Emerging Strategies for Heart Failure Roundtable; Stop it before it happens—the prevention of heart failure?

Clyde W. Yancy, MD, MSc
Professor of Medicine, Professor, Medical Social Science
Chief, Cardiology
Associate Director, Bluhm CV Institute
&
Vice-Dean, Diversity & Inclusion
Northwestern University, FSM
&
Deputy Editor, JAMA Cardiology

No relevant disclosures
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The prevention of heart failure?
Stages, Phenotypes and Treatment of HF

**STAGE A**
At high risk for HF but without structural heart disease or symptoms of HF

- e.g., Patients with:
  - HTN
  - Atherosclerotic disease
  - DM
  - Obesity
  - Metabolic syndrome

- Patients
  - Using cardiotoxins
  - With family history of cardiomyopathy

**THERAPY**
- Goals
  - Heart healthy lifestyle
  - Prevent vascular, coronary disease
  - Prevent LV structural abnormalities
- Drugs
  - ACEI or ARB in appropriate patients for vascular disease or DM
  - Statins as appropriate

**STAGE B**
Structural heart disease but without signs or symptoms of HF

- e.g., Patients with:
  - Previous MI
  - LV remodeling including LVH and low EF
  - Asymptomatic valvular disease

**THERAPY**
- Goals
  - Prevent HF symptoms
  - Prevent further cardiac remodeling
- Drugs
  - ACEI or ARB as appropriate
  - Beta blockers as appropriate
- In selected patients
  - ICD
  - Revascularization or valvular surgery as appropriate

**STAGE C**
Structural heart disease with prior or current symptoms of HF

- e.g., Patients with:
  - Known structural heart disease and HF signs and symptoms

**THERAPY**
- Goals
  - Control symptoms
  - Improve HRQOL
  - Prevent hospitalization
  - Prevent mortality
- Drugs for routine use
  - Diuretics for fluid retention
  - ACEI or ARB
  - Beta blockers
  - Aldosterone antagonists
- Drugs for use in selected patients
  - Hydralazine/isosorbide dinitrate
  - ACEI and ARB
  - Digoxin
- In selected patients
  - CRT
  - ICD
  - Revascularization or valvular surgery as appropriate

**STAGE D**
Refractory HF

- e.g., Patients with:
  - Marked HF symptoms at rest
  - Recurrent hospitalizations despite GDMT

**THERAPY**
- Goals
  - Control symptoms
  - Improve HRQOL
  - Reduce hospital readmissions
  - Establish patient’s end-of-life goals
- Options
  - Advanced care measures
  - Heart transplant
  - Chronic inotropes
  - Temporary or permanent MCS
  - Experimental surgery or drugs
  - Palliative care and hospice
  - ICD deactivation

**At Risk for Heart Failure**
- Patients with:
  - Known structural heart disease and HF signs and symptoms
  - Patients with:
    - Previous MI
    - LV remodeling including LVH and low EF
    - Asymptomatic valvular disease
  - Patients with:
    - HTN
    - Atherosclerotic disease
    - DM
    - Obesity
    - Metabolic syndrome
  - Patients
    - Using cardiotoxins
    - With family history of cardiomyopathy

**Heart Failure**

- Patients with:
  - Marked HF symptoms at rest
  - Recurrent hospitalizations despite GDMT

- Patients with:
  - Previous MI
  - LV remodeling including LVH and low EF
  - Asymptomatic valvular disease

- Patients
  - HTN
  - Atherosclerotic disease
  - DM
  - Obesity
  - Metabolic syndrome
  - Using cardiotoxins
  - With family history of cardiomyopathy

Yancy C, Jessup M, Bozkurt B et al. JACC, 2013
Prevalence and prognostic significance of HF Stages

Survival (years)

Ammar et al. *Circulation* 2007; 115:1563
Comparison of short-term vs lifetime cumulative risks of CHF for men and women at selected index ages

ONE IN FIVE INDIVIDUALS WILL DEVELOP HF

FRAMINGHAM Donald M. Lloyd-Jones et al Circulation 2002;106:3068
Lifetime risk for HF; indexed to blood pressure & sex

- Men:
  - BP <140/<90: 15.6%
  - BP 140-159/90-99: 23.2%
  - BP ≥160/≥100: 27.4%

- Women:
  - BP <140/<90: 12%
  - BP 140-159/90-99: 20.4%
  - BP ≥160/≥100: 29.5%
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Go to 'View - Normal' to return to slides

HTN to HF; what is the pathophysiology?
The 7 pathways in the progression from hypertension to heart failure.

