Introduction: Statistics for Chronic Kidney Disease (CKD)
Kidney Disease Statistics for the United States: Prevalence

Age-Adjusted Prevalence of CKD Stages 1–4 by Gender 1999–2012

Age-Adjusted Prevalence of CKD Stages 1–4 by Race/Ethnicity 1999–2012
Kidney Disease Statistics for the United States: Costs

• Medicare spending for patients with CKD ages 65 and older exceeded $81 billion in 2018 and represented 22% of all Medicare spending in this age group.

• More than 70% of Medicare spending for CKD patients age 65 and older was incurred by those who also had diabetes, congestive heart failure or both.

• Spending was more than twice as high for patients with all three chronic conditions of CKD, diabetes, congestive heart failure ($57,965) than in patients with only CKD ($25,734).

• Total Medicare-related expenditures for beneficiaries with ESRD rose to $49.2B in 2018 and accounted for 7.2% of Medicare fee-for-service expenditures.
Kidney Disease Statistics for the United States: Mortality

All-cause mortality rates (per 1,000 patient years at risk) for Medicare patients aged 66+, by CKD status and year, 2001–2013 (adjusted)
Burden, access, and disparities in kidney disease


KEYWORDS: acute kidney injury; end stage renal disease; global health; health equity; social determinants of health

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### Table 1 | World Bank country group chronic kidney disease gaps

<table>
<thead>
<tr>
<th>CKD care</th>
<th>Low-income countries (%)</th>
<th>Lower-middle-income countries (%)</th>
<th>Upper middle-income countries (%)</th>
<th>High-income countries (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Governmental recognition of CKD as a health priority</td>
<td>59</td>
<td>50</td>
<td>17</td>
<td>29</td>
</tr>
<tr>
<td>Government funds all aspects of CKD care</td>
<td>13</td>
<td>21</td>
<td>40</td>
<td>53</td>
</tr>
<tr>
<td>Availability of CKD management and referral guidelines (international, national, or regional)</td>
<td>46</td>
<td>73</td>
<td>83</td>
<td>97</td>
</tr>
<tr>
<td><strong>Existence of current CKD detection programs</strong></td>
<td><strong>6</strong></td>
<td><strong>24</strong></td>
<td><strong>24</strong></td>
<td><strong>32</strong></td>
</tr>
<tr>
<td>Availability of dialysis registries</td>
<td>24</td>
<td>48</td>
<td>72</td>
<td>89</td>
</tr>
<tr>
<td>Availability of academic centers for renal clinical trial management</td>
<td>12</td>
<td>34</td>
<td>62</td>
<td>63</td>
</tr>
</tbody>
</table>
Mean Annual Health Care Cost Per Patient with CKD (developed countries)

• Progression from CKD G1–G2 to CKD G3a-3b was associated with a 1.1–1.7 fold increase in per patient mean annual health care cost

• Mean annual total health care costs per patient:
  o CKD G1-G3b: $1,600 to $25,037
  o CKD G4–G5: $5,367 to $53,186
  o Kidney failure: $20,110 to $100,593
Screening for CKD: Barriers to Early Identification & Intervention
Early identification of CKD

- Screening
- Risk stratification
- Treatment

https://www.pinterest.com/pin/374361787748770734/
Professional organizations have been discordant on whether or not to screen for CKD.
In the absence of direct evidence to support screening, we have to make tough choices using all available evidence.
KDIGO Early Identification & Intervention in CKD Controversies Conference
KDIGO Early Identification & Intervention in CKD Controversies Conference

(Official hashtag: #KDIGOEarlyCKD)
Outline: Four Major Topics

1. The selection of candidate populations for CKD early detection
2. The relative diagnostic and predictive characteristics of tests for kidney disease and their potential costs
3. The evidence base for treatments that could reduce the risk of CKD progression and cardiovascular events
4. The implementation strategies for CKD early detection and treatment programs and the key factors determining resource allocation and cost-effectiveness
Conceptual framework of a CKD screening, risk stratification, and treatment program
WHO Screening Principles Apply to CKD

- Public health problem
- Early asymptomatic phase
- Detectable by affordable testing
- Treatments are effective and available
- Disease progression understood
- Screening treatment must be ongoing, not just one episode
- Affordable for overall healthcare budget
Additional Considerations

• Patients overwhelmingly prefer earlier CKD screening and diagnosis.

• Patient education has the potential to improve self-management and disease prognosis.

• Economic rationale must favor some program of early CKD screening/risk stratification/treatment, given the costs of kidney failure to healthcare systems and society.
Approaches considered to CKD screening, risk-stratification and treatment

• Identification of all persons with CKD
• Identification of individuals within high-risk populations to maximize testing yield
• Identification of individuals with CKD who are most likely to progress to kidney failure or experience cardiovascular or other CKD complications
• Additional topics:
  – Definitions of high-risk populations
  – Optimal frequency of rescreening
Decisions concerning the age to initiate testing, the frequency of repeat testing, and the time to forgo or end testing should all be **individualized** based upon:

- Risk factors
- Preferences
- Life expectancy
Person with hypertension, diabetes, and cardiovascular disease should be screened for CKD.
Conclusion 1: Persons with hypertension, diabetes, and cardiovascular disease should be screened for CKD.
Screening Strategy

CKD screening should be implemented for groups with these well-accepted CKD risk factors:

- Hypertension,
- Diabetes, and/or
- Cardiovascular disease
Controversies Conference Report

Conclusion 2:

CKD screening and treatment programs should be also implemented in other high-risk individuals and populations based on comorbidities, environmental exposures, or genetic factors.
Conclusion 2: CKD screening and treatment programs should also be implemented in other high-risk individuals and populations based on comorbidities, environmental exposures, or genetic factors.

- Older age
- Race/ethnicity
- SLE
- HIV
- Family History
- Genetic Risk Factors
- Low Socioeconomic Status
- Environmental Exposures
- Prior AKI
- Preeclampsia
- Nephrotoxins
- Obesity
Conclusion 2: CKD screening and treatment programs should also be implemented in other high-risk individuals and populations based on comorbidities, environmental exposures, or genetic factors.

<table>
<thead>
<tr>
<th>Conditions of ↑CKD risk</th>
<th>Consider screening for CKD</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hypertension</td>
<td>• Urinary albumin–creatinine ratio (ACR) to detect albuminuria</td>
</tr>
<tr>
<td>• Diabetes</td>
<td>• Serum creatinine and cystatin C(^b) to estimate glomerular filtration rate (eGFR)</td>
</tr>
<tr>
<td>• Cardiovascular disease</td>
<td></td>
</tr>
<tr>
<td>• AKI/hospitalization history</td>
<td></td>
</tr>
<tr>
<td>• Family history of kidney disease</td>
<td></td>
</tr>
<tr>
<td>• Obesity</td>
<td></td>
</tr>
<tr>
<td>• Older age(^a)</td>
<td></td>
</tr>
<tr>
<td>• Other high-risk comorbidities,</td>
<td></td>
</tr>
<tr>
<td>environmental exposures, or genetic factors</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion 3:

The initiation, frequency, and cessation of CKD screening should be individualized based on kidney and cardiovascular risk profiles and individual preferences.
Conclusion 3: The initiation, frequency, and cessation of CKD screening should be individualized based on kidney and cardiovascular risk profiles and individual preferences.

The **timing of initiation of CKD screening** should be based on comorbidities and individualized risk assessment, rather than at a specific chronologic age.
The frequency of testing is a critical aspect of CKD screening programs and has substantial impact on costs.

- Must be individualized and could range from 1 to 10 years.
- Risk equations that estimate future CKD probabilities could be used to guide the timing of the subsequent testing.

Research

JAMA | Original Investigation

Development of Risk Prediction Equations for Incident Chronic Kidney Disease

Robert G. Nelson, MD, PhD; Morgan E. Grams, MD, PhD; Shoshana H. Ballew, PhD; Yingying Sang, MS; Feeridouan Azizi, MD; Steven J. Chadban, MD, PhD; Layal Chaker, MD, PhD; Stephan C. Dunning, MBA; Caroline Fox, MD; Yoshihisa Hirakawa, MD; Kunijoshi Iseki, MD, PhD; Joachim Ikx, MD, MAS; Tazeen H. Jafar, MD, MPH; Anna Köttgen, MD, MPH; David M. J. Naimark, MD, MSc; Takayoshi Ohkubo, MD, PhD; Gordon J. Prescott, BSc, MSc, PhD, CStat; Casey M. Rebholz, PhD; Charumathi Sabanayagam, PhD; Toshimi Sairenchi, PhD; Ben Schöttker, PhD; Yugo Shibagaki, MD; Marcello Tonelli, MD, SM; Luxia Zhang, MD; Ron T. Gansevoort, MD, PhD; Kunihiro Matsushita, MD, PhD; Mark Woodward, PhD; Josef Coresh, MD, PhD; Varda Shalev, MD; for the CKD Prognosis Consortium

**IMPORTANCE** Early identification of individuals at elevated risk of developing chronic kidney disease (CKD) could improve clinical care through enhanced surveillance and better management of underlying health conditions.

**OBJECTIVE** To develop assessment tools to identify individuals at increased risk of CKD, defined by reduced estimated glomerular filtration rate (eGFR).

**DESIGN, SETTING, AND PARTICIPANTS** Individual-level data analysis of 34 multinational cohorts from the CKD Prognosis Consortium including 5,222,711 individuals from 28 countries. Data were collected from April 1970 through January 2017. A 2-stage analysis was performed, with each study first analyzed individually and summarized overall using a weighted average. Because clinical variables were often differentially available by diabetes status, models were developed separately for participants with diabetes and without diabetes. Discrimination and calibration were also tested in 9 external cohorts (n = 2,253,540).
Overdiagnosis vs the greater relative burden of CKD on the elderly

Prevalence of Chronic Kidney Disease in the United States

Josef Coresh, MD, PhD
Elizabeth Selvin, PhD, MPH
Lesley A. Stevens, MD, MS
Jane Manzi, PhD
John W. Kusek, PhD
Paul Egerds, PhD
Frederick Van Lente, PhD
Andrew S. Levey, MD

Context The prevalence and incidence of kidney failure treated by dialysis and transplantation in the United States have increased from 1988 to 2004. Whether there have been changes in the prevalence of earlier stages of chronic kidney disease (CKD) during this period is uncertain.

Objective To update the estimated prevalence of CKD in the United States.


Main Outcome Measures Chronic kidney disease prevalence was determined based on persistent albuminuria and decreased estimated glomerular filtration rate (GFR).

