Essential Hypertension and Treatment

András Tislér M.D., Ph.D.
1st Dept. of Med. Semmelweis University, Budapest
August 2008
Overview

• Note on the pathogenesis of HTN
• Note on home blood pressure measurement
• Note on therapy
PHYSIOLOGIC CONTROL OF ARTERIAL PRESSURE*

ARTHUR C. GUYTON, THOMAS G. COLEMAN, JACQUES C. FOURCADE, AND L. GABRIEL NAVAR

Department of Physiology and Biophysics
University of Mississippi School of Medicine
Jackson, Miss.
Fig. 2. Equilibration of the normal renal function curve for output of extracellular fluid with the normal curve for intake of extracellular fluid.
Fig. 3. Equilibration of output and intake of extracellular fluid in a human being with various renal abnormalities.
Fig. 4. Computer predictions of changes in circulatory function when total peripheral resistance is suddenly increased threefold or decreased threefold but without altering renal resistances.
HTN „follows the kidney” after transplantation

Control normotensive kidney Tx

Change in blood pressure in genetically normotensive rat (F1H) after transplanting kidney from a genetically hypertensive rat (SHRSP) strain

Am J Physiol 1993;265:F104
Normotension “follows the kidney” after transplantation

Change in blood pressure after transplanting salt-resistant rat kidney (R) in genetically salt sensitive (S) rat

Circ Res 1975;36:692
Change in blood pressure after transplanting kidneys from hypertensive and non-hypertensive donors in human

- Kidneys from donors with head injury or cerebral tumor
- Kidneys from donors with subarachnoid hemorrhage
Distribution and function of AT1 receptors

• Kidney: vasoconstriction, antinatriuresis
• Vascular smooth muscle cells: vasoconstriction
• Adrenals: aldosterone production
• CNS: pressure response
AT$_{1a}$ receptor knock-out cross-transplantation mice

Wild-Type

Systemic KO

Kidney KO

Total KO

J Clin Invest 2005;115:1092
Blood pressure response to Ang II infusion

Proc Natl Acad Sci U SA 2006;103:17985
Conclusion

- Decreased salt excreting ability of the kidneys is sufficient to cause sustained HTN

- Vasoconstriction alone, without impairment in salt-excretion, is not sufficient to cause sustained HTN
Overview

• Note on the pathogenesis of HTN

• Note on home blood pressure measurement (HBPM)

• Note on therapy
Total cardiovascular risk is determined by:

- Level of blood pressure
- Presence of risk factors
- Presence of metabolic syndrome & diabetes
- Presence of organ damage
- Presence of established cardiovascular or renal disease
Stratification of total cardiovascular risk into categories

<table>
<thead>
<tr>
<th>Blood pressure (mmHg)</th>
<th>Normal SBP 120-129 or DBP 80-84</th>
<th>High normal SBP 130-139 or DBP 85-89</th>
<th>Grade 1 HT SBP 140-159 or DBP 90-99</th>
<th>Grade 2 HT SBP 160-179 or DBP 100-109</th>
<th>Grade 3 HT SBP ≥180 or DBP ≥110</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other risk factors, OD or disease</td>
<td>Average risk</td>
<td>Average risk</td>
<td>Low added risk</td>
<td>Moderate added risk</td>
<td>High added risk</td>
</tr>
<tr>
<td>No other risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2 risk factors</td>
<td>Low added risk</td>
<td>Low added risk</td>
<td>Moderate added risk</td>
<td>Moderate added risk</td>
<td>Very high added risk</td>
</tr>
<tr>
<td>3 or more risk factors, MS, OD or diabetes</td>
<td>Moderate added risk</td>
<td>High added risk</td>
<td>High added risk</td>
<td>High added risk</td>
<td>Very high added risk</td>
</tr>
<tr>
<td>Established CV or renal disease</td>
<td>Very high added risk</td>
<td>Very high added risk</td>
<td>Very high added risk</td>
<td>Very high added risk</td>
<td>Very high added risk</td>
</tr>
</tbody>
</table>
Types of blood pressure measurement

- Office
- Home
- Ambulatory
- During exercise or laboratory stress
- Central
- Beat-to-beat
Fig. 1.—Comparison of clinic and home blood pressure readings in a patient with essential hypertension.
Is HBPM considered to be part of standard hypertension patient care? „Yes”

<table>
<thead>
<tr>
<th>Country</th>
<th>%</th>
<th>Stat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hungary</td>
<td>98</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Ontario</td>
<td>52</td>
<td></td>
</tr>
</tbody>
</table>

J Hypertens 2006;24:1429  
J Hypertens 2008;26:446
“How often do you encourage your patient to measure BP at home?”

