Delaying Progression

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Disclosure

• **Paul Drawz, MD, MHS, MS** has no financial relationships with commercial interest(s).
Learning Objective

• Identify strategies for delaying the progression of CKD in at-risk patients.
Session Outline

- Recognize evidence-based management strategies that will help delay CKD progression in at-risk patients and improve outcomes.
  - ACEI/ARBs
  - DM control
- Recognize that BP lowering does not slow progression of CKD
- Recognize unconventional treatment strategies to slow progression of CKD
Self Assessment Questions

• 1. Target blood pressure in non-dialysis diabetic CKD with a albumin-to-creatinine ratio of <30mg/g should be:
  o <120/80mmHg
  o <140/90mmHg
  o <150/90mmHg
  o <130/80mmHg

• 2. A 55 year-old Caucasian-American man, with a history of type 2 diabetes (15 years), hypertension (3 years) dyslipidemia (5 years) and cardiovascular disease (myocardial infarction 3 years ago). He was recently diagnosed with CKD. His most recent labs reveal an eGFR of 45 ml/min/1.73m² and an ACR of 38 mg/g. Which of the following should be avoided?
  o ACE and ARB in combination
  o Daily low-dose aspirin
  o NSAIDs
  o Statins
  o A and C
Steps to CKD Patient Care

1. Does the patient have CKD?
2. Assess GFR, albuminuria
3. Determine etiology
4. Assess for evidence of progression
5. Assess for associated complications
6. Patient education
7. Assess life expectancy and patient wishes for dialysis/transplantation
Delaying Progression of CKD
CKD - Progression of Kidney Failure Concept

Variable depending on several factors including (1) type of disease and (2) how well it is treated.
## ACEI/ARBs to Slow CKD Progression

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline Proteinuria</th>
<th>ACEI/ARB</th>
<th>Reduction in Renal Events</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RENAAL</td>
<td>UACR ~1250mg/g</td>
<td>losartan</td>
<td>21 (5 to 34)^A</td>
</tr>
<tr>
<td>IDNT</td>
<td>Uprot 2.9g/24hr</td>
<td>irbesartan</td>
<td>33 (13 to 48)^D</td>
</tr>
<tr>
<td>Lewis, et al.</td>
<td>Uprot 2.7g/24hr</td>
<td>captopril</td>
<td>48 (16 to 69)^D</td>
</tr>
<tr>
<td>HOPE</td>
<td>32% microalbuminuria</td>
<td>ramipril</td>
<td>24 (3 to 40)^B</td>
</tr>
<tr>
<td><strong>Non-diabetic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REIN 2</td>
<td>Uprot 5.3g/24hr</td>
<td>ramipril</td>
<td>48 (9 to 70)^A</td>
</tr>
<tr>
<td>AIPRI</td>
<td>Uprot 1.8g/24hr</td>
<td>benazepril</td>
<td>53 (27 to 70)^A</td>
</tr>
<tr>
<td>REIN 1</td>
<td>Uprot 1.7g/24hr</td>
<td>ramipril</td>
<td>63 (18 to 84)^C</td>
</tr>
<tr>
<td>AASK</td>
<td>Uprot/Cr 0.5g/24hr</td>
<td>ramipril</td>
<td>38 (10 to 58)^E</td>
</tr>
<tr>
<td>Hou, et al.</td>
<td>Uprot 1.7g/24hr</td>
<td>Benazepril</td>
<td>40 (P=0.02)^C</td>
</tr>
</tbody>
</table>

Outcomes: A: doubling of serum creatinine or ESRD; B: overt nephropathy defined by 24 h urine albumin ≥300mg, 24 h urine protein ≥500mg, or urine albumin/creatinine ratio >36mg/mmol; C: ESRD; D: doubling of serum creatinine; E: 50% decline in GFR or ESRD
ACEI/ARBs to Slow CKD Progression

• With proteinuria
  o ACEi or ARB +/- diuretic
• No proteinuria
  o ACEi or ARB preferred