Results The prevalence of both albuminuria and decreased GFR increased from 1988-1994 to 1999-2004. The prevalence of CKD stages 1 to 4 increased from 10.0% (95% confidence interval [CI], 9.2%-10.9%) in 1988-1994 to 13.1% (95% CI, 12.0%-14.1%) in 1999-2004.

Age and Association of Kidney Measures With Mortality and End-stage Renal Disease

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Marcello Tonelli, MD, SM
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Alestra Levin, MD
Chi-Pang Wen, MD, MPH, DrPH
Josef Coresh, MD, PhD
for the Chronic Kidney Disease Prognosis Consortium

Context Chronic kidney disease (CKD) is prevalent in older individuals, but the risk implications of low estimated glomerular filtration rate (eGFR) and high albuminuria across the full age range are controversial.

Objective To evaluate possible effect modification (interaction) by age of the association of eGFR and albuminuria with clinical risk, examining both relative and absolute risks.

Design, Setting, and Participants Individual-level meta-analysis including 205124 participants from 33 general population or high-risk (of vascular disease) cohorts and 13 CKD cohorts from Asia, Australasia, Europe, and North/South America, conducted in 1972-2011 with a mean follow-up time of 5.8 years (range, 0-31 years).

Main Outcome Measures Hazard ratios (HRs) of mortality and end-stage renal disease (ESRD) according to eGFR and albuminuria were meta-analyzed across age categories after adjusting for sex, race, cardiovascular disease, diabetes, systolic blood pressure, cholesterol, body mass index, and smoking. Absolute risks were estimated using HRs and average incidence rates.

Results Mortality (112325 deaths) and ESRD (8411 events) risks were higher at lower eGFR and higher albuminuria in every age category. In general and high-risk cohorts, relative mortality risk for reduced eGFR decreased with increasing age; adjusted HRs at an eGFR of 45 mL/min/1.73 m2 vs 80 mL/min/1.73 m2 were 3.50 (95% CI, 2.55-4.81), 2.21 (95% CI, 2.02-2.41), 1.59 (95% CI, 1.42-1.77), and 1.35 (95% CI, 1.23-1.48) in age categories 18-54, 55-64, 65-74, and ≥75 years, respectively (P < .05 for age interaction). Absolute risk differences for the same comparisons were higher at older age (9.0 [95% CI, 6.0-12.8], 12.2 [95% CI, 10.3-14.3], 13.3 [95% CI, 9.0-18.6], and 27.2 [95% CI, 13.5-45.5] excess deaths per 1000 person-years, respectively). For increased

Measures of chronic kidney disease and risk of incident peripheral artery disease: a collaborative meta-analysis of individual participant data

Kumihiro Matsushita, Shoshane H Ballew, Josef Coresh, Hisatomi Arima, Johan Amlod, Massimo Cozzo, Natalie Ebert, Jade S Hiramoto, Heejin Kim, Michael G Shlipak, Frank L Vissines, Ron T Gansevoort, Csaba P Kovcsy, Varala Shalen, Mark Woodward, Florian Koenen, for the Chronic Kidney Disease Prognosis Consortium

ISN | ISN Passport | ISN International Society of Nephrology
Potential CKD mechanisms
- Environmental
- Vascular
- Inflammatory
- Neurodegenerative
- Genetic

CKD Risk factors
- Emerging risk factors:
  C-Reactive protein, oxidative stress, homocysteine, serum albumin, hemoglobin concentration, malnutrition, anemia.
- Traditional risk factors: albuminuria, hypertension, smoking, elevated cholesterol, diabetes.
- Neural toxicity and degeneration: uremic toxins, endogenous toxins, putative neurotoxins (e.g. parathyroid hormone, nitrogen metabolism); environmental toxins.

Anatomic diagnosis
- Chronic Kidney Disease

Clinical outcomes
- Cognitive impairment
  - cerebrovascular disease: e.g. stroke; white matter lesions; silent brachial infarction; endothelial dysfunction.
Potential harms associated with CKD overdiagnosis in older adults can be mitigated using available diagnostic and risk tools.

1.4.3.5: We suggest measuring cystatin C in adults with eGFRcreat 45-59 ml/min/1.73m² who do not have markers of kidney damage if confirmation of CKD is required. (2C)

- If eGFRcys/eGFRcreat-cys is also <60 ml/min/1.73 m², the diagnosis of CKD is confirmed.
- If eGFRcys/eGFRcreat-cys is ≥60 ml/min/1.73 m², the diagnosis of CKD is not confirmed.
Older adults should not be excluded from CKD screening programs
Conclusion 4:

CKD screening and risk stratification must consist of a dual assessment of estimated glomerular filtration rate (eGFR) and albuminuria (UACR).
Conclusion 4: CKD screening and risk stratification must consist of a dual assessment of estimated glomerular filtration rate (eGFR) and albuminuria (UACR).

<table>
<thead>
<tr>
<th>GFR categories (ml/min per 1.73 m²) Description and range</th>
<th>Persistent albuminuria categories Description and range</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 Normal or high ≥90</td>
<td>A1 Normal to mildly increased</td>
</tr>
<tr>
<td>G2 Mildly decreased 60–89</td>
<td>A2 Moderately increased 30–300 mg/g 3–30 mg/mmol</td>
</tr>
<tr>
<td>G3a Mildly to moderately decreased 45–59</td>
<td>A3 Severely increased &gt;300 mg/g &gt;30 mg/mmol</td>
</tr>
<tr>
<td>G3b Moderately to severely decreased 30–44</td>
<td></td>
</tr>
<tr>
<td>G4 Severely decreased 15–29</td>
<td></td>
</tr>
<tr>
<td>G5 Kidney failure &lt;15</td>
<td></td>
</tr>
</tbody>
</table>

Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.
Measurements for Early CKD

The *ideal initial screening and diagnosis approach* would consist of the *triple marker panel*:

- Serum creatinine
- Serum cystatin C, and
- Urine albumin-to-creatinine ratio (UACR)
Use of Clinical Decision Support to Improve Primary Care Identification and Management of Chronic Kidney Disease (CKD)

Cara B. Litwin, MD, MS, J. Madison Hyer, MS, and Steven M. Ornstein, MD

Primary care physicians’ familiarity, beliefs, and perceived barriers to practice guidelines in non-diabetic CKD: a survey study

Khaled Abdel-Kader1, Raquel C. Greer2,3, L Ebony Boulware4 and Mark L Unruh5

Incident chronic kidney disease: trends in management and outcomes

Robert M. Perkins1, Alex R. Chang1, Kenneth E. Wood2, Josef Coresh3, Kunihiro Matsushita4 and Morgan Grams3

1Bayer HealthCare, Whippany, NJ, USA, 2Geisinger Medical Center, Danville, PA, USA, 3Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University, Baltimore, MD, USA and 4Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
Low rates of albuminuria testing in CKD

In a US study of more than one million patients with eGFR < 60 ml/min/1.73 m², only 19% of the participants had the necessary ACR testing to calculate the 4-variable KFRE.

Further examples:

Cleveland Clinic: 36% of patients with CKD had no proteinuria assessed

UK Cohort: 17% reported ACR testing within the first year of registration of CKD

In this population of incident CKD Stage G3 patients, quantification rates of urinary protein excretion doubled over the study period, but remained low in absolute terms; less than half of the incident CKD population in 2010–12 underwent urinary protein quantification.

How attuned are PCPs to isolated albuminuria abnormalities?

Primary care physicians’ familiarity, beliefs, and perceived barriers to practice guidelines in non-diabetic CKD: a survey study

Khaled Abdel-Kader¹*, Raquel C Greer²,³, L Ebony Boulware⁴ and Mark L Unruh⁵

![Figure 1 PCPs reporting that a non-diabetic older adult with the specified characteristics has CKD. Colors indicate CKD risk categories as classified in KDIGO guidelines. Yellow – moderate, orange – high, red – very high. N = 154.](image-url)
Poor Adherence to CKD Screening Guidelines in Patients with CKD Risk Factors (e.g., diabetes, hypertension)

- Albuminuria testing in persons with diabetes
  - 41.8% of Medicare
  - 49% of Optum Clinformatics™

- Albuminuria testing – HTN alone
  - 6.6% of Medicare
  - 7.1% of Optum Clinformatics™

2018 USRDS Annual Data Report. NIDDK, 2018

Capacities of primary health care services for CKD (by income groups): Qualitative urinalysis using test strips for albumin or protein or both was available in 41% of low-income countries, 58% of high-income countries in primary care. Only one-third of low-income countries were able to measure serum creatinine in primary care, and none was able to access eGFR.
Poor Adherence to CKD Screening Guidelines in Patients with CKD Risk Factors (e.g., diabetes, hypertension)

Screening and Recognition of CKD in VA Health Care System Primary Care Clinics


Percentage of patients with diabetes (DM), hypertension (HTN), or both who had screening tests in the chart

Within each criterion of CKD, green box represents the percentage of patients who were recognized to have CKD
Conversion of Urine Protein-Creatinine Ratio or Urine Dipstick Protein to Urine Albumin-Creatinine Ratio for Use in Chronic Kidney Disease Screening and Prognosis

An Individual Participant-Based Meta-analysis

Keiichi Sumida, MD, MPH, PhD*; Girish N. Nadkarni, MD, MPH*; Morgan E. Grams, MD, PhD; Yingying Sang, MSc; Shoshana H. Ballew, PhD; Josef Coresh, MD, PhD; Kunihiro Matsushita, MD, PhD; Aditya Surapaneni, PhD; Nigel Brunskill, MD, PhD; Steve J. Chadban, MD, PhD; Alex R. Chang, MD, MS; Massimo Cirillo, MD; Kenn B. Dara, PhD; Ron T. Gansevoort, MD, PhD; Amit X. Garg, MD, PhD; Licia Iacoviello, MD, PhD; Takamasa Kayama, MD, PhD; Tsuneo Konta, MD, PhD; Csaba P. Kovessy, MD; James Lash, MD; Brian J. Lee, MD; Rupert W. Major, MD, PhD; Marie Metzger, PhD; Katsuyuki Miura, MD, PhD; David M.J. Naimark, MD, MSc; Robert G. Nelson, MD, PhD; Simon Sawhney, MD, PhD; Nikita Stempniewicz, MSc; Mila Tang, MSc; Raymond R. Townsend, MD; Jamie P. Traynor, MD; José M. Valdivielso, PhD; Jack Wetzel, MD, PhD; Kevan R. Polkinghorne, MBChB, PhD†; and Hiddo J.L. Heerspink, PhD†; for the Chronic Kidney Disease Prognosis Consortium‡

Background: Although measuring albuminuria is the preferred method for defining and staging chronic kidney disease (CKD), total urine protein or dipstick protein is often measured instead.

