Hypertension in Geriatrics

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Major risk factors for cardiovascular disease

**UNHEALTHY LIFESTYLE**
- Cigarette smoking
- Physical inactivity
- Diet high in fat

**HIGH RISK DISEASES**
- Hypertension
- Diabetes
- Hyperlipidemia
- Obesity

**END ORGAN DAMAGE**
- Heart disease
- Stroke
- Peripheral artery disease
- Chronic kidney disease
- Eye sight failure

**NON-MODIFIABLE FACTORS**
- Age
- Family history of premature coronary artery disease (CAD)
Cardiovascular Mortality Rates are Higher among Dialysis Patients

Cardiovascular Disease in CKD: Multifactorial Pathogenesis

- Elevated PTH/2HPT
- Duration of dialysis
- Oxidative stress
- Anaemia
- Chronic inflammation
- Hyperphosphatemia
- Exogenous Ca intake
- Elevated Ca x P product
- Dyslipidemia
- Hypertension
- Diabetes Mellitus
- Genetics
- Smoker
- Age
- Elevated Ca x P product

- High prevalence of traditional risk factors
- As renal function deteriorates, non-traditional factors play an increasing role in GFR loss and cardiovascular damage

Traditional risk factors
Non Traditional risk factors
Goal of BP Control in CKD and Elderly

- Reduction of Proteinuria
- Retardation of CKD progression
- Reduction of Mortality
- Reduction of CVD
DOC VADER

TALKS

"END-OF-LIFE"
Baseline eGFR threshold below which risk for ESRD exceeded risk for death for each age group.

- 0.75-1 ml/min/year (normal aging)
- 3-5 ml/min/year (DM nephropathy)

Ann M. O'Hare et al. JASN 2007;18:2758-2765
Goal of BP Control in CKD and Elderly

- Reduction of Proteinuria
- Retardation of CKD progression
- Reduction of Mortality
- Reduction of CVD

Risk of ESRD > risk of death
Risk of death > risk of ESRD
What is Your Target BP Treatment for Elderly Patients to Reduce Risks of Cardiovascular Diseases?

A. Same as general population
B. Somewhat higher than general population
C. Lower than general population
D. Depends on “how old” is the patient
Hypertension in the Elderly

• Fastest growing segment of the population
• Prevalence of hypertension is very high
• Several issues make managing HTN unique:
  – Often present with isolated systolic HTN
  – More likely to present with comorbidities
  – Many clinical trials in HTN have excluded these patients (particularly for those 80 years and older)
  – Elderly are more susceptible to certain adverse effects (orthostatic hypotension)
Arterial stiffness is a cumulative measure of the damaging effects of CV risk factors on the arterial wall with aging.

Peter M. Nilsson et al. Hypertension. 2009;54:3-10
JNC-8 Recommendations

• In patients >60 years of age, start medications at blood pressure of ≥150/90mm Hg and treat to goal of <150/90mm Hg

• In patients >60 years of age, treatment does not need to be adjusted if achieved blood pressure is lower than goal and well-tolerated

## Comparisons to Other Guidelines

<table>
<thead>
<tr>
<th>BP Goal</th>
<th>JNC-7</th>
<th>JNC-8</th>
<th>ASH/ISH</th>
<th>ESC/ESH</th>
<th>CHEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 60</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
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<tr>
<td>Age 60-79</td>
<td>&lt;140/90</td>
<td>&lt;150/90</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
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<tr>
<td>Age 80+</td>
<td>&lt;140/90</td>
<td>&lt;150/90</td>
<td>&lt;150/90</td>
<td>&lt;150/90</td>
<td>&lt;150/90</td>
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<tr>
<td>Diabetes</td>
<td>&lt;130/80</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;140/85</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>CKD</td>
<td>&lt;130/80</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;130/90</td>
<td>&lt;140/90</td>
</tr>
</tbody>
</table>

HYVET

• HYpertension in the Very Elderly Trial
  – Randomized, double-blind trial
  – Included patients aged 80 or older with SBP ≥ 160mmHg
  – Randomized to indapamide +/- perindopril or placebo
  – Target BP of 150/80mmHg
  – Primary outcome of fatal or nonfatal stroke

HYVET

• Results
  – Mean BP at the end of the trial
    • Indapamide +/- perindopril - 143/78 mm Hg
    • Placebo – 158/84 mm Hg
  – 48.0% of indapamide patients achieved goal BP vs. 19.9% of placebo patients (p<0.001)
  – Outcomes with indapamide +/- perindopril
    • 30% reduction in stroke (p=0.06)
    • 64% reduction in heart failure (p<0.001)
    • 21% reduction in all-cause mortality (p=0.02)

HYVET and earlier trials demonstrated that treatment of HTN to goal BP less than 150/80 mm Hg in patients >80 years old was safe and effective.

