Chronic Kidney Disease Management 2022: Advancing the American Kidney Health Initiative

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Director of Ascension Kidney Care
Ascension Health System
37,000,000 Americans have kidney diseases

>726,000 Americans have kidney failure

>100,000 Americans begin dialysis each year and nearly 60% of those will die within the first 5 years of treatment

~100,000 Americans are on the kidney transplant waiting list
NIH Spending per Patient

- **HIV/AIDS**: $2563, $3.1 B for 1.2 M patients
- **Cancer**: $319, $7.4 B for 23.3 M patients
- **Heart Disease**: $53, $1.6 B for 30.3 M patients
- **Kidney Disease**: $19, $0.72 B for 37 M patients
Advancing American Kidney Health initiative

Goals:

• Reduce the Risk of Kidney Failure
• Improve Access to and Quality of Person-Centered Treatment Options
• Increase Access to Kidney Transplants
Executive Order on Advancing American Kidney Health
10 July 2019
whitehouse.gov/presidential-actions/executive-order-advancing-american-kidney-health
Designed by: Tejas Desai, MD | @nephondemand

**Goals**

- 80% of incident ESRD patients receive either home dialysis therapy or transplantation by CY 2025
- Standardize organ procurement reduce percentage of discarded organs
- Remove financial barriers for living kidney donors
- Encourage development of the artificial kidney
- Restructure payment models to incentivize prevention, home therapy/transplantation

**Payment Models**

- **ETC | KCF**
  - CKCC Graduated
  - CKCC Pro/Global

  ![Randomized](icon)
  - ESRD Treatment Choices (ETC)
    - Mandatory randomization: no crossover/dropout allowed
  - Conventional Payment Model
    - Payment not affected

  ![Mandatory](icon)
  - **MANDATORY**
    - Receive capitated payments for CKD 4-5 and ESRD patients
    - Receive bonus $ for patients transplanted (distributed over 3 year period if transplant remains “successful”)
    - Same as KCF
    - Assume 50-100% risk as well as 50-100% of shared savings

  ![Optional](icon)
  - **OPTIONAL**
    - Kidney Care First (KCF)
    - Kidney Care Organization + Nephrolist
A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommend immediate implementation of the <strong>CKD-EPI creatinine equation refit without the race variable</strong> in all laboratories in the U.S. The equation refit excludes race in the calculation and reporting, includes diversity in its development, is immediately available to all labs in the U.S. and has acceptable performance characteristics and potential consequences that do not disproportionately affect any one group of individuals.</td>
</tr>
<tr>
<td>Recommend national efforts to facilitate increased, routine, and timely use of cystatin C, especially to confirm eGFR in clinical decision-making</td>
</tr>
<tr>
<td>Encourage and fund research on GFR estimation with new endogenous filtration markers and on interventions to eliminate racial and ethnic disparities</td>
</tr>
<tr>
<td>The Task Force gathered input from diverse stakeholders and carefully reviewed the evidence to create these recommendations</td>
</tr>
</tbody>
</table>

AJKD DOI: 10.1053/j.ajkd.2021.08.003, JASN DOI: 10.1681/ASN.2021070988 
Visual Graphic by Edgar Lerma, MD, FASN
Eliminating Race Coefficient in CKD-EPI

**Potential Benefits:**

- Expand Access to Care
- Expanding Medicare coverage for medical nutrition therapy (0.47%) and kidney disease education (0.14%)
- Increase nephrology referrals
- Potentially earlier transplant referral

**Potential Unintended Consequences**

- Medication limitations (i.e., SGLT2i candidacy)
- Financial implications (higher insurance costs)
- Possible ineligibility for living donor (2.1% disqualified in Diao/NHANES study)
- Clinical trial enrollment eligibility
60-year-old man has a known diagnosis of type 2 diabetes (micro- and macrovascular disease). He has established chronic kidney disease, hyperlipidemia, hypertension, and proteinuria. Which of the following statements is true?