Hypertension

1. 

2. No MI

3. MI

"Transition to failure"

4. MI

5. No MI

6. cLVH

7. Low EF

Symptomatic Heart Failure with Normal EF

Symptomatic Heart Failure with Low EF

Mark H. Drazner Circulation. 2011;123:327-334
Change in Hemodynamic Profile With Age; hypertension leading to heart failure

Hemodynamics: \[ BP = CO \times TPR \]

Borderline Hypertension

Established Hypertension

Heart Failure

Mild

Severe

Cardiac Output

Peripheral Resistance

Age (years)

20 40 60 80

Figure 5
A new pathophysiological model—
from HTN to HF

HTN → LVH

- Microtubule dysfunction
- T-tubule dysfunction
- Collagen synthesis
- Myocardial fibrosis

→ Mechanical dysfunction

- Stiffness / Abnormal relaxation

→ Heart Failure
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Scale to full screen size if necessary.

Click image, go to 'Format - Send to Back'

Go to 'View - Normal' to return to slides

HTN to HF; what is the natural history?
STAGE A HF:
Hypertension as a Risk Factor for HF in African Americans

Incidence of heart failure in young African Americans

**IHD Rates by SBP, DBP and Age**

**Lower Blood Pressure Is Better**

**A: Systolic Blood Pressure**

<table>
<thead>
<tr>
<th>Age at risk:</th>
<th>IHD Mortality (Floating Absolute Risk and 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>80-89 Years</td>
<td>256</td>
</tr>
<tr>
<td>70-79 Years</td>
<td>128</td>
</tr>
<tr>
<td>60-69 Years</td>
<td>64</td>
</tr>
<tr>
<td>50-59 Years</td>
<td>32</td>
</tr>
<tr>
<td>40-49 Years</td>
<td>16</td>
</tr>
<tr>
<td>30-39 Years</td>
<td>8</td>
</tr>
<tr>
<td>20-29 Years</td>
<td>4</td>
</tr>
<tr>
<td>10-19 Years</td>
<td>2</td>
</tr>
<tr>
<td>0-9 Years</td>
<td>1</td>
</tr>
</tbody>
</table>

Usual Systolic Blood Pressure (mm Hg)

**B: Diastolic Blood Pressure**

<table>
<thead>
<tr>
<th>Age at risk:</th>
<th>IHD Mortality (Floating Absolute Risk and 95% CI)</th>
</tr>
</thead>
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<td>20-29 Years</td>
<td>4</td>
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<tr>
<td>10-19 Years</td>
<td>2</td>
</tr>
<tr>
<td>0-9 Years</td>
<td>1</td>
</tr>
</tbody>
</table>

Usual Diastolic Blood Pressure (mm Hg)

**IHD: Ischemic Heart Disease**

Blood Pressure Lowering Treatment Based on CV Risk: A Meta-analysis of Individual Patient Data

