What we are going to be talking about

• **Hot Topic**
  - SGLT2 Inhibitors and kidney disease progression

• Review the most recent epidemiology CKD/ESRD Trends

• Management of CKD Complications
  - HTN
  - Lipids
  - Metabolic Acidosis

• Conclusions
What is all the BUZZ about Sodium-Glucose Cotransporter (SGLT2) Inhibitors
eGFR < 30
eGFR 45-30: Do not initiate (Maybe)
How Do We Get Here?

• Approved by the FDA in 2013 + 2014
  - Canagliflozin, Dapagliflozin, Empagliflozin

• Several trials were required to meet regulatory requirements for CV safety
  - EMPA-REG OUTCOME: 14% reduction in CV composite endpoints (Zinman B. NEJM 2015)
  - CANVAS + R: 14% reduction in CV composite endpoints (Neal B. NEJM 2017)
  - DECLARE: 17% reduction in CV death or hospitalization for heart failure (Wiviott S.D NEJM 2018)
4401 DM2, ACR > 300 mg/g, eGFR (90-30) on maximum tolerated RAAS blockade and randomized Canagliflozin or placebo

Primary Outcome: Composite of ESRD (dialysis, kidney transplant, eGFR < 15), doubling of creatinine, or death from renal or CV disease @ 5 years

Baseline characteristics: 63 yo, 67% female, 66% white, HgbA1C 8.3 (duration of DM ~ 16 years), CVD (50%), SBP: 140/78, ~ ACR 900 mg/g, eGFR 56
CREDENENCE TRIAL

30% Reduction of Primary Outcome (ESRD, Kidney Transplant, eGFR < 15)

During Trial (median follow-up = 2.62 years)
Number Needed to Treat (NNT) = 22

Hazard ratio, 0.70 (95% CI, 0.59–0.82)
P=0.00001
33% Reduction in ESRD

34% Reduction in ESRD, Doubling SC, or Renal Death

Number Needed to Treat (NNT) = 43

Number Needed to Treat (NNT) = 28

Evaluation of the Benefits and Risk of Aspirin in the Secondary Prevention of Cardiovascular and Cerebrovascular Events
Weisman S JAMA 2002
6 Trials (~ 6300 people); NNT to Prevent Death: 1:67

Perkovic V. NEJM 2019
No Difference in Death from CV or Death

**E** Death from Cardiovascular Cause

<table>
<thead>
<tr>
<th>Patients with an Event (%)</th>
<th>Months since Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Placebo</td>
<td>0</td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>0</td>
</tr>
</tbody>
</table>

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

**F** Death from Any Cause

<table>
<thead>
<tr>
<th>Patients with an Event (%)</th>
<th>Months since Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Placebo</td>
<td>0</td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>0</td>
</tr>
</tbody>
</table>

Hazard ratio, 0.83 (95% CI, 0.68–1.02)

**No. at Risk**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>2199</th>
<th>2185</th>
<th>2160</th>
<th>2106</th>
<th>1818</th>
<th>1220</th>
<th>688</th>
<th>189</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canagliflozin</td>
<td>2202</td>
<td>2187</td>
<td>2155</td>
<td>2120</td>
<td>1835</td>
<td>1263</td>
<td>687</td>
<td>212</td>
<td></td>
</tr>
</tbody>
</table>

Perkovic V. NEJM 2019
CREDENCE Trial
Difference in HgbA1C (-0.11%)
Difference in Blood Pressure (2.4/1.4 mmHg)
CREDENCE Trial
Weight Loss (0.88 kg)