Delaying CKD Progression: ACEi/ARB

- Check labs after initiation
  - If less than 25% SCr increase, continue and monitor
  - If more than 25% SCr increase, stop ACEi and evaluate for RAS
- Continue until contraindication arises, no absolute eGFR cutoff
- Better proteinuria suppression with low Na diet (<2 g of sodium; or <5 g sodium chloride per day) and diuretics
- Avoid volume depletion and NSAIDs

**QUESTION - TRUE OR FALSE -**
ACEI-ARBs have been shown to slow progression of CKD in patients with proteinuria?
Session Outline

• Recognize evidence-based management strategies that will help delay CKD progression in at-risk patients and improve outcomes.
  o ACEI/ARBs
  o DM control
• Recognize that BP lowering does not slow progression of CKD
• Recognize unconventional treatment strategies to slow progression of CKD
Managing Hyperglycemia

- Hyperglycemia is a fundamental cause of vascular complications, including CKD.
- Poor glycemic control has been associated with albuminuria in type 2 diabetes.
- Risk of hypoglycemia increases as kidney function becomes impaired.
- Declining kidney function may necessitate changes to diabetes medications and renally-cleared drugs.
- Target HbA1c ~7.0%
  - Can be extended above 7.0% with comorbidities or limited life expectancy, and risk of hypoglycemia.

Role of Intensive Glucose Control in Development of Renal End Points in Type 2 Diabetes Mellitus

Systematic Review and Meta-analysis

Steven G. Coca, DO, MS; Faramarz Ismail-Beigi, MD, PhD; Nowreen Haq, MD, MPH; Harlan M. Krumholz, MD, SM; Chirag R. Parikh, MD, PhD

- 7 studies
- 28,065 participants
- Conventional control versus intensive control
  - A1c 7.3 to 9.1 versus 6.4 to 7.4
**A** Microalbuminuria

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight, %</td>
<td>M-H, Random (95% CI)</td>
</tr>
<tr>
<td>ACCORD(^8,14)</td>
<td>720</td>
<td>3250</td>
<td>27.3</td>
<td>0.88 (0.80-0.96)</td>
</tr>
<tr>
<td>ADVANCE(^12)</td>
<td>1318</td>
<td>5571</td>
<td>29.3</td>
<td>0.92 (0.86-0.98)</td>
</tr>
<tr>
<td>Kumamoto(^4,15)</td>
<td>5</td>
<td>52</td>
<td>1.3</td>
<td>0.44 (0.16-1.17)</td>
</tr>
<tr>
<td>UKPDS 33(^16)</td>
<td>368</td>
<td>2277</td>
<td>19.6</td>
<td>0.88 (0.75-1.04)</td>
</tr>
<tr>
<td>UKPDS 34(^17)</td>
<td>79</td>
<td>342</td>
<td>12.2</td>
<td>1.00 (0.77-1.30)</td>
</tr>
<tr>
<td>VADT(^11)</td>
<td>43</td>
<td>442</td>
<td>7.6</td>
<td>0.74 (0.51-1.07)</td>
</tr>
<tr>
<td>VA Feasibility Trial(^5)</td>
<td>7</td>
<td>42</td>
<td>2.5</td>
<td>0.26 (0.13-0.52)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>11976</td>
<td>10750</td>
<td>100.0</td>
<td>0.86 (0.76-0.96)</td>
</tr>
<tr>
<td>Total events</td>
<td>2540</td>
<td>2631</td>
<td></td>
<td>0.064</td>
</tr>
<tr>
<td>Heterogeneity: (\tau^2 = 0.01); (\chi^2 = 16.71); (P = .01); (I^2 = 64%) &amp; Heterogeneity: (\tau^2 = 0.00); (\chi^2 = 5.73); (P = .33); (I^2 = 13%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: (z = 2.60); (P = .009) &amp; Test for overall effect: (z = 4.24); (P = .001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**B** Macroalbuminuria