<table>
<thead>
<tr>
<th></th>
<th>Hungary</th>
<th>Ontario</th>
</tr>
</thead>
<tbody>
<tr>
<td>almost always</td>
<td>57%</td>
<td>23%</td>
</tr>
<tr>
<td>often</td>
<td>37%</td>
<td>39%</td>
</tr>
<tr>
<td>sometimes</td>
<td>3%</td>
<td>27%</td>
</tr>
<tr>
<td>occasionally</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>almost never</td>
<td>3%</td>
<td>3%</td>
</tr>
</tbody>
</table>

p<0.001

J Hypertens 2006;24:1429
J Hypertens 2008;26:446
Frequency of use of HBPM

- US: 38% in 2000, 55% in 2005
- Italy: 75% hypertension clinic
- MD recommends its use (USA): 35% in 2000, 47% in 2005

The Gallup Study of the Hypertension Market, 2006
Blood Press 2005;14:251
Call to Action on Use and Reimbursement for Home Blood Pressure Monitoring
A Joint Scientific Statement From the American Heart Association, American Society of Hypertension, and Preventive Cardiovascular Nurses Association

Thomas G. Pickering, MD, DPhil, FAHA, Chair; Nancy Houston Miller, RN, BSN, FAHA; Gbenga Ogedegbe, MD, MPH, FAHA; Lawrence R. Krakoff, MD, FAHA; Nancy T. Artinian, PhD, RN, BC, FAHA; David Goff, MD, PhD, FAHA

European Society of Hypertension guidelines for blood pressure monitoring at home: a summary report of the Second International Consensus Conference on Home Blood Pressure Monitoring
Gianfranco Parati\textsuperscript{a}, George S. Stergiou\textsuperscript{b}, Roland Asmar\textsuperscript{c}, Grzegorz Bilo\textsuperscript{a}, Peter de Leeuw\textsuperscript{d}, Yutaka Imai\textsuperscript{e}, Kazuomi Kario\textsuperscript{f}, Empar Lurbe\textsuperscript{g}, Athanasios Manolis\textsuperscript{h}, Thomas Mengden\textsuperscript{i}, Eoin O’Brien\textsuperscript{j}, Takayoshi Ohkubo\textsuperscript{k}, Paul Padfield\textsuperscript{l}, Paolo Palatini\textsuperscript{m}, Thomas Pickering\textsuperscript{n}, Josep Redon\textsuperscript{o}, Miriam Revera\textsuperscript{a}, Luis M. Ruilope\textsuperscript{p}, Andrew Shennan\textsuperscript{q}, Jan A. Staessen\textsuperscript{r}, Andras Tisler\textsuperscript{s}, Bernard Waebere\textsuperscript{t}, Alberto Zanchetti\textsuperscript{u} and Giuseppe Mancia\textsuperscript{v}, on behalf of the ESH Working Group on Blood Pressure Monitoring
Key issues related to the methodology of HBPM

- Need of medical supervision and patient training
- Need of independent validation
  - www.dableducational.com
  - www.bhsoc.org/blood_pressure_list.htm
- Checking device accuracy in individual patients
Methods of HBPM: measurement

- Most frequent errors during HBP measurement
  - No rest period prior to measurement (90%)
  - No back support or legs crossed (70%)
  - Incorrect correct cuff placement (50%)
  - Talking during measurement (46%)
  - Arm not supported at heart level (30%)
  - Constrictive clothing (9%)

- Use of cuffs that are inappropriate for the arm

Blood Press Monit 2004;9:143
Devices

• **Recommended**
  – Auscultatory, finger cuff, wrist cuff* not recommended
  – Small and large adult cuffs should be available
  – Semiautomated, preferably automated oscillometric recommended
  – Large display, sufficient memory, computation of whole period averages

• **Optional**
  – Detection of arm movement, irregular heart beats,
  – Separate evening, morning averages
  – Automated night time measurement
  – Telemonitoring capability may be useful

* Under evaluation for special situations  

J Hypertens 2008;26:1505
How many home readings are needed?