D) Body weight

End of study difference
-0.88 kg
(95% CI: -1.69, -0.07)
CREDENCE Trial

31% Reduction in Proteinuria

31% reduction in proteinuria
# Side Effects

<table>
<thead>
<tr>
<th>Event</th>
<th>Canagliflozin</th>
<th>Placebo</th>
<th>Canagliflozin</th>
<th>Placebo</th>
<th>Hazard ratio (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperkalemia</td>
<td>151/2200</td>
<td>181/2197</td>
<td>29.7</td>
<td>36.9</td>
<td>0.80 (0.65–1.00)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>86/2200</td>
<td>98/2197</td>
<td>16.9</td>
<td>20.0</td>
<td>0.85 (0.64–1.13)</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>11/2200</td>
<td>1/2197</td>
<td>2.2</td>
<td>0.2</td>
<td>10.80 (1.39–83.65)</td>
</tr>
<tr>
<td>Osmotic diuresis</td>
<td>51/2200</td>
<td>40/2197</td>
<td>10.0</td>
<td>8.2</td>
<td>1.25 (0.83–1.89)</td>
</tr>
<tr>
<td>Volume depletion</td>
<td>144/2200</td>
<td>115/2197</td>
<td>28.4</td>
<td>23.5</td>
<td>1.25 (0.97–1.59)</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>225/2200</td>
<td>240/2197</td>
<td>44.3</td>
<td>48.9</td>
<td>0.92 (0.77–1.11)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>245/2200</td>
<td>221/2197</td>
<td>48.3</td>
<td>45.1</td>
<td>1.08 (0.90–1.29)</td>
</tr>
<tr>
<td>Genital mycotic infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28/1439</td>
<td>3/1466</td>
<td>8.4</td>
<td>0.9</td>
<td>9.30 (2.83–30.60)</td>
</tr>
<tr>
<td>Female</td>
<td>22/761</td>
<td>10/731</td>
<td>12.6</td>
<td>6.1</td>
<td>2.10 (1.00–4.45)</td>
</tr>
</tbody>
</table>
Absolute eGFR Difference
1.52 ml/min (95% CI, 1.11-1.93)
How Are SGLT Renoprotective?

Kidney protection

1. Transport work
   - Renal O₂ consumption
   - Albuminuria

2. Kidney growth
   - Albuminuria
   - Inflammation

3. Blood glucose

4. NHE3

5. Insulin need/levels
   - Glucagon

6. Lipolysis and hepatic gluconeogenesis

7. Mild ketosis

ECV/blood pressure
- Uric acid levels
- Body fat and weight
Afferent

Efferent

SGLT2-I
Vasoconstricts

ACE/ARB
Vasodilates

Normal

Diabetes

Decreased pressure

Dilated afferent arteriole

Constricted efferent arteriole (increased pressure)

Glomerular loss of proteins

Proteins stored in cytoplasm cause cell activation and inflammation

Proximal tubule

CREDENCE Conclusions

Benefits

• Renal outcomes were primary endpoints!
• Renal benefits were achieved IN ADDITION to RAAS blockade
• Higher Risk population derived benefit
  - eGFR (60-30)
  - Proteinuria

Limitations

• Minorities underrepresented
• Off treatment eGFR not measured after study stopped
• Increase risk of DKA and mycotic GU infections
• $$$$$$$$$$$$$$$$

EMPA-KIDNEY: GFR 20-90, ACR > 200, DIABETIC AND NON-DIABETIC
What we are going to be talking about

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• Conclusions
What is the Major Cause of ESRD in the US in 2017?

1. Hypertension
2. Diabetes Mellitus
3. Glomerulonephritis
4. Analgesic Nephropathy
Latest Etiology of ESRD in 2017

65% are modifiable

- DM: 45% → 38%
- HTN: 31% → 26%
- GN: 9% → 15%
- Cystic Disease: 5% → 2%
- Unknown/Other causes: 15% → 9%
Trends in the number of ESRD prevalence, by modality, in the U.S. population by Year

2015 Incident 124,114 new cases/year

ESRD mortality is ~ 20% per year

USRDS Annual Data Report 2017
Trends in the prevalence of ESRD, by age group, and race in the U.S. population by Year

Native American, Pacific Islanders: 9.5x
Black: 3.7x
American Indians/Alaska Natives: 1.5x
Asians: 1.3x

USRDS Annual Data Report 2017
Trends in number of prevalent ESRD cases using home dialysis, by type of therapy, in the United States by Year

- All home dialysis
- Home hemodialysis
- Peritoneal dialysis

~50,000 people
~10,000 people

USRDS Annual Data Report 2017
On average, ESRD reduces an individual's expected lifespan by

1. 70%
2. 50%
3. 25%
4. No change
Expected lifetime (years) by age, sex, and treatment modality in transplant patients, and the general U.S.

