Strategies for Cardiovascular Risk Assessment in hypertensive patients in low-resources settings.

Focus on sub-Saharan African Low-and Middle Income Countries

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a.i. Steering Committee
Executive General Secretary

CVR: what is known?

- Why from a certain level of arterial blood pressure is considered as dangerous?
  - The relationship between blood pressure and adverse health effects displays a non-linear but continuous relationship
    John KJ Li 2000.

- The classifying people into ‘hypertensive’ and ‘normotensive’ groups is encouraged by a consideration of ‘excess risk’ or by ‘proven treatment benefit’ in clinical trials for a certain level of blood pressure.
  - Birkett 1997

- BUT: The evaluation of this ‘excess risk’ must include blood pressure related risk factors => Total Cardiovascular Risk
**CVR: what is debated?**

- **Factors to be included:** Although we have a common understanding about the physiopathology of most of the factors, and the role they play in increasing the risk for / from blood pressure, we know also they have different burden in different populations.
  
  Twagirumukiza M et al, J.Human Hypert, 2010  
  Modesti Prati et al, Journal of Hypertension, 2014

- **Assessment of identified risk factors:** What to do when some laboratory equipment are not optimal, doesn’t exist or are not accessible to everybody?
  
  Modesti Prati et al, Journal of Hypertension, 2014  

- **Predictive equations/algorithm/score:** Can the Framingham, Eu SCORE, WHO|ISH, etc be applied in African settings?
  
  Twagirumukiza M et al, J.Human Hypert, 2010

- **Using it CVR to tailor treatment to individuals:** Threshold, staging, treatment accessibility but also drug of choice.

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**Population distribution of cardiovascular risk (factors)**
CVR: Different population, different burden

- The Framingham and other similar studies provide the basis for the equations upon which many of the existing cardiovascular risk-profiling packages have been developed.

- However, such risk profiling protocols lack universal applicability
  Brindle PM, et al. Heart 2006
CVR: Different population, different burden

The WHO/ISH risk prediction charts

- Risk factors:
  1. Age (40 years +): lower for sub-Saharan Africa?
  2. Sex
  3. Smoking
  4. SBP (140 mm Hg +),
  5. Blood cholesterol (TC), and
  6. Presence or absence of diabetes

- where blood cholesterol can be measured.
- cross-sectional population samples from: Nigeria, Iran, China, Pakistan, Georgia, Nepal, Cuba, and Sri Lanka

This is just a predicted CVR not validated with real data

Prevalence of Hypertension in SSA (11 countries)
Analysis of the problem of HT in SSA
Prevalence and burden

A literature search: population studies, 1998-2008

2008 in SSA: **75 million** people with hypertension and a prevalence of **16.2%**

2025 in SSA: **125 million** people with hypertension and a prevalence of **17.4%**

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**CVR: Different population, different burden - HT**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>SSA (1)</th>
<th>England (2)</th>
<th>USA (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–24</td>
<td>5 897</td>
<td>5.2</td>
<td>NA</td>
</tr>
<tr>
<td>25–34</td>
<td>18 431</td>
<td>9.8</td>
<td>442 215</td>
</tr>
<tr>
<td>35–44</td>
<td>9 822</td>
<td>17.9</td>
<td>487 692</td>
</tr>
<tr>
<td>45–54</td>
<td>6 081</td>
<td>30.3</td>
<td>389 053</td>
</tr>
<tr>
<td>55–64</td>
<td>5 086</td>
<td>46.0</td>
<td>355 094</td>
</tr>
<tr>
<td>65–74</td>
<td>1 544</td>
<td>62.4</td>
<td>256 966</td>
</tr>
<tr>
<td>75+</td>
<td>NA</td>
<td>NA</td>
<td>288 820</td>
</tr>
</tbody>
</table>

| All ages, standardized (4) | 23.3 | 20.0 | 22.2 |

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(1) Pooled Hypertension Prevalence, from 15 studies pertaining to 11 countries.
(3) Fields LE, Hypertension, 2004

(4) standardized to every country population.
(5) adjusted prevalence to World Health Organization (WHO) standard population [Ahmad O et al. WHO, 2001]
Urban vs Rural and Gender hypertension prevalence by age

<table>
<thead>
<tr>
<th>Gender</th>
<th>Urban vs. Rural OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age ≥ 15 years</td>
</tr>
<tr>
<td></td>
<td>Age 25-64 years</td>
</tr>
<tr>
<td>Men</td>
<td>2.09 (1.73 to 2.52)</td>
</tr>
<tr>
<td>Women</td>
<td>1.75 (1.47 to 2.08)</td>
</tr>
<tr>
<td>Both sexes</td>
<td>1.93 (1.70 to 2.19)</td>
</tr>
</tbody>
</table>

(a) Based on studies reporting gender data, the risk of becoming hypertensive in adult (≥15 years+) was in urban areas 2 times higher than in rural areas in men and 1.75 times higher in women, but the difference between two sexes was not statistically significant.