<table>
<thead>
<tr>
<th>SBP (Per 10 mmHg increase)</th>
<th>Screening</th>
<th>Home 1-day</th>
<th>2-day</th>
<th>1-week</th>
<th>2-week</th>
<th>Multiple</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke RH and 95% CI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage increase in risk (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8% (−1% to 18%)</td>
<td>19% (8%−31%)</td>
<td>20% (8%−33%)</td>
<td>27% (13%−43%)</td>
<td>31% (16%−47%)</td>
<td>35% (20%−51%)</td>
</tr>
</tbody>
</table>

J Hypertens 2004;22:1099
How often and how many times to measure?

- At initial assessment, treatment changes, before clinic visits
  - 7 day measurement
  - 2 measurement on each session
  - 2 sessions per day (morning evening)
  - Assess average with the first day data discarded

- Long term follow-up
  - 1-2 measurements per week
Reference values and target home blood pressure

- Diagnostic threshold
  - $\geq 135/85$ mmHg

- Goal BP
  - $< 135/85$ mmHg
  - Probably lower in high risk individuals
    - „each mmHg reduction is important”
Frequency of cardiovascular events according to office and home blood pressure levels in the SHEAF-study

Normal home BP <135/85 mmHg, normal office BP <140/90 mmHg

n=4939, 3y f/u JAMA 2004;291:11342
Development of stage 5 CKD according to the level of home and office (routine) BP

n=217, 3.5 y f/u, Kidney Int 2006;69:406
Risk of CV mortality according to the number of methods (office, home, ambulatory) by which high blood pressure was detected

PAMELA study n=2051, 148 mo f/u, Hypertension 2006;47:846
Flow-sheet for evaluating need for treatment

Office BP Raised

Target organ Damage

Present

Absent

Continue To Monitor

Home BP

<125/76

<130/80

>125/76 <135/85

>130/80

24 Hr BP

Start Treatment

Hypertension 2008;52:10
Indications for HBPM in treated patients

• All patients receiving antihypertensive treatment
• Evaluation of white coat HTN
• Evaluation of masked HTN
• Evaluation of resistant HTN
• To improve compliance
• To improve HTN control rates
The effect of HBPM on blood pressure: meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Weighted mean difference (95% CI) in fall in systolic blood pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carnahan 1975</td>
<td></td>
</tr>
<tr>
<td>Pierce 1984</td>
<td></td>
</tr>
<tr>
<td>Binstock 1988</td>
<td></td>
</tr>
<tr>
<td>Midanik 1991</td>
<td></td>
</tr>
<tr>
<td>Soghikian 1992</td>
<td></td>
</tr>
<tr>
<td>Muhlhauser 1993</td>
<td></td>
</tr>
<tr>
<td>Friedman 1996</td>
<td></td>
</tr>
<tr>
<td>Bailey 1999</td>
<td></td>
</tr>
<tr>
<td>Mehos 2000</td>
<td></td>
</tr>
<tr>
<td>Vetter 2000</td>
<td></td>
</tr>
<tr>
<td>Artinian 2001</td>
<td></td>
</tr>
<tr>
<td>Broege 2001</td>
<td></td>
</tr>
<tr>
<td>Rogers 2001</td>
<td></td>
</tr>
<tr>
<td>Overall (95% CI)</td>
<td>4.25 (1.55 to 6.95)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Weighted mean difference (95% CI) in fall in diastolic blood pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carnahan 1975</td>
<td></td>
</tr>
<tr>
<td>Haynes 1976</td>
<td></td>
</tr>
<tr>
<td>Johnson 1978</td>
<td></td>
</tr>
<tr>
<td>Pierce 1984</td>
<td></td>
</tr>
<tr>
<td>Stahl 1984</td>
<td></td>
</tr>
<tr>
<td>Binstock 1988</td>
<td></td>
</tr>
<tr>
<td>Midanik 1991</td>
<td></td>
</tr>
<tr>
<td>Soghikian 1992</td>
<td></td>
</tr>
<tr>
<td>Muhlhauser 1993</td>
<td></td>
</tr>
<tr>
<td>Friedman 1996</td>
<td></td>
</tr>
<tr>
<td>Bailey 1999</td>
<td></td>
</tr>
<tr>
<td>Mehos 2000</td>
<td></td>
</tr>
<tr>
<td>Vetter 2000</td>
<td></td>
</tr>
<tr>
<td>Artinian 2001</td>
<td></td>
</tr>
<tr>
<td>Broege 2001</td>
<td></td>
</tr>
<tr>
<td>Rogers 2001</td>
<td></td>
</tr>
<tr>
<td>Overall (95% CI)</td>
<td>2.37 (1.25 to 3.49)</td>
</tr>
</tbody>
</table>

