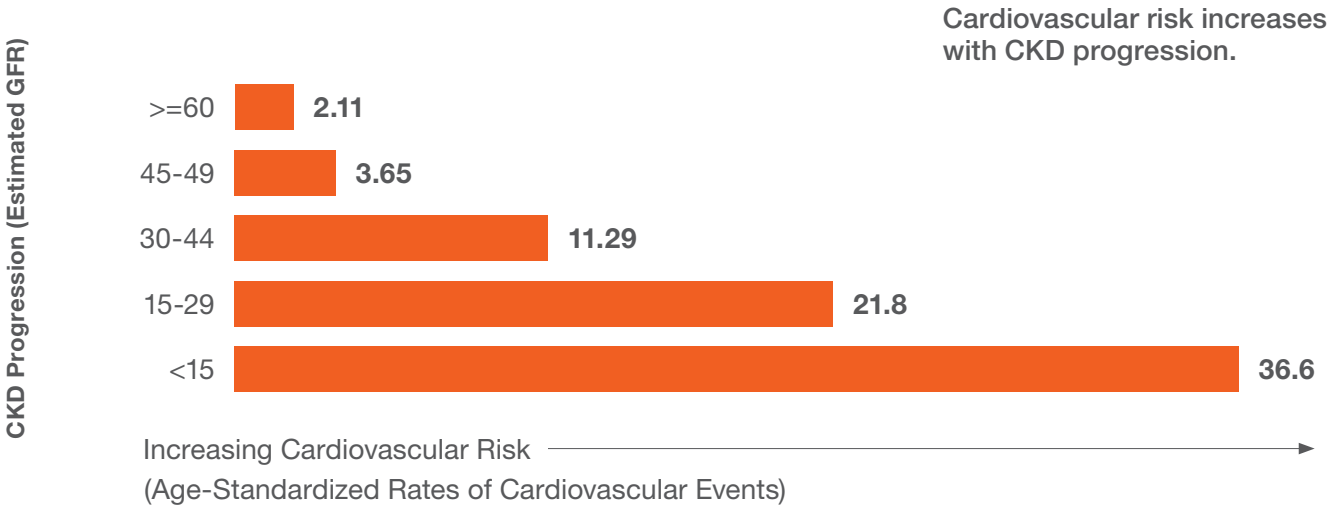
Chronic Kidney Disease (CKD) and Risk of Cardiovascular Events



Source: Go , A.S., et al., Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *New England Journal of Medicine,* 2004;351(13):1296-1305.

Barriers to use and interpretation exist for both of these tests. Ordering CKD laboratory tests is not a simple "stroke" or "click." In many cases, a clinician must search through the laboratory order requisition or online compendium to identify the various laboratory tests for CKD. They are often not located near each other or are not labeled with clear indications that kidney disease is their focus.

ESTIMATED GLOMERULAR FILTRATION RATE (eGFR)

The estimated glomerular filtration rate (eGFR) is commonly calculated and reported by clinical laboratories in the U.S. The two common eGFR equations utilized in the U.S. are the MDRD study and the CKD-EPI creatinine 2009 eGFR equations. The CKD-EPI creatinine 2009 eGFR equation is substantially more accurate than the MDRD study equation in the population with eGFR near 60 ml/min/1.73m^2.[4] Investigation of the two widely used equations shows the CKD-EPI creatinine 2009 eGFR equation more accurately predicts clinical risk for people with CKD.[4]

ALBUMIN-CREATININE RATIO (ACR)

There is a particular problem with ordering a spot or random urine albumin-creatinine ratio (ACR), which is the test for CKD recommended by the National Kidney Foundation (NKF)[4], American Diabetes Association (ADA)[8], and others. There is confusion among ordering clinicians regarding the urinary albumin-creatinine ratio, which is currently called "microalbumin with creatinine" test.[9,10] The current Common Procedural Terminology (CPT®) code for the microalbumin test (CPT 82043) is used to report the concentration of urinary albumin alone. Some labs only report urine albumin concentration to thresholds of >97 mg/dL or >300 mg/L, which does not permit accurate calculation of the albumin to creatinine ratio.

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When the ACR is reported, the laboratory must perform and report both microalbumin (CPT 82043) and urinary creatinine (CPT 82570). Many laboratories offer the ability to order the ACR wherein they will report the albumin, urinary creatinine, and the ratio. Even if the ACR is reported, the units for albumin and creatinine concentration are not uniform across laboratories (e.g., Quest Diagnostics reports the ratio in mcg albumin/mg creatinine, and LabCorp reports report the ratio in mg albumin/g creatinine) although the actual numeric values are the same. In addition, there is another, less-sensitive urinary albumin assay with a corresponding CPT code (82042) that is not appropriate for routine evaluation of patients at risk for CKD.