<table>
<thead>
<tr>
<th>Active  (n/N)</th>
<th>Control (n/N)</th>
<th>Mean BP difference, mm Hg</th>
<th>Risk difference (95% CI)</th>
<th>Risk ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-year risk of stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4.0%</td>
<td>175/10497</td>
<td>286/14743</td>
<td>4.4/3.0</td>
<td>-1.06 (-1.53 to 0.60)</td>
</tr>
<tr>
<td>4.0-5.4%</td>
<td>196/5608</td>
<td>266/6648</td>
<td>5.1/3.1</td>
<td>-1.05 (-1.87 to 0.73)</td>
</tr>
<tr>
<td>5.4-7.2%</td>
<td>205/4445</td>
<td>257/4529</td>
<td>7.5/3.5</td>
<td>-1.49 (-2.67 to 0.32)</td>
</tr>
<tr>
<td>&gt;7.2%</td>
<td>206/2781</td>
<td>255/2970</td>
<td>6.1/2.6</td>
<td>-1.78 (-3.35 to 0.22)</td>
</tr>
<tr>
<td>p(het)=0.17 (p(trend)=0.06)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 5-year risk of CHD |
| <5% | 164/10373 | 251/14382 | 5.0/3.1 | -0.47 (-0.90 to 0.05) | 0.85 (0.70 to 1.04) |
| 5-7% | 183/5546 | 232/6950 | 5.3/3.2 | -0.28 (-1.03 to 0.47) | 0.94 (0.78 to 1.15) |
| 7-11% | 182/4187 | 233/4530 | 6.3/2.8 | -1.14 (-2.20 to 0.07) | 0.85 (0.70 to 1.02) |
| >11% | 189/2870 | 225/2957 | 6.2/2.9 | -1.57 (-3.19 to 0.04) | 0.87 (0.72 to 1.04) |
| p(het)=0.07 (p(trend)=0.10) | |

| 5-year risk of heart failure |
| <2.6% | 102/14560 | 119/20070 | 4.8/3.1 | -0.42 (-0.36 to 0.11) | 0.91 (0.70 to 1.18) |
| 2.6-4.5% | 104/4503 | 118/4839 | 5.7/3.0 | -0.26 (-0.99 to 0.47) | 0.93 (0.71 to 1.21) |
| 4.5-7.0% | 101/2362 | 120/2376 | 7.2/2.9 | -1.04 (-2.52 to 0.44) | 0.87 (0.67 to 1.12) |
| >7.0% | 90/1651 | 131/1674 | 6.3/2.8 | -3.28 (-5.30 to 1.25) | 0.72 (0.55 to 0.93) |
| p(het)=0.001 (p(trend)=0.09) | |

| 5-year risk of cardiovascular death |
| <5% | 190/12870 | 274/17722 | 4.6/3.0 | -0.30 (-0.64 to 0.05) | 0.88 (0.72 to 1.06) |
| 5-8% | 203/4967 | 261/5788 | 5.9/3.0 | -0.78 (-1.67 to 0.11) | 0.88 (0.72 to 1.05) |
| 8-13% | 212/2985 | 257/3138 | 7.4/3.3 | -1.68 (-3.32 to 0.05) | 0.87 (0.72 to 1.04) |
| >13% | 220/2554 | 243/2301 | 8.4/3.4 | -1.20 (-3.36 to 0.96) | 0.93 (0.78 to 1.10) |
| p(het)=0.001 (p(trend)=0.21) | |

| 5-year risk of death |
| <6% | 318/11659 | 446/16314 | 4.7/3.1 | -0.32 (-0.81 to 0.17) | 0.93 (0.81 to 1.07) |
| 6-10% | 340/4875 | 424/5860 | 5.7/3.1 | -0.72 (-1.79 to 0.36) | 0.92 (0.80 to 1.06) |
| 10-16% | 343/3001 | 421/3435 | 5.5/3.1 | -1.16 (-2.81 to 0.49) | 0.92 (0.80 to 1.05) |
| >16% | 379/1611 | 384/1623 | 7.3/3.0 | -0.71 (-3.49 to 2.07) | 0.97 (0.85 to 1.10) |
| p(het)=0.48 (p(trend)=0.21) | |

Favours active treatment
Favours control

Lancet 2014; 384 (August 16 2014)
Blood Pressure Lowering Treatment Based on CV Risk: A Meta-analysis of Individual Patient Data
**SPRINT Hypertension Trial**

- **Study Type:** Interventional Study
  - **Design:** Allocation: Randomized
  - **Endpoint Classification:** Efficacy Study
  - **Intervention Model:** Parallel Assignment
  - **Masking:** Single Blind (Outcomes Assessor)