BMJ 2004;329:145
Self-Monitoring of Blood Pressure Promotes Achievement of Blood Pressure Target in Primary Health Care

Laura Halme, Risto Vesaainen, Mika Kaaja, Ilkka Kantola, for the HOMER (HOme MEasuReement of blood pressure) study group

N=269, HBPM vs office BP, office goal <140/85, home goal <135/80 mmHg 6 mo f/u
Self-Measurement of Blood Pressure at Home Reduces the Need for Antihypertensive Drugs
A Randomized, Controlled Trial

HOMERUS trial
N=430 office vs. Home BP guided Rx, goal 120-140/80-90mmHg, 1y f/u

(Hypertension. 2007;50:1019-1025.)
Limitations

• May not work in atrial fibrillation and frequent arrhythmias

• In patients where HBPM causes anxiety, preoccupation with BP and self-medication
Overview

- Note on the pathogenesis of HTN
- Note on home blood pressure measurement
- Note on therapy
### Initiation of antihypertensive treatment

<table>
<thead>
<tr>
<th>Other risk factors, OD or disease</th>
<th>Normal SBP 120-129 or DBP 80-84</th>
<th>High normal SBP 130-139 or DBP 85-89</th>
<th>Grade 1 HT SBP 140-159 or DBP 90-99</th>
<th>Grade 2 HT SBP 160-179 or DBP 100-109</th>
<th>Grade 3 HT SBP ≥180 or DBP ≥110</th>
</tr>
</thead>
<tbody>
<tr>
<td>No other risk factors</td>
<td>No BP intervention</td>
<td>No BP intervention</td>
<td>Lifestyle changes for several weeks then drug treatment if BP uncontrolled</td>
<td>Lifestyle changes for several weeks then drug treatment if BP uncontrolled</td>
<td>Lifestyle changes + immediate drug treatment</td>
</tr>
<tr>
<td>1-2 risk factors</td>
<td>Lifestyle changes</td>
<td>Lifestyle changes</td>
<td>Lifestyle changes for several weeks then drug treatment if BP uncontrolled</td>
<td>Lifestyle changes for several weeks then drug treatment if BP uncontrolled</td>
<td>Lifestyle changes + immediate drug treatment</td>
</tr>
<tr>
<td>3 or more risk factors, MS, OD or diabetes</td>
<td>Lifestyle changes</td>
<td>Lifestyle changes and consider drug treatment</td>
<td>Lifestyle changes + drug treatment</td>
<td>Lifestyle changes + drug treatment</td>
<td>Lifestyle changes + immediate drug treatment</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Lifestyle changes</td>
<td>Lifestyle changes + drug treatment</td>
<td>Lifestyle changes + drug treatment</td>
<td>Lifestyle changes + drug treatment</td>
<td>Lifestyle changes + immediate drug treatment</td>
</tr>
<tr>
<td>Established CV or renal disease</td>
<td>Lifestyle changes + immediate drug treatment</td>
<td>Lifestyle changes + immediate drug treatment</td>
<td>Lifestyle changes + immediate drug treatment</td>
<td>Lifestyle changes + immediate drug treatment</td>
<td>Lifestyle changes + immediate drug treatment</td>
</tr>
</tbody>
</table>

J Hypertens 2007;25:1105
• „the primary goal of treatment is to achieve maximum reduction in total risk of CV disease”

• „This requires treatment of raised BP per se as well as of all associated reversible risk factors”

• „BP should be reduced to at least below 140/90 mmHg (systolic/diastolic) and to lower values, if tolerated, in all hypertensive patients”

• „Target BP should be at least <130/80 mmHg in diabetics and in high or very high risk patients, such as those with associated clinical conditions (stroke, myocardial infarction, renal dysfunction, proteinuria)”

J Hypertens 2007;25:1105
Objective
- To compare diuretic/placebo (less intensive) with diuretic/felodipine (more intensive) over 5 years

Patients
- N= 9711, 50-79y, hypertension plus 1CV event or 2 risk factors

Outcome
- Primary: stroke
- Secondary: CV events, all cause mortality
Blood pressure during the FEVER study

SBP

DBP

Diff: 4.2/2.1 mmHg

J Hypertens 2007;23:2157
FEVER study: main outcome

Hazard ratio (95% CI)

- Stroke
  - Fatal
  - Non-fatal
- All cardiovascular events
- All cardiac events
- All cause death
- Cardiovascular death
- Coronary events
- Heart failure
- New onset diabetes
- Cancer