Objective: To develop equations for converting urine protein-creatinine ratio (PCR) and dipstick protein to urine albumin-creatinine ratio (ACR) and to test their diagnostic accuracy in CKD screening and staging.

Design: Individual participant-based meta-analysis.

Setting: 12 research and 21 clinical cohorts.

Participants: 919,383 adults with same-day measures of ACR and PCR or dipstick protein.

Measurements: Equations to convert urine PCR and dipstick protein to ACR were developed based on a median of 956,174 measurements of PCR or greater, trace to +, and ++ for screening for ACR values greater than 30 mg/g and classification into stages A2 and A3, respectively, had moderate sensitivity (62%, 36%, and 78%) and high specificity (88%, 88%, and 98%). For individual risk prediction, the estimated 2-year 4-variable kidney failure risk equation using predicted ACR from PCR had discrimination similar to that of using observed ACR.

Limitation: Diverse methods of ACR and PCR quantification were used; measurements were not always performed in the same urine sample.

Conclusion: Urine ACR is the preferred measure of albuminuria; however, if ACR is not available, predicted ACR from PCR or urine dipstick protein may help in CKD screening, staging, and prognosis.
For CKD screening, staging and prognosis: is urine dipstick protein good enough?

### Study Design & Cohort

- **Individual participant-based meta-analysis**
  - 12 research cohorts
  - 21 clinical cohorts
  - 919,383 adults

### Equations derived:

- From Urine PCR & dipstick protein values
- To predict A/C ratios
- To detect Presence of CKD (ACR ≥ 30mg/g)
- And to classify Stage A2 or A3 (moderately or severely increased albuminuria)

### Results

<table>
<thead>
<tr>
<th>Source of predictive ACR</th>
<th>Predicted state or classification</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR</td>
<td>CKD</td>
<td>91%</td>
<td>87%</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>75%</td>
<td>89%</td>
</tr>
<tr>
<td></td>
<td>A3</td>
<td>87%</td>
<td>98%</td>
</tr>
<tr>
<td>Dipstick</td>
<td>Trace</td>
<td>62%</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>36%</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td>++</td>
<td>78%</td>
<td>98%</td>
</tr>
</tbody>
</table>

**Conclusion:** Urine ACR is the preferred measure of albuminuria; however, if ACR is not available, predicted ACR from PCR or urine dipstick protein may help in CKD screening, staging, and prognosis.

Sumida, K., Nadkami, G., Grams, M et al. *Conversion of Urine Protein–Creatinine Ratio or Urine Dipstick Protein to Urine Albumin–Creatinine Ratio for Use in Chronic Kidney Disease Screening and Prognosis An Individual Participant–Based Meta-analysis*. doi: 10.7326/M20-0529

VA by @AnnaGaddy
Controversies Conference Report

Conclusion 5:

Accurate GFR estimation includes both creatinine and cystatin C measurement for initial diagnosis and staging.
Conclusion 5: Accurate GFR estimation includes both creatinine and cystatin C measurement for initial diagnosis and staging.
Cystatin C versus Creatinine in Determining Risk Based on Kidney Function

Comparisons of eGFR Using Creatinine, Cystatin C, or both with All-Cause Mortality

N= 90,750
12,351 deaths

The use of cystatin C alone or in combination with creatinine strengthens the association between the eGFR and the risks of death and end-stage renal disease across diverse populations.
Cystatin C has the additional advantage of offering GFR estimates that do not require the incorporation of a race coefficient, as is required for creatinine.
Controversies Conference Report

Conclusion 6:

The combination of Creatinine, Cystatin C, and UACR for CKD screening is affordable in high income settings.
Conclusion 6: The combination of Creatinine, Cystatin C, and UACR for CKD screening is affordable in high income settings.

SCREEN

RISK STRATIFY

Conditions of ↑CKD risk
- Hypertension
- Diabetes
- Cardiovascular disease
- AKI/hospitalization history
- Family history of kidney disease
- Obesity
- Older age
- Other high-risk comorbidities, environmental exposures, or genetic factors

Consider screening for CKD
- Urinary albumin–creatinine ratio (ACR) to detect albuminuria
- Serum creatinine and cystatin C to estimate glomerular filtration rate (eGFR)

Is any of the following present for 3 months or more?
- eGFR < 60 ml/min/1.73 m²
- ACR ≥ 30 mg/g (3 mg/mmol)
- Markers of kidney disease

Classify/risk stratify CKD stage
- Assign eGFR category (ml/min/1.73 m²):
  G1 = ≥ 90; G2 = 60 – 89; G3a = 45 – 59; G3b = 30 – 44; G4 = 15 – 29; G5 = < 15
- Identify and treat specific cause of CKD
- Assign albuminuria category:
  A1 (normal or mild): <30 mg/g or < 3 mg/mmol; A2 (moderately ↑): 30–300 mg/g or 3–30 mg/mmol; A3 (severely ↑): > 300 mg/g or > 30 mg/mmol

Yes

Yes

No

Periodically repeat evaluation

Yes
Original Investigation

Multinational Assessment of Accuracy of Equations for Predicting Risk of Kidney Failure
A Meta-analysis

Navdeep Tangri, MD, PhD, FRCP, Morgan E. Grams, MD, PhD; Andrew S. Levey, MD; Josef Coresh, MD, PhD; Lawrence J. Appel, MD; Brad C. Astor, PhD, MPH; Gabriel Chodick, PhD; Allan J. Collins, MD; Ogjenjka Ojurdej, MSc; C. Rania Eley, MBChB, PhD; Marie Evans, MD, PhD; Amit X. Garg, MD, PhD; Stein I. Hallan, MD, PhD; Lesley A. Inker, MD, MS; Sadayoshi Ito, MD, PhD; Sun Ha, Jee, PhD; Csaba P. Kovacs, MD; Florian Kronenberg, MD; Hidde J. L. Heerspink, PharmD, PhD; Angharad Marks, MBChB, MRCP, MSc, PhD; Girish N. Nadkarni, MD, MPH; Sankar D. Navaneethan, MD, MPH; Robert G. Nelson, MD, PhD; Stephanie Titze, MD, MSc; Mark J. Sarnak, MD, MS; Benedicte Stengel, MD, PhD; Mark Woodward, PhD; Kunitoshi Iseki, MD, PhD; for the CKD-Prognosis Consortium

Figure 3. Discrimination Statistics (C Statistics) for Original 4-Variable and 8-Variable Equations at 2 and 5 Years by Subgroup

Table A: 4-Variable equation

<table>
<thead>
<tr>
<th>Cohort</th>
<th>No. of Patients</th>
<th>C Statistic (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>140947</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>126536</td>
</tr>
<tr>
<td>Black</td>
<td>Yes</td>
<td>13125</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>236463</td>
</tr>
<tr>
<td>Age, y ≥65</td>
<td>196626</td>
<td>0.903 (0.879-0.926)</td>
</tr>
<tr>
<td>&lt;65</td>
<td>70847</td>
<td>0.898 (0.874-0.922)</td>
</tr>
</tbody>
</table>

Table B: 8-Variable equation

<table>
<thead>
<tr>
<th>Cohort</th>
<th>No. of Patients</th>
<th>C Statistic (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>17770</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>22233</td>
</tr>
<tr>
<td>Black</td>
<td>Yes</td>
<td>3311</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>31420</td>
</tr>
<tr>
<td>Age, y ≥65</td>
<td>24336</td>
<td>0.905 (0.882-0.927)</td>
</tr>
<tr>
<td>&lt;65</td>
<td>15678</td>
<td>0.891 (0.876-0.905)</td>
</tr>
</tbody>
</table>

Figure 3. Discrimination Statistics (C Statistics) for Original 4-Variable and 8-Variable Equations at 2 and 5 Years by Subgroup
Interventions for CKD
<table>
<thead>
<tr>
<th>G1</th>
<th>G2</th>
<th>G3a</th>
<th>G3b</th>
<th>G4</th>
<th>G5</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>A2</td>
<td>A3</td>
<td>A1</td>
<td>A2</td>
<td>A3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifestyle modification</td>
<td>Smoking cessation</td>
<td>RAS inhibition</td>
<td>Optimize blood pressure control</td>
<td>Statins</td>
<td>Optimize glycemic control</td>
</tr>
</tbody>
</table>
Controversies Conference Report

Conclusion 7:

A key rationale for CKD screening is the availability of many effective interventions to delay CKD progression and reduce cardiovascular risk.
Conclusion 7: A key rationale for CKD screening is the availability of many effective interventions to delay CKD progression and reduce cardiovascular risk.
Lifestyle Improvements May Help Reduce Progression at All Stages of CKD
ACEi/ARB Reduce the Risk of CKD Progression and Kidney Failure

## Benefits of Intensive BP Lowering in CKD

### Intensive versus Standard Blood-Pressure Control

<table>
<thead>
<tr>
<th></th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Targeted Systolic Blood Pressure:</strong></td>
<td>&lt;120 mmHg Systolic</td>
<td>&lt;140 mmHg Systolic</td>
</tr>
<tr>
<td><strong>N:</strong></td>
<td>4678</td>
<td>4683</td>
</tr>
<tr>
<td><strong>First Occurrence of MI, ACS, Stroke, HF or Death from CVS Cause:</strong></td>
<td>5.2% (HR 0.75; 95% CI, 0.64 to 0.89; P&lt;0.001)</td>
<td>6.8%</td>
</tr>
<tr>
<td><strong>Death from Any Cause:</strong></td>
<td>3.3% (HR 0.73; 95% CI, 0.60 to 0.90; P=0.003)</td>
<td>4.5%</td>
</tr>
</tbody>
</table>

**N Engl J Med 2015; 373:2103-2116**

**SPRINT Research Group, visualmed.org**
Mortality Benefits of Intensive BP Lowering in CKD

Cheung AK et al. JASN. 28: 2812–2823, 2017


Malhotra et al. systematic review and meta-analysis

SPRINT

HR (95% CI) 0.72 (0.53-0.99)

Cheung AK et al. JASN. 28: 2812–2823, 2017
Statins Lower CVD Risk in Persons with CKD G3 or G4

Impact of renal function on the effects of LDL cholesterol lowering with statin-based regimens: a meta-analysis of individual participant data from 28 randomised trials