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight, %</td>
<td>M-H, Random (95% CI)</td>
</tr>
<tr>
<td>ACCORD(^8,14)</td>
<td>195</td>
<td>4397</td>
<td>39.3</td>
<td>0.72 (0.60-0.86)</td>
</tr>
<tr>
<td>ADVANCE(^12)</td>
<td>230</td>
<td>5571</td>
<td>42.5</td>
<td>0.79 (0.67-0.93)</td>
</tr>
<tr>
<td>Kumamoto(^4,15)</td>
<td>0</td>
<td>52</td>
<td>0.2</td>
<td>0.11 (0.01-1.94)</td>
</tr>
<tr>
<td>UKPDS 33(^16)</td>
<td>72</td>
<td>2277</td>
<td>10.4</td>
<td>0.90 (0.60-1.35)</td>
</tr>
<tr>
<td>VADT(^11)</td>
<td>20</td>
<td>693</td>
<td>6.2</td>
<td>0.56 (0.33-0.96)</td>
</tr>
<tr>
<td>VA Feasibility Trial(^5)</td>
<td>3</td>
<td>24</td>
<td>1.4</td>
<td>0.35 (0.11-1.13)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>13014</td>
<td>11712</td>
<td>100.0</td>
<td>0.74 (0.65-0.85)</td>
</tr>
<tr>
<td>Total events</td>
<td>520</td>
<td>647</td>
<td></td>
<td>0.13%</td>
</tr>
<tr>
<td>Heterogeneity: (\tau^2 = 0.00); (\chi^2 = 10.97); (P = .04); (I^2 = 13%) &amp; Heterogeneity: (\tau^2 = 0.00); (\chi^2 = 5.73); (P = .33); (I^2 = 13%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: (z = 4.24); (P = .001) &amp; Test for overall effect: (z = 4.24); (P = .001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Doubling of Serum Creatinine

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>Risk Ratio M-H, Random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>ACCORD³,¹⁴</td>
<td>392</td>
<td>5041</td>
<td>357</td>
</tr>
<tr>
<td>ADVANCE¹²</td>
<td>67</td>
<td>5571</td>
<td>61</td>
</tr>
<tr>
<td>UKPDS 33¹⁶</td>
<td>7</td>
<td>2150</td>
<td>7</td>
</tr>
<tr>
<td>VADT¹¹</td>
<td>78</td>
<td>882</td>
<td>78</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>13644</td>
<td>12383</td>
<td>100.0</td>
</tr>
</tbody>
</table>

- Total events: 544
- Heterogeneity: $\tau^2=0.00$; $\chi^2=3.46$; $P=.33$; $I^2=13\%$
- Test for overall effect: $z=0.76$; $P=.44$

### ESRD

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>Risk Ratio M-H, Random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>ACCORD³,¹⁴</td>
<td>138</td>
<td>5119</td>
<td>151</td>
</tr>
<tr>
<td>ADVANCE¹²</td>
<td>11</td>
<td>5571</td>
<td>31</td>
</tr>
<tr>
<td>UKPDS 33¹⁶</td>
<td>16</td>
<td>2729</td>
<td>9</td>
</tr>
<tr>
<td>UKPDS 34¹⁷</td>
<td>2</td>
<td>342</td>
<td>2</td>
</tr>
<tr>
<td>VADT¹¹</td>
<td>7</td>
<td>882</td>
<td>11</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>14643</td>
<td>13117</td>
<td>100.0</td>
</tr>
</tbody>
</table>

- Total events: 204
- Heterogeneity: $\tau^2=0.09$; $\chi^2=7.08$; $P=.13$; $I^2=43\%$
- Test for overall effect: $z=1.72$; $P=.09$
# Intensive Diabetes Therapy and Glomerular Filtration Rate in Type 1 Diabetes