But...what about a lower BP goal?

And...what about the patients age 60-80?

Perry, Davis et al. (2000) JAMA
Dahlof, Lindholm et al. (1991) Lancet
Staessen, Fagard et al. (1997) Lancet

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HYVET</th>
<th>SHEP</th>
<th>STOP</th>
<th>Syst-Eur</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean treatment BP reduction, SBP/DBP, mmHg</td>
<td>−29/−13</td>
<td>−27/−9</td>
<td>−29/−17</td>
<td>−23/−7</td>
</tr>
<tr>
<td>Stroke, % reduction</td>
<td>−30</td>
<td>−32</td>
<td>−47</td>
<td>−42</td>
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<tr>
<td>Coronary disease, % reduction</td>
<td>−23*</td>
<td>−27</td>
<td>−13</td>
<td>−30</td>
</tr>
<tr>
<td>Heart failure, % reduction</td>
<td>−64</td>
<td>−55</td>
<td>−51</td>
<td>−29</td>
</tr>
</tbody>
</table>

HYVET, Hypertension in Very Elderly Trial (66); SHEP, Systolic Hypertension in the Elderly Program (55); STOP, Swedish Trial in Old Patients (56); Syst-Eur, European Systolic Hypertension in the Elderly (57); DBP, diastolic BP; SBP, systolic BP.

*Percentage of cardiovascular mortality reduction.
Hypertension in the Elderly

- Two “treat-to-target” trials in this age group
  - Japanese Trial to Assess Optimal SBP (JATOS)
    - 4416 patients aged 65-85 (average age of 74)
    - Randomized to SBP<140 vs. SBP 140-160
    - Achieved BP of 136/75 vs. 146/78
    - No difference in CV events or renal failure (p=0.99)
  - VALISH trial
    - 3079 patients aged 70-84 (average age of 76)
    - Randomized to SBP<140 or SBP 140-149
    - No significant reductions in stroke, CV events, or renal failure
  - Overall event rates were lower than anticipated in both of these studies

Systolic Blood Pressure Intervention Trial (SPRINT)

Examine effect of more intensive high blood pressure treatment than is currently recommended