Figure 2: Effects on major coronary events per mmol/L reduction in LDL cholesterol, by baseline renal function

Data for participants with missing creatinine values at baseline are included in totals. Black squares and horizontal lines represent 99% CIs. White diamonds represent 95% CIs. Vertical dotted line represents overall RR for each outcome. eGFR=estimated glomerular filtration rate. RR=rate ratio.
Glucose Control Lowers Risk of CKD Progression in Type 2 Diabetes

Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials

The Collaborators on Trials of Lowering Glucose (CONTROL) group

### Supplementary Table 3. Effects of more versus less intensive glucose control on the primary outcomes by years of follow up

<table>
<thead>
<tr>
<th>Event number</th>
<th>Pooled HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>More intensive</td>
<td>Less intensive</td>
<td></td>
</tr>
<tr>
<td>Primary kidney outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1 years</td>
<td>120</td>
<td>112</td>
</tr>
<tr>
<td>0-2 years</td>
<td>264</td>
<td>279</td>
</tr>
<tr>
<td>0-3 years</td>
<td>408</td>
<td>456</td>
</tr>
<tr>
<td>0-4 years</td>
<td>584</td>
<td>655</td>
</tr>
<tr>
<td>0-5 years</td>
<td>761</td>
<td>865</td>
</tr>
</tbody>
</table>
SGLT2 Inhibitors: the New Cardiorenal Miracle Drugs

## Effects of SGLT2 Inhibitors on Major Kidney Outcomes*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Events</th>
<th>Patients</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis, transplantation, or death due to kidney disease</td>
<td>252</td>
<td>38723</td>
<td>0.67 (0.52–0.86)</td>
</tr>
<tr>
<td>ESKD</td>
<td>335</td>
<td>38723</td>
<td>0.65 (0.53–0.81)</td>
</tr>
<tr>
<td>Substantial loss of kidney function, ESKD, or death due to kidney disease</td>
<td>967</td>
<td>38671</td>
<td>0.58 (0.51–0.66)</td>
</tr>
<tr>
<td>Substantial loss of kidney function, ESKD, or death due to cardiovascular or kidney disease</td>
<td>2323</td>
<td>38676</td>
<td>0.71 (0.63–0.82)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>943</td>
<td>38684</td>
<td>0.75 (0.66–0.85)</td>
</tr>
</tbody>
</table>

*based on CANVAS, DECLARE-TIMI 58, EMPA-REG, and CREDEENCE

---

Effects of SGLT2 Inhibitors on Early CKD*

Effect of SGLT2 inhibitors on substantial loss of kidney function, kidney failure, or death due to kidney disease as stratified by baseline GFR

*based on CANVAS, DECLARE-TIMI 58, EMPA-REG, and CREDENCE

Neuen BL et al. Lancet Diabetes Endocrinol. 7: 845-854, 2019
Effects of SGLT2 Inhibitors on Early CKD*

Effect of SGLT2 inhibitors on substantial loss of kidney function, kidney failure, or death due to kidney disease as stratified by baseline albuminuria

*based on CANVAS, DECLARE-TIMI 58, EMPA-REG, and CREDENCE

Neuen BL et al. Lancet Diabetes Endocrinol. 7: 845-854, 2019
### SGLT2 Inhibitors: Evidence Summary of Cardiovascular and Kidney Benefits

#### a Kidney outcome

<table>
<thead>
<tr>
<th>Study ID</th>
<th>HR (95% CI)</th>
<th>No diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPA-HF</td>
<td>0.67 (0.30–1.49)</td>
<td></td>
</tr>
<tr>
<td>EMPEROR-Reduced</td>
<td>0.42 (0.19–0.97)</td>
<td></td>
</tr>
<tr>
<td>DAPA-CKD</td>
<td>0.50 (0.35–0.72)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (I² = 0.0%, P = 0.714)</td>
<td>0.51 (0.38–0.69)</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAPA-HF</td>
<td>0.73 (0.39–1.34)</td>
<td></td>
</tr>
<tr>
<td>EMPEROR-Reduced</td>
<td>0.53 (0.31–0.90)</td>
<td></td>
</tr>
<tr>
<td>DAPA-CKD</td>
<td>0.64 (0.52–0.79)</td>
<td></td>
</tr>
<tr>
<td>CANVAS</td>
<td>0.60 (0.47–0.77)</td>
<td></td>
</tr>
<tr>
<td>CREDENCE</td>
<td>0.66 (0.53–0.81)</td>
<td></td>
</tr>
<tr>
<td>EMPA-Reg</td>
<td>0.54 (0.40–0.75)</td>
<td></td>
</tr>
<tr>
<td>DECLARE-TIMI</td>
<td>0.53 (0.43–0.66)</td>
<td></td>
</tr>
<tr>
<td>VERTIS-CV</td>
<td>0.81 (0.63–1.04)</td>
<td></td>
</tr>
<tr>
<td>SCORED</td>
<td>0.71 (0.46–1.08)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (I² = 6.6%, P = 0.380)</td>
<td>0.63 (0.57–0.69)</td>
<td></td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td>0.62 (0.57–0.67)</td>
</tr>
</tbody>
</table>

#### b Hospitalisation for heart failure or cardiovascular death

<table>
<thead>
<tr>
<th>Study ID</th>
<th>HR (95% CI)</th>
<th>No diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPA-HF</td>
<td>0.73 (0.60–0.89)</td>
<td></td>
</tr>
<tr>
<td>EMPEROR-Reduced</td>
<td>0.78 (0.64–0.97)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (I² = 0.0%, P = 0.650)</td>
<td>0.75 (0.65–0.87)</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAPA-HF</td>
<td>0.75 (0.63–0.90)</td>
<td></td>
</tr>
<tr>
<td>EMPEROR-Reduced</td>
<td>0.72 (0.60–0.87)</td>
<td></td>
</tr>
<tr>
<td>CANVAS</td>
<td>0.78 (0.67–0.91)</td>
<td></td>
</tr>
<tr>
<td>CREDENCE</td>
<td>0.69 (0.57–0.83)</td>
<td></td>
</tr>
<tr>
<td>EMPA-Reg</td>
<td>0.66 (0.55–0.79)</td>
<td></td>
</tr>
<tr>
<td>DECLARE-TIMI</td>
<td>0.83 (0.73–0.95)</td>
<td></td>
</tr>
<tr>
<td>VERTIS-CV</td>
<td>0.88 (0.75–1.03)</td>
<td></td>
</tr>
<tr>
<td>SCORED</td>
<td>0.77 (0.66–0.91)</td>
<td></td>
</tr>
<tr>
<td>SOLOIST</td>
<td>0.68 (0.53–0.88)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (I² = 16.1%, P = 0.299)</td>
<td>0.76 (0.72–0.81)</td>
<td></td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td>0.76 (0.72–0.80)</td>
</tr>
</tbody>
</table>

**SGLT2 Inhibitors: Primary Kidney Outcome Trials**

---

**Table: Albuminuria stages, description and range**

<table>
<thead>
<tr>
<th>Albuminuria stages</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Normal to mildly increased</td>
<td>Moderately increased</td>
<td>Severely increased</td>
</tr>
<tr>
<td>Range</td>
<td>&lt;30 mg/g</td>
<td>30 – 300 mg/g</td>
<td>&gt;300 mg/g</td>
</tr>
</tbody>
</table>

---

**CREDENCE (DKD)**
- eGFR ≥30 to <90 mL/min/1.73 m² and UACR ≥300 mg/g

**DAPA-CKD (CKD)**
- eGFR ≥25 to <75 mL/min/1.73 m² and UACR ≥200 mg/g

**EMPA-KIDNEY (CKD)**
- eGFR ≥45 to <75 mL/min/1.73 m² and UACR ≥200 mg/g OR eGFR ≥20 to <45 mL/min/1.73 m²

---

**GFR categories**

<table>
<thead>
<tr>
<th>GFR category</th>
<th>EGFRA1</th>
<th>EGFRA2</th>
<th>EGFRA3</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>≥90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G2</td>
<td>60 – 89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G3a</td>
<td>45 – 59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G3b</td>
<td>30 – 44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G4</td>
<td>15 – 29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G5</td>
<td>&lt;15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

The cardiovascular outcome trials are indicated in the circles and positioned based on their mean eGFR and median UACR.

---

**References**


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*Courtesy of Dr. Peter Rossing*
# CREDENCE: Canagliflozin and renal outcomes in type 2 diabetes and nephropathy

## Study design and participants
- 4401 patients with T2DM & UACR >300 mg/g
- 62 years
- eGFR 57
- UACR 927 mg/g

## Intervention
- Stable on maximum dose tolerated ACEi or ARB for 4 weeks
- Canagliflozin
- Placebo

## Outcomes
- **Primary outcome**
  - Doubling of serum creatinine, ESKD, death due to cardiovascular or kidney disease
  - **HR 0.70** (95% CI 0.59-0.82)
  - **NNT 21**

- **End-stage kidney disease**
  - **HR 0.68** (95% CI 0.54-0.86)
  - **NNT 42**

- No increased risk of:
  - Amputations
    - HR 1.10 (95% CI 0.79-1.56)
  - Fractures
    - HR 0.98 (95% CI 0.70-1.37)

## Conclusion
In patients with type 2 diabetes and kidney disease, canagliflozin reduces the risk of kidney failure and cardiovascular events.
Does Dapagliflozin compared to placebo reduce the risk of kidney failure and CV events in CKD patients with and without T2DM?

**21 Countries
286 Centers**

**N=4304**

**DAPAGLIFLOZIN**
- Standard Care
- N=2152
- HR 0.61
- (95% CI 0.51-0.72)
- p<0.001
- NNT=19

**PLACEDO**
- Standard Care
- N=2152
- HR 0.56
- (95% CI 0.45-0.68)
- p<0.001

**Benefit of Dapagliflozin on primary end-point was consistent in patients with and without T2DM**

% of patients who discontinued the drug or who experienced SAE was similar in both groups

DKA, 2 in placebo group vs none in Dapagliflozin group

No DKA or severe hypoglycemia in patients without T2DM

**CONCLUSION:** Dapagliflozin compared to placebo significantly reduced the risk of kidney failure, CV death or hospitalization for HF and all-cause mortality in patients with CKD with and without T2DM. Dapagliflozin was well-tolerated, in keeping with its established safety profile.

