Pre Hypertension

Is it Time to Change the Definitions of Hypertension and to Change the Risk Tables?
Primary and secondary prevention of cardiovascular disease

• The high-risk strategy - greatest risk (e.g. 10-year coronary heart disease risk $\geq 20\%$) - benefits the individual

• A mass strategy- lifestyle change for the entire population:
  – Is designed to shift the distribution of risk to lower levels
  – Can potentially prevent more events than a high-risk strategy
Modified mass strategy

• Larger segments of the population are defined at risk
• Moving the level of risk requiring treatment to progressively lower levels.
Blood pressure related events

• Identifying another segment of the population at-risk for blood pressure related events

• Could they potentially benefit from pharmacologic/ non pharmacologic intervention?

• Is there a reduced risk for progression to hypertension and for cardiovascular events?
RANGE OF NORMAL BLOOD PRESSURE: A STATISTICAL AND CLINICAL STUDY OF 11,383 PERSONS

- SAMUEL C. ROBINSON, M.D.; MARSHALL BRUCER

- *Arch Intern Med (Chic).* 1939;64(3):409-444
• Defined BPs in the range of 120–139/80–89mmHg as pre-hypertensive
• They observed both that most future hypertensives originated from the prehypertensive range
• These individuals had roughly double the mortality rate of people with BP of <120/80mmHg.
2007 Guidelines for the Management of Arterial Hypertension- ESH/ESC

Table 1 Definitions and classification of blood pressure (BP) levels (mmHg)

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Normal</td>
<td>120–129</td>
<td>80–84</td>
</tr>
<tr>
<td>High normal</td>
<td>130–139</td>
<td>85–89</td>
</tr>
<tr>
<td>Grade 1 hypertension</td>
<td>140–159</td>
<td>90–99</td>
</tr>
<tr>
<td>Grade 2 hypertension</td>
<td>160–179</td>
<td>100–109</td>
</tr>
<tr>
<td>Grade 3 hypertension</td>
<td>180</td>
<td>110</td>
</tr>
<tr>
<td>Isolated systolic</td>
<td>140</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>
JNC-7 2003

• Systolic blood pressure of 120–139 mmHg or a diastolic blood pressure of 80–89 mmHg - prehypertensive

• Require health-promoting lifestyle modifications to prevent CVD
Staging Prehypertension

- Stage 1’ prehypertension: 120–129/80–84mmHg
- Stage 2’ prehypertension: 130–139/85–89mmHg
Stage 2 prehypertensives vs. normotensives

• 3-fold or greater risk for progression to established hypertension

• Double the risk of clinical cardiovascular disease independently of progression to hypertension.
These individuals are not associated with optimal health
Risk Factors & Sub Clinical TOD

- Hypertriglyceridemia
- Reduced concentrations of HDL-cholesterol
- Greater numbers of small, dense LDL-cholesterol particles
- High levels of fibrinogen, plasminogen activator inhibitor-1 (PAI-1), adipokines and inflammatory cytokines
- Endothelial dysfunction, left ventricular hypertrophy
Pre-disease or a disease?
Aortic Stiffness, Blood Pressure Progression, and Incident Hypertension

JAMA. 2012;308(9):875-881
Speed of the wave is related to the stiffness of the artery it is traveling in.

The stiffer the artery the higher the wave speed.
Windkessel Model (windbag model)

Since the aorta and attached large arteries are rich in elastic fibers, they expand and store blood as blood is flushed into them. Blood is delivered to the arteries during the systole, but the blood stored in large arteries is delivered to the periphery during the diastole by the elasticity of the arteries. In this way, the blood output by a heart beat can be continuously delivered to the periphery even when the heart is resting because the blood is first stored in the arteries.
A, When the arteries are normally compliant, a substantial fraction of the stroke volume is stored in the arteries during ventricular systole. The arterial walls are stretched.

B, During ventricular diastole the previously stretched arteries recoil. The volume of blood that is displaced by the recoil furnishes continuous capillary flow throughout diastole.

C, When the arteries are rigid, virtually none of the stroke volume can be stored in the arteries.

D, Rigid arteries cannot recoil appreciably during diastole.
The speed at which the outgoing and reflected waves travel is dependent on the stiffness of the arteries.