**Official Title:** Systolic Blood Pressure Intervention Trial

**Primary Outcome Measures:** First occurrence of a myocardial infarction (MI), acute coronary syndrome (ACS), stroke, heart failure (HF), or CVD death [Time Frame: 6 years] [Designated as safety issue: No]

**Secondary Outcome Measures:** All-cause mortality; Development of end stage renal disease (ESRD), Dementia, Decline in cognitive function, Small vessel cerebral ischemic disease

- **Estimated Enrollment:** 9250
  - **Study Start Date:** October 2010
  - **Estimated Study Completion Date:** December 2018
  - **Estimated Primary Completion Date:** October 2018 (Final data collection date for primary outcome measure)
Increased CV risk as defined by SPRINT:

- clinical or subclinical cardiovascular disease other than stroke;
- chronic kidney disease, excluding polycystic kidney disease, with an estimated glomerular filtration rate (eGFR) of 20 to less than 60 ml per minute per 1.73 m$^2$ of body-surface area, calculated with the use of the four-variable Modification of Diet in Renal Disease equation;
- a 10-year risk of cardiovascular disease of 15% or greater on the basis of the Framingham risk score;
- or an age of 75 years or older
Systolic Blood Pressure in the Two Treatment Groups over the Course of the Trial.

![Graph showing systolic blood pressure over time for the two treatment groups.](image)

<table>
<thead>
<tr>
<th>Years</th>
<th>Standard treatment</th>
<th>Intensive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>150</td>
<td>130</td>
</tr>
<tr>
<td>1</td>
<td>140</td>
<td>130</td>
</tr>
<tr>
<td>2</td>
<td>130</td>
<td>130</td>
</tr>
<tr>
<td>3</td>
<td>120</td>
<td>130</td>
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<tr>
<td>4</td>
<td>120</td>
<td>130</td>
</tr>
<tr>
<td>5</td>
<td>120</td>
<td>130</td>
</tr>
</tbody>
</table>

No. with Data

<table>
<thead>
<tr>
<th>Years</th>
<th>Standard treatment</th>
<th>Intensive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4683</td>
<td>4678</td>
</tr>
<tr>
<td>1</td>
<td>4345</td>
<td>4375</td>
</tr>
<tr>
<td>2</td>
<td>4222</td>
<td>4231</td>
</tr>
<tr>
<td>3</td>
<td>4092</td>
<td>4091</td>
</tr>
<tr>
<td>4</td>
<td>3997</td>
<td>4029</td>
</tr>
<tr>
<td>5</td>
<td>3904</td>
<td>3920</td>
</tr>
</tbody>
</table>

Mean No. of Medications

<table>
<thead>
<tr>
<th>Years</th>
<th>Standard treatment</th>
<th>Intensive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.9</td>
<td>2.3</td>
</tr>
<tr>
<td>1</td>
<td>1.8</td>
<td>2.7</td>
</tr>
<tr>
<td>2</td>
<td>1.8</td>
<td>2.8</td>
</tr>
<tr>
<td>3</td>
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<td>2.8</td>
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<tr>
<td>4</td>
<td>1.8</td>
<td>2.8</td>
</tr>
<tr>
<td>5</td>
<td>1.8</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Primary Outcome and Death from Any Cause.

A  Primary Outcome

Cumulative Hazard

Hazard ratio with intensive treatment, 0.75 (95% CI, 0.64–0.89)

Standard treatment

Intensive treatment

No. at Risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard treatment</td>
<td>4683</td>
<td>4437</td>
<td>4228</td>
<td>2829</td>
<td>721</td>
</tr>
<tr>
<td>Intensive treatment</td>
<td>4678</td>
<td>4436</td>
<td>4256</td>
<td>2900</td>
<td>779</td>
</tr>
</tbody>
</table>

B  Death from Any Cause

Cumulative Hazard

Hazard ratio with intensive treatment, 0.73 (95% CI, 0.60–0.90)