**DAPA-CKD**


DOI: 10.1056/NEJMoa2024816

Visual Abstract by: Ana Naidas, MD
CRENCE: DM + eGFR of 30 to <90 ml/min/1.73 m² and albuminuria (UACR >300 to 5000)

ESKD, doubling of serum creatinine, death from kidney causes or CV death

Primary composite outcome

↓ 30% RRR  
\( p = 0.000001 \)

CV death or HHF

Secondary outcomes

↓ 31% RRR  
\( p < 0.001 \)

3P-MACE

↓ 20% RRR  
\( p = 0.01 \)

HHF

↓ 39% RRR  
\( p < 0.001 \)

DAPA-CKD: noDM & DM + eGFR of 25 to <75 ml/min/1.73 m² and albuminuria (UACR >200 to 5000)

Decline in eGFR ≥50%; ESKD*; renal or CV death

Primary composite outcome

↓ 39% RRR  
\( p = 0.000000028 \)

≥50% sustained decline in eGFR or reaching ESRD or renal death

Secondary outcomes

↓ 44% RRR  
\( p = 0.000000018 \)

CV death or HHF

↓ 29% RRR  
\( p = 0.008 \)

TOTAL death

↓ 31% RRR  
\( p = 0.0035 \)

*Defined as eGFR <15 ml/min/1.73 m², need for chronic dialysis and/or renal transplantation
GLP-1 RA Recommended for Persons with Diabetes and eGFR <30 ml/min/1.73 m²

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug</strong></td>
<td>Lixisenatide</td>
<td>Liraglutide</td>
<td>Semaglutide</td>
<td>Exenatide</td>
<td>Albiglutide</td>
<td>Dulaglutide</td>
<td>Semaglutide (oral)</td>
</tr>
<tr>
<td><strong>Total number of participants</strong></td>
<td>6068</td>
<td>9340</td>
<td>3297</td>
<td>14,752</td>
<td>9463</td>
<td>9901</td>
<td>3183</td>
</tr>
<tr>
<td><strong>% with CVD</strong></td>
<td>100%</td>
<td>81.3%</td>
<td>81%</td>
<td>73%</td>
<td>100%</td>
<td>31.5%</td>
<td>84.7%</td>
</tr>
<tr>
<td><strong>eGFR criteria for enrollment (ml/min per 1.73 m²)</strong></td>
<td>&gt;30 ml/min per 1.73 m²</td>
<td>Most had eGFR ≥30, but did include 220 patients with eGFR 15 to 30</td>
<td>Not reported</td>
<td>≥30</td>
<td>≥30</td>
<td>≥15</td>
<td>≥30 (whichever 0.9% had eGFR &lt;30)</td>
</tr>
<tr>
<td><strong>Mean eGFR at enrollment (ml/min per 1.73 m²)</strong></td>
<td>76</td>
<td>80</td>
<td>~75</td>
<td>76</td>
<td>79</td>
<td>79.5</td>
<td>74 ± 21</td>
</tr>
<tr>
<td><strong>% with eGFR &lt;60 ml/min per 1.73 m²</strong></td>
<td>23</td>
<td>26.7 with eGFR 30 to 59 ml/min per 1.73 m², 2.4 with eGFR &lt;10 ml/min per 1.73 m²</td>
<td>28.5</td>
<td>22.9</td>
<td>Not reported</td>
<td>22.2</td>
<td>26.9</td>
</tr>
<tr>
<td><strong>ACR</strong></td>
<td>10% with micro-albuminuria and 7% with severely increased albuminuria</td>
<td>Not reported</td>
<td>Not reported</td>
<td>3.5% with severely increased albuminuria</td>
<td>Not reported</td>
<td>7.9% with severely increased albuminuria</td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>Follow-up time</strong></td>
<td>25 mo</td>
<td>3.8 yr</td>
<td>2.1 yr</td>
<td>3.2 yr</td>
<td>1.6 yr</td>
<td>5.4 yr</td>
<td>15.9 mo</td>
</tr>
<tr>
<td><strong>CV outcome definition</strong></td>
<td>CV death, MI, stroke, or hospitalization for unstable angina</td>
<td>CV death, nonfatal MI, or nonfatal stroke</td>
<td>CV death, nonfatal MI, or nonfatal stroke</td>
<td>CV death, nonfatal MI, or nonfatal stroke</td>
<td>CV death, nonfatal MI, or nonfatal stroke</td>
<td>CV death, nonfatal MI, or nonfatal stroke</td>
<td>CV death, nonfatal MI, or nonfatal stroke</td>
</tr>
<tr>
<td><strong>CV outcome results</strong></td>
<td>HR 1.02 (0.89–1.17)</td>
<td>HR 0.87 (0.78–0.97)</td>
<td>HR 0.74 (0.58–0.95)</td>
<td>HR 0.91 (0.83–1.00)</td>
<td>HR 0.78 (0.68–0.90)</td>
<td>HR 0.88 (0.79–0.99)</td>
<td>HR 0.79 (0.57–1.1)</td>
</tr>
<tr>
<td><strong>Kidney outcome (secondary end points)</strong></td>
<td>New-onset severely increased albuminuria and doubling of SCR</td>
<td>New-onset persistent severely increased albuminuria, persistent doubling of the SCR level, ESRD, or death due to kidney disease</td>
<td>Persistent severely increased albuminuria, persistent doubling of SCR, a COG of &lt;45 ml/min, or need for KRT</td>
<td>Two kidney composite outcomes: (1) 40% eGFR decline, kidney replacement, or renal death, (2) 40% eGFR decline, kidney replacement, renal death, or severely increased albuminuria</td>
<td>Not reported</td>
<td>New severely increased albuminuria, ACR of ≥3.9 mg/ g, or death due to kidney disease</td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>Kidney outcome results</strong></td>
<td>New-onset severely increased albuminuria: adjusted HR 0.81 (0.66–0.99), P = 0.04; Doubling of SCR: adjusted HR 1.16 (0.74–1.83), P = 0.51</td>
<td>HR 0.78 (0.67–0.92)</td>
<td>HR 0.64 (0.46–0.88)</td>
<td>40% eGFR decline, kidney replacement, or renal death: adjusted HR 0.87 (0.71–1.04), P = 0.13, 40% eGFR decline, kidney replacement, renal death, or severely increased albuminuria: adjusted HR 0.85 (0.74–0.98), P = 0.009</td>
<td>Not reported</td>
<td>HR 0.85 (0.77–0.93) Similar for eGFR ≥60 vs. &lt;60 ml/min per 1.73 m², no albuminuria vs. albuminuria, no ACE/ARB vs. ACE/ARB</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
Effects of GLP-1RA on All-Cause Mortality and CV Outcomes*

*based on ELIXA, EXSCEL, HARMONY, LEADER, PIONEER 6, REWIND, SUSTAIN-6

Kristensen SL et al. Lancet Diabetes Endocrinol. 7: 776-785, 2019
Effects of GLP-1RA on Kidney Outcomes and Heart Failure*

<table>
<thead>
<tr>
<th>Outcome Description</th>
<th>Study</th>
<th>Event Rate</th>
<th>Event Rate</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital admission for heart failure</td>
<td>ELIXA</td>
<td>122/3034 (4%)</td>
<td>127/3034 (4%)</td>
<td>0.96 (0.75-1.23)</td>
</tr>
<tr>
<td></td>
<td>LEADER</td>
<td>218/4668 (5%)</td>
<td>248/4672 (5%)</td>
<td>0.87 (0.73-1.05)</td>
</tr>
<tr>
<td></td>
<td>SUSTAIN-6</td>
<td>59/1648 (4%)</td>
<td>54/1649 (3%)</td>
<td>1.11 (0.77-1.61)</td>
</tr>
<tr>
<td></td>
<td>EXSCEL</td>
<td>219/7356 (3%)</td>
<td>231/7396 (3%)</td>
<td>0.94 (0.78-1.13)</td>
</tr>
<tr>
<td></td>
<td>Harmony Outcomes</td>
<td>79/4731 (2%)</td>
<td>111/4732 (2%)</td>
<td>0.71 (0.53-0.94)</td>
</tr>
<tr>
<td></td>
<td>REWIND</td>
<td>213/4949 (4%)</td>
<td>226/4952 (5%)</td>
<td>0.93 (0.77-1.12)</td>
</tr>
<tr>
<td></td>
<td>PIONEER 6</td>
<td>21/1591 (1%)</td>
<td>24/1592 (2%)</td>
<td>0.86 (0.48-1.44)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>936/27977 (3%)</td>
<td>1016/28027 (4%)</td>
<td>0.91 (0.83-0.99)</td>
</tr>
</tbody>
</table>

Composite kidney outcome including macroalbuminuria

<table>
<thead>
<tr>
<th>Outcome Description</th>
<th>Study</th>
<th>Event Rate</th>
<th>Event Rate</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ELIXA</td>
<td>172/2639 (6%)</td>
<td>203/2647 (6%)</td>
<td>0.84 (0.68-1.02)</td>
</tr>
<tr>
<td></td>
<td>LEADER</td>
<td>268/4668 (6%)</td>
<td>337/4672 (7%)</td>
<td>0.78 (0.67-0.92)</td>
</tr>
<tr>
<td></td>
<td>SUSTAIN-6</td>
<td>62/1648 (4%)</td>
<td>100/1649 (6%)</td>
<td>0.64 (0.46-0.88)</td>
</tr>
<tr>
<td></td>
<td>EXSCEL</td>
<td>366/6256 (6%)</td>
<td>407/6222 (7%)</td>
<td>0.88 (0.76-1.01)</td>
</tr>
<tr>
<td></td>
<td>REWIND</td>
<td>848/4949 (17%)</td>
<td>970/4952 (20%)</td>
<td>0.85 (0.77-0.93)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>1716/20160 (9%)</td>
<td>2017/20142 (10%)</td>
<td>0.83 (0.78-0.89)</td>
</tr>
</tbody>
</table>

Worsening of kidney function

<table>
<thead>
<tr>
<th>Outcome Description</th>
<th>Study</th>
<th>Event Rate</th>
<th>Event Rate</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ELIXA</td>
<td>35/3032 (1%)</td>
<td>41/3031 (1%)</td>
<td>1.16 (0.74-1.83)</td>
</tr>
<tr>
<td></td>
<td>LEADER</td>
<td>87/4668 (2%)</td>
<td>93/4672 (2%)</td>
<td>0.89 (0.67-1.19)</td>
</tr>
<tr>
<td></td>
<td>SUSTAIN-6</td>
<td>18/1648 (1%)</td>
<td>14/1649 (1%)</td>
<td>1.28 (0.64-2.58)</td>
</tr>
<tr>
<td></td>
<td>EXSCEL</td>
<td>246/4945 (4%)</td>
<td>273/4958 (4%)</td>
<td>0.88 (0.74-1.05)</td>
</tr>
<tr>
<td></td>
<td>REWIND</td>
<td>169/4949 (3%)</td>
<td>237/4952 (5%)</td>
<td>0.70 (0.57-0.85)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>555/20753 (3%)</td>
<td>662/20762 (3%)</td>
<td>0.87 (0.73-1.03)</td>
</tr>
</tbody>
</table>