So if a person has stiffer arteries, the waves will travel out and back quicker, arriving earlier back at the heart.
Pressure Wave Reflection at the Heart

This earlier return to the heart of the reflected pressure wave (due to stiffening of the arteries) changes the aortic root pressure waveform.

This gives three important clinical implications.
Pressure Wave Reflection at the Heart

First, the central systolic pressure and central pulse pressure is increased.

An increase in the central pulse pressure that drives cerebral blood flow increases stroke risk.
## Table 3. Correlates of Blood Pressure During Examination Cycle 8 (N = 1759)

<table>
<thead>
<tr>
<th>Dependent Variable During Examination Cycle 8&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Predictor Variables During Examination Cycle 7&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Estimated Regression Coefficient (95% CI)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>Systolic blood pressure</td>
<td>6.8 (5.9 to 7.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Forward wave amplitude</td>
<td>1.3 (0.5 to 2.1)</td>
<td>.002</td>
</tr>
<tr>
<td></td>
<td>CFPWV</td>
<td>1.5 (0.5 to 2.6)</td>
<td>.000</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>Diastolic blood pressure</td>
<td>5.3 (4.7 to 5.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Systolic blood pressure</td>
<td>−1.1 (−1.7 to −0.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>CFPWV</td>
<td>−0.7 (−1.3 to −0.1)</td>
<td>.03</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>Mean arterial pressure</td>
<td>5.1 (4.5 to 5.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Pulse pressure</td>
<td>−0.9 (−1.5 to −0.3)</td>
<td>.005</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>Pulse pressure</td>
<td>6.4 (5.6 to 7.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Forward wave amplitude</td>
<td>2.0 (1.3 to 2.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>CFPWV</td>
<td>2.1 (1.2 to 2.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Mean arterial pressure</td>
<td>−1.1 (−1.8 to −0.4)</td>
<td>.003</td>
</tr>
<tr>
<td></td>
<td>Augmentation index</td>
<td>0.7 (0 to 1.4)</td>
<td>.04</td>
</tr>
</tbody>
</table>

Abbreviation: CFPWV, carotid-femoral pulse wave velocity.

<sup>a</sup>Models were adjusted for age, sex, body mass index (calculated as weight in kilograms divided by height in meters squared), height, heart rate, total cholesterol, high-density lipoprotein cholesterol, triglycerides, fasting glucose, diabetes, current smoking, and time between examination cycles 7 and 8.

<sup>b</sup>Derived from a single multivariable model for each blood pressure measure during examination cycle 8 and are presented per 1-SD difference in the value of predictor variables (SDs appear in Table 2).
Table 5. Correlates of Tonometry Measures During Examination Cycle 8 (N = 1759)

<table>
<thead>
<tr>
<th>Dependent Variable During Examination Cycle 8&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Predictor Variables During Examination Cycle 7&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Estimated Regression Coefficient (95% CI)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFPWV</td>
<td>CFPWV</td>
<td>17.5 (16.2 to 18.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Forward wave amplitude</td>
<td>Pulse pressure</td>
<td>4.3 (3.4 to 5.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Forward wave amplitude</td>
<td>Forward wave amplitude</td>
<td>3.5 (2.7 to 4.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CFPWV</td>
<td>Diastolic blood pressure</td>
<td>2.8 (1.8 to 3.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Augmentation index</td>
<td>Augmentation index</td>
<td>−0.9 (−1.6 to −0.2)</td>
<td>.01</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>Augmentation index</td>
<td>4.6 (4.0 to 5.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CFPWV</td>
<td>Systolic blood pressure</td>
<td>1.1 (0.4 to 1.8)</td>
<td>.001</td>
</tr>
<tr>
<td>CFPWV</td>
<td>Augmentation index</td>
<td>−1.1 (−1.9 to −0.2)</td>
<td>.01</td>
</tr>
</tbody>
</table>

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<sup>a</sup> Models were adjusted for age, sex, body mass index (calculated as weight in kilograms divided by height in meters squared), height, heart rate, total cholesterol, high-density lipoprotein cholesterol, triglycerides, fasting glucose, diabetes, antihypertensive treatment, current smoking, and time between examination cycles 7 and 8.

