NIH Support of International Tobacco Control Research

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Tobacco Control Research Branch
Tobacco Control as a Global Cancer Research Priority

- November 2012 - Research leaders from 15 countries came to NIH to discuss priorities in global cancer research.
- “With respect to modifiable lifestyle risk factors for cancer, there is a consensus that tobacco use remains, by far, the most important at a global level”
- Measures that can already be taken to control tobacco use include removing tobacco products from trade agreements, increasing taxes on tobacco products, controlling tobacco industry marketing, building support among health professionals.

Tobacco Is a Risk Factor for 6 of the World’s 8 Leading Causes of Death

Global Tobacco Burden

• Tuberculosis:
  - Substantially increases risk of infection and death from TB
  - >20% of global TB incidence attributed to tobacco smoking

• Maternal and Child Health
  • Maternal smoking and secondhand smoke cause of poor pregnancy outcome in many countries
  • Women’s tobacco use may be increasing in LMICs

• Tobacco use - $500 billion annual cost to world’s economy.
  • Health care costs and loss of income through illness and premature death
  • Diversion of family resources (up to 10%) from food, shelter, health care, education and other family needs
  • In many countries the poor have higher tobacco use prevalence, and related disease, death, and economic burden
Global Tobacco Mortality is Growing and Shifting to the Developing World

• Tobacco use kills about 6 million people annually worldwide.

• Tobacco-related deaths are expected to rise to 8 million by 2030, and more than 80% of deaths will occur in low and middle-income countries (LMICs).

• Countries increasingly face a “double burden” of disease: diseases of poverty and chronic diseases caused by risk factors such as tobacco use.

• Tobacco use and exposure among women in LMICs is rising threatening to impede or reverse efforts to improve maternal and child health.
International Tobacco and Health Research and Capacity Building Program

Program Review 2002-2012
Features of the TOBAC Program: Scientific Objectives

The Funding Announcement set out Scientific Objectives for both Research Activity and Research Capacity Building

• Long Term Goals for Capacity Building: build “scientific competence and skills” and develop a cadre of tobacco researchers beyond the term of the grant award

• Capacity building also provides opportunity for HIC researchers to gain experience with working in an LMIC.

• Aim to build institutional capacity as well, supporting and linking research institutions in LMICs.

FIC Information: www.fic.nih.gov
Features of the TOBAC Program: Special Requirements

- Collaboration: Requires both PI from US/HIC and PI from LMIC.
- Relevant Research Priorities: Demonstrate how proposed research reflects the priorities of the collaborating LMIC.
- Dissemination: Dissemination plan should describe how results will support tobacco control in the host country.
- Continued Collaboration: Plan for continued collaboration and mentoring after initial training period.
- Network meetings: Budget for periodic grantee network meetings.
- Evaluation: Track long term impact of training and capacity building efforts and use of research findings in country.
The International Tobacco and Health Research and Capacity Building Program (TOBAC) Country Collaborators, 2001-2013
<table>
<thead>
<tr>
<th>Hungary</th>
<th>Syria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Tobacco sales tax increase nine-times over from 2007-2011.</td>
<td>• Supported the first-ever population surveys, toxicity and addiction studies for waterpipe use.</td>
</tr>
<tr>
<td>• Passage of national clean air laws</td>
<td>• Information generated by the project has been used to inform the country's health policies, including a ban on public smoking.</td>
</tr>
</tbody>
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**China**

- TOBAC-funded research, in coordination with the Chinese Center for Disease Control and Prevention and the State Administration of Taxation, found that 2009 tobacco taxation adjustments in China had generated an additional RMB 50 billion in tax revenue.

- This TOBAC-funded work informed Chinese health officials who subsequently endorsed national policy changes regarding tobacco sales.
USAID and NIH Partnerships for Enhanced Engagement in Research (PEER) Health

• Supports developing country researchers in low and middle income countries (LMICs)
• Focus on “implementation science”
• Partner Agencies: NIH, CDC, Department of State, Department of Defense
• Cycle 2 (2014) solicitations for Philippines and Indonesia

http://sites.nationalacademies.org/PGA/dsc/peerhealth/PGA_086555
PEER Tobacco Control Projects

Impact of reduced in-home secondhand smoke exposure on low birthweight prevalence and neonate health
*PI: Yayi Suryo Prabandari, Faculty of Medicine, Gadjah Mada University*

Effects of air pollution in early life on infant and maternal health
*PI: Nikmah Salamia Idris, University of Indonesia*

Effect of a smoking cessation intervention program for families of children diagnosed with TB
*PI: Benjamin Sablan, Philippine Ambulatory Pediatric Association*
Waterpipe Tobacco Smoking: Epidemiologic, Clinical and Laboratory Research