The terms “microalbumin” and “macroalbumin” also cause confusion, and practitioners may incorrectly believe that microalbumin is testing for excretion of a small albumin molecule rather than a low level of urinary albumin excretion. The current terms were derived from the detection limits of certain urine dipstick tests, and have caused widespread use of arbitrary decision points that do not reflect the continuously increasing cardiovascular risk associated with progression of urine albumin concentrations.[9] Recent clinical practice guidelines have recommended that the “microalbumin test” term be replaced because of misinterpretation as “small albumin” or a specific test value range, rather than the test itself.[4]

CKD*intercept* OBJECTIVES:

1. Establish protection and preservation of kidney health as a national public health priority. Integrate CKD testing for at-risk populations into routine primary care.
2. Provide training and materials so that clinicians apply CKD interventions in practice, and are able to consistently make sense of the test results and diagnosis for patients.
3. Engage CKD patients in ongoing interactions to ensure that they have the information and resources they need to make informed choices to protect their kidney health.

STRATEGY

The CKD*intercept* strategy for overcoming the obstacles to establishing kidney disease testing for at-risk populations as routine standard of care in primary practice includes five elements:

1. Address confusion about albuminuria testing by building consensus regarding unified terminology and laboratory reporting formats.
2. Foster consensus within the laboratory community to report eGFR using the 2009 CKD-EPI creatinine eGFR equation.
3. Recommend the creation of a standardized laboratory-specific “Kidney Profile” that combines estimated glomerular filtration rate (eGFR). The “Kidney Profile” is distinct from the Renal Function Panel (CPT 80069). The former is intended for detection and monitoring, whereas the latter is used only for monitoring individuals with diagnosed CKD.

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4. Educate the ordering clinician community about the changes effected by this plan and ensure that clinicians have patient-directed materials to facilitate education about CKD in their practices.
5. Measure the utilization of the new "Kidney Profile" and its relationship to diagnosis of CKD in primary care.

After working with members of the laboratory community, these five strategic elements were translated into the development priorities described below.

DEVELOPMENT PRIORITIES

PRIORITY 1: STANDARDIZE OR HARMONIZE THE DESCRIPTIVE LANGUAGE AND REPORTING OF THE RANDOM OR SPOT URINARY ALBUMIN-CREATININE RATIO

NKF convened the initial discussion of the Laboratory Engagement Advisory Group (Advisory Group) regarding this priority in early 2016. After several rounds of discussion on this topic, the Advisory Group recommends that the name for the random or spot urinary albumin-creatinine ratio be standardized to: **Albumin-creatinine ratio, urine**

It is also recommended that the reporting format for this test be harmonized to: **mg/gram**

It is suggested that appropriate aliases for "albumin-creatinine ratio, urine" in US laboratory information systems (LIS) that have character limitations include:

- Albumin-creatinine ratio, urine (29 characters)
- Albumin/creatinine ratio urine (28 characters)
- Albumin/creat. ratio urine (25 characters)
- Album/creat ratio, urine (22 characters)

PRIORITY 2: STANDARDIZE THE USE OF THE CKD-EPI CREATININE 2009 eGFR EQUATION TO REPORT ESTIMATED GLOMERULAR FILTRATION RATE (eGFR)

The Advisory Group recommends the 2009 CKD-EPI creatinine eGFR equation as the most accurate and least biased routinely available method to report eGFR.

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PRIORITY 3: DEVELOP CONSENSUS FOR A LABORATORY-SPECIFIC "KIDNEY PROFILE" WITH THE CLINICAL LABORATORY COMMUNITY

The advisory group recommends that NKF promote the industry-wide implementation of:

Kidney Profile (eGFR + albumin-creatinine ratio, urine)

Frequently utilized panels could be combined with the Kidney Profile at the discretion of the laboratory:

Kidney Profile + BMP (Basic Metabolic Panel)

Kidney Profile + CMP (Comprehensive Metabolic Panel)

Kidney Profile + RFP (Renal Function Panel)

PRIORITY 4: DEVELOP A PROFESSIONAL EDUCATION CAMPAIGN TO ENSURE THAT CLINICIANS APPROPRIATELY ORDER CKD TESTS FOR THEIR AT-RISK PATIENTS

The Advisory Group recommended that NKF collaborate with the American Society of Clinical Pathology (ASCP) to develop educational materials to raise clinician awareness of the changes described above, while raising awareness of the importance of guideline-concordant assessment for CKD.