Standard treatment

Intensive treatment

No. at Risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard treatment</td>
<td>4683</td>
<td>4528</td>
<td>4383</td>
<td>2998</td>
<td>789</td>
</tr>
<tr>
<td>Intensive treatment</td>
<td>4678</td>
<td>4516</td>
<td>4390</td>
<td>3016</td>
<td>807</td>
</tr>
</tbody>
</table>
Primary and Secondary Outcomes and Renal Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants (N = 4678)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary outcome†</td>
<td>243 (5.2)</td>
<td>319 (6.8)</td>
<td>0.75 (0.64–0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>97 (2.1)</td>
<td>116 (2.5)</td>
<td>0.83 (0.64–1.09)</td>
<td>0.19</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>40 (0.9)</td>
<td>40 (0.9)</td>
<td>1.00 (0.64–1.55)</td>
<td>0.99</td>
</tr>
<tr>
<td>Stroke</td>
<td>62 (1.3)</td>
<td>70 (1.5)</td>
<td>0.89 (0.63–1.25)</td>
<td>0.50</td>
</tr>
<tr>
<td>Heart failure</td>
<td>62 (1.3)</td>
<td>100 (2.1)</td>
<td>0.62 (0.45–0.84)</td>
<td>0.002</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>37 (0.8)</td>
<td>65 (1.4)</td>
<td>0.57 (0.38–0.85)</td>
<td>0.005</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>155 (3.3)</td>
<td>210 (4.5)</td>
<td>0.73 (0.60–0.90)</td>
<td>0.003</td>
</tr>
<tr>
<td>Primary outcome or death</td>
<td>332 (7.1)</td>
<td>423 (9.0)</td>
<td>0.78 (0.67–0.90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Participants with CKD at baseline (N = 1330)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite renal outcome‡</td>
<td>14 (1.1)</td>
<td>15 (1.1)</td>
<td>0.89 (0.42–1.87)</td>
<td>0.76</td>
</tr>
<tr>
<td>≥50% reduction in estimated GFR§</td>
<td>10 (0.8)</td>
<td>11 (0.8)</td>
<td>0.87 (0.36–2.07)</td>
<td>0.75</td>
</tr>
<tr>
<td>Long-term dialysis</td>
<td>6 (0.5)</td>
<td>10 (0.8)</td>
<td>0.57 (0.19–1.54)</td>
<td>0.27</td>
</tr>
<tr>
<td>Kidney transplantation</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incident albuminuria¶</td>
<td>49/526 (9.3)</td>
<td>59/500 (11.8)</td>
<td>0.72 (0.48–1.07)</td>
<td>0.11</td>
</tr>
<tr>
<td>Participants without CKD at baseline (N = 3332)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30% reduction in estimated GFR to &lt;60 ml/min/1.73 m²§</td>
<td>127 (3.8)</td>
<td>37 (1.1)</td>
<td>3.49 (2.44–5.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Incident albuminuria¶</td>
<td>110/1769 (6.2)</td>
<td>135/1831 (7.4)</td>
<td>0.81 (0.63–1.04)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

* CI denotes confidence interval, and CKD chronic kidney disease.
† The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.
‡ The composite renal outcome for participants with CKD at baseline was the first occurrence of a reduction in the estimated GFR of 50% or more, long-term dialysis, or kidney transplantation.
§ Reductions in the estimated GFR were confirmed by a second laboratory test at least 90 days later.
¶ Incident albuminuria was defined by a doubling of the ratio of urinary albumin (in milligrams) to creatinine (in grams) from less than 10 at baseline to greater than 10 during follow-up. The denominators for number of patients represent those without albuminuria at baseline.
|| No long-term dialysis or kidney transplantation was reported among participants without CKD at baseline.