The DCCT/EDIC Research Group*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Diabetes Therapy</th>
<th>Conventional Diabetes Therapy</th>
<th>Risk Reduction with Intensive Therapy†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Events</td>
<td>Incidence Rate/1000 Person-Yr</td>
<td>No. of Events</td>
<td>Incidence Rate/1000 Person-Yr</td>
</tr>
<tr>
<td>Impaired GFR‡</td>
<td>24</td>
<td>1.6</td>
<td>46</td>
<td>3.0</td>
</tr>
<tr>
<td>Onset during DCCT</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Onset during EDIC</td>
<td>23</td>
<td>1.6</td>
<td>43</td>
<td>2.5</td>
</tr>
<tr>
<td>Estimated GFR &lt;45 ml/min/1.73 m²</td>
<td>24</td>
<td>1.6</td>
<td>39</td>
<td>2.5</td>
</tr>
<tr>
<td>Estimated GFR &lt;30 ml/min/1.73 m²§</td>
<td>13</td>
<td>0.8</td>
<td>23</td>
<td>1.5</td>
</tr>
<tr>
<td>End-stage renal disease§</td>
<td>8</td>
<td>0.5</td>
<td>16</td>
<td>1.1</td>
</tr>
<tr>
<td>Combined outcome of impaired GFR or death¶</td>
<td>53</td>
<td>3.4</td>
<td>80</td>
<td>5.2</td>
</tr>
</tbody>
</table>

*P-values were calculated by a Cox proportional hazards analysis, with the usual assumptions, after adjustment for age, sex, baseline estimated GFR, duration of diabetes, duration of intervention, and randomization stratum.
Session Outline

• Recognize evidence-based management strategies that will help delay CKD progression in at-risk patients and improve outcomes.
  o ACEI/ARBs
  o DM control

• **Recognize that BP lowering does not slow progression of CKD**

• Recognize unconventional treatment strategies to slow progression of CKD
Low BP targets and renal outcomes

- Toto et al.
- Lewis – collaborative study group
- REIN-2
- MDRD
- AASK
Toto et al. – 1995

- CKD patients (GFR < 70), normal urine sediment, Uprot < 2g/d
- Randomized
  - Strict (DBP 65 to 80, n = 42)
  - Conventional (DBP 85 to 95, n = 35)
- Follow up ~40mo, mean DBP 81.1 and 87.1
- GFR decline
  - -0.31 vs -0.050 (P > 0.25)
- Secondary outcome – 50% decline GFR, doubling Cr, ESRD or death
  - 12 vs 7 (P > 0.25)
Type 1 DM with nephropathy

• 129 subjects – Cr <4
• Randomized
  o Low MAP of 92 to 100 mmHg
  o High MAP of 100 to 107 mmHg
• Follow up >2yrs, avg MAP difference 6 mmHg
• All treated with ramipril
• Primary outcome – absolute change in iGFR
  o Low MAP – 62 to 54
  o High MAP – 64 to 58
• Secondary outcome – 24hr Uprot lower in low MAP group

Lewis JB, AJKD, 1999, pg 809.
REIN-2

• 335 non-DM patients receiving ramipril
  o 1-3gm/24hr with CrCl <45
  o ≥ 3gm/24hr with CrCl <70
• Randomized
  o DBP <90
    o Intensified BP control (< 130/80)
• Median f/u 19mo; difference in BP: 4.1/2.8 mmHg
• ESRD
  o 20% in conventional arm
  o 23% in intensified arm (P = 0.99)
• No difference in rate of GFR decline or Uprot

MDRD

- Usual BP – MAP 107 mmHg (140/90)
- Low BP – MAP 92 mmHg (125/75)
- Study 1 – 585 subjects GFR 25 to 55
  - Mean decline in GFR (ml/min/3yrs)
    - 12.3 in usual vs 10.8 in low BP target (P = 0.18)
- Study 2 – 255 subjects GFR 13 to 24
  - Mean decline in GFR (ml/min/yr)
    - 4.2 in usual vs 3.7 in low BP target (P = 0.28)

Klahr S, NEJM, 1994, pg 877.
Effect of low BP target depends on baseline level of proteinuria

![Graph showing the effect of low BP target on the mean rate of GFR decline based on baseline urinary protein levels.](image)

- **Study 1**
  - Low BP target: ○
  - Usual BP target: ●
  - Baseline urinary protein levels:
    - <1 g/day: n = 420
    - 1–<3 g/day: n = 104
    - ≥3 g/day: n = 54

- **Study 2**
  - Low BP target: ○
  - Usual BP target: ●
  - Baseline urinary protein levels:
    - <1 g/day: n = 136
    - 1–<3 g/day: n = 63
    - ≥3 g/day: n = 32