<table>
<thead>
<tr>
<th>Age</th>
<th>General U.S. population 2013</th>
<th>ESRD patients 2013</th>
<th>Dialysis</th>
<th>Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>0-14</td>
<td>70.7</td>
<td>75.4</td>
<td>23.8</td>
<td>23.1</td>
</tr>
<tr>
<td>15-19</td>
<td>59.7</td>
<td>64.4</td>
<td>21.8</td>
<td>19.1</td>
</tr>
<tr>
<td>20-24</td>
<td>55.0</td>
<td>59.5</td>
<td>18.8</td>
<td>16.1</td>
</tr>
<tr>
<td>25-29</td>
<td>50.3</td>
<td>54.6</td>
<td>16.2</td>
<td>14.1</td>
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<td>30-34</td>
<td>45.7</td>
<td>49.7</td>
<td>14.1</td>
<td>12.6</td>
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<tr>
<td>35-39</td>
<td>41.0</td>
<td>45.0</td>
<td>12.6</td>
<td>11.5</td>
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<tr>
<td>40-44</td>
<td>36.5</td>
<td>40.3</td>
<td>11.0</td>
<td>10.3</td>
</tr>
<tr>
<td><strong>45-49</strong></td>
<td><strong>32.0</strong></td>
<td><strong>35.6</strong></td>
<td><strong>9.3</strong></td>
<td><strong>8.8</strong></td>
</tr>
<tr>
<td>50-54</td>
<td>27.7</td>
<td>31.1</td>
<td>7.9</td>
<td>7.7</td>
</tr>
<tr>
<td>55-59</td>
<td>23.7</td>
<td>26.8</td>
<td>6.6</td>
<td>6.6</td>
</tr>
<tr>
<td>60-64</td>
<td>19.9</td>
<td>22.6</td>
<td>5.5</td>
<td>5.7</td>
</tr>
<tr>
<td><strong>65-69</strong></td>
<td><strong>16.2</strong></td>
<td><strong>18.6</strong></td>
<td><strong>4.6</strong></td>
<td><strong>4.8</strong></td>
</tr>
<tr>
<td>70-74</td>
<td>12.8</td>
<td>14.8</td>
<td>3.8</td>
<td>4.0</td>
</tr>
<tr>
<td>75-79</td>
<td>9.8</td>
<td>11.4</td>
<td>3.2</td>
<td>3.5</td>
</tr>
<tr>
<td>80-84</td>
<td>7.1</td>
<td>8.4</td>
<td>2.6</td>
<td>2.9</td>
</tr>
<tr>
<td>85+</td>
<td>3.8</td>
<td>4.4</td>
<td>2.1</td>
<td>2.3</td>
</tr>
</tbody>
</table>
What’s Worse: Cancer Versus ESRD

Estimated Remaining Years of Life

Ages 45-54
- US Resident: 29.9
- Colon Cancer: 6.9
- ESRD: 2.7
- Lung Cancer: 2.6

Ages 55-64
- US Resident: 21.6
- Colon Cancer: 9.8
- ESRD: 5.3
- Lung Cancer: 2.6

Pastan S. Dialysis Therapy. NEJM. 1998
Reduction in ESRD mortality and comorbidity-specific Medicare populations aged 65 & older

Mortality declined by 28% for ESRD
What is the leading cause of death in patients with CKD?