*based on ELIXA, EXSCEL, HARMONY, LEADER, PIONEER 6, REWIND, SUSTAIN-6

Kristensen SL et al. Lancet Diabetes Endocrinol. 7: 776-785, 2019
For more information on pharmacotherapies for patients with diabetes and CKD, please refer to the KDIGO Speaker’s Guide noted below:

KDIGO Diabetes in CKD Guideline Website:
https://kdigo.org/guidelines/diabetes-ckd/

KDIGO Diabetes in CKD Speaker’s Guide Direct Download:
Management of Metabolic Acidosis

A randomized trial comparing the safety, adherence and pharmacodynamics profiles of two doses of sodium bicarbonate in CKD: The BASE Pilot Trial.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaHCO₃ 0.8 meq/kg-LBW/d (n=90)</td>
<td>Safe</td>
</tr>
<tr>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>NaHCO₃ 0.5 meq/kg-LBW/d (n=52)</td>
<td>✓</td>
</tr>
<tr>
<td>Placebo (n=52)</td>
<td>Reference Group</td>
</tr>
</tbody>
</table>

Conclusion: Both NaHCO₃ doses were safe and tolerable. Neither increased BP or weight. The higher dose raised serum bicarbonate and lowered urinary ammonium more than the lower dose. ACR increased in both groups, but the magnitude was greater with the higher dose.

doi: 10.1681/ASN.2019030287
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Conclusion 8:

Accurate diagnosis and staging of CKD are necessary to utilize treatments effectively.
Conclusion 8: Accurate diagnosis and staging of CKD are necessary to utilize treatments effectively.
Drug Factors associated with increased risk of nephrotoxicity

- **↑ Kidney exposure to drug**
  - Dose and duration of therapy
  - Intravenous route of administration

- **Immune drug effects**
  - Haptens/prohaptens
  - Molecular mimicry
  - Antibody formation
  - Increased T-cell activation

- **Combinations of nephrotoxic drugs**
  - NSAIDs
  - Radiocontrast
  - ACE-I/ARB
  - Cisplatin
  - Aminoglycosides

- **Direct drug nephrotoxicity**
  - Drug-Uromodulin interaction (cast formation)

- **Intracellular drug accumulation**

- **↑ Drug concentrations within cells (transporter competition)**

- **Insoluble drug in urine (crystal formation)**

- **Abbreviations**
  - HES: Heidelberg Education Society
  - Tr: Transporter
Conditions of ↑CKD risk
- Hypertension
- Diabetes
- Cardiovascular disease
- AKI/hospitalization history
- Family history of kidney disease
- Obesity
- Older age
- Other high-risk comorbidities, environmental exposures, or genetic factors

Consider screening for CKD
- Urinary albumin–creatinine ratio (ACR) to detect albuminuria
- Serum creatinine and cystatin C to estimate glomerular filtration rate (eGFR)

Is any of the following present for 3 months or more?
- eGFR < 60 ml/min/1.73 m²
- ACR ≥ 30 mg/g (3 mg/mmol)
- Markers of kidney disease

Classify/risk stratify CKD stage

Periodically repeat evaluation

• Assign eGFR category (ml/min/1.73 m²):
  - G1 = ≥ 90
  - G2 = 60 – 89
  - G3a = 45 – 59
  - G3b = 30 – 44
  - G4 = 15 – 29
  - G5 = < 15

• Identify and treat specific cause of CKD

• Assign albuminuria category:
  - A1 (normal or mild): <30 mg/g or < 3 mg/mmol
  - A2 (moderately): 30–300 mg/g or 3–30 mg/mmol
  - A3 (severely): > 300 mg/g or > 30 mg/mmol
**Treatment**

**Patient safety**
- All patients eGFR < 60: patient safety risk:
  - Dose medications based on eGFR
  - Reduce risk of AKI from volume depletion
  - Adopt “sick day rules” as needed
  - Avoid dual ACEi and ARB blockade
  - Contrast-associated AKI prevention:
    - Use lowest possible radiocontrast dose
    - Adequate hydration before, during, and after the procedure, consider isotonic saline infusion
    - Withhold ACEi or ARBs, diuretics, and other nephrotoxic agents before and after procedure
- eGFR 45 – 59:
  - Avoid prolonged NSAIDs
- eGFR 30 – 44:
  - Avoid prolonged NSAIDs
  - Use metformin with close monitoring at 50% dose
- eGFR < 30:
  - Avoid any NSAIDs
  - Avoid bisphosphonates
  - Avoid metformin
  - Avoid PICC lines for access preservation
  - If on warfarin: monitor PT-INR closely given increased risk of bleeding

**Slowing CKD progression and reducing complications**
- Treat high blood pressure:
  - ACEi or ARB if ACR > 30mg/g or 3 mg/mmol
  - Diuretic often required
  - Dietary sodium < 2000 mg/d
- Type 2 diabetes - target HbA1c < 6.5% to < 8.0%:
  - For those with CKD and type 2 diabetes and eGFR > 30, start SGLT2 inhibitor and metformin
  - If glycemic target not achieved with metformin and SGLT2 inhibition, add GLP1-RA
- CKD complications testing:
  - Anemia – evaluate if CKD G3–G5 and Hb < 13 g/dl for men and < 12 g/dl for women
  - Treat iron deficiency first. Consider starting erythropoiesis-stimulating agents (ESAs) if Hb 9–10 g/dl (avoid Hb > 11.5 g/dl)
  - Acidosis – correct to normal range using bicarbonate supplementation if bicarbonate < 22 mmol/l in CKD G3–G5
- Influenza vaccination
- Pneumococcal and hepatitis B vaccination in CKD G4–G5
- Screen for hepatitis C

**Reduction of CVD complications**
- CKD = ↑CVD risk
- Blood pressure systolic target < 120 mm Hg²
  - Consider BP target of < 130/80 mm Hg in kidney transplant recipients
- Start lipid-lowering therapy:
  - If CKD and age ≥ 50 years, statin is recommended
  - If CKD and age 18–49 years, statin if known CAD, diabetes mellitus, prior stroke, or high ASCVD risk
- Aspirin for secondary prevention unless bleeding risk outweighs benefits

**When to refer to nephrology:**
- AKI or abrupt sustained fall in GFR
- eGFR < 30 ml/min/1.73 m²
- Consistent significant albuminuria (ACR > 300 mg/g or 30 mg/mmol)
- Progression of CKD
- Urinary red cell casts or RBC > 20 per high power field sustained and not readily explained
- CKD and hypertension refractory to treatment with 4 or more antihypertensive agents
- Persistent abnormalities of serum potassium
- Recurrent or extensive nephrolithiasis
- Hereditary kidney disease
Controversies Conference Report

Conclusion 9:

Patient engagement is a critical component of efforts to screen for and treat CKD.
Conclusion 9: Patient engagement is a critical component of efforts to screen for and treat CKD

Potential benefits:

• Improved patient activation
• Improved access to healthcare
• Improved access and adherence to medications
• Timely nephrology referral, dietician referral, and diabetes education
Measures for Defining Success in CKD Screening, Risk Stratification and Treatment Programs

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process (pertaining to health systems, providers, or patients)</td>
<td>• Screening with the correct tests (eGFR and UACR)</td>
</tr>
<tr>
<td></td>
<td>• Timely and appropriate follow-up testing</td>
</tr>
<tr>
<td></td>
<td>• Dietary, exercise, and smoking cessation counseling</td>
</tr>
<tr>
<td></td>
<td>• Clinician CKD awareness as measured by documentation</td>
</tr>
<tr>
<td></td>
<td>• Patient adherence to treatment plan</td>
</tr>
<tr>
<td></td>
<td>• Appropriate nephrology/kidney transplant referrals</td>
</tr>
<tr>
<td></td>
<td>• Availability of essential medicines and testing</td>
</tr>
<tr>
<td>Patient-centered</td>
<td>• Patient awareness of and attitudes toward CKD diagnosis</td>
</tr>
<tr>
<td></td>
<td>• Patient experience and satisfaction</td>
</tr>
<tr>
<td></td>
<td>• CKD-specific knowledge</td>
</tr>
<tr>
<td></td>
<td>• Trust in physician</td>
</tr>
<tr>
<td></td>
<td>• Quality of life</td>
</tr>
<tr>
<td></td>
<td>• Shared decision-making for modality choice, including kidney replacement therapy and conservative management</td>
</tr>
<tr>
<td>Intermediate clinical</td>
<td>• Blood pressure control</td>
</tr>
<tr>
<td></td>
<td>• Glycemic control</td>
</tr>
<tr>
<td></td>
<td>• Statin use</td>
</tr>
<tr>
<td></td>
<td>• ACEI/ARB use</td>
</tr>
<tr>
<td></td>
<td>• SGLT2 inhibitor use</td>
</tr>
<tr>
<td></td>
<td>• Vaccinations</td>
</tr>
<tr>
<td></td>
<td>• Management of CKD-specific complications</td>
</tr>
<tr>
<td></td>
<td>• Drug dosing/adverse drug events</td>
</tr>
<tr>
<td>Clinical</td>
<td>• CKD progression—eGFR slope, 40% decline in eGFR, doubling of serum creatinine, kidney failure</td>
</tr>
<tr>
<td></td>
<td>• Hospitalization or emergency department visits</td>
</tr>
<tr>
<td></td>
<td>• Cardiovascular events</td>
</tr>
<tr>
<td></td>
<td>• Acute kidney injury events</td>
</tr>
<tr>
<td></td>
<td>• Emergency dialysis starts</td>
</tr>
<tr>
<td></td>
<td>• Pre-emptive transplant rates</td>
</tr>
<tr>
<td></td>
<td>• All-cause mortality</td>
</tr>
</tbody>
</table>
Educational Interventions for Patients With CKD: A Systematic Review

Pamela A. Lopez-Vargas, MPH, Allison Tong, PhD, Martin Howell, PhD and Jonathan C. Craig, PhD