A. Intensive treatment of blood pressure in diabetics improves survival

B. Early start of dialysis is associated with improved survival

C. Intensive treatment of lipid level improves survival

D. The use of SGLT2 in moderate CKD is associated with improved renal outcomes

E. Intensive treatment of blood pressure in CKD preserves kidney function
Proteinuria Significance

- Powerful predictor of progressive renal disease
- Even low level (1+ dipstick) is associated with twofold increased risk of ESRD
- Hallmark of diabetic and hypertensive nephropathy (accounts for the majority of patients with proteinuria)
- Significant (>1g/day) in absence of identifiable cause warrants further investigation
<table>
<thead>
<tr>
<th>Urine Studies</th>
<th>Protein</th>
<th>Pointers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipstick</td>
<td>![Protein Dipstick]</td>
<td>• Albumin / negatively charged proteins</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Can miss microalbuminurin/+ proteins (Ig)</td>
</tr>
<tr>
<td>Spot Urine</td>
<td><strong>Albumin/creatinine ratio (UACR)</strong></td>
<td>• More precise at lower concentrations</td>
</tr>
<tr>
<td>UACR</td>
<td>• &lt; 30 mg/g: Normal</td>
<td>○ Albumin only</td>
</tr>
<tr>
<td></td>
<td>• 30-300: Microalbuminuria</td>
<td>○ Screening increased risk of CKD (ie DM, HTN, glomerular disease)</td>
</tr>
<tr>
<td></td>
<td>○ &gt; 300: Macroalbuminuria</td>
<td>○ One of the first proteins to pass</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Protein-creatinine ratio (UPCR)</strong></td>
</tr>
<tr>
<td></td>
<td>• &lt; 0.15 g/g (150 mg/g): Normal</td>
<td>• Check UPCR if HIGH UACR</td>
</tr>
<tr>
<td></td>
<td>• 0.15-3.0 (150-3000): Proteinuria</td>
<td>○ Checks non-albumin + albumin</td>
</tr>
<tr>
<td></td>
<td>• &gt; 3.5 mg/g: Nephrotic range</td>
<td>• Closely correlates to 24-hour urine protein</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Trend proteinuria</td>
</tr>
<tr>
<td>24-hour urine</td>
<td><strong>Albumin</strong></td>
<td>• Gold standard</td>
</tr>
<tr>
<td>collection</td>
<td>• 30-300 mg/dL: microalbuminuria</td>
<td>• Cumbersome</td>
</tr>
<tr>
<td></td>
<td>• &gt; 300 mg/dL: macroalbuminuria</td>
<td>• Significant collection errors (missed samples, timing)</td>
</tr>
<tr>
<td></td>
<td><strong>Protein</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• &gt; 150 mg/dL: proteinuria</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• &gt; 3-3.5 g/dL: nephrotic</td>
<td></td>
</tr>
</tbody>
</table>
- Normal:
  - e.g. Bence-Jones proteinuria

- Overflow:
  - e.g. albuminuria

- Glomerular:
  - e.g. β₂- or α₁-microglobulinuria

- Tubular:
  - e.g. Tamm-Horsfall proteinuria

- Secreted:
  - e.g. Bence-Jones proteinuria
Differential diagnosis of glomerular diseases

Diseases presented by either nephrotic and nephritic can be idiopathic or secondary to other causes.
Strategies for Preventing Progressive Nephropathy in Type 2 Diabetes

- **Target glomerular hemodynamics**
  - Efferent vasodilation (RAASi)
  - Afferent vasoconstriction (SGLT2i)
  - BP control

- **CV risk reduction strategies**

- **Glucose control**

- **Future therapies**
  - Anti-inflammatory, anti-fibrotics
### Renoprotection with RAAS Inhibition

<table>
<thead>
<tr>
<th>Trial</th>
<th>Population</th>
<th>N</th>
<th>Intervention</th>
<th>Conclusions</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROADMAP</td>
<td>T2DM without microalbuminuria</td>
<td>4,449</td>
<td>Olmesartan vs placebo</td>
<td>Olmesartan delayed the onset of microalbuminuria</td>
<td>Olmesartan group had lower BPs and more CV deaths</td>
</tr>
<tr>
<td>IRMA-2</td>
<td>T2DM and microalbuminuria</td>
<td>590</td>
<td>Irbesartan 150 mg vs irbesartan 300 mg vs placebo</td>
<td>Irbesartan reduced the development of overt proteinuria</td>
<td>Subgroup analysis suggested a dose-dependent effect</td>
</tr>
<tr>
<td>Captopril Trial</td>
<td>T1DM with proteinuria</td>
<td>409</td>
<td>Captopril 25 mg 3x/d vs placebo</td>
<td>Captopril reduced the risk for doubling of SCr as a primary outcome and death, dialysis therapy, or transplantation as a secondary outcome</td>
<td></td>
</tr>
<tr>
<td>IDNT</td>
<td>T2DM with proteinuria and reduced kidney function</td>
<td>1,715</td>
<td>Irbesartan vs amlodipine vs placebo</td>
<td>Irbesartan reduced the risk for doubling of SCr, ESRD, or death</td>
<td></td>
</tr>
<tr>
<td>RENAAL</td>
<td>T2DM with proteinuria and reduced kidney function</td>
<td>1,513</td>
<td>Losartan vs placebo</td>
<td>Losartan reduced the risk for doubling of SCr, ESRD, or death</td>
<td></td>
</tr>
</tbody>
</table>
SGLT2 Inhibition

