Pre-Hypertension: Clinical Profile

- Autonomic nervous system alterations
- Early cardiovascular structural alterations
- Increased association with metabolic abnormalities
- Increased CV risk
Sympathetic Nerve Traffic
in Optimal (n = 24), Normal (n = 27) and High-Normal (n = 38) BP Subjects

Seravalle, Lonati, Buzzi, Cairo, Quartì Trevano, Dell’Oro, Facchetti, Mancia, Grassi, J Hypertens 2015; 33: 1411-1417
Suggested pathway from normotension to hypertension and target organ damage

From Davis et al., J Am Coll Cardiol 2012; 59: 2206

Prehypertension and the risk of stroke: a meta-analysis
Neurology 2014,82:1153-1161

Prehypertension and the risk of coronary heart disease in Asian and Western populations: a meta-analysis.
J Am Heart Ass 2015,19:e001519

PAMELA

Pressioni Arteriose Monitorate E Loro Associazioni

Monitored Blood Pressures and Their Associations
PAMELA Study

- 3600 subjects representative of Monza population for age/gender and other characteristics (MONICA criteria)
- Age: 25 to 74 years
- Office BP → 2 visits (3 measurements per visit)
- Home BP → morning / evening measurements (semiautomatic device)
- 24h ambulatory BP monitoring (Spacelabs device / readings at 20 min intervals)
- CVD history / CV risk assessment
- Smoking
- Blood glucose / lipid profile
- Echocardiogram / ECG
PAMELA STUDY

1st PAMELA Project
(years 1992-1998)

Study performed in more than 3200 subjects representative of the general population living in Monza and Brianza Area.
Main goals: To define

A. to define normality BP values for ABPM and home according to age ranges
B. Relationships between ABPM and TOD (cross-sectional)
C. BP control in the population
D. Home BP, Clinic BP and target organ damage
Relationship of Clinic BP to Home BP, 24 h Average BP and Daytime Average BP in the Subjects of the PAMELA Study

Mancia G et al., J Hypertens 1995; 13: 1377-1390
### SBP / DBP Normality Values (mmHg)

<table>
<thead>
<tr>
<th></th>
<th>PAMELA</th>
<th>ESH/ESC Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinic</td>
<td>140/90</td>
<td>140/90</td>
</tr>
<tr>
<td>Home</td>
<td>132/83</td>
<td>135/85</td>
</tr>
<tr>
<td>24h</td>
<td>125/79</td>
<td>125-130/80</td>
</tr>
</tbody>
</table>
PAMELA Study: SBP Values and LVH Prevalence

Sega et al., Circulation 2001
PAMELA Population

n \(\rightarrow\) 2051 (64% of original sample, representative of Monza population)

Office / Home / 24h BP
Lipid Profile
Blood Glucose
Body Mass Index
Abdominal circumference
Smoking
Family / Personal History
LVMI (Echo)

Mean FU 148 months (up to 1/10/2004)
CV deaths* or (%)
CV events (if hospitalized)
All cause deaths* or (%)

Surviving subjects restudied
10 years after initial examination

* death certificate
2nd PAMELA Project
(years 2000-2003)

Prospective follow-up study, with a temporal window > 10 years aimed at investigating the impact of different clinic, ambulatory ad home BPs and variabilities on:

A. CV morbidity
B. CV mortality
C. TOD
D. Metabolic alterations

Cross sectional assessment of cognitive function and relationships with various BPs and variabilities.
Survival Free of CV Morbid / Fatal Events in Subjects with Combined or Selective Elevation in Office / Home / Ambulatory BP (PAMELA Population)

Office vs 24h BP

Office vs Home BP
Incidence and 10-year Age- and Gender-adjusted Risk of NOD or IFG Development according to Baseline BP Classification from Clinic and ABP

NOD

<table>
<thead>
<tr>
<th>Baseline BP Classification</th>
<th>NOD</th>
<th>NOD + IFG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WCH</td>
<td>6.5</td>
<td>13.8</td>
</tr>
<tr>
<td>Masked H</td>
<td>6.6</td>
<td>11.1</td>
</tr>
<tr>
<td>Sustained H</td>
<td>6.1</td>
<td>13.0</td>
</tr>
</tbody>
</table>

NOD + IFG

<table>
<thead>
<tr>
<th>Baseline BP Classification</th>
<th>NOD + IFG</th>
<th>NOD + IFG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension</td>
<td>2.89</td>
<td>P = 0.007</td>
</tr>
<tr>
<td>WCH</td>
<td>2.70</td>
<td>P = 0.03</td>
</tr>
<tr>
<td>Masked H</td>
<td>2.23</td>
<td>P = 0.04</td>
</tr>
<tr>
<td>Sustained H</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* P < 0.01 vs. N

Mancia et al., J Hypertens 2009; 27: 1672-1678
Other Descriptive Data from PAMELA

- Characteristics of dipping phenomenon
- $\Delta$ home/24h BP with age (vs $\Delta$ clinic BP)
- Ambulatory / home BP control by treatment in HT population
- LVH in untreated / treated / controlled HTs
- LVH in WCH / masked HT
- Use of PAMELA data as control group for variety of comparisons
- BP values and job characteristics
- Weekly / Seasonal BP variations
Masked hypertension

BP variability and CV risk

Prognostic importance of LVH

Relationship of BP to metabolic risk factors / Prognostic relevance of MS

Body mass index / WC and CV events

Contribution to genetic studies
Incidence and 10-year Age/gender-adjusted Risk of Developing Sustained (True) Hypertension in True N, WCH and Masked H