### Samples of Successful CKD Education Efforts

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient Population</th>
<th>Participants (N)</th>
<th>Study Design</th>
<th>Education Topic(s)</th>
<th>Intervention</th>
<th>Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Patients at risk for AKI on the basis of prescription for hypertension or diabetes medications</td>
<td>152</td>
<td>Prospective cohort study</td>
<td>NSAID avoidance</td>
<td>Pharmacist-led education intervention administered during prescription pickup or pharmacy purchase</td>
<td>Increased knowledge of risks associated with NSAIDs; patient-reported intentions to limit NSAID use</td>
</tr>
<tr>
<td>115</td>
<td>Adult patients with eGFR &lt; 60 ml/min per 1.73 m² not on dialysis</td>
<td>89</td>
<td>Randomized, controlled clinical trial</td>
<td>Protein intake</td>
<td>Addition of nutrition education materials to a dietary counseling program</td>
<td>Reduced protein intake in the intervention compared with the control group; adherence rates did not differ between groups</td>
</tr>
<tr>
<td>6</td>
<td>Patients with progressive CKD expected to require RRT within 6–18 mo (sCr &lt; 3.4 mg/dl)</td>
<td>297</td>
<td>Inception cohort, prospective, randomized, controlled trial</td>
<td>Healthy kidney function, kidney diseases, RRT modalities, diet/nutrition, medications, lifestyle changes</td>
<td>90-min one-on-one slide-based teaching sessions supported by a printed 60-page booklet and 10-min telephone support calls every 3 wk</td>
<td>Delayed dialysis initiation in the intervention group; knowledge acquisition was directly associated with time to dialysis</td>
</tr>
<tr>
<td>8</td>
<td>Patients with eGFR &lt; 30 ml/min per 1.73 m²</td>
<td>70</td>
<td>Randomized, controlled trial</td>
<td>Self-care dialysis (i.e., peritoneal dialysis, home hemodialysis)</td>
<td>Two-phase education program, including educational booklets and a 15-min video (phase 1) as well as a 90-min interactive small group session (phase 2)</td>
<td>Increase in patient-reported intention to use self-care dialysis among intervention compared with usual care group</td>
</tr>
<tr>
<td>11</td>
<td>Patients with progressive CKD expected to require RRT (sCr &lt; 3.96 mg/dl and increasing)</td>
<td>335</td>
<td>Randomized, controlled trial</td>
<td>Normal kidney function, kidney diseases, dietary management, RRT modalities</td>
<td>60- to 75-min one-on-one slide lecture presentation supplemented by a 22-page booklet summarizing the presentation content</td>
<td>The intervention group survived an average of 8 mo longer after dialysis initiation than the usual care group</td>
</tr>
<tr>
<td>116</td>
<td>Patients on hemodialysis</td>
<td>118</td>
<td>Randomized, controlled trial</td>
<td>BP control</td>
<td>Nurse-led education program incorporating monitoring, goal setting, and reinforcement</td>
<td>The intervention group had reduced systolic and diastolic BPs compared with the control group</td>
</tr>
</tbody>
</table>

sCr, serum creatinine; NSAID, nonsteroidal anti-inflammatory drug.
Role of Information Technology in CKD Care

Health information technology (IT) to improve the care of patients with chronic kidney disease (CKD)

Clarissa J Diamantidis\(^1,2\)* and Stefan Becker\(^3\)

**Abstract**

Several reports show that patients with chronic disease who are empowered with information technology (IT) tools for monitoring, training and self-management have improved outcomes, however there are few such applications employed in kidney disease. This review explores the current and potential uses of health IT platforms to advance kidney disease care by offering innovative solutions to inform, engage and communicate with individuals with CKD.

**Keywords:** Chronic kidney disease, Health information technology, Mobile health, Patient safety
National Kidney Disease Education Program

The National Kidney Disease Education Program (NKDEP) (2000–2019) promoted evidence-based interventions to improve understanding, detection, and management of kidney disease, including identification of patients at greatest risk for progression to kidney failure. NIDDK carries forward the content and outreach and promotion activities developed under the program to meet ongoing need.

Identify & Manage Patients
- Identify and Evaluate Patients With CKD
- Manage Patients with CKD
- Training for CDEs, RDs, and PharmDs

Learn more about Patient Management

GFR Calculators
- MDRD for Adults (Conventional Units)
- MDRD for Adults (SI Units)
- CKD–EPI for Adults (Conventional Units)
- CKD–EPI for Adults (SI Units)
- For Children (Conventional Units)
- For Children (SI Units)

Learn more about GFR Calculators
Types of Telehealth Applications to Enhance CKD Knowledge and Awareness

<table>
<thead>
<tr>
<th>Telehealth Application</th>
<th>Definition</th>
<th>Kolb’s Learning Theory</th>
<th>Current Uses</th>
<th>Potential Future Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Web-based applications</td>
<td>Internet Web site with educational text or links to educational materials</td>
<td>Knowledge</td>
<td>Patient: education about CKD</td>
<td>Patient: inclusion in self-management training and risk factor education for CKD prevention</td>
</tr>
<tr>
<td>Videoconferencing</td>
<td>Synchronous discussion among peers that are physically distant, broadcast over video</td>
<td>Knowledge and understanding</td>
<td>Patient: awareness of CKD and empowerment with virtual support groups</td>
<td>Provider: nephrology clinical support tools (protocols, treatment algorithms)</td>
</tr>
<tr>
<td>Text messaging</td>
<td>Mobile phone based text messages delivered over telephone cables or broadband</td>
<td>Knowledge</td>
<td>Patient: CKD self-management (medication adherence, appointment reminders)</td>
<td>Patient: eHealth communities for psychosocial support, including those around kidney donation</td>
</tr>
<tr>
<td>Interactive voice response</td>
<td>Telephone-based automated voice recognition system that delivers/captures personalized data</td>
<td>Knowledge; limited understanding</td>
<td>Patient: education about CKD and healthy lifestyles</td>
<td>Provider: intra-professional nephrology education during training</td>
</tr>
<tr>
<td>Mobile applications</td>
<td>Wireless communication among objects that provide individualized data</td>
<td>Knowledge and understanding</td>
<td>Patient: self-management with personal data</td>
<td>Patient: self-management (medication titration)</td>
</tr>
<tr>
<td>Store and forward communication</td>
<td>Asynchronous communication using text and/or pictures</td>
<td>Knowledge and understanding</td>
<td>Patient: education about community resources</td>
<td>Provider: proactive preventive consultation</td>
</tr>
</tbody>
</table>

### Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

<table>
<thead>
<tr>
<th>GFR categories (mL/min per 1.73 m²)</th>
<th>Description and range</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Normal or high</td>
<td>≥90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G2</td>
<td>Mildly decreased</td>
<td>60–89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G3a</td>
<td>Mildly to moderately decreased</td>
<td>45–59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G3b</td>
<td>Moderately to severely decreased</td>
<td>30–44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G4</td>
<td>Severely decreased</td>
<td>15–29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Persistent albuminuria categories**

- Normal to mildly increased
- Moderately increased
- Severely increased

<table>
<thead>
<tr>
<th></th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal to mildly increased</td>
<td>Moderately increased</td>
<td>Severely increased</td>
</tr>
<tr>
<td></td>
<td>&lt;30 mg/g</td>
<td>30–300 mg/g</td>
<td>&gt;300 mg/g</td>
</tr>
<tr>
<td></td>
<td>&lt;3 mg/mmol</td>
<td>3–30 mg/mmol</td>
<td>&gt;30 mg/mmol</td>
</tr>
</tbody>
</table>

Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.
Controversies Conference Report

Conclusion 10:

CKD screening and treatment efforts require multi-stakeholder implementation strategies to overcome barriers to high quality CKD care.
Conclusion 10: CKD screening and treatment efforts require multi-stakeholder implementation strategies to overcome barriers to high quality CKD care.
<table>
<thead>
<tr>
<th><strong>PATIENT RELATED BARRIERS</strong></th>
<th><strong>HEALTH SYSTEM RELATED BARRIERS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Low patient knowledge of CKD and its associated risks, and social risk factors, such as limited financial resources and low health literacy</td>
<td>• Perceived lack of urgency for detecting early CKD among primary care clinicians</td>
</tr>
<tr>
<td></td>
<td>• Lack of knowledge of CKD guidelines</td>
</tr>
<tr>
<td></td>
<td>• Lack of incentives for CKD interventions</td>
</tr>
<tr>
<td></td>
<td>• Lack of CKD-specific clinical quality measures</td>
</tr>
<tr>
<td></td>
<td>• Suboptimal communication between specialties</td>
</tr>
</tbody>
</table>
Health System-Level Approaches for Improving Early CKD Identification and Management

Framework for developing initiatives

Conceptual
- Understand patient flow through the health system and identify possible tactics for engagement
- Develop risk-based approaches to identifying and treating CKD
- Integrate novel program processes with existing health services and processes
  - Augment/strengthen in view of early CKD identification and intervention
- Actively engage with:
  - Patients
  - Health care clinicians
  - Health system administrators and policy makers
- Develop monitoring and improvement strategies

Practical
- Determine population for screening based on local risk factors
- Identify existing screening programs for other diseases, such as cardiovascular
- Assess whether there is necessary political commitment
- Specify available resources (workforce/material/funding)
- Develop a technical package, strategies using the best available evidence, for CKD screening and management
- Provide specific, actionable recommendations with level of evidence
- Develop targeted versions of the guideline summary aimed at patients and primary-care providers\(^{103,104}\)
- Develop visually appealing infographics and apps to aid in knowledge translation
- Integrate guideline recommendations in laboratory information systems and electronic health records with clinical decision support
- Engage medical educators to teach guideline-based CKD care in medical schools
- Engage all stakeholders—professional societies (such as ISN), patients, payers, health systems, and disease-specific foundations—in dissemination strategies
- Establish governance for monitoring, evaluation, and improvement
Health System-Level Approaches for Improving Early CKD Identification and Management

Framework for continued advocacy and expansion of efforts

- Identify the full health and economic burdens of kidney diseases
- Establish kidney disease registries and use collected data to drive surveillance, feedback, and integration
- Collaborate with other guideline bodies and professional societies to maximize consistency in recommendations (e.g., primary care, cardiology, endocrinology, geriatrics)
- Develop evidence-based quality measures for CKD care
- Document real-world health and economic consequences of successful interventions and models of care
- Identify methods for sustainable financing of optimal services
- Generate and promote evidence linking health promotion to improved health and economic outcomes regarding kidney diseases
- Continue advocacy from researchers, clinicians, and policy makers for healthy environments and lives
- Focus investments and reforms to develop effective primary-care systems, including pharmaceuticals and behavioral interventions
- Invest in research to identify novel risk factors for kidney diseases
- Implement cost-effective strategies to target care to individuals at increased risk of kidney disease
Measures for Defining Success in CKD Screening, Risk Stratification and Treatment Programs