**Normal TGF**
- Appropriate afferent arteriole tone
- Macula densa
- Normal GFR
- SGLT-2
- Na+/glucose reabsorption

**Impaired TGF**
- Elevated GFR
- Decreased Na+ delivery to macula densa
- Afferent arteriole vasodilation
- Increased Na+/glucose reabsorption

**Restored TGF**
- Normalization of GFR
- Increased Na+ delivery to macula densa
- SGLT-2 inhibition in proximal tubule
- Glucosuria

**Normal physiology**
- Hyperfiltration in early stages of diabetic nephropathy

**SGLT-2 inhibition reduces hyperfiltration via TGF**
49-year-old man with type 2 DM and a recent hemoglobin A1c of 8.9%. He has recently started empagliflozin. Which is true regarding empagliflozin?

A. Empagliflozin is effective in patients with an eGFR <20 ml/min/per 1.73 m²

B. The risk of urinary tract infections is not increased with empagliflozin

C. There is an increased risk of ketoacidosis with empagliflozin

D. The risk of genital fungal infection is not increased with empagliflozin
Renal, Cardiovascular, and Safety Outcomes of Canagliflozin By Baseline Kidney Function: Post hoc Secondary Analysis of the CREDENCE Randomized Trial

### METHODS

4401 participants with T2DM and screening eGFR 30-<90 mL/min/1.73m²

- 41%: 30-<45 mL/min/1.73m²
- 30%: 45-<60 mL/min/1.73m²
- 29%: 60-<90 mL/min/1.73m²

#### Effect of Canagliflozin on Kidney and Cardiovascular Outcomes

<table>
<thead>
<tr>
<th>Screening eGFR</th>
<th>HR (95% CI)</th>
<th>1000 patients/2.6 years (95% CI)</th>
<th>Absolute risk reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-stage kidney disease, doubling of serum creatinine, or renal or cardiovascular death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-&lt;45 mL/min/1.73m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-&lt;60 mL/min/1.73m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-&lt;90 mL/min/1.73m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization for heart failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-&lt;45 mL/min/1.73m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-&lt;60 mL/min/1.73m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-&lt;90 mL/min/1.73m²</td>
<td></td>
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</tr>
</tbody>
</table>

CONCLUSION In CREDENCE, canagliflozin safely reduced the risk of renal and cardiovascular events with consistent results across eGFR subgroups, including those initiating treatment with eGFR 30-<45 mL/min/1.73m². Absolute benefits for renal outcomes were greatest in lower initial eGFR subgroups.

doi: 10.1681/ASN.2019111168
Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy—CREDENCE Trial

A Primary Composite Outcome

- Hazard ratio: 0.70 (95% CI: 0.63–0.80)
- P=0.00003

- Canagliflozin
- Placebo

No. at Risk
Placebo: 2138
Canagliflozin: 2137

B Renal-Specific Composite Outcome

- Hazard ratio: 0.86 (95% CI: 0.73–0.99)
- P=0.0007

- Canagliflozin
- Placebo

No. at Risk
Placebo: 2139
Canagliflozin: 2138

C End-Stage-Kidney Disease

- Hazard ratio: 0.48 (95% CI: 0.39–0.57)
- P<0.0002

- Canagliflozin
- Placebo

No. at Risk
Placebo: 2139
Canagliflozin: 2138

D Dialysis, Kidney Transplantation, or Renal Death

- Hazard ratio: 0.70 (95% CI: 0.54–0.94)

