Identifying biomarkers of household air pollution exposure and cardiovascular risk for intervention evaluation in China

Global Alliance for Clean Cookstoves
December 16, 2014

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McGill University
China’s health transition: leading causes of death

<table>
<thead>
<tr>
<th>Disorder</th>
<th>1990 Rank (95% UI)</th>
<th>2010 Rank (95% UI)</th>
<th>% Change (95% UI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower respiratory infections</td>
<td>1 (1 to 3)</td>
<td>1 (1 to 1)</td>
<td>21 (-13 to 37)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2 (1 to 3)</td>
<td>2 (1 to 1)</td>
<td>21 (-13 to 37)</td>
</tr>
<tr>
<td>COPD</td>
<td>3 (2 to 10)</td>
<td>3 (2 to 1)</td>
<td>81 (25 to 103)</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>4 (4 to 8)</td>
<td>4 (4 to 5)</td>
<td>-45 (-51 to -39)</td>
</tr>
<tr>
<td>Drowning</td>
<td>5</td>
<td>5</td>
<td>64 (-9 to 188)</td>
</tr>
<tr>
<td>Neonatal encephalopathy</td>
<td>6 (4 to 12)</td>
<td>6 (3 to 6)</td>
<td>37 (17 to 75)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>7 (6 to 10)</td>
<td>7 (7 to 9)</td>
<td>-11 (-24 to 5)</td>
</tr>
</tbody>
</table>

- Dietary risks
- High blood pressure
- Tobacco smoking
- Ambient particulate matter pollution
- Household air pollution from solid fuels
Household air pollution & blood pressure in China

Baumgartner et al. Environ Health Perspect 2011; PNAS, 2014
The potential cardiovascular benefits of population-based energy interventions

Association of usual SBP with risk of stroke in Asian cohorts

Age at risk

≥ 70 years

60-69 years

< 60 years

Usual systolic blood pressure (mm Hg)

<table>
<thead>
<tr>
<th>Hazard ratio and 95% CI</th>
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<tbody>
<tr>
<td>0.25</td>
</tr>
<tr>
<td>0.5</td>
</tr>
<tr>
<td>1.0</td>
</tr>
<tr>
<td>2.0</td>
</tr>
<tr>
<td>4.0</td>
</tr>
<tr>
<td>8.0</td>
</tr>
<tr>
<td>16.0</td>
</tr>
<tr>
<td>32.0</td>
</tr>
<tr>
<td>64.0</td>
</tr>
</tbody>
</table>

< 8 mmHg decrease

> 30% reduction in stroke

> 25% reduction in CHD

Asia-Pacific Cohort Studies Collaboration Journal of Hypertension 2003
Evaluation of improved energy interventions

- Thermal insulation
- Efficient windows and doors

Insulation in rural houses

- Water heaters and lighting
- Radiant floor heating

Use of passive solar energy

- Gasifiers and new generation stoves
- Coupled heating-cooking systems

Raise the efficiency of energy technologies

- Processed biomass fuels
- Gaseous fuels

Alternative domestic fuels

- Use of more-efficient fuels

Active energy-saving methods

Passive energy-saving methods
The IGNITE Study: Improving air quality, health and environment through energy interventions in the Tibetan Plateau
Women’s average 48-hr PM$_{2.5}$ exposure in summer:

- **Mean:** 137 µg/m$^3$
- **Range:** 29-1129 µg/m$^3$

• Typical kitchen and traditional wood-burning cookstoves
IGNITE study design

- 5-year intervention evaluation study; ~200 women in 8 villages
- 200 homes (~120 intervention / 80 controls); not randomized
- Measurements of air pollution exposure and CV biomarkers on 2-6 days every 6 months for 3-years

2012: Pilot study; Pellet factory built

Summer 2014: Baseline environmental / health measurements begin

Spring 2015: ~120 homes receive stoves; measurements continue

2016: Evaluate stove success; environ/health measurements continue

2017: Control homes receive energy package (...)