<sup>b</sup> Derived from a single multivariable model for each tonometry measure during examination cycle 8 and are presented per 1-SD difference in the value of predictor variables.
• In this cohort, higher aortic stiffness, FWA, and augmentation index were associated with higher risk of incident hypertension
The Endothelium

Intima
- endothelium
- connective tissue

Media
- smooth muscle
- protein matrix of elastin/collagen
- internal elastic lamina

Adventitia
- strong, fibrous tissue to maintain vessel shape

Elevated Endothelin-1 Vasoconstrictor Tone in Prehypertensive Adults

Figure 3  Endothelium-dependent and -independent vasodilation. Forearm blood flow responses to acetylcholine (A) and sodium nitroprusside (B) in normotensive and prehypertensive adults. Values are mean ± SEM. *<ce:italic> P</ce:italic> < 0.05.

Brian R. Weil, Christian M. Westby, Jared J. Greiner, Brian L. Stauffer, Christopher A. DeSouza

Canadian Journal of Cardiology Volume 28, Issue 3 2012 347 - 353

http://dx.doi.org/10.1016/j.cjca.2011.11.006
Figure 4  Endothelium-dependent vasodilation with ET A receptor blockade. Forearm blood flow responses to acetylcholine in the presence and absence of ET A receptor blockade with BQ-123 in normotensive (A) and prehypertensive (B) adults. Val...

Brian R. Weil, Christian M. Westby, Jared J. Greiner, Brian L. Stauffer, Christopher A. DeSouza

Elevated Endothelin-1 Vasoconstrictor Tone in Prehypertensive Adults

Canadian Journal of Cardiology Volume 28, Issue 3 2012 347 - 353

http://dx.doi.org/10.1016/j.cjca.2011.11.006
Fig. 1  A and B: presence of perivascular adipose tissue (PVAT) in mesenteric artery and its branch. C: mRNA expression of angiotensinogen (ATG) and angiotensin I-converting enzyme (ACE) from adipocytes of mesenteric PVAT. D: presence of angiotensin II.

Chao Lu, Li-Ying Su, Robert M.K.W. Lee, Yu-Jing Gao

Mechanisms for perivascular adipose tissue-mediated potentiation of vascular contraction to perivascular neuronal stimulation: The role of adipocyte-derived angiotensin II

European Journal of Pharmacology Volume 634, Issues 1-3 2010 107 - 112

http://dx.doi.org/10.1016/j.ejphar.2010.02.006
Effects of ACE inhibitor and angiotensin II type I receptor antagonist on the contractile response to electrical field stimulation

Chao Lu, Li-Ying Su, Robert M.K.W. Lee, Yu-Jing Gao

Mechanisms for perivascular adipose tissue-mediated potentiation of vascular contraction to perivascular neuronal stimulation: The role of adipocyte-derived angiotensin II

European Journal of Pharmacology Volume 634, Issues 1-3 2010 107 - 112

http://dx.doi.org/10.1016/j.ejphar.2010.02.006
Treatment ?
Pharmacological treatment

- Anti hypertensive medications
- non anti hypertensive medications
Feasibility of Treating Prehypertension with an Angiotensin-Receptor Blocker

• Trial of Preventing Hypertension (TROPHY) Study Investigators
  • N Engl J Med 2006; 354:1685-1697
TROPHY (Trial of Preventing Hypertension) study design (upper panel) and Kaplan-Meier analysis (lower panel) of new-onset clinical hypertension.

Reprinted with permission from Julius et al. (11).
Kaplan–Meier Analysis of New-Onset Clinical Hypertension.

**TROPHY Study: ARB in ‘Prehypertension’**

![Graph showing cumulative incidence over study years](image)

- **Placebo**
- **Candesartan**

*Julius NEJM 2006; 354: 1685-97*
The PHARAO study: prevention of hypertension with the angiotensin-converting enzyme inhibitor ramipril in patients with high-normal blood pressure - a prospective, randomized, controlled prevention trial of the German Hypertension League

*J Hypertens.* 2008 Jul;26(7):1487-96
The PHARAO study: prevention of hypertension with the angiotensin-converting enzyme inhibitor ramipril in patients with high-normal blood pressure - a prospective, randomized, controlled prevention trial of the German Hypertension League.

