HOPE Trial
Heart Outcomes Prevention Evaluation (NEJM 2000;342:145-53)

- **Trail Design**
  - Randomized, Double-blind
  - Placebo-controlled

- **Patient Enrollment**
  - n = 9,541 patients, age>55 years
  - CAD, CVA or PVD without a low LVEF
  - Diabetes + ≥ 1 Risk Factor

- **Duration**
  - Planned 6.0 years
  - Halted after 4.5 years

- **Primary Endpoints**
  - MI, stroke, CV death, 5-year mean follow-up
  - ACEI (ramipril) reduced by 22% the relative risk for CV death, nonfatal acute MI or stroke.

HOPE Baseline Demographics

Mean Age: 65.9 Years
Female: 26.7%
Any CAD: 80.6%
Previous MI: 52.8%
Diabetes: 38.3%
Hypertension: 46.5%
Hypercholesterolemia: 65.8%
Peripheral Vascular Disease: 43.4%
Stoke or TIA: 10.8%

HOPE: Ramipril 10 mg Benefits to Subgroups

<table>
<thead>
<tr>
<th>Event</th>
<th>No of Patients</th>
<th>Relative Risk in Ramipril Group</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality in Diabetics</td>
<td>38%</td>
<td>0.60</td>
<td>0.80</td>
</tr>
<tr>
<td>Stroke</td>
<td>32%</td>
<td>0.80</td>
<td>1.00</td>
</tr>
<tr>
<td>New-Onset of Diabetes</td>
<td>30%</td>
<td>1.00</td>
<td>1.20</td>
</tr>
<tr>
<td>Cardiovascular Deaths</td>
<td>26%</td>
<td>1.20</td>
<td>1.40</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>23%</td>
<td>1.40</td>
<td>1.60</td>
</tr>
<tr>
<td>MI, Stroke &amp; CV mortality</td>
<td>22%</td>
<td>1.60</td>
<td>1.80</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>20%</td>
<td>1.80</td>
<td>2.00</td>
</tr>
<tr>
<td>Diabetic Complications</td>
<td>16%</td>
<td>2.00</td>
<td>2.20</td>
</tr>
<tr>
<td>Total Mortality</td>
<td>16%</td>
<td>2.20</td>
<td>2.40</td>
</tr>
<tr>
<td>Revascularization Procedures</td>
<td>15%</td>
<td>2.40</td>
<td>2.60</td>
</tr>
</tbody>
</table>

HOPE: Baseline SBP vs. Global Endpoint


Baseline Systolic Blood Pressure Quartiles
- Average Baseline SBP (mmHg):
  - 124
  - 130
  - 141
  - 158
- δ SBP (mmHg) with Ramipril:
  - -3.0
  - -3.3
  - -3.3
  - -3.3
- δ DBP (mmHg) with Ramipril:
  - -1.5
  - -2.2
  - -2.2
  - -1.7

HOPE: Decrement in SBP and DBP

HOPE OBP (n=9541)
end of trial 4.5 years

Ramipril SBP: -2.17
Placebo SBP: 0.14
Ramipril DBP: -3.13
Placebo DBP: -2.09

NEJM 2000;342:145-153
HOPE: Decrement in SBP and DBP

<table>
<thead>
<tr>
<th></th>
<th>HOPE OBP (n = 9541)</th>
<th>HOPE ABP (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>end of trial 4.5 years</td>
<td>measured at 1 year</td>
</tr>
<tr>
<td>Ramipril SBP</td>
<td>-2.17</td>
<td>NS</td>
</tr>
<tr>
<td>Placebo SBP</td>
<td>0.14</td>
<td>-2.8</td>
</tr>
<tr>
<td>Ramipril DBP</td>
<td>-3.13</td>
<td>NS</td>
</tr>
<tr>
<td>Placebo DBP</td>
<td>-2.59</td>
<td>-1.0</td>
</tr>
</tbody>
</table>

10 mmHg
P < 0.03
4 mmHg
P < 0.03

NEJM 2000;342:145
Hypertension 2001;38:e28

HOPE: Ambulatory Blood Pressures

Comparative Effects of Ramipril on Ambulatory and Office Blood Pressures
A HOPE Substudy

- Study comprised of 38 patients with peripheral arterial disease
- Patients underwent 24-hour ambulatory blood pressure (ABP) measurement before randomization and after 1 year
- Ramipril did not reduce OBP or day ABP after 1 year
- 24-hour ABP was reduced significantly because of pronounced blood pressure lowering effect at night
- The night/day ratio also was lowered significantly in the ramipril group
- The effects on cardiovascular morbidity and mortality observed with ramipril in the HOPE study may relate to effects on blood pressure patterns over the 24-hour period


HOPE: Primary Outcome in Diabetics, n= 3577

Cardiovascular death, myocardial infarction or stroke

Kaplan-Meier rates

Risk Reduction 25% RR p = 0.0004

Duration of Follow-up (days)


HOPE & MICRO-HOPE
Primary Endpoints

Total Mortality
Stroke
MI
CV Death

Patients With Diabetes  Overall