MDRD – long term outcomes

Kidney failure

Usual BP

Low BP

Kidney failure or all-cause mortality

Usual BP

Low BP

AASK

- African American, non-DM, GFR 20-65
- Randomized
  - Usual MAP (102 to 107 mmHg)
  - Low MAP (92 mmHg)
- Achieved BP 141/85 vs 128/78
- GFR decline (ml/min/1.73m$^2$/yr)
  - Usual: 1.95
  - Low: 2.21 (P = 0.24)
- No difference in 50% decline GFR, death, ESRD or composite

AASK – Doubling of Cr, ESRD or Death According to Baseline Proteinuria Status

According to Baseline Proteinuria Status

• Renal Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Active treatment</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DBP 115 to 129 mmHg</td>
<td>2/70</td>
<td>0/73</td>
<td>0.146</td>
</tr>
<tr>
<td>DBP 90 to 114 mmHg</td>
<td>3/191</td>
<td>0/186</td>
<td>0.089</td>
</tr>
</tbody>
</table>
UKPDS 38

- 1148 subjects – type 2 DM, median fu 8.4yrs
- At 9 years
  - No difference in Cr or proportion of patients with a doubling of Cr

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Tight control</th>
<th>Less tight control</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ualb &gt; 50mg/l</td>
<td>28.8%</td>
<td>33.1%</td>
<td>0.87 (0.60 to 1.26)</td>
</tr>
<tr>
<td>Ualb &gt; 300mg/l</td>
<td>7.0%</td>
<td>6.6%</td>
<td>1.06 (0.42 to 2.67)</td>
</tr>
</tbody>
</table>

Systolic Hypertension in the Elderly Study (SHEP)

• 4736 men and women
• Randomized
  o Active tx – target SBP < 160 mmHg (or decrease 20 mmHg if baseline < 180 mmHg)
  o Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group</th>
<th>Active</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr ≥ 2mg/dl</td>
<td>DM</td>
<td>4.5%</td>
<td>4.1%</td>
</tr>
<tr>
<td></td>
<td>Non-DM</td>
<td>2.6%</td>
<td>2.1%</td>
</tr>
<tr>
<td>≥ 1+ UProt</td>
<td>DM</td>
<td>32.3%</td>
<td>34.6%</td>
</tr>
<tr>
<td></td>
<td>Non-DM</td>
<td>17.2%</td>
<td>19.8%</td>
</tr>
</tbody>
</table>

Curb JD et al, JAMA, 1996, pg 1886.
4,733 participants with type 2 DM  
SBP target <120mmHg vs. <140mmHg  
Achieved SBP 119mmHg vs. 133.5mmHg

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intense</th>
<th>Standard</th>
<th>HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary*</td>
<td>1.87 %/yr</td>
<td>2.09 %/yr</td>
<td>0.88 (0.73-1.06)</td>
<td>0.20</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.32 %/yr</td>
<td>0.53 %/yr</td>
<td>0.59 (0.39-0.89)</td>
<td>0.01</td>
</tr>
<tr>
<td>Death</td>
<td>1.28 %/yr</td>
<td>1.19 %/yr</td>
<td>1.07 (0.85-1.35)</td>
<td>0.55</td>
</tr>
<tr>
<td>eGFR &lt;30</td>
<td>4.2 %</td>
<td>2.2 %</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>6.6 %</td>
<td>8.7 %</td>
<td>0.009</td>
<td></td>
</tr>
</tbody>
</table>

* Nonfatal MI, nonfatal stroke, or death from CV causes.
BP targets in CKD – **CV risk reduction**

- **Target blood pressure in non-dialysis CKD:**
  - ACR <30 mg/g: ≤140/90 mm Hg
  - ACR 30-300 mg/g: ≤140/90 mm Hg*
  - ACR >300 mg/g: ≤140/90 mm Hg*
  - Individualize targets and agents according to age, coexistent CVD, and other comorbidities

- **Avoid ACEi and ARB in combination**
  - Risk of adverse events (impaired kidney function, hyperkalemia)

**QUESTION – True or False –**

Intense BP lowering slows progression of CKD?