Luders, Stephan; Schrader, Joachim; Berger, Jurgen; Unger, Thomas; Zidek, Walter; Bohm, Michael; Middeke, Martin; Motz, Wolfgang; Lubcke, Cornelia; Gansz, Andrea; Brokamp, Ludmer; Schmieder, Roland; Trenkwalder, Peter; Haller, Herrmann; Dominiak, Peter


Trial profile. ABPM, ambulatory blood pressure monitoring.
• Ramipril proved to be more effective in reducing the incidence of manifest office hypertension in patients with baseline ambulatory blood pressure monitoring high-normal blood pressure.
• The incidence of cerebrovascular and cardiovascular events showed no statistically significant differences between the two groups.
Blood pressure of all randomized patients. (a) Office BP. (b) Twenty-four-hour ABPM BP. ABPM, ambulatory blood pressure monitoring; BP, blood pressure.
Ambulatory blood pressure control with bedtime aspirin administration in subjects with prehypertension.

- a significant effect on BP of low dose aspirin only when ingested at bedtime by prehypertensive subjects

- decrease of 6/3 mm Hg in the 24-h mean of systolic (SBP)/diastolic BP (DBP), respectively; \(P < 0.001\)
Uric acid reduction rectifies prehypertension in obese adolescents.

Hypertension. 2012 Nov;60(5):1148-56.
Flow diagram for the prevention of hypertension in obese adolescents trial.

Soletsky B, and Feig D | Hypertension 2012;60:1148-1156
<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>-13.7) 14.3 (14.8</td>
<td>-13.1) 14.1 (15.2</td>
<td>-13.5) 14.5 (15.3</td>
<td>-13.0) 14.2 (15.3</td>
<td>0.878</td>
<td>0.902</td>
<td>0.541</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>35.7</td>
<td>35.8</td>
<td>36.3</td>
<td>33.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-34.0) 37.7 (39.7</td>
<td>-31.9) 39.7 (40.9</td>
<td>-33.9) 40.9 (37.1</td>
<td></td>
<td>0.491</td>
<td>0.121</td>
<td>0.039</td>
</tr>
<tr>
<td>Serum uric acid, mg/dL</td>
<td>(7.1–6.5) 6.8</td>
<td>(7.1–5.9) 6.6</td>
<td>(7.5–6.3) 6.8</td>
<td>(7.2–6.2) 6.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-h SBP, mm Hg</td>
<td>122.3</td>
<td>121.9</td>
<td>122.5</td>
<td>122.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-119.3) 124.1</td>
<td>-116.3) 125.0</td>
<td>-119.4) 125.6</td>
<td>-118.9) 126.2</td>
<td>0.099</td>
<td>0.338</td>
<td>0.952</td>
</tr>
<tr>
<td>24-h DBP, mm Hg</td>
<td>-67.2) 68.7 (64.2</td>
<td>67.5 (67.5</td>
<td>68.5 (66.1)</td>
<td>69.7 (66.7)</td>
<td>0.126</td>
<td>0.093</td>
<td>0.186</td>
</tr>
<tr>
<td></td>
<td>(70.1) 69.8 (70.7</td>
<td>(73.1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nocturnal dip SBP, %</td>
<td>-6.9) 9.6 (12.7</td>
<td>-7.2) 9.7 (12.2</td>
<td>-6.6) 9.4 (12.1</td>
<td>-6.7) 9.8 (12.9</td>
<td>0.115</td>
<td>0.942</td>
<td>0.993</td>
</tr>
<tr>
<td></td>
<td>(14.6) 14.6 (20.2</td>
<td>(16.4) 16.4 (19.7</td>
<td>(15.1) 15.1 (20.3</td>
<td>-7.8) 12.2 (16.5</td>
<td>0.381</td>
<td>0.104</td>
<td>0.374</td>
</tr>
</tbody>
</table>
### End Points at the Conclusion of the 2-mo Treatment Phase