1. Malignancy
2. Infections
3. Cardiovascular Disease
4. Renal Failure
Mortality Rate by GFR

1.12 million patients followed over 2.84 years

Death:
- from any cause
- from CV event

Rate of Death (per 100 person-years)*

<table>
<thead>
<tr>
<th>e-GFR:</th>
<th>≥60</th>
<th>45-59</th>
<th>30-44</th>
<th>15-29</th>
<th>&lt;15</th>
</tr>
</thead>
<tbody>
<tr>
<td>(ml/min/1.73 m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>0.76</td>
<td>1.08</td>
<td>3.65</td>
<td>11.36</td>
<td>21.8</td>
</tr>
<tr>
<td>45-59</td>
<td>2.11</td>
<td></td>
<td>4.76</td>
<td>11.29</td>
<td>14.14</td>
</tr>
<tr>
<td>30-44</td>
<td></td>
<td></td>
<td></td>
<td>11.36</td>
<td>14.14</td>
</tr>
<tr>
<td>15-29</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>36.6</td>
</tr>
<tr>
<td>&lt;15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Age-Standardized Rate

Go A. NEJM 2004

Courtesy of Joe Nally
Etiology of Death in ESRD in 2017

~ 55% of all ESRD death is due to CVD

Excludes missing/unknown causes of death
**Prevalence of CKD in the US Population**

Prevalence CKD: 14.8% US population

CKD stage 3 (6.4%)

Relative stable since 1999

### Prognosis of chronic kidney disease by GFR and albuminuria

<table>
<thead>
<tr>
<th>Glomerular filtration rate</th>
<th>Albuminuria normal to mildly increased (ACR &lt; 30 mg/g or &lt; 3 mg/mmol)</th>
<th>Albuminuria moderately increased (ACR 30–299 mg/g or 3–29 mg/mmol)</th>
<th>Albuminuria severely increased (ACR ≥ 300 mg/g or ≥ 30 mg/mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal or high (&gt; 90 mL/min/1.73 m²)</td>
<td>Low risk(^a)</td>
<td>Moderately increased risk</td>
<td>High risk</td>
</tr>
<tr>
<td>Mildly decreased (60–89 mL/min/1.73 m²)</td>
<td>Low risk(^a)</td>
<td>Moderately increased risk</td>
<td>High risk</td>
</tr>
<tr>
<td>Mildly to moderately decreased (45–59 mL/min/1.73 m²)</td>
<td>Moderately increased risk</td>
<td>High risk</td>
<td>Very high risk</td>
</tr>
<tr>
<td>Moderately to severely decreased (30–44 mL/min/1.73 m²)</td>
<td>High risk</td>
<td>Very high risk</td>
<td>Very high risk</td>
</tr>
<tr>
<td>Severely decreased (15–29 mL/min/1.73 m²)</td>
<td>Very high risk</td>
<td>Very high risk</td>
<td>Very high risk</td>
</tr>
<tr>
<td>Kidney failure (&lt; 15 mL/min/1.73 m²)</td>
<td>Very high risk</td>
<td>Very high risk</td>
<td>Very high risk</td>
</tr>
</tbody>
</table>

\(^a\)If no other markers of kidney disease are present and the patient does not have chronic kidney disease

ACR = albumin-creatinine ratio, GFR = glomerular filtration rate

### 2016 Costs
- CKD $79B
- ESRD $35B
- Total = 114 B
What percentage of CKD 4 patients progress to ESRD?

1. 80%
2. 60%
3. 40%
4. 20%
5. 10%
CKD Patients Are More Likely to Die Than Progress to ESRD

27,998 CKD patients and observed them over 5 years

Keith D. Arch Intern Med 2004
Slide courtesy of Joe Nally
Goal to CKD Management: EARLY DETECTION

- Identify Cause
- Slow Progression
- Cardiovascular Risk
- Improved Survival
- Decreased ESRD
- Decreased Burden on Individual and HealthCare System
Management of Hypertension in CKD
What is the Prevalence of HTN in Stage 3B CKD?