- Canagliflozin
- Placebo

No. at Risk
Placebo: 2139
Canagliflozin: 2138

E Deaths from Cardiovascular Cause

- Hazard ratio: 0.78 (95% CI: 0.61–1.00)
- P=0.05

- Canagliflozin
- Placebo

No. at Risk
Placebo: 2139
Canagliflozin: 2138

F Deaths from Any Cause

- Hazard ratio: 0.83 (95% CI: 0.68–1.12)

- Canagliflozin
- Placebo

No. at Risk
Placebo: 2139
Canagliflozin: 2138

A Urinary Albumin-to-Creatinine Ratio

- Geometric Mean

- Canagliflozin
- Placebo

No. of Patients
Placebo: 2113
Canagliflozin: 2114

B Change from Baseline in Estimated GFR

- Baseline (ml/min/1.73 m²)

- Canagliflozin
- Placebo

No. of Patients
Placebo: 2178
Canagliflozin: 2179


380:2295-2306
Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes- EMPA-REG OUTCOME

Effects of empagliflozin versus placebo on cardiovascular and kidney outcomes were across the KDIGO risk categories

<table>
<thead>
<tr>
<th>EMPA-REG OUTCOME</th>
<th>Randomization</th>
<th>Empagliflozin</th>
<th>Placebo</th>
<th>HR (95% CI)</th>
<th>P values for treatment by subgroup interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 Diabetes</td>
<td></td>
<td>Empagliflozin 10 mgs daily</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atherosclerotic Cardiovascular Disease (ASCVD)</td>
<td></td>
<td>Empagliflozin 10 mgs daily</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR ≥ 30 mL/min/1.73 m²</td>
<td></td>
<td>Empagliflozin 25 mgs daily</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Classified by KDIGO Risk categories</td>
<td></td>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 6,592</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

CV Outcomes (3-point MACE): Empagliflozin 10.5%, Placebo 12.1%, HR (95% CI) 0.86 (0.74, 0.99), p = 0.26-0.85

Kidney Outcomes (Doubling of Creatinine initiation of KRT or death from kidney disease): Empagliflozin 1.7%, Placebo 3.1%, HR (95% CI) 0.54 (0.40, 0.75), p = 0.16-0.60

In all KDIGO risk categories, placebo and empagliflozin had similar adverse events rates, the notable exception being genital infection events, which were more common with empagliflozin for each category.

Conclusions: The observed effects of empagliflozin vs placebo on cardiovascular and kidney outcomes were consistent across the KDIGO risk categories.

Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes - EMPA-REG OUTCOME

A Incident or Worsening Nephropathy

Hazard ratio, 0.61 (95% CI, 0.53–0.70)
P < 0.001

No. at Risk
Placebo 4124 3994 3848 3669 3371 2279 1887 1219 290
Empagliflozin 2061 1946 1836 1703 1433 1016 833 521 106

B Post Hoc Renal Composite Outcome

Hazard ratio, 0.54 (95% CI, 0.40–0.75)
P < 0.001

No. at Risk
Placebo 7020 6986 6931 6864 6765 6696 6651 6088 5114 3961 3488 2707 1703
Empagliflozin 2323 2295 2267 2205 2121 2064 1927 1981 1763 1479 1262 1123 977 731 448
Empagliflozin, 10 mg 2322 2290 2264 2235 2162 2114 2012 2064 1839 1540 1314 1180 1024 785 513
Empagliflozin, 25 mg 2322 2288 2269 2216 2156 2111 2066 2067 1871 1563 1340 1207 1063 838 524

No. In Follow-up
Analysis Total 7020 7020 6996 6931 6864 6765 6696 6651 6088 5114 3961 3488 2707 1703

Dapagliflozin in Patients with Chronic Kidney Disease - DAPA-CKD Trial

Could dapagliflozin improve kidney and cardiovascular outcomes in patients with CKD?

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Kidney</th>
<th>Cardiovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>14.5%</td>
<td>6.4%</td>
</tr>
<tr>
<td>GFR 25-75 ml/min</td>
<td>11.3%</td>
<td>Hospitalization for heart failure</td>
</tr>
<tr>
<td>N= 4304</td>
<td></td>
<td>Death from cardiovascular causes</td>
</tr>
<tr>
<td>Dapagliflozin 10mg/d</td>
<td>N= 2152</td>
<td>6.8%</td>
</tr>
<tr>
<td>67.5% diabetes type 2</td>
<td>9.2%</td>
<td>Death from any cause</td>
</tr>
<tr>
<td>ACR 200-5000mg/g</td>
<td>6.6%</td>
<td>P=0.004</td>
</tr>
<tr>
<td></td>
<td>4.6%</td>
<td>P=0.009</td>
</tr>
</tbody>
</table>

**Conclusion:** Among patients with chronic kidney disease, the risk of any composite kidney or cardiovascular outcomes or death was significantly lower with dapagliflozin than with placebo.