(a) The differences in prevalence of hypertension between urban and rural populations are of comparable magnitude for men and women.
CVR: Extended cardiovascular risk factors

**ESH and ESC Guidelines**

2013 ESH/ESC Guidelines for the management of arterial hypertension

*The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)*

Source: "2013 ESC/ESH Recommendations" (Mancia and others 2013)

CVR: New stratification in LMIC from Bukavu Observ Study

β coefficient in linear regression of systolic blood pressure and diastolic blood pressure by physical activity and fruits/vegetables consumption after adjusted for age, waist circumference and body mass index

Source: “Bukavu Observ Study” DRC, AISoH investigators, Circulation 2014, In press
Bukavu CVR Cohort study- ObServ Project
General Methodology Framework

Assessment of identified risk factors for CVR
CVR: Limitations in assessment of identified risk factors

- In low-income countries, with limited testing facilities, laboratory analysis (Lipid profiles, diabetes screening) can be too expensive or not available.

- Few studies compared CVR prediction charts with and without the need for cholesterol testing with any of the standard prediction rules or validated in any cohort.

- Can a prediction rule that does not need laboratory testing predict cardiovascular disease events as effectively as one that uses laboratory-based values?
  - Yes (So far)
  - But in this study they introduced the Body-Mass-Index!

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**Laboratory-based versus non-laboratory-based method for assessment of cardiovascular disease risk: the NHANES I Follow-up Study cohort**

CVR Stratification: Challenges

- A consensus is needed:
  Modesti Prati et al, Journal of Hypertension, 2014

CVR Stratification: Challenges

- Easy obesity measurements (BMI or waist circumferences) are not included in the WHO/ISH charts, although there is strong evidence of the importance of obesity to guide intervention strategies aimed at reducing the incidence of type 2 diabetes.
  Modesti Prati et al, Journal of Hypertension, 2014

- Therefore to include waist circumferences in the risk assessment could enhance awareness.
CVR Stratification: Challenges

- Assessment of proteinuria is also not included in WHO charts, although recognizing that CVD risk may be higher than indicated in the chart in people with proteinuria.

- A guideline is needed but this task should come from a specific LMIC composed professionals/academics.

  Modesti Prati et al, Journal of Hypertension, 2014

- In extreme case when the resources are really limited, it is a preferred strategy to work only on hypertension and smoking and not on lipid and diabetes because a lower risk is attributed to them.

Using it CVR to tailor treatment to individuals

...not forget affordability!
**Stratification of Cardiovascular Risk**

<table>
<thead>
<tr>
<th>Other risk factors, asymptomatic organ damage or disease</th>
<th>Blood pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High normal SBP 130–139 or DBP 85–89</td>
</tr>
<tr>
<td>No other RF</td>
<td>Low risk</td>
</tr>
<tr>
<td>1–2 RF</td>
<td>Low risk</td>
</tr>
<tr>
<td>≥3 RF</td>
<td>Low to moderate risk</td>
</tr>
<tr>
<td>OD, CKD stage 3 or diabetes</td>
<td>Moderate to high risk</td>
</tr>
<tr>
<td>Symptomatic CVD, CKD stage ≥ 4 or diabetes with OO/RF's</td>
<td>Very high risk</td>
</tr>
</tbody>
</table>

Source: "2013 ESC/ESH Recommendations" (Mancia and others 2013)

**Initiation of lifestyle changes treatment.**

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<tbody>
<tr>
<td></td>
<td>High normal SBP 130–139 or DBP 85–89</td>
</tr>
<tr>
<td>No other RF</td>
<td>• No BP intervention</td>
</tr>
<tr>
<td>1–2 RF</td>
<td>• Lifestyle changes</td>
</tr>
<tr>
<td>≥3 RF</td>
<td>• Lifestyle changes</td>
</tr>
<tr>
<td>OD, CKD stage 3 or diabetes</td>
<td>• Lifestyle changes</td>
</tr>
<tr>
<td>Symptomatic CVD, CKD stage ≥ 4 or diabetes with OO/RF's</td>
<td>• Lifestyle changes</td>
</tr>
</tbody>
</table>

Source: "2013 ESC/ESH Recommendations" (Mancia and others 2013)
Decrease in BP with antihypertensive drug treatments and ethnicity

*Source:* Adapted from Brewster et al (Mensah GA. 2003)

DDD prices adjusted to PPP per capita

DDD prices adjusted to PPP per capita

![Graph showing adjusted prices for different countries, with high prices for Amlodipine in Burundi & DRC.]