Randomized Controlled Trial
Target Systolic BP

Intensive Treatment
Goal SBP < 120 mm Hg

Standard Treatment
Goal SBP < 140 mm Hg

SPRINT design details available at:
- ClinicalTrials.gov (NCT01206062)
<table>
<thead>
<tr>
<th>Demographic and Baseline Characteristics</th>
<th>Total N=9361</th>
<th>Intensive N=4678</th>
<th>Standard N=4683</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age, years</td>
<td>67.9 (9.4)</td>
<td>67.9 (9.4)</td>
<td>67.9 (9.5)</td>
</tr>
<tr>
<td>% ≥75 years</td>
<td>28.2%</td>
<td>28.2%</td>
<td>28.2%</td>
</tr>
<tr>
<td>Female, %</td>
<td>35.6%</td>
<td>36.0%</td>
<td>35.2%</td>
</tr>
<tr>
<td>White, %</td>
<td>57.7%</td>
<td>57.7%</td>
<td>57.7%</td>
</tr>
<tr>
<td>African-American, %</td>
<td>29.9%</td>
<td>29.5%</td>
<td>30.4%</td>
</tr>
<tr>
<td>Hispanic, %</td>
<td>10.5%</td>
<td>10.8%</td>
<td>10.3%</td>
</tr>
<tr>
<td>Prior CVD, %</td>
<td>20.1%</td>
<td>20.1%</td>
<td>20.0%</td>
</tr>
<tr>
<td>Mean 10-year Framingham CVD risk, %</td>
<td>20.1%</td>
<td>20.1%</td>
<td>20.1%</td>
</tr>
<tr>
<td>Taking antihypertensive meds, %</td>
<td>90.6%</td>
<td>90.8%</td>
<td>90.4%</td>
</tr>
<tr>
<td>Mean (SD) number of antihypertensive meds</td>
<td>1.8 (1.0)</td>
<td>1.8 (1.0)</td>
<td>1.8 (1.0)</td>
</tr>
<tr>
<td>Mean (SD) Baseline BP, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>139.7 (15.6)</td>
<td>139.7 (15.8)</td>
<td>139.7 (15.4)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>78.1 (11.9)</td>
<td>78.2 (11.9)</td>
<td>78.0 (12.0)</td>
</tr>
</tbody>
</table>
## Selected Baseline Laboratory Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Intensive</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$N=9361$</td>
<td>$N=4678$</td>
<td>$N=4683$</td>
</tr>
<tr>
<td>Mean (SD) eGFR, mL/min/1.73 m$^2$</td>
<td>71.7 (20.6)</td>
<td>71.8 (20.7)</td>
<td>71.7 (20.5)</td>
</tr>
<tr>
<td>% with eGFR &lt; 60 mL/min/1.73 m$^2$</td>
<td>28.3</td>
<td>28.4</td>
<td>28.1</td>
</tr>
<tr>
<td>Mean (SD) Urine albumin/creatinine, mg/g</td>
<td>42.6 (166.3)</td>
<td>44.1 (178.7)</td>
<td>41.1 (152.9)</td>
</tr>
<tr>
<td>Mean (SD) Total cholesterol, mg/dL</td>
<td>190.1 (41.2)</td>
<td>190.2 (41.4)</td>
<td>190.0 (40.9)</td>
</tr>
<tr>
<td>Mean (SD) Fasting plasma glucose, mg/dL</td>
<td>98.8 (13.5)</td>
<td>98.8 (13.7)</td>
<td>98.8 (13.4)</td>
</tr>
</tbody>
</table>
Systolic BP During Follow-up

Year 1

Mean SBP
136.2 mm Hg

Mean SBP
121.4 mm Hg

Standard

Intensive

Average number of antihypertensive medications

Average SBP
(During Follow-up)

Standard: 134.6 mm Hg

Intensive: 121.5 mm Hg

Number of participants

4876 4375 4231 4091 4029 3920 3204 2035 1048 286 274

Standard N  Intensive N
All-cause Mortality
Cumulative Hazard

Hazard Ratio = 0.73 (95% CI: 0.60 to 0.90)

Figure 2B: All-Cause Mortality Cumulative Hazards

During Trial (median follow-up = 3.26 years)
Number Needed to Treat (NNT) to Prevent a death = 90
Summary and Conclusions

- **SPRINT** examined effects of more intensive antihypertensive therapy than currently recommended.

- Participants were US adults ≥50 years with hypertension and additional risk for CVD.

- Rapid and sustained difference in SBP achieved between the two treatment arms.

- Trial stopped early, due to benefit, after median follow-up of 3.26 years.

- Incidence of primary outcome (composite of CVD events) 25% lower in Intensive compared to Standard Group and all-cause mortality reduced by 27%.

- Treatment effect similar in all six pre-specified groups of interest.

- The “number needed to treat” to prevent primary outcome event or death 61 and 90, respectively.
Summary and Conclusions

• In participants with CKD at baseline, no differences in renal outcomes

• In participants without CKD at baseline, incidence of eGFR reduction ≥ 30% more common in Intensive Group

• No overall difference in serious adverse events (SAEs) between treatment groups

• SAEs associated with hypotension, syncope, electrolyte abnormalities, and hospital discharge reports of acute kidney injury or acute renal failure more common in Intensive Group

• Overall, benefits of more intensive BP lowering exceeded the potential for harm
The combination of efficacy and discontinuation information to estimate the overall control rates separate by age categories.
30 Famous Local Foods to Eat in Singapore Before You Die
Ethnic Differences in Older Americans: Awareness, Knowledge, and Beliefs about Hypertension