**Incidence**

<table>
<thead>
<tr>
<th>Classification</th>
<th>N</th>
<th>WCH</th>
<th>Masked H</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline clinic BP</td>
<td>18.2</td>
<td>42.6</td>
<td>47.1</td>
</tr>
<tr>
<td>Baseline 24h BP</td>
<td>13.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Odds Ratio**

- N: 2.51, P<0.0001
- WCH: 1.78, P<0.0001

*Mancia et al., Hypertension 2009*
Distribution of the PAMELA population according to BP status

- Optimal: 26.72% (N = 440, Age: 48.2 ± 13.1)
- Prehypertension: 40.07% (N = 660, Age: 47.2 ± 12.6)
- Hypertension: 33.21% (N = 547, Age: 55.6 ± 11.5)
BP and HR values in optimal, prehypertensive and hypertensive patients

**Office**

**Home**

**24-h ABPM**

<table>
<thead>
<tr>
<th></th>
<th>Optimal</th>
<th>PreHT</th>
<th>HT</th>
<th></th>
<th>Optimal</th>
<th>PreHT</th>
<th>HT</th>
<th></th>
<th>Optimal</th>
<th>PreHT</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mmHg</strong></td>
<td><strong>90</strong></td>
<td><strong>80</strong></td>
<td><strong>70</strong></td>
<td><strong>40</strong></td>
<td><strong>100</strong></td>
<td><strong>80</strong></td>
<td><strong>70</strong></td>
<td><strong>40</strong></td>
<td><strong>160</strong></td>
<td><strong>140</strong></td>
<td><strong>120</strong></td>
</tr>
<tr>
<td><strong>b/min</strong></td>
<td><strong>70</strong></td>
<td><strong>60</strong></td>
<td><strong>50</strong></td>
<td><strong>30</strong></td>
<td><strong>80</strong></td>
<td><strong>60</strong></td>
<td><strong>50</strong></td>
<td><strong>30</strong></td>
<td><strong>120</strong></td>
<td><strong>100</strong></td>
<td><strong>80</strong></td>
</tr>
</tbody>
</table>

* indicates significant difference.
Anthropometric and metabolic profile in optimal, prehypertensive and hypertensive patients

- **BMI**
- **Cholesterol**
- **HDL-chol**
- **Triglycerides**
- **Glucose**
- **Uric acid**

<table>
<thead>
<tr>
<th></th>
<th>Optimal</th>
<th>PreHT</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* denotes significant difference.
LVMI and LVH in optimal, prehypertensive and hypertensive patients

LVMI and LVH levels in different blood pressure categories.

- LVMI: Lower values in optimal, intermediate in prehypertension, and higher in hypertension.
- LVH: Rising trend from optimal to prehypertension, with a significant increase in hypertension.
Fatal and non-fatal CV events at follow-up

Optimal
Not adjusted
Prehypertension
Hypertension

CV events 2004

Optimal
Prehypertension
Hypertension

Not adjusted
Adjusted for age and gender

CV mortality 2004

Optimal
Prehypertension
Hypertension

p = 0.0324
p < 0.0001
p = 0.0023
p = 0.3643
p = 0.7081
p = 0.0289
p = 0.6839
p = 0.5538
Prevalence of different BP groups
PAMELA 1 vs PAMELA 2

<table>
<thead>
<tr>
<th>BP Group</th>
<th>PAMELA 1</th>
<th>PAMELA 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>347</td>
<td>154</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>492</td>
<td>47</td>
</tr>
<tr>
<td>Hypertension</td>
<td>86</td>
<td>178</td>
</tr>
</tbody>
</table>

PAMELA 2:
- Blue: Optimal
- Yellow: Prehypertension
- Red: Hypertension
- Pink: On treatment
New cases of left ventricular hypertrophy
PAMELA 1 vs PAMELA 2

Not adjusted

Adjusted for age and gender

Optimal

Prehypertension

Hypertension

p < 0.0001

p = 0.0014

p < 0.0001

p < 0.0001
New cases of metabolic syndrome
PAMELA 1 vs PAMELA 2

Not adjusted

Adjusted for age and gender

Optimal

Prehypertension

Hypertension

HR

HR

p=0.0071

p=0.0024

p=0.0114

p=0.0134
New cases of diabetes
PAMELA 1 vs PAMELA 2

Optimal

Prehypertension

Hypertension

Not adjusted

Adjusted for age and gender

HR

0.5 1 5 10 50

p = 0.0144

p = 0.0060

p = 0.0486

p = 0.0386
PAMELA Project: Past, Present and Future


Cross sectional → Longitudinal → Longitudinal
Distribution of the PAMELA population according to BP status

- **Optimal**: 26.72%, 440 individuals, age 48.2 ± 13.1
- **Normal**: 22.83%, 376 individuals, age 47.2 ± 12.6
- **Prehypertension**: 17.24%, 284 individuals
- **Hypertension**: 33.21%, 547 individuals, age 55.6 ± 11.5
### Prevalence of different BP groups

#### PAMELA 1 vs PAMELA 2

<table>
<thead>
<tr>
<th>BP Category</th>
<th>PAMELA 1</th>
<th>PAMELA 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>74.04</td>
<td>37.35</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>37.35</td>
<td>13.42</td>
</tr>
<tr>
<td>Hypertension</td>
<td>154</td>
<td>47</td>
</tr>
</tbody>
</table>

- PAMELA 1: Optimal 47%, Prehypertension 170%, Hypertension 189%
- PAMELA 2: Optimal 34.79%, Prehypertension 12.65%, Hypertension 34.79%

[Bar chart showing the prevalence of different BP groups for PAMELA 1 and PAMELA 2]