<table>
<thead>
<tr>
<th><em>End Point (units)</em></th>
<th>Placebo</th>
<th>$p^+$</th>
<th>Allopurinol $p^+$</th>
<th>$P$ Allopurinol vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum uric acid, mg/dL (Change from baseline)</td>
<td>6.3 (5.8 to 6.8)</td>
<td>$-0.3$ ($-0.1$ to $-0.7$)</td>
<td>4.1 (3.4 to 4.7)</td>
<td>$-2.8$ ($-2.1$ to $-3.6$)</td>
</tr>
<tr>
<td>24-h SBP, mm Hg (Change from baseline)</td>
<td>120.0 (114.9 to 125.1)</td>
<td>$+1.9$ ($-0.4$ to 2.4)</td>
<td>113.5 (110.3 to 117.3)</td>
<td>$-9.2$ ($-6.7$ to $-11.3$)</td>
</tr>
<tr>
<td>24-h DBP, mm Hg (Change from baseline)</td>
<td>68.7 (66.4 to 71.1)</td>
<td>$+1.3$ (0.2 to 3.5)</td>
<td>62.4 (60.4 to 64.5)</td>
<td>$-6.1$ ($-4.6$ to $-9.0$)</td>
</tr>
</tbody>
</table>
Prevention of hypertension in patients with pre-hypertension: protocol for the PREVER-prevention trial

Trials. 2011 Mar 5;12:65

TRIAL REGISTRATION:
Clinical Trials NCT00970931
POTENTIALLY ELIGIBLE (Time 0)
- Consent form
- Males/ Females, 30 - 70 years old
- Office average blood pressure: 120-139/80-89 mmHg
- If diabetes mellitus: Systolic BP: 120-130 mmHg

LIFESTYLE MODIFICATION (Months 1 to 3)
- Weight control
- Dash diet like
- Low sodium
- Stop smoking
- Physical activity

RANDOMIZATION (Month 3)
- Consent form
- Prehypertension at office blood pressure
- Blood tests
- Urine analysis
- ECG

FOLLOW-UP VISITS (Months 6 to 15)
- Re-assessment
- Office blood pressure
- Side-effects

OUTCOMES (Month 18)
- Hypertension
- Adverse events
- Target-organ damage
- Cardiovascular disease
Males or females, 30 to 70 years old, prehypertension (office blood pressure); no antihypertensive treatment, without allergy to chlortalidone and amiloride, and no previous CHD, severe chronic disease, or pregnant women

Lifestyle modification

Prehypertension

Chlortalidone and Amiloride

Placebo

3 m
6 m
9 m
12 m
15 m

Hypertension
Adverse effects
Target-organ damage

3 m
6 m
9 m
12 m
15 m

Hypertension
Adverse effects
Target-organ damage

TW SUMC
Myocardial infarction
Unstable angina requiring hospitalization
Stroke and Ischemic Transitory Attack
Heart failure requiring hospitalization
Peripheral vascular disease requiring hospitalization
New subclinical evidence of vascular atherosclerotic disease
Sudden death
Non pharmacological treatment

DASH Pyramid

Source: http://www.nhlbi.nih.gov/

(c) 2007, Margo N. Woods, DSc
Protein supplementation lowers blood pressure in overweight adults: effect of dietary proteins on blood pressure (PROPRES), a randomized trial

Am J Clin Nutr. 2012 Apr;95(4):966-71
Flow diagram of participants in the effect of dietary proteins on blood pressure (PROPRES) study.

216 individuals screened

- 93 excluded
  - 41 blood pressure too low/high
  - 20 medication use
  - 32 other

123 started run-in

- 24 dropped out

99 randomly assigned

51 maltodextrin

- 0 dropped out

48 protein

- 5 dropped out
  - 2 adverse effects
  - 2 started medication
  - 1 other

94 included in analysis

- 51 maltodextrin
- 43 protein

Baseline and run-in characteristics \((n = 94)\)

<table>
<thead>
<tr>
<th></th>
<th>Protein group</th>
<th>Maltodextrin group</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants ((n))</td>
<td>43</td>
<td>51</td>
<td>—</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27±0.4</td>
<td>28.8±0.4</td>
<td>0.11</td>
</tr>
<tr>
<td>Age (y)</td>
<td>55.3±1.1</td>
<td>55.0±1.3</td>
<td>0.90</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>147.7±1.9</td>
<td>150.1±2.0</td>
<td>0.41</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>95.9±1.1</td>
<td>95.9±1.1</td>
<td>0.45³</td>
</tr>
</tbody>
</table>
Maltodextrin group (black, n = 51) and protein group (white, n = 43).