1. 30%
2. 50%
3. 70%
4. 90%
Prevalence and Control of Hypertension in CKD

- Prevalance
- Controlled < 140/90
- Controlled < 130/80

Muntner P, AJKD 2009
Number Medications Required to Treat Blood Pressure Targets (and Lack of Success)

- No anti-HTN med: 2%
- 1 anti-HTN med: 15%
- 2 anti-HTN meds: 25%
- 3 anti-HTN meds: 26%
- 4+ anti-HTN meds: 32%

Bar chart:
- 1 med: 75% controlled, 50% <140/90 mmHg
- 2 meds: 73% controlled, 51% <140/90 mmHg
- 3 meds: 69% controlled, 49% <140/90 mmHg
- 4+ meds: 61% controlled, 40% <140/90 mmHg

Legend: 
- SBP/DBP <140/90 mmHg
- SBP/DBP <130/80 mmHg
Mechanism of HTN in CKD

1. ↑ Vasoconstriction due to enhanced RAAS
2. ↑ Volume expansion due to impaired pressure natriuresis
3. ↑ Total peripheral resistance due to increased SNS activity
4. ↑ Sodium reabsorption from All effects
Management of Hypertension in Patients With CKD

Treatment of hypertension in patients with CKD

BP goal <130/80 mm Hg (Class I)

Albuminuria (≥300 mg/d or ≥300 mg/g creatinine)

Yes

ACE inhibitor (Class IIa)

No

Usual “first-line” medication choices

ACE inhibitor intolerant

Yes

ARB* (Class IIb)

No

ACE inhibitor* (Class IIa)

*CKD stage 3 or higher or stage 1 or 2 with albuminuria ≥300 mg/d or ≥300 mg/g creatinine
Efficacy and Safety of Benazepril for Advanced Chronic Renal Insufficiency

Fan Fan Hou, M.D., Ph.D., Xun Zhang, M.D., Guo Hua Zhang, M.D., Ph.D., Di Xie, M.D., Ping Yan Chen, M.D., Wei Ru Zhang, M.D., Ph.D., Jian Ping Jiang, M.D., Min Liang, M.D., Ph.D., Guo Bao Wang, M.D., Zheng Rong Liu, M.D., and Ren Wen Geng, M.D.

422 CKD Patients, Proteinuria ~ 1.6 g/day

Group 1: 104 patients serum creatinine 1.5-3 mg/dl (eGFR 38)
  Group 1: Benazepril 20 mg/day

Group 2: 224 patients serum creatinine 3.1 – 5 mg/dl (eGFR 26)
  Group 2A: 112 were assigned benazepril 20 mg/d
  Group 2B: 112 were assigned placebo

Outcome: Doubling SC, ESRD, or Death
ACE-I Decreased Renal Progression While Initiating in Advanced CKD

Group 1: 22% reached endpoint
2A: 41% reached endpoint
2B: Placebo: 60% reached endpoint

No Difference in Adverse Events

Serum Creatinine 3.1-5 mg/dl

No. at Risk

<table>
<thead>
<tr>
<th>Group at Risk</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1, benazepril</td>
<td>102</td>
</tr>
<tr>
<td>Group 1, placebo</td>
<td>108</td>
</tr>
<tr>
<td>Group 2, benazepril</td>
<td>107</td>
</tr>
<tr>
<td>Group 2, placebo</td>
<td>108</td>
</tr>
</tbody>
</table>

Hou F. NEJM 2006
General Rules and Expectations

- **Thiazides**
  - Chlorthalidone > HCTZ
  - Thiazides not effective in GFR < 30

- **ACE-I/ARBS/RAAS**
  - Impaired anti-proteinuric effects with a high salt diet and enhanced with a low salt diet or diuretic. (Heeg. KI 1989)
  - Rule of 30 (Kunz R. Ann Intern Med. 2008, IDNT,RENAAL,REIN)
  - Spirolactone (~25 mg/day) will reduce proteinuria by ~ 800 mg/day (Navaneethan CJASN 2009)
  - Angioedema with ACE-I **CAN** receive ARB 6 weeks after ACE discontinuation (2018 ACC/AHA)
Management of Hyperlipidemia in CKD
58 year old male with CKD 4 from DM and HTN
PMH = No CAD, CVA, CHF
Lipids = Chol 180, LDL 95, TG 145

Effective LDL-lowering therapy will accomplish which of the following?