<table>
<thead>
<tr>
<th></th>
<th>Whites (%)</th>
<th>Hispanics (%)</th>
<th>African Americans (%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medications only way to Control BP</td>
<td>23.3</td>
<td>55.5</td>
<td>50.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Weight reduction</td>
<td>93.6</td>
<td>89.0</td>
<td>87.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Reduce alcohol use</td>
<td>80.6</td>
<td>77.9</td>
<td>72.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Quit smoking</td>
<td>90.8</td>
<td>85.8</td>
<td>83.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Reduce salt Intake</td>
<td>90.3</td>
<td>87.9</td>
<td>90.7</td>
<td>NS</td>
</tr>
<tr>
<td>Take aspirin</td>
<td>63.5</td>
<td>61.4</td>
<td>54.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Exercise &gt;=3x per wk</td>
<td>95.0</td>
<td>91.4</td>
<td>86.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Emotional stress reduction</td>
<td>94.6</td>
<td>89.3</td>
<td>90.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Since lifestyle changes made BP has improved</td>
<td>58.0</td>
<td>67.0</td>
<td>75.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Seen HTN info on television</td>
<td>73.1</td>
<td>71.2</td>
<td>84.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obtain most information on HTN from MD/hospital only</td>
<td>16.4</td>
<td>30.5</td>
<td>22.0</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Category</th>
<th>Odds of Adequate Control</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African Americans</td>
<td>White</td>
<td>0.69</td>
<td>0.44–1.09</td>
</tr>
<tr>
<td>Hispanics</td>
<td></td>
<td>0.67</td>
<td>0.41–1.01</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td>0.74</td>
<td>0.51–1.06</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>0.91</td>
<td>0.07–1.28</td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td>0.92</td>
<td>0.90–0.96</td>
</tr>
<tr>
<td>Medication only way to treat blood pressure</td>
<td>Yes</td>
<td>1.87</td>
<td>1.27–2.75</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>1.33</td>
<td>0.84–2.11</td>
</tr>
<tr>
<td>Decreasing alcohol use will improve BP control</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>1.33</td>
<td>0.84–2.11</td>
</tr>
</tbody>
</table>

Differences in knowledge and beliefs about HTN were significantly associated with self-reported BP levels and control rates.

Okonofua, Cutler et al. (2005) Am J Hypertens
Randomly assigned 585 overweight and 390 normal-weight elderly individuals who had mild hypertension (145/85) and were taking a single antihypertensive medication randomly assigned to sodium restriction (1.8 g/24 h), weight reduction (goal 10 lb), both, or usual care

Primary end points were the development of hypertension (190/110 mmHg at a single visit or mean pressure of 150/90 mmHg) after withdrawal of medication
Evaluation of BP

Pre-HD CKD and PD
• Clinic BP (standard vs nonstandard)
• Home BP
• Ambulatory BP monitoring

Haemodialysis patients
• Pre-HD
• Post-HD
• Home BP
Role of ABPM

- **White coat ↑BP**: Clinic SBP > 140 but normal home BP or ABPM without target organ damage (TOD)
- **Masked ↑BP**: Clinic SBP < 140 but home SBP or ABPM > 140 ± TOD
- **Nocturnal BP > 125/75**
- **Nondipper**: DBP and SBP ↓ by <10 and 20% during sleep respectively
- **Reverse dipper**: no drop in SBP or DBP during sleep
- **BP load**: <25% above normal over 24h
# Comparisons to Other Guidelines

<table>
<thead>
<tr>
<th></th>
<th>JNC-7</th>
<th>JNC-8</th>
<th>ASH/ISH</th>
<th>ESC/ESH</th>
<th>CHEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>No DM or CKD</td>
<td>Thiazide</td>
<td>Thiazide, ACEI, ARB, CCB</td>
<td>&lt;60:ACEI,ARB &gt;60:CCB, thiazide</td>
<td>Thiazide, ACEI, ARB, CCB, BB</td>
<td>Thiazide, ACEI, ARB (BB if &lt;60)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>ACEI, ARB, CCB, BB, thiazide</td>
<td>CCB, thiazide, ACEI, ARB</td>
<td>ACEI, ARB</td>
<td>ACEI, ARB, CCB, thiazide</td>
<td>ACEI, ARB</td>
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<tr>
<td>CKD</td>
<td>ACEI, ARB</td>
<td>ACEI, ARB</td>
<td>ACEI, ARB</td>
<td>ACEI, ARB</td>
<td>ACEI, ARB</td>
</tr>
</tbody>
</table>