**Tropical Medicine and International Health, 2010; 15:350-361.**

Pharmacoeconomic model 1: cost of antihypertensive drugs (estimates for SSA needs)

![Graph showing cost per year for SSA in various countries, with highlighted costs for specific drugs.]
### Pharmacoeconomic model 1: cost of antihypertensive drugs (estimates for SSA needs)

<table>
<thead>
<tr>
<th>Form and dosage</th>
<th>DDD</th>
<th>DDD Price ($ US cents)</th>
<th>Cost per year per capita ($ US)</th>
<th>Estimates for the cost per year for SSA (bn $ US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amlodipine 5mg</td>
<td>5mg</td>
<td>20.00</td>
<td>73.00</td>
<td>5.45</td>
</tr>
<tr>
<td>Atenolol 100mg</td>
<td>75mg</td>
<td>3.00</td>
<td>10.95</td>
<td>0.82</td>
</tr>
<tr>
<td>Atenolol 50mg</td>
<td>75mg</td>
<td>4.05</td>
<td>14.78</td>
<td>1.10</td>
</tr>
<tr>
<td>Captopril 25mg</td>
<td>50mg</td>
<td>4.20</td>
<td>15.33</td>
<td>1.15</td>
</tr>
<tr>
<td>Enalapril 5mg</td>
<td>10mg</td>
<td>16.00</td>
<td>58.40</td>
<td>4.36</td>
</tr>
<tr>
<td>HCTZ 25mg</td>
<td>25mg</td>
<td>0.50</td>
<td>1.83</td>
<td>0.14</td>
</tr>
<tr>
<td>Nifedipine LP 20mg</td>
<td>30mg</td>
<td>10.58</td>
<td>38.60</td>
<td>2.88</td>
</tr>
<tr>
<td>AAS Junior</td>
<td>100mg</td>
<td>0.01</td>
<td>0.04</td>
<td>0.02</td>
</tr>
<tr>
<td>Reserpine</td>
<td>0.1mg</td>
<td>0.35</td>
<td>1.28</td>
<td>0.10</td>
</tr>
<tr>
<td>Prazosin</td>
<td>1mg</td>
<td>2.08</td>
<td>7.59</td>
<td>0.57</td>
</tr>
</tbody>
</table>

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**Concrete guidelines for daily clinical practice**
Management strategies

**Research question**

- What could be the management strategy for hypertension in SSA with context of limited resources to reduce the number of cases reaching hospitals with last stage of complications?

**Answer:**

- ENCREASE AWARENESS
- early detection,
- early treatment and efficient control in SSA.

**Detection at Community level!**

Non-physician health-care workers (NPHWs) can be retrained to reliably and effectively assess and manage cardiovascular risks in primary health-care settings where there are no attending physicians.
Detection at Community level!

**Use of algorithms**
- Community level:
  - Community health worker
  - Only detection and control

- Health center level:
  - Nurse
  - Prescription of limited number of drugs → Algorithms

Management strategies

**Prerequisites**

- Community health worker:
  - BP devices + training
- Health center:
  - ECG, BP devices + training
  - Core drugs based on what is on NEMLS (hydrochlorothiazide) + reserpine? and prazosin?.
  - Good storage of medicines
  - Training
- Population sensitization programs
HTN Management strategies

Example of algorithm

Algorithms can be adapted to the local situation

Monotherapy vs. drug combination strategies to achieve target BP

*Mild BP elevation Low/moderate CV risk* Choose between *Marked BP elevation High/very high CV risk*

- Single agent
- Two-drug combination

Switch to different agent
Previous agent at full dose
Previous combination at full dose
Add a third drug

- Full dose monotherapy
- Two drug combination at full doses
- Switch to different two-drug combination
- Three drug combination at full doses

BP = blood pressure; CV = cardiovascular.

*Source: “2013 ESC/ESH Recommendations” (Mancia and others 2013)*
Conclusions

1. We should use adopt after adapting them by adding obesity measurement surrogates (BMI or waist circumferences) and proteinuria

2. Validation studies are needed before advocating them,

3. CVR assessment in LMIC can reduce unnecessary drug treatment to low-risk patients.

4. Threshold of cardiovascular risk for deciding the start of drug treatment can be adjusted to suit the country context.

5. WHO proposed different 10-year total CVD risk thresholds for intensive intervention based on countries resource level (20% for high-resource setting; 30% for medium-resource setting; 40% for low-resource setting).
Conclusions

6. Very high-risk individuals (have already CHD, etc) do not require risk scoring: the risk score will be an underestimate in these settings.

7. Individuals who do not fall into the very high-risk category:
   Risk scoring using well-documented key risk factors is appropriate to estimate the total cardiovascular risk in asymptomatic adults.

8. Furthermore, risk scoring is especially important in individuals with the CVR factors help to install preventive/treatment measures.

MANAGEMENT OF ARTERIAL HYPERTENSION AND STROKE IN SSA

“Although the nature tries classifying people into richest and poorest, it is an ethical obligation for scholars and scientists to find how health care can reach everyone!”

Marc Twagirumukiza

Thanks for your attention
Strategies for Cardiovascular Risk Assessment in hypertensive patients in low-resources settings.

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