Effect of dietary protein supplementation on blood pressure: a randomized, controlled trial.

Circulation. 2011 Aug 2;124(5):589-95
Flow diagram of participants in the Protein and Blood Pressure (ProBP) study.

1,626 Participants assessed for eligibility

1,235 Excluded
931 Failed to meet criteria
304 Declined to participate

391 Underwent run-in

39 Excluded due to non-compliance

352 Randomized

Group A
117 Received soy protein
101 Received milk protein
93 Received carbohydrate

Group B
117 Received milk protein
104 Received carbohydrate
92 Received soy protein

Group C
118 Received carbohydrate
101 Received soy protein
88 Received milk protein

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Randomization Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
</tr>
<tr>
<td>Age, y</td>
<td>(11.5) 48.4</td>
</tr>
<tr>
<td>Male, %</td>
<td>59.0</td>
</tr>
<tr>
<td>Black, %</td>
<td>33.3</td>
</tr>
<tr>
<td>Some college education, %</td>
<td>92.3</td>
</tr>
<tr>
<td>Current smoking, %</td>
<td>5.1</td>
</tr>
<tr>
<td>Alcohol drinking, %</td>
<td>39.3</td>
</tr>
<tr>
<td>Physical activity [μτεθυ] 3 times/wk, %</td>
<td>56.9</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>(4.5) 29.0</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>(9.3) 127.2</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>(5.9) 81.6</td>
</tr>
</tbody>
</table>
Net changes (95% confidence interval) in systolic and diastolic blood pressure (BP) associated with dietary protein supplementations.

Determinants of Blood Pressure Response to Low Salt Intake in a Healthy Adult Population

*J Clin Hypertens (Greenwich)*. 2011 Nov;13(11):795-800
Salt intake recommendation

• The current level of sodium intake among Americans is much higher than the recommended level of 2300 mg/day.

• Although much evidence supports the beneficial effect of lowering sodium intake down to 1500 mg/day according to the 2010 guideline

US department of Health and Human Services. Dietary guideline for Americans
Old Order Amish community of Lancaster County, PA
Patients & Methods

- Study subjects consumed a standardized high sodium (Na) diet (280 meq/day = 6440 mg/day) for 6 days
- 6–14 day washout period
- A standardized low Na diet - 40 meq/day = 920 mg/day for 6 days.
- **Measurement of 24-hour ambulatory blood pressure**
Specially outfitted kitchen by an Amish cook
## Basic characteristics for the HAPI population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n = 245)</th>
<th>Women (n = 220)</th>
<th>All (n = 465)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.2 ±12.9</td>
<td>45.5 ±13.7</td>
<td>43.8 ±13.4</td>
<td>0.006</td>
</tr>
<tr>
<td>PISBP (mmHg)</td>
<td>120.9 ±13.5</td>
<td>120.9 ±16.7</td>
<td>120.9 ±15.1</td>
<td>0.27</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.4</td>
<td>27.4</td>
<td>26.4</td>
<td>0.0001 &gt;</td>
</tr>
<tr>
<td>Activity (counts) (× 1000)</td>
<td>511.9 ±235.3</td>
<td>357.3 ±185.4</td>
<td>436.7 ±225.9</td>
<td>0.0001 &gt;</td>
</tr>
</tbody>
</table>
Mean (± SD) urinary sodium/creatinine and potassium/creatinine excretion before and during dietary intervention

<table>
<thead>
<tr>
<th></th>
<th>Pre Intervention</th>
<th>High Salt</th>
<th>Low Salt</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na/Cr</td>
<td>(5.5) 12.8</td>
<td>(5.4) 11.9</td>
<td>(1.2) 2.1</td>
</tr>
<tr>
<td>K/Cr</td>
<td>(2.4) 3.3</td>
<td>(1.5) 3.4</td>
<td>(1.4) 4.3</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na/Cr</td>
<td>(12.8) 17.1</td>
<td>(8.1) 17.4</td>
<td>(2.4) 3.2</td>
</tr>
<tr>
<td>K/Cr</td>
<td>(3.2) 4.2</td>
<td>(2.5) 4.5</td>
<td>2.1) 5.2</td>
</tr>
</tbody>
</table>
### SBP response to low salt diet