Underuse of ACEI/ARB

- Physicians’ beliefs that drug interventions for which benefits may not be evident for several years are not warranted in elderly patients with already limited life expectancy
- Fear an increased risk for hyperkalemia or additional decrease in renal function on initiation of such therapy in elderly patients

Winkelmayer, Fischer et al. (2005) Am J Kidney Dis
Young vs. Old on ACEI/ARB

- RAS may become less active with aging
- Reduction in renin and aldosterone level
- Benefits:
  - Target on increased peripheral resistance and decreased arterial compliance
  - Improvement on endothelial dysfunction
## ACEI vs. diuretic agents

Prospective, open-label trial with blinded assessment study design

6083 patients who had hypertension and were aged 65 to 84 years during a median of 4.1 years no increase in risks despite effective BP reduction were noted with the ACEI

<table>
<thead>
<tr>
<th>All Subjects</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
<th>ACE Inhibitors Superior</th>
<th>Diuretics Superior</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cardiovascular events or death from any cause</td>
<td>0.89 (0.79–1.00)</td>
<td>0.05</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>First cardiovascular event or death from any cause</td>
<td>0.89 (0.79–1.01)</td>
<td>0.06</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>0.90 (0.75–1.09)</td>
<td>0.27</td>
<td>0.2</td>
<td>1.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Male Subjects</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
<th>ACE Inhibitors Superior</th>
<th>Diuretics Superior</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cardiovascular events or death from any cause</td>
<td>0.83 (0.71–0.97)</td>
<td>0.02</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>First cardiovascular event or death from any cause</td>
<td>0.83 (0.71–0.97)</td>
<td>0.02</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>0.83 (0.66–1.06)</td>
<td>0.14</td>
<td>0.2</td>
<td>1.0</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Female Subjects</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
<th>ACE Inhibitors Superior</th>
<th>Diuretics Superior</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cardiovascular events or death from any cause</td>
<td>1.00 (0.83–1.21)</td>
<td>0.98</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>First cardiovascular event or death from any cause</td>
<td>1.00 (0.83–1.20)</td>
<td>0.98</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>1.01 (0.76–1.35)</td>
<td>0.94</td>
<td>0.2</td>
<td>1.0</td>
</tr>
</tbody>
</table>
Losartan vs. Atenolol

1326 men and women aged 55 through 80 years (mean, 70 years) Systolic blood pressure of 160 to 200 mm Hg and diastolic blood pressure of less than 90 mm Hg (mean, 174/83 mm Hg) - reduced by 28/9 and 28/9 mm Hg in the losartan and atenolol arms

Patients receiving losartan had fewer

- Cardiovascular mortality (8.7 vs 16.9 events per 1000 patient-years; RR, 0.54; 95% CI, 0.34-0.87; P = .01)
- Nonfatal and fatal stroke (10.6 vs 18.9 events per 1000 patient-years; RR, 0.60; 95% CI, 0.38-0.92; P = .02)
- New-onset diabetes (12.6 vs 20.1 events per 1000 patient-years; RR, 0.62; 95% CI, 0.40-0.97; P = .04)
- Total mortality (21.2 vs 30.2 events per 1000 patient-years; RR, 0.72; 95% CI, 0.53-1.00; P = .046)

Losartan decreased ECG-LVH more than atenolol (P<.001) and was better tolerated
Tolerability of ARBs in the Older Patient Population

Among the best tolerated antihypertensive agents
Potential for ARBs to cause hyperkalaemia and/or worsening renal function
  Volume-depleted
  Bilateral renal artery stenosis
Prompt achievement of BP goals is a critical determinant of outcomes
  With ARBs as first-line therapy, treatment be initiated with medium or high doses

Hyperkalaemia (K>5.5)

- Dietary indiscretion - eg bananas, potatoes, coconut and Nyoni juice
- Or NSAIDs, dehydration, absence of a kalliuretic diuretic (thiazide or frusemide)
- If K 5.5-6, review diet, K binding resins ± hold of RAAS blocker temporarily
- Long term K binding resins - Resonium/Kayalexate/Partiromer/Zirconium cyclosilicate
Rising creatinine