09/11/2015; Announcement of premature termination of SPRINT for benefit

• “... treating high-risk hypertensive adults 50 years of age and older to a target of 120 mm Hg significantly reduced cardiovascular events by 30% and reduced all-cause mortality by nearly 25% when compared with patients treated to a target of 140 mm Hg...”
Hypertension, Obesity, Diabetes and HF Free Survival

• The Cardiovascular Lifetime Risk Pooling Project
• Framingham Heart, Framingham Offspring, Chicago Heart Association Detection Project, ARIC
• 471,988 person-years of follow-up, beginning at age 45
• Men and women without HTN, obesity or DM lived an average 35-37 years without HF. Those with HTN, obesity and/or DM had shorter survival – 3 to 11 years
Heart Failure-Free Survival and Survival after Incident Heart Failure by Risk Factors (HTN, Obesity, DM) for Men and Women at Index Age of 45 Years
## Treatment of Hypertension to Prevent HF:

### Treatment effects of blood pressure lowering on heart failure outcomes in landmark hypertension trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Inclusion criteria</th>
<th>Intervention</th>
<th>Duration (yr)</th>
<th>Mean BP difference between groups (mmHg)</th>
<th>Absolute rates of heart failure</th>
<th>Relative reduction of heart failure (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHEP 1997</td>
<td>4,736</td>
<td>≥ 60 yrs; SBP ≥ 160 mmHg</td>
<td>Chlorothalidone ± atenolol</td>
<td>4.5</td>
<td>-26.0 / -8.9</td>
<td>2.3% vs. 4.4%</td>
<td>RR 0.51 (0.37-0.71)</td>
</tr>
<tr>
<td>HYVET 2008</td>
<td>3,845</td>
<td>≥ 80 yrs; SBP ≥ 160 mmHg</td>
<td>Indapamide ± perindopril</td>
<td>2.1</td>
<td>-15.0 / -6.1</td>
<td>5.3% vs. 14.8%</td>
<td>RR 0.36 (0.22-0.58)</td>
</tr>
<tr>
<td>ALLHAT 2002</td>
<td>33,357</td>
<td>≥ 55 years; HTN + 1 CV risk factor</td>
<td>Chlorothalidone vs. Amlodipine;</td>
<td>4.9</td>
<td>-0.8 / +0.8</td>
<td>7.7% vs. 10.2%</td>
<td>RR 0.62 (0.48-0.75)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chlorothalidone vs. Lisinopril</td>
<td></td>
<td>-2.0 / 0</td>
<td>7.7% vs. 8.7%</td>
<td></td>
</tr>
<tr>
<td>HOPE 2000</td>
<td>9,297</td>
<td>≥ 55 years; vascular disease or DM + 1 CV risk factor</td>
<td>Ramipril</td>
<td>4.5</td>
<td>-3 / -2</td>
<td>9.0% vs. 11.5%</td>
<td>RR 0.77 (0.67-0.87)</td>
</tr>
<tr>
<td>SPRINT 2015</td>
<td>9,361</td>
<td>SBP ≥ 130 mmHg; increased CVD risk without DM</td>
<td>SBP target &lt;120 mmHg vs. SBP target &lt;140 mmHg</td>
<td>3.3</td>
<td>-18.2 / -9.4</td>
<td>1.3%/yr vs. 2.1%/yr</td>
<td>HR 0.62 (0.45-0.84)</td>
</tr>
</tbody>
</table>

For ALLHAT, mean blood pressure differences. Data for the Chlorothalidone vs. doxazosin comparison is not presented since this arm was terminated early due to harm from doxazosin.
Kaplan-Meier Analysis of Major Adverse Cardiovascular Events in the Full Study Sample and in Participants With BNP ≥50 pg/mL

BNP indicates brain-type natriuretic peptide. Major adverse cardiovascular events included arrhythmia, transient ischemic attack, stroke, myocardial infarction, peripheral or pulmonary thrombosis/embolus, or heart failure. In the full sample, 51 (7.3%) of 697 patients were admitted for major adverse cardiovascular events in the intervention group and 71 (10.5%) of 677 were admitted in the control group. In participants with BNP ≥50 pg/mL, 35 (13.3%) of 263 were admitted for major adverse cardiovascular events in the intervention group and 45 (19.1%) of 235 were admitted in the control group.
A Bold New Direction in Heart Failure

• **Prevention**
  – Heart failure is a preventable illness and we should shift our focus in part to prevention