*Reasonable to select a goal of 140/90 mm Hg, especially for moderate albuminuria (ACR 30-300 mg/g.)*

1) 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults - Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8), JAMA. 2014;311(5):507-520
Session Outline

• Recognize evidence-based management strategies that will help delay CKD progression in at-risk patients and improve outcomes.
  o ACEI/ARBs
  o DM control

• Recognize that BP lowering does not slow progression of CKD

• Recognize unconventional treatment strategies to slow progression of CKD
Metabolic Acidosis

- Often becomes apparent at GFR < 25-30 ml/min
- More severe with higher protein intake
- May contribute to bone disease, protein catabolism, and progression of CKD
- Correction of metabolic acidosis may slow CKD progression and improve patients functional status\(^1,2\)

Adults with CKD (eGFR 15-30 ml/min/1.73m\(^2\)) with bicarbonate 16-20 mmol/L; treated with sodium bicarbonate for 2 years to normalize serum bicarbonate concentration\(^2\)

Metabolic Acidosis

• Maintain serum bicarbonate > 22 mmol/L
  o Start with 0.5-1 mEq/kg per day
  o **Sodium bicarbonate tablets**
    • 325mg, 625 mg tablets; 1 g = 12 mEq
  o **Sodium citrate solution**
    • 1 mEq/ml
    • Avoid if on aluminum phosphate binders
  o **Baking soda**
    • 54 mmol/level tsp
Allopurinol?

- Randomized controlled trial
- 54 patients with either Uprot > 0.5g/24hr or Cr >1.35mg/dL (but <4.5)
  - Uric acid >7.6mg/dL
- Allopurinol 100mg/d versus placebo
  - Cr 1.64 to 1.99 versus 1.86 to 2.89 (P=0.08)
  - Deterioration in renal function: 16% versus 46% (P=0.02)

Allopurinol RCT #2

- 113 patients – eGFR <60 ml/min/1.73m²
- Allopurinol 100mg/day versus usual therapy
- After 24 months, treatment with allopurinol:
  - Lowered uric acid: 6.0 vs 7.5 (P<0.001)
  - Stabilized eGFR: 42.2 vs. 35.9 (P<0.001)
- No effect on albuminuria
- No effect on blood pressure
- HR for new CV events: 0.29 (0.09 to 0.86)

Impact of primary care CKD detection with a patient safety approach

Improved diagnosis creates opportunity for strategic preservation of kidney function

Discuss Take Home Points
Self Assessment Questions

1. Target blood pressure in non-dialysis diabetic CKD with a albumin-to-creatinine ratio of <30mg/g should be:
   - A. 120/80mmHg
   - B. *140/90mmHg*
   - C. 150/90mmHg
   - D. 130/80mmHg
   **B Rationale**: Comparison of Guideline Recommendations for CKD Blood Pressure Targets among reliable sources, including JAMA2014 and KDIGO2012, contain similar recommendations as less than 140/90 mm Hg in CKD

2. A 55 year-old Caucasian-American man, with a history of type 2 diabetes (15 years), hypertension (3 years) dyslipidemia (5 years) and cardiovascular disease (myocardial infarction 3 years ago). He was recently diagnosed with CKD. His most recent labs reveal an eGFR of 45 ml/min/1.73m² and an ACR of 38 mg/g. Which of the following should be avoided?
   - A. ACE and ARB in combination
   - B. Daily low-dose aspirin
   - C. NSAIDs
   - D. Statins
   - E. *A and C*
   **E. Rationale**: ACE and ARBs used in combination have been shown to increase adverse events, particularly impaired kidney function and hyperkalemia. NSAIDs have been shown to cause kidney damage and increase CKD progression. Statins are indicated based on KDIGO guidelines and a daily low-dose aspirin is not contraindicated in CKD.
Questions and Answers
Additional Resources

- KDOQI Clinical Practice Guideline For Diabetes: Update 2012
  https://www.kidney.org/professionals/guidelines/guidelines_comments

  http://www2.kidney.org/professionals/KDOQI/guidelines_bp/

- National Kidney Foundation Tool: *Self-Management, Diabetes and CKD*
  https://www.kidney.org/sites/default/files/12_10_2095_SelfManagement.pdf