1. Reduce major atherosclerotic events
2. Reduce patient mortality
3. Slow the progression of CKD
4. Reduce the incidence of ESRD
Study of Heart and Renal Protection (SHARP TRIAL)

- 9270 “CKD patients”
  - Male ≥ 1.7, Female ≥ 1.5)
  - Age 62, 13% smokers, 23% DM
  - 3023 (33%) on RRT (IHD or PD)
- No MI or CABG
- Median Follow up 4.9 years
- Does combination simvastatin/ezetimibe therapy reduce CV events in CKD patients for primary prevention?
SHARP TRIAL: 17% Reduction of Atherosclerotic Events

Risk Ratio 0.83 (0.74 – 0.94)
Log-rank 2P = 0.0021

Proportion with events (%) vs Years of follow-up
SHARP: Conclusions

• Benefit in primary prevention for reducing CV events in CKD patients
• No benefit in lipid lowering therapy in ESRD population (AURORA and 4D)
• No benefit in slowing CKD progression
• No increase risk in malignancy or rhabdomyolysis
Lipid Management in CKD

- ACC/AHA and KDIGO guidelines no longer specify lipid targets but rather target CV risk

- 2013 KDIGO Lipid guidelines:
  - Adults ≥ 50 years old with eGFR < 60 ml/min should be started on treatment with statin or statin/ezetimibe combination (1A)
  - Adults 18-49 years old with CKD, suggest statin therapy in people with one or more of the following conditions (2A)
    - CAD
    - DM
    - Ischemic stroke
    - 10 year risk of coronary death or non fatal MI > 10%

- Treat according to the “fire and forget” strategy, unless measuring lipids will alter management
<table>
<thead>
<tr>
<th>Statin</th>
<th>eGFR G1-G2</th>
<th>eGFR G3a-G5, including patients on dialysis or with a kidney transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lovastatin</td>
<td>GP</td>
<td>nd</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>GP</td>
<td>80(^1)</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>GP</td>
<td>20(^2)</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>GP</td>
<td>10(^3)</td>
</tr>
<tr>
<td>Simvastatin/Ezetmibe</td>
<td>GP</td>
<td>20/10(^4)</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>GP</td>
<td>40</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>GP</td>
<td>40</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>GP</td>
<td>2</td>
</tr>
</tbody>
</table>
Management of Metabolic Acidosis in CKD
Metabolic Acidosis in CKD

- Metabolic acidosis occurs as CKD progresses due to a decrease in renal acid secretion.
- > 30% of CKD 4 patients develop metabolic acidosis.
- Metabolic acidosis is associated with renal osteodystrophy, protein wasting, impaired myocardial contractility, SNS overactivity, and respiratory disturbances.
Treatment of Metabolic Acidosis with Sodium Bicarbonate in CKD Patients Will Most Likely Result In Which Of The following?

1. Edema
2. Worsening of hypertension
3. Slowing the progression of CKD
4. Improved patient survival
RCT, 134 patients with CKD 4 and HCO 16-20 mmol/L

Groups:
- Intervention: Received NaHCO (~1.8 grams/day) to target HCO > 22
- Control: No treatment

Outcomes: CKD progression after 2 years
Sodium Bicarbonate Reduces eGFR Loss

NaHCO group had decrease in GFR loss (1.88 vs 5.93 ml/min) p<0.0001 [CI 0.6-0.4]
NaHCO group had lower risk of ESRD (33% versus 46.5%) p<0.001 [0.04-0.4]
Metabolic Acidosis in CKD

• Mechanism of Action
  - Acidosis results in CKD progression due to activation of complement, endothelin, and RAAS systems

• Conclusions
  - Use NaHCO₃ 650 mg PO BID
  - Target HCO₃ is ≥ 23 mEq/L (2B)
  - Treatment prevents bone disease and CKD progression
Conclusions

- CKD is prevalent and often underdiagnosed
- Early recognition of kidney disease is important to minimize complications of CKD
- Treatment of hypertension, proteinuria reduction using RAAS blockade, and alkali therapy for metabolic acidosis has been proven to slow CKD progression
- Treatment with a statin has been shown to reduce cardiovascular events which are prevalent in CKD
- SGLT2 inhibition in proteinuric DM2 (eGFR 90-30) has been shown to decrease CV mortality and decrease renal progression
QUESTIONS

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