Visual abstract: Denisse Arellano, MD @deniise_am
Dapagliflozin in Patients with Chronic Kidney Disease-
DAPA-CKD Trial
### FDA-approved SGLT2 inhibitors

<table>
<thead>
<tr>
<th>Generic agent (brand)</th>
<th>Canagliflozin (Invokana)</th>
<th>Dapagliflozin (Farxiga)</th>
<th>Empagliflozin (Jardiance)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial dose</strong></td>
<td>100 mg/d if eGFR is 45 to &lt;60 and 300 mg/d if eGFR ≥60</td>
<td>5 mg/d (10 mg/d)</td>
<td>10 mg/d (25 mg/d)</td>
</tr>
<tr>
<td><strong>Renal dosage adjustments</strong></td>
<td>Discontinue if eGFR is persistently &lt;45 (Contraindicated if eGFR &lt;30)</td>
<td>Do not administer/discontinue with eGFR &lt;60</td>
<td>Do not initiate/discontinue with eGFR persistently &lt;45 (Contraindicated if eGFR &lt;30)</td>
</tr>
<tr>
<td><strong>Hepatic dosage adjustments</strong></td>
<td>No adjustment for mild to moderate impairment; not recommended in severe impairment (has not been studied)</td>
<td>None to note</td>
<td>None to note</td>
</tr>
<tr>
<td><strong>Drug interactions</strong></td>
<td>If receiving concurrent UGT enzyme inducers and eGFR is 45 to &lt;60, consider alternative antihyperglycemic therapy</td>
<td>None to note</td>
<td>None to note</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Administer prior to first meal</td>
<td>Administer in the morning without regard to food</td>
<td></td>
</tr>
<tr>
<td><strong>Common adverse effects</strong></td>
<td>Genital mycotic infections, urinary tract infections, volume-related effects such as dizziness and hypotension</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Available combination products, generic (brand)</strong></td>
<td>canagliflozin + metformin (Invokamet)</td>
<td>dapagliflozin + metformin ER (Xigduo)</td>
<td>empagliflozin + metformin (Synjardy) empagliflozin + linagliptan (Glyxambi)</td>
</tr>
</tbody>
</table>
Side effects

- Euglycemic DKA
- Genital Infections
- Peripheral vascular disease/amputations (Empagliflozin only, not Dapagliflozin)
- Possibly bladder Ca (Dapagliflozin only)
- Hypotension/AKI (diuretic)
- Increased LDL-C
- NOT hypoglycemia
Does finerenone slow progression of CKD and reduce cardiovascular mortality in patients with type 2 diabetes?

**Phase 3, Double-Blind, Multicenter, Randomized, Controlled Trial**

5674 Patients with type 2 diabetes and CKD

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients</th>
<th>Primary Composite Outcome: Kidney Failure with &gt;40% decrease in eGFR over 4-week period or death from renal causes</th>
<th>Secondary Composite Outcome: Death from cardiovascular causes or hospitalization for any cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finerenone</td>
<td>n = 2833</td>
<td>17.8% (504/2833) HR 0.82 (0.73 - 0.93) p = 0.001</td>
<td>13.0% (367/2833) HR 0.86 (0.75 - 0.99) p = 0.03</td>
</tr>
<tr>
<td>Placebo</td>
<td>n = 2841</td>
<td>21.1% (600/2841)</td>
<td>14.8% (420/2841)</td>
</tr>
</tbody>
</table>

2.6 year median follow up

In patients with CKD and type 2 diabetes, treatment with finerenone resulted in lower risk of CKD progression and cardiovascular events than placebo.