<table>
<thead>
<tr>
<th></th>
<th>daytime</th>
<th>nighttime</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35&gt;</td>
<td>0.01±4.60</td>
<td>0.03±5.29−</td>
</tr>
<tr>
<td>50–35</td>
<td>0.85±5.30−</td>
<td>0.93±5.63−</td>
</tr>
<tr>
<td><strong>50&lt;</strong></td>
<td><strong>1.05±6.60−</strong></td>
<td><strong>2.86±5.94−</strong></td>
</tr>
<tr>
<td>p for difference by age</td>
<td>0.001</td>
<td>5.10E-06</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>men</td>
<td>0.33±5.72−</td>
<td>0.85±5.49−</td>
</tr>
<tr>
<td><strong>women</strong></td>
<td><strong>1.10±5.31−</strong></td>
<td><strong>1.97±5.78−</strong></td>
</tr>
<tr>
<td>p for difference by sex</td>
<td>0.12</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>pre-intervention SBP</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>120&gt;</td>
<td>0.21±4.74−</td>
<td>0.97±5.34−</td>
</tr>
<tr>
<td><strong>140&gt;−120=&lt;=</strong></td>
<td><strong>0.30±5.79−</strong></td>
<td><strong>1.18±5.85−</strong></td>
</tr>
<tr>
<td>140=&lt;=</td>
<td>4.48±7.96−</td>
<td>4.33±6.66−</td>
</tr>
<tr>
<td>p for difference by pre-intervention SBP</td>
<td>2.70E-06</td>
<td>8.80E-06</td>
</tr>
</tbody>
</table>

TW SUMC
Lifestyle interventions reduce coronary heart disease risk: results from the PREMIER Trial

Circulation. 2009 Apr 21;119(15):2026-31
Patients & Primary outcome

- Participants were 810 adults with prehypertension or stage 1 hypertension who met JNC-7 criteria for a 6-month trial of nonpharmacological BP.
- The change in estimated 10-year CHD risk at 6 months compared with baseline using the sex-specific Framingham risk equations.
Figure 1. Flow of participants in the PREMIER trial. *Number of participants with complete covariates for Framingham risk equations.

Maruthur N M et al. Circulation 2009;119:2026-2031
Figure 2. Median 10-year CHD risk in the PREMIER trial by randomized group at baseline and 6 months.

RRR = 0.88, P < 0.001

RRR = 0.86, P < 0.001

Median 10-Year CHD Risk (%)

Advice Only  EST  EST+DASH

Baseline  6 Months

Maruthur N M et al. Circulation 2009;119:2026-2031
Exercise
Effects of Swimming Training on Blood Pressure and Vascular Function in Adults >50 Years of Age

Am J Cardiol. 2012 Apr 1;109(7):1005-10
Methods

• They were assigned at random to one of two groups.
• The first group received 12 weeks of swimming instruction and swam 15 to 45 minutes a day, three to four days a week.
• The second, or control, group spent that time stretching and learning relaxation exercises.
Results

• Casual systolic BP decreased significantly from 131 ± 3 to 122 ± 4 mm Hg in the swimming training group. Significant decreases in systolic BP were also observed in ambulatory (daytime) and central (carotid) BP measurements.
<table>
<thead>
<tr>
<th></th>
<th>IY</th>
<th>EUC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 6</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>(3) 132</td>
<td>(2) 133</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>(2) 83</td>
<td>(1) 83</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>(2) 99</td>
<td>(1) 99</td>
</tr>
<tr>
<td>Heart rate (mmHg)</td>
<td>(2) 70</td>
<td>(1) 70</td>
</tr>
</tbody>
</table>
IY- Iyengar yoga
IY- Iyengar yoga
Iyengar Yoga versus Enhanced Usual Care on Blood Pressure in Patients with Prehypertension to Stage I Hypertension: a Randomized Controlled Trial.

Evid Based Complement Alternat Med. 2011;2011:546428
Summary

• High risk patients
• The benefit from medical treatment- not proven
• Probably non pharmacological treatment has beneficial effect
• Probably ABPM is needed to make an accurate diagnosis of pre hypertension
Pre Hypertension

Is it Time to Change the Definitions of Hypertension and to Change the Risk Tables?
Thank You