NNT for 5 years: 42
NNT for 5 years: 80

J Hypertens 2007;23:2157
• The role of small achieved blood pressure difference during treatment is substantial even in low risk patients

• First trial to show benefit of lowering blood pressure below the recommended systolic value of 140 mmHg in this population
Treatment of Hypertension in Patients 80 Years of Age or Older
HYVET background

**Total mortality**
- Double-blind trials (meta-analysis) (RR = 1.14, P = 0.05)
- All trials (meta-analysis) (RR = 1.06, P = 0.30)
- HYVET-Pilot (diuretic) (RR = 1.307, P = 0.34)
- HYVET-Pilot (ACE) (RR = 1.149, P = 0.65)
- HYVET-Pilot (all active) (RR = 1.227, P = 0.42)

**Stroke events**
- Double-blind trials (meta-analysis) (RR = 0.64, P = 0.01)
- All trials (meta-analysis) (RR = 0.67, P = 0.01)
- HYVET-Pilot (diuretic) (RR = 0.813, P = 0.01)
- HYVET-Pilot (ACE) (RR = 0.629, P = 0.21)
- HYVET-Pilot (all active) (RR = 0.471, P = 0.02)
HYVET

- **Objective**
  - To determine if treatment of HTN in patients ≥ 80 years of age was beneficial

- **Methods**
  - n= 3845, ≥ 160 mmHg, indapamid+perindopril vs. placebo, goal <150/80 mmHg, median f/u 1.8y

- **Outcome**
  - Primary: stroke
  - Secondary: all cause mortality CV events and mortality

NEJM May 1st 2008
HYVET: change in blood pressure

Median follow-up 1.8 years

15 mmHg

6 mmHg

Follow-up (years)

Blood Pressure (mmHg)

Placebo

Indapamide SR +/- perindopril

NEJM May 1st 2008
HYVET: outcome data (intention to treat analysis)

<table>
<thead>
<tr>
<th>Event</th>
<th>HR</th>
<th>95% CI</th>
<th>NNT/5y</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Stroke</td>
<td>0.70</td>
<td>(0.49, 1.01)</td>
<td>38</td>
</tr>
<tr>
<td>Stroke Death</td>
<td>0.61</td>
<td>(0.38, 0.99)</td>
<td></td>
</tr>
<tr>
<td>All cause mortality</td>
<td>0.79</td>
<td>(0.65, 0.95)</td>
<td>16</td>
</tr>
<tr>
<td>NCV/Unknown death</td>
<td>0.81</td>
<td>(0.62, 1.06)</td>
<td></td>
</tr>
<tr>
<td>CV Death</td>
<td>0.77</td>
<td>(0.60, 1.01)</td>
<td></td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>0.71</td>
<td>(0.42, 1.19)</td>
<td></td>
</tr>
<tr>
<td>Heart Failure</td>
<td>0.36</td>
<td>(0.22, 0.58)</td>
<td></td>
</tr>
<tr>
<td>CV events</td>
<td>0.66</td>
<td>(0.53, 0.82)</td>
<td></td>
</tr>
</tbody>
</table>
• Treatment of very old hypertensive patients decreases the risk of death from stroke and the risk of any death

• Trial evidence to expand the age range of the treatment of HTN
The main benefits of antihypertensive therapy are due to lowering of BP *per se*.

Five major classes of antihypertensive agents:
- thiazide diuretics
- calcium antagonists
- ACE inhibitors
- angiotensin receptor antagonists
- β- blockers

are suitable for the initiation and maintenance of antihypertensive treatment, alone or in combination.

β-blockers, especially in combination with a thiazide diuretic, should not be used in patients with the metabolic syndrome or at high risk of incident diabetes.
Primary

Is ATII receptor blocking equivalent to ACE inhibition among high risk patients?