N Engl J Med 2020;
FIGARO-DKD trial

RESEARCH SUMMARY

Cardiovascular Events with Finnerenone in Kidney Disease and Type 2 Diabetes

Pitt B et al. DOI: 10.1056/NEJMoa2110956

CLINICAL PROBLEM
Finnerenone, a selective nonsteroidal mineralocorticoid receptor antagonist, improves cardiovascular outcomes in patients with stage 3 or 4 chronic kidney disease (CKD) with severely elevated albuminuria and type 2 diabetes. Whether finnerenone is beneficial in patients with diabetes and less-advanced CKD is unclear.

CLINICAL TRIAL
Design: A phase 3, multicenter, randomized, placebo-controlled trial examined the efficacy and safety of finnerenone in adults with type 2 diabetes and a range of CKD stages.
Interventions: 7457 patients with diabetes and CKD treated with a maximum-dose renin-angiotensin system inhibitor were assigned to receive oral finnerenone or placebo. Eligible patients had persistent, moderately elevated albuminuria plus an estimated glomerular filtration rate (eGFR) of 25 to 90 ml per minute per 1.73 m² (stage 2 to 4 CKD) or persistent, severely elevated albuminuria plus an eGFR of at least 60 ml per minute per 1.73 m² (stage 1 or 2 CKD). The primary outcome was a composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure.

RESULTS
Efficacy: During a median 3.4 years of follow-up, the incidence of primary outcome events was lower with finnerenone than with placebo, a difference driven mainly by a lower incidence of hospitalization with finnerenone.
Safety: The incidence of serious adverse events was similar in the two groups. Hypokalemia occurred more often with finnerenone but did not result in any deaths and rarely resulted in treatment discontinuation.

LIMITATIONS AND REMAINING QUESTIONS
- Few Black patients were included. Patients with symptomatic heart failure with a reduced ejection fraction were excluded.
- Current clinical guidance recommends sodium-glucose cotransporter 2 inhibitors or glucagon-like peptide-1 receptor agonists in patients with type 2 diabetes and CKD. Whether using finnerenone with these agents offers additive cardiovascular benefits is unclear.

Death from Cardiovascular Causes, Nonfatal MI, Nonfatal Stroke, or Hospitalization for Heart Failure

<table>
<thead>
<tr>
<th></th>
<th>Finnerenone</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR</td>
<td>0.63</td>
<td>0.76</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.43 to 0.90</td>
<td>0.60 to 1.00</td>
</tr>
</tbody>
</table>

Hospitalization for Heart Failure

<table>
<thead>
<tr>
<th></th>
<th>Finnerenone</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR</td>
<td>0.71</td>
<td>0.90</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.50 to 0.96</td>
<td>0.50 to 1.00</td>
</tr>
</tbody>
</table>

Safety Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Finnerenone</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse events</td>
<td>35.4%</td>
<td>32.9%</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>10.8%</td>
<td>5.4%</td>
</tr>
<tr>
<td>Treatment discontinuation due to hypokalemia</td>
<td>1.2%</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

CONCLUSIONS
The mineralocorticoid receptor antagonist finnerenone lowered the risk of major adverse cardiovascular events among patients with type 2 diabetes and a wide range of CKD stages.

Links: Full Article | NEJM Quick Take
**Methods**

46 patients
- Age ≥18 years
- UACR 100-3500 mg/24-hour
- eGFR >30 - <90 ml/min/1.73m²
- Stable (>4 weeks) dose of ACEi or ARB

Dapagliflozin
- 10 mg

Eplerenone
- 50 mg

Eplerenone 50 mg

Dapagliflozin 10 mg

4-weeks treatment in random order with 4-weeks wash-out in between

**Outcomes**

**UACR change (%) from baseline**
- Dapagliflozin: 19.3
- Eplerenone: 33.7
- Dapagliflozin-Eplerenone: 53.0

*combination vs. dapa: p<0.001*
*combination vs. eple: p=0.0127*

**Change from baseline in serum K (mmol/L)**
- Dapagliflozin: 0.03
- Eplerenone: 0.36
- Dapagliflozin-Eplerenone: 0.23

*combination vs. dapa: p<0.0018*
*combination vs. eple: p=0.0296*

**Conclusion**

Dapagliflozin in combination with eplerenone reduced albuminuria to a greater extent than either drug alone. Compared to eplerenone, dapagliflozin-eplerenone combined decreased serum potassium.

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Advancing American Kidney Health Initiative

- Appropriate identification of at risk population with appropriate screening tools
- Management of risk factor progression via proper therapeutic interventions
- Preparation for optimal decision making based on risk factors