The NKF and ASCP are working to develop and deploy the following materials:

a. Summary of recommendations for CKD assessment (for pathologists and clinicians)
b. Presentation summarizing CKD assessment and management in primary care
c. Frequently asked questions (for clinicians)
d. Infographic summarizing the program
e. Frequently asked questions (for patients)
f. Patient brochure on CKD
g. Webpage dedicated to this initiative

The campaign to raise awareness of CKD and the new strategy for ordering its assessment is anticipated to be deployed in February 2018.

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PRIORITY 5: DEVELOP A PUBLIC EDUCATION CAMPAIGN FOR PEOPLE WITH AND AT RISK FOR CKD TO UNDERSTAND THEIR CKD TEST RESULTS

As noted above, ASCP volunteered to partner with NKF to produce the educational materials that will be distributed as part of this collaboration.

PRIORITY 6: MEASURE THE IMPACT OF THE "KIDNEY PROFILE" UTILIZATION AND CONSIDER RELATED METRICS FOR IMPROVING CKD RECOGNITION.

Assessing Uptake of Recommendations by the Laboratory Community

To establish a baseline to assess the integration of the recommendations in this document and their impact, the American Association of Bioanalysts (AAB), in collaboration with National Independent Laboratory Association (NILA) team members, disseminated the following assessment questions in their ongoing laboratory proficiency testing:

1. **Do you use the term "albumin-creatinine ratio, urine" as an alias?**
   Yes
   No
   Other, specify:_____
2. **How do you report albumin-creatinine ratio, urine?**
   mg/g
   mcg/mg
   Do not report a ratio, but report albumin and creatinine concentration separately
   Do not know
   Other, specify:_____
3. **Do you offer a "kidney profile" test that consists of the estimated GFR and albumin-creatinine ratio, urine?**
   Yes
   No
   Other, specify:_____

The AAB fielded the 3 questions above to the laboratory community. The results from this initial national survey (September 27, 2017) included responses from 44 laboratories in the U.S. Of these laboratories, 0/44 reported use of "albumin-creatinine ratio, urine" as an alias in their systems. Only 8 of 44 laboratories report albumin-creatinine ratio, urine (or microalbumin tests) as mg/g. None of the responding laboratories (0/44) offer a "Kidney Profile" option for ordering CKD tests. It is the goal of the initiative to reassess these questions in January 2019.

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Assessing Uptake of Kidney Profile and Guideline Concordant Testing by Ordering Clinicians

The NKF is also discussing how collaborating laboratories can capture data to measure the impact of Kidney Profile use on CKD assessment, recognition and diagnosis. The methodology proposed below is currently in draft form:

The objective is to increase appropriate testing for CKD to reduce the gap in unidentified CKD.

CKD for this purpose is defined by the use of ICD-10 codes (N18.1, N18.2, N18.3, etc.)

Changes in urine ACR and Kidney Profile test volume could also be assessed (most likely a relative change based on potential competitive nature of sharing test volume) among at-risk population including those with diabetes and hypertension ICD-10 codes.

Change in newly diagnosed (based on ICD-10 code) CKD post-launch of campaign:

1. Track patients who are identified based on ICD-10 codes in four calendar quarters following launch and at least one serum creatinine in prior year. A
2. Identify the A patients who had a prior eGFR <60 ml/min/1.73m^2 in prior one year. (For this purpose assume non-African American.) B
3. Identify the A patients who had a prior eGFR >60 ml/min/1.73m^2 in prior year. (For this purpose assume non-African American.) C
4. B/(A-C) = D represents fraction of newly identified patients who could have been recognized earlier.
5. Run the same analysis (steps 1-4 for prior one year period). This will provide baseline as to fraction who were identified prior to campaign. E
6. The ratio of D/E = F reflects the impact of the campaign.

One could add refinements such as multiple measurements of eGFR to confirm diagnosis, adjustments to deal with patients tested at the beginning or end of a year, but that is irrelevant when doing this comparison because these factors affect both D and E equally. The model above represents a simple, feasible approach that is easy to explain. Nevertheless, alternative suggestions are most welcome.

A. Tracking relative change in albumin-creatinine ratio, urine and Kidney Profile testing can be performed quarterly.

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