2013: Begin field testing new stove designs
High efficiency, low emission heating and cooking stove interventions

Traditional stoves

Biomass pellets + semi-gasifier stove for cooking & heating
Measurement of air pollution exposure

- Integrated PM$_{2.5}$ and black carbon exposure for 48-144 hours every 6 months in adult women and some men
- Measurement in winter and summer
Health and other covariate measurements

- Central and brachial blood pressure
- Arterial stiffness
- Collection of spot urine, dried blood spots, buccal cells
- Cardiopulmonary function
- Anthropometrics
- Physical activity
- Salt intake
- Co-morbidities & previous cardiovascular events
- Socioeconomic status
- Nutrition & alcohol
- Secondhand smoking
- Medication use
Effects of higher personal PM$_{2.5}$ exposure (>58 $\mu$g/m$^3$; median) on vascular function and cellular aging in Sichuan women (n=25)

Univariate (I) and age/BMI-adjusted (II) linear models

<table>
<thead>
<tr>
<th></th>
<th>(I) Difference (95% CI) (univariate)</th>
<th>(II) Difference (95% CI) (multivariate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial SBP (mm Hg)</td>
<td>5.2 (-7.4, 17.7)</td>
<td>4.6 (-7.8, 16.9)</td>
</tr>
<tr>
<td>Central SBP (mm Hg)</td>
<td>3.6 (-8.0, 15.2)</td>
<td>3.1 (-8.4, 14.5)</td>
</tr>
<tr>
<td>Central pulse pressure (mm Hg)</td>
<td>5.0 (-3.7, 13.7)</td>
<td>4.1 (-4.2, 12.4)</td>
</tr>
<tr>
<td>Augmentation index (Alx, %)</td>
<td>2.7 (-1.5, 7.0)</td>
<td>2.8 (-1.6, 7.2)</td>
</tr>
<tr>
<td>Pulse wave velocity (cfPWV; m/s)</td>
<td>0.0 (-1.0, 1.0)</td>
<td>0.0 (-0.1, 0.1)</td>
</tr>
<tr>
<td>Relative telomere length</td>
<td>-33% (-99, 32)</td>
<td>-43% (-113, 28)</td>
</tr>
</tbody>
</table>

Shan et al., *Environ Res* 2014
Biomarker study: The INTERMAP-China site and participants (enrolled in the 1990s)

- 839 men and women, 40-59 years in the 1990s
- Multiple visits and measurements of fuel use, diet, alcohol, weight, height, nutrition, blood pressure, and socio-demographic variables
- Two 24-h urine collections
Study platform

- Intervention
  - Risk factor exposure
  - Biomarkers of exposure
  - Biomarkers of early effect
  - Clinical symptoms
Measuring household air pollution exposures and clinical markers

- Current energy (fuel/stove) use, housing, and changes in energy use
- 48-hr personal PM exposure
- Dietary intake
- Active and second-hand smoking
- Health conditions and diagnoses since enrolment in 1990s
- Socio-demographic variables

- Brachial and central blood pressure, arterial stiffness, and cardiopulmonary function
- 24-hour urine; dried blood spots; and blood samples
Identifying biomarkers of exposure and vascular function

Metabolome-Wide Association Study Identifies Multiple Biomarkers that Discriminate North and South Chinese Populations at Differing Risks of Cardiovascular Disease: INTERMAP Study

Ivan K. S. Yap,†,§ Ian J. Brown,†,§ Queenie Chan,†,§ Anisha Wijeyesekera,†,‡ Isabel Garcia-Perez,†,‡ Magda Bictash,†,‡ Ruey Leng Loo,† Marc Chadeau-Hyam,‡ Timothy Ebbels,† Maria De Iorio,† Elaine Maibaum,† Liancheng Zhao,‖ Hugo Kesteloot,‖ Martha L. Daviglus,§ Jeremiah Stamler,§ Jeremy K. Nicholson,†,§ Paul Elliott,*†,†§ and Elaine Holmes*†,†§

<table>
<thead>
<tr>
<th></th>
<th>N China (N=523)</th>
<th>S China (N=244)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg)</td>
<td>123.8 (18.6)</td>
<td>115.4 (13.0)</td>
</tr>
<tr>
<td>Ur Na (mmol/24h)</td>
<td>271.4 (88.3)</td>
<td>139.2 (55.5)</td>
</tr>
<tr>
<td>Ur (Na/K ratio)</td>
<td>7.8 (2.4)</td>
<td>3.7 (1.5)</td>
</tr>
<tr>
<td>Ca (mg/1000 kcal)</td>
<td>136.5 (48.4)</td>
<td>175.0 (62.5)</td>
</tr>
<tr>
<td>Mg (mg/1000 kcal)</td>
<td>133.2 (38.7)</td>
<td>198.2 (27.2)</td>
</tr>
</tbody>
</table>
Outcomes and impacts of ongoing China studies

- Environmental exposure and health data in four regions and 2-3 time points
- Potential biomarker discovery
- Intervention evaluation

- Impacts on
  - Sustainability agenda in energy and housing
  - NCD prevention and clinical guideline development
  - Provincial and county-level projects
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