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Indicators</th>
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| **Process (pertaining to health systems, providers, or patients)** | • Screening with the correct tests (eGFR and UACR)  
• Timely and appropriate follow-up testing  
• Dietary, exercise, and smoking cessation counseling  
• Clinician CKD awareness as measured by documentation  
• Patient adherence to treatment plan  
• Appropriate nephrology/kidney transplant referrals  
• Availability of essential medicines and testing |
| **Patient-centered**                         | • Patient awareness of and attitudes toward CKD diagnosis  
• Patient experience and satisfaction  
• CKD-specific knowledge  
• Trust in physician  
• Quality of life  
• Shared decision-making for modality choice, including kidney replacement therapy and conservative management |
| **Intermediate clinical**                    | • Blood pressure control  
• Glycemic control  
• Statin use  
• ACEI/ARB use  
• SGLT2 inhibitor use  
• Vaccinations  
• Management of CKD-specific complications  
• Drug dosing/adverse drug events |
| **Clinical**                                 | • CKD progression—eGFR slope, 40% decline in eGFR, doubling of serum creatinine, kidney failure  
• Hospitalization or emergency department visits  
• Cardiovascular events  
• Acute kidney injury events  
• Emergency dialysis starts  
• Pre-emptive transplant rates  
• All-cause mortality |
Controversies Conference Report
Conclusion 11:

Financial and nonfinancial incentives need to be aligned toward CKD screening, risk stratification, and treatment.
Conclusion 11: Financial and non-financial incentives need to be aligned toward CKD screening, risk stratification and treatment.

Advancing American Kidney Health Executive Order

Infographic courtesy of Dr. Tejas Desai
Controversies Conference Report

Conclusion 12:

CKD screening in high-risk groups is likely to be cost-effective.
Conclusion 12: CKD screening in high-risk groups is likely to be cost-effective.

The Preventable Productivity Burden of Kidney Disease in Australia

Feby Savira,1,2 Zanfina Ademi,1 Bing H. Wang,1,2 Andrew R. Kompa,3 Alice J. Owen,1 Danny Liew,1 and Ella Zomer1

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Savira et al. JASN 2021; doi: https://doi.org/10.1681/ASN.2020081148

This Australian study demonstrated that even a modest 10% reduction in CKD incidence translated into the prevention of 1503 cases of CKD G3, 117 cases of CKD G4-G5, and six new cases of kidney failure per year and would result in a gain of 7590 productivity-adjusted life years (PALYs), with an associated cost savings of US$1.1 billion.
Conclusion 12: CKD screening in high-risk groups is likely to be cost-effective.

Using CKD risk scores may also allow clinicians to cost-effectively identify a broader population for CKD screening with testing for albuminuria and potentially detect people with CKD at earlier stages of the disease than current approaches of screening only persons with diabetes or hypertension.
Conclusion 12: CKD screening in high-risk groups is likely to be cost-effective.

Future research direction: we need new cost effectiveness analyses to overcome limitations of prior studies.

- Predominant focus on proteinuria
- Minimal inclusion of cardiovascular outcomes: the key complication of CKD that drive hospitalizations and mortality
- Assumption of annual screening: costly and probably unnecessary
- Models did not incorporate patient perspectives and patient-reported outcomes
- Few cost-effectiveness studies included low and middle income countries (LMICs)
Controversies Conference Report

Conclusion 13:

CKD screening approaches may differ in LMIC countries.
Conclusion 13: CKD screening approaches may differ in LMIC countries
CKD is highly prevalent, costly, and its worldwide disease burden is increasing.

There are low-cost and accurate tests for CKD. Serum creatinine and cystatin C are accurate tests to estimate GFR. UACR is a sensitive measurement of kidney damage but urine dipstick proteinuria could be considered in low-resource settings.

CKD is asymptomatic until late stages. The asymptomatic stage contributes to low awareness of CKD in patients with the diagnosis. Therefore, a screening program could shift recognition of CKD into much earlier stages relative to current practice.

Individuals with CKD often express a preference for early communication about a CKD diagnosis.

Treatments for recognized CKD can be initiated during early stages, are accepted, and are highly effective.

CKD screening in high-risk groups is likely to be cost-effective.
### Responses to Common Criticisms of CKD Early Detection and Treatment Proposals

<table>
<thead>
<tr>
<th>Criticism</th>
<th>KDIGO Controversies Conference Conclusion</th>
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</table>
| **CKD testing is too expensive.**                   | - The three measures recommended for CKD detection and risk stratification (creatinine, cystatin C, UACR) are all feasible on auto-analyzers, and can be measured together for less than $20 USD. Models that exclude cystatin C are acceptable for low-resource settings  
  - Higher volume testing would further lower the costs per individual  
  - The costs of a monitoring program are largely driven by the frequency of testing; the intervals for CKD monitoring could be tailored to the individual’s prior testing and risk factor profile |
| **All patients get a serum creatinine test anyway.** | - Many persons with CKD are not actively engaged in medical care and may not have had a GFR assessment at appropriate frequency  
  - Persons with abnormal albuminuria but preserved GFR represent a substantial proportion of the CKD population, and they are woefully under-detected in current clinical care |
| **All CKD patients already have diabetes or hypertension, and diagnosing CKD would not change management.** | - A significant proportion of patients, especially in LMIC have CKD in absence of prior diabetes or hypertension and limiting screening to those with these conditions would miss a large fraction of CKD  
  - Persons with diabetes or hypertension are not effectively monitored with appropriate kidney measures (e.g., UACR)  
  - CKD diagnosis may impact choice of antihypertensive agent, medication dosing, indication for statin therapy, SGLT2 inhibitor therapy, avoidance of nephrotoxins, and prognostication |
## Responses to Common Criticisms of CKD Early Detection and Treatment Proposals

<table>
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</table>
| Older adults do not have “real” CKD.                                      | - Older adults have the highest prevalence of CKD across all GFR and albuminuria stages, and CKD impacts physical and cognitive function, medication safety, and prognosis for older adults  
  - As with all screening programs, testing must be consistent with that person’s goals of care and life expectancy, but this would not justify excluding older adults from CKD detection and monitoring                                                                                                                                                                                                                                                                                     |
| There are no effective treatments for CKD, even if it is detected.        | - Several available treatments can reduce CKD progression and the risk of cardiovascular disease for persons with CKD, including ACEi/ARBs, statins, BP and diabetes management, and SGLT2 inhibitors  
  - Earlier initiation of preventive therapies may slow progression across stages and ultimately reduce both the incidence and prevalence of kidney failure and risk of future development of cardiovascular disease. Benefits have been observed for some therapies in reducing all-cause mortality and risk for heart failure.                                                                                                                                                                                                 |
Responses to Common Criticisms of CKD Early Detection and Treatment Proposals

<table>
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<th>KDIGO Controversies Conference Conclusion</th>
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</thead>
</table>
| Notifying patients of CKD would cause more harm and anxiety than any benefit | · With proper communication about CKD staging and education regarding lifestyle and treatment options, patients with newly detected CKD can make positive choices that will reduce their risk of progression  
· Patient representatives have expressed their desire for early detection strategies and for prognostic information, while lamenting that their own CKD diagnosis occurred too late |
| The requirement for confirmatory testing at 90-days to diagnose CKD is a barrier to effective treatment | · The 90-day period might be useful to distinguish the chronicity of kidney disease, but it is not essential to establish that kidney disease is present  
· Persons with high-risk CKD should be treated expeditiously without waiting for confirmatory testing |
Conclusions

• The KDIGO Controversies Conference participants were unanimous that the bulk of evidence supports systematic approaches to screen for, risk stratify, and treat persons with CKD.

• Because interventions to slow CKD progression and reduce cardiovascular risk are evidence-based and have been shown to improve outcomes, the focus should be on strategies to maximize deployment of CKD screening, risk stratification, and treatment efforts.
Key conclusions from KDIGO Controversies Conference on Early Identification and Intervention

Populations for CKD screening, risk stratification, and treatment

**Conclusion 1.** Persons with hypertension, diabetes, or cardiovascular disease should be screened for CKD.
**Conclusion 2.** CKD screening and treatment programs should also be implemented in other high-risk individuals and populations based on comorbidities, environmental exposures, or genetic risk factors.
**Conclusion 3.** The initiation, frequency, and cessation of CKD screening should be individualized based on kidney and cardiovascular risk profiles and individual preferences.

Measurements for early CKD

**Conclusion 4.** CKD screening and risk stratification must consist of a dual assessment of estimated glomerular filtration rate (eGFR) and albuminuria (UACR).
**Conclusion 5.** Accurate GFR estimation includes both creatinine and cystatin C measurements for initial diagnosis and staging.
**Conclusion 6.** The combination of creatinine, cystatin C, and UACR for CKD screening is affordable in high-income settings.

Interventions for CKD

**Conclusion 7.** A key rationale for CKD screening is the availability of many effective interventions to delay CKD progression and reduce cardiovascular risk.
**Conclusion 8.** Accurate diagnosis and staging of CKD are necessary to utilize treatments effectively.
**Conclusion 9.** Patient engagement is a critical component of efforts to screen for and treat CKD.

Health system and economic factors

**Conclusion 10.** CKD screening and treatment efforts require multi-stakeholder implementation strategies to overcome barriers to high-quality CKD care.
**Conclusion 11.** Financial and nonfinancial incentives need to be aligned toward CKD screening, risk stratification, and treatment.
**Conclusion 12.** CKD screening in high-risk groups is likely to be cost-effective.
**Conclusion 13.** CKD screening approaches may differ in LMIC countries.

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; LMICs, low- and middle-income countries; UACR, urine albumin-to-creatinine ratio.
Future Research

- **Pragmatic trials** should be designed to test CKD early identification and intervention programs across various high-risk populations using different combinations of measures.

- Implementation efforts should engage policy makers, local clinicians, the community at large and broader stakeholders in an iterative process.

- Ultimately, **large-scale randomized controlled trials** should be conducted to evaluate the effects of CKD screening, risk stratification, and treatment programs compared with usual care on clinical endpoints.
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