- Always check creatinine 1-2 weeks after starting or changing RAAS blocker
- <30% ↑ is acceptable
- ≥30% - dehydration, recent hypotension, ischaemia, NSAID, interstitial nephritis
- Screening for renal artery stenosis
- Hold off agent and review in 2-4 weeks and ↓ thiazide dose to 12.5mg
Goal of BP Control in CKD and Elderly

• Reduction of Proteinuria
• Retardation of CKD progression
• Reduction of Mortality
• Reduction of CVD

Risk of ESRD > risk of death
Risk of death > risk of ESRD
RAAS blockade- GFR decline at the expense of improvement in proteinuria (beyond BP control)

<table>
<thead>
<tr>
<th></th>
<th>Without RAAS blockade BP&gt;140/90</th>
<th>Without RAAS blockade but BP 130/80</th>
<th>With RAAS blockade BP 130/80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline GFR</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Baseline proteinuria (g/day)</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Expected GFR decline/year</td>
<td>5-10mL/min/yr</td>
<td>4-6mmL/min/yr</td>
<td>2-3mL/min/yr</td>
</tr>
<tr>
<td>(normal decline 1mL/min/yr)</td>
<td></td>
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</tr>
<tr>
<td>GFR after 2 years</td>
<td>20</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>Proteinuria after 2 years</td>
<td>6</td>
<td>2.8</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>DM number</th>
<th>Protocol</th>
<th>FU</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril trial — Lewis EJ et al NEJM 1993</td>
<td>Type 1DM N=490 BP 135/86 UACR&gt;0.5g/d Crt 220</td>
<td>Captopril 25mg tds vs placebo</td>
<td>3y</td>
<td>Doubling of Crt ↓48% Cct ↓11±21 vs 17±20ml/min/y</td>
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<tr>
<td>RENAAL-Reduction of Endpoints in NIDDM with Angiogen II Antagonist Losartan Brenner BM et al NEJM 2001</td>
<td>Type 2 DM N=1513 BP150/80 UACR 1.2g/d Crt 170</td>
<td>Losartan 50-100mg vs placebo</td>
<td>3.5y</td>
<td>UTP↓ 36% Doubling of Crt ↓26% ESRD ↓28% GFR↓ 4.4 vs 5.2ml/min/y</td>
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<tr>
<td>Irbesartan in Patients with DM2Nephropathy Diabetes trial Lewis EJ, NEJM 2001</td>
<td>Type 2 DM N=1715 BP 160/85 UACR 1.9g/d Crt 141</td>
<td>Irbesartan 75-300mg/d vs Amlodipine 10mg vs Placebo</td>
<td>2.6y</td>
<td>UTP↓ 33% Doubling of Crt↓ 33-37% ESRD↓ 23% Cct 5.5 vs 6.5-6.8ml/min/y</td>
</tr>
</tbody>
</table>

Cct = creatinine clearance
Age-specific subgroup analyses (from RENAAL)

• 1,513 participants, 421 (27.8%) were aged 65 years (maximum age 74 years)
• Age did not modify the efficacy of losartan in reducing the risk of the primary outcome
• Elderly patients had the same level of benefits and risks as younger patients from treatment with losartan

## My Opinion

<table>
<thead>
<tr>
<th></th>
<th>JNC-7</th>
<th>JNC-8</th>
<th>ASH/ISH</th>
<th>ESC/ESH</th>
<th>CHEP</th>
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</thead>
<tbody>
<tr>
<td>No DM or CKD</td>
<td>Thiazide</td>
<td>Thiazide, ACEI, ARB, CCB</td>
<td>&lt;60:ACEI,ARB &gt;60:CCB, thiazide</td>
<td>Thiazide, ACEI, ARB, CCB, BB</td>
<td>Thiazide, ACEI, ARB (BB if &lt;60)</td>
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<tr>
<td>Diabetes</td>
<td>ACEI, ARB, CCB, BB, thiazide</td>
<td>CCB, thiazide, ACEI, ARB</td>
<td>ACEI, ARB, CCB, thiazide</td>
<td>ACEI, ARB</td>
<td>ACEI, ARB, CCB, thiazide</td>
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<tr>
<td>CKD</td>
<td>ACEI, ARB</td>
<td>ACEI, ARB</td>
<td>ACEI, ARB</td>
<td>ACEI, ARB</td>
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</tr>
</tbody>
</table>

Thank You!

Questions?