Secondary

Is double blockade better than ACE inhibition?
Inclusion Criteria

ONTARGET
- ≥55 y
- High risk
  - CAD
  - PAD
  - Stroke
  - DM + target organ damage

HOPE
- ≥55 y
- High risk
  - CAD
  - PAD
  - Stroke
  - DM + 1 risk factor
Planned. Actual = 25,620

Planned. Actual = 5,926

* Planned. Actual = 25,620

† Planned. Actual = 5,926
Outcome

ONTARGET
- CV mortality
- AMI
- Stroke
- CHF with admission

HOPE
- CV mortality
- AMI
- Stroke
## Baseline data

<table>
<thead>
<tr>
<th>Demography</th>
<th>ONTARGET (n = 25,620)</th>
<th>HOPE (n = 9,541)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.4</td>
<td>65.9</td>
</tr>
<tr>
<td>Male (%)</td>
<td>73.3</td>
<td>73.3</td>
</tr>
<tr>
<td>Body mass index</td>
<td>28.2</td>
<td>27.7</td>
</tr>
<tr>
<td>Waist–hip ratio</td>
<td>0.9</td>
<td>0.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical history</th>
<th>ONTARGET (n = 25,620)</th>
<th>HOPE (n = 9,541)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (%)</td>
<td>68.3</td>
<td>46.5</td>
</tr>
<tr>
<td>MI (%)</td>
<td>48.7</td>
<td>52.8</td>
</tr>
<tr>
<td>Stable angina (%)</td>
<td>34.8</td>
<td>55.8</td>
</tr>
<tr>
<td>Stroke/TIA (%)</td>
<td>20.7</td>
<td>10.8</td>
</tr>
<tr>
<td>Claudication (%)</td>
<td>11.8</td>
<td>15.9</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>37.3</td>
<td>38.3</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>12.5</td>
<td>14.1</td>
</tr>
</tbody>
</table>
Occurrence of the primary outcome in the three groups of ONTARGET

- Telmisartan: 1.01 [0.94-1.09]
- Ramipril: 0.99 [0.92-1.07]
- Telmisartan plus ramipril: 0.99 [0.92-1.07]
## Outcome in Ontarget and HOPE

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ramipril</th>
<th>Telmisartan</th>
<th>Comb.</th>
<th>HOPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>16.5</td>
<td>16.7</td>
<td>16.3</td>
<td></td>
</tr>
<tr>
<td>CV mort. + AMI + stroke</td>
<td>14.1</td>
<td>13.9</td>
<td>14.1</td>
<td>14.0</td>
</tr>
<tr>
<td>MI</td>
<td>4.8</td>
<td>5.2</td>
<td>5.2</td>
<td>9.9</td>
</tr>
<tr>
<td>stroke</td>
<td>4.7</td>
<td>4.3</td>
<td>4.4</td>
<td>3.4</td>
</tr>
<tr>
<td>CHF hosp.</td>
<td>4.1</td>
<td>4.6</td>
<td>3.9</td>
<td></td>
</tr>
<tr>
<td>CV mort.</td>
<td>7.0</td>
<td>7.0</td>
<td>7.3</td>
<td>6.1</td>
</tr>
</tbody>
</table>
Discontinuation of study medication and selected reasons

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ramipril (N=8576)</th>
<th>Telmisartan (N=8542)</th>
<th>Combination Therapy (N=8502)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of discontinuations†</td>
<td>2099 (24.5)</td>
<td>1962 (23.0)</td>
<td>2495 (29.3) *</td>
</tr>
<tr>
<td>Reason for permanent discontinuation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotensive symptoms</td>
<td>149 (1.7)</td>
<td>229 (2.7) *</td>
<td>406 (4.8) *</td>
</tr>
<tr>
<td>Syncope</td>
<td>15 (0.2)</td>
<td>19 (0.2)</td>
<td>29 (0.3)</td>
</tr>
<tr>
<td>Cough</td>
<td>360 (4.2)</td>
<td>93 (1.1) *</td>
<td>392 (4.6)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12 (0.1)</td>
<td>19 (0.2)</td>
<td>39 (0.5) *</td>
</tr>
<tr>
<td>Angioedema</td>
<td>25 (0.3)</td>
<td>10 (0.1) *</td>
<td>18 (0.2)</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>60 (0.7)</td>
<td>68 (0.8)</td>
<td>94 (1.1) *</td>
</tr>
</tbody>
</table>

(29% in HOPE)  

* p<0.01
• Telmisartan is similarly effective than ramipril in high risk patients but better tolerated (angioedema, cough)

• Double blockade is no more effective than ramipril alone and less tolerated
Summary

• Note on the pathogenesis of HTN
  – Decreased salt excretion capacity of the kidneys is necessary for sustained hypertension

• Note on home blood pressure measurement
  – Inclusion into everyday clinical practice is supported by recent guidelines

• Note on therapy
  – FEVER: evidence to treat HTN <140 mmHg systolic
  – HYVET: evidence to treat HTN in those ≥80 years of age
  – ONTARGET: no evidence for difference in efficacy between ramipril and telmisartan among high risk patients