PIs: Wasim Maziak (Florida International University) and Alan Shihadeh (American University of Beirut)
The “Hoffmann List” of probable causative agents in cigarette smoke and related disorders

<table>
<thead>
<tr>
<th>disorder</th>
<th>contributing agents</th>
<th>possible enhancing agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>tobacco dependence</td>
<td>major: nicotine</td>
<td>acetaldehyde</td>
</tr>
<tr>
<td></td>
<td>minor: secondary <em>Nicotiana</em> alkaloids, flavor components</td>
<td></td>
</tr>
<tr>
<td>cardiovascular disease</td>
<td>major: carbon monoxide, nitrogen oxides, hydrogen cyanide, tar</td>
<td>nicotine, alkylating species</td>
</tr>
<tr>
<td></td>
<td>minor: cadmium, zinc</td>
<td></td>
</tr>
<tr>
<td>chronic obstructive pulmonary disease</td>
<td>hydrogen cyanide, volatile aldehydes, nitrogen oxides, carbon monoxide, tar</td>
<td></td>
</tr>
<tr>
<td>lung and larynx cancer</td>
<td>major: PAH, NNK</td>
<td>catechol, tumor promoters</td>
</tr>
<tr>
<td></td>
<td>minor: $^{210}$polonium, formaldehyde, acetaldehyde, butadiene, metals (Cr, Cd, Ni)</td>
<td>acetaldehydes, diet, alkylating species</td>
</tr>
<tr>
<td>oral cavity cancer</td>
<td>major: NNN, NNK</td>
<td><em>herpes simplex</em>, irritation</td>
</tr>
<tr>
<td></td>
<td>minor: PAH</td>
<td></td>
</tr>
<tr>
<td>esophageal cancer</td>
<td>NNN</td>
<td>ethanol, diet</td>
</tr>
<tr>
<td>pancreas cancer</td>
<td>NNK, NNAL</td>
<td>diet</td>
</tr>
</tbody>
</table>

*Hoffmann et al, 2001; Hecht 1997*
Do waterpipes emit toxicants?

Health Warning: Smoking is a main cause of Lung cancer, Lung diseases and of Heart and arteries diseases.
Waterpipe Research Questions: Transdisciplinary Research for Policy

• What toxicants are waterpipe users exposed to?
  – Measure puff topography patterns in “field” study (waterpipe café)
  – Program smoking robot to reproduce puff patterns and analyze smoke contents using standardized testing protocol

• What level of toxicants gets absorbed by the waterpipe user?
  – Measure biomarkers (cotinine, carcinogen metabolites) in smoker vs non-smoker

• Does waterpipe smoking emit toxicants into the environment?
  – Controlled measurement of toxicants emitted by burning waterpipe and exhaled by user
  – Measure PM2.5 in waterpipe cafes
Find out how people smoke

Shihadeh, Antonius, Azar, BRIMC, 2005

Average puff topography
- Volume
- Duration
- Frequency
- Number

Puff topography record
Program smoking robot & sample/analyze smoke

human participant puff topography record

vacuum pump

data acquisition and control system

data acquisition

puff control valve

mass flow meter

particulate traps

glass fiber filters

CO grab bag

sealed diaphragm pump

volatile aldehydes sampler

coated SPA trap

waterpipe

Shihadeh & Azar, JAM, 2006
Carcinogen exposure over 24 hours: waterpipe vs cigarette

• Hospital setting, cross-over design, N=13 dual users
• All day *ad libitum* cigarette smoking (11 cpd mean) versus 3 WTS use sessions
• Measurements on day 4 of 4-day protocol.

Chamber study of waterpipe environmental emissions

\[
\frac{dN_k}{dt} = \frac{1}{2} \sum_{i=1}^{\infty} \beta(v_i, v_j) N_i N_j - N_k \sum_{i=1}^{\infty} \beta(v_i, v_k) N_i - \gamma N_k
\]
WP emits more of everything measured cf cigarettes

<table>
<thead>
<tr>
<th></th>
<th>waterpipe SS</th>
<th>cigarette SS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( N = 12 )</td>
<td>( N = 9 )</td>
</tr>
<tr>
<td>Carbon monoxide, mg</td>
<td>( 2269 \pm 108 )</td>
<td>( 65.5 \pm 5.5 )</td>
</tr>
<tr>
<td>PAH, ng</td>
<td>( N = 11 )</td>
<td>( N = 3 )</td>
</tr>
<tr>
<td>Total PAH</td>
<td>( 1193 \pm 226 )</td>
<td>( 305 \pm 49 )</td>
</tr>
<tr>
<td>Particle number emissions</td>
<td>( N = 4 )</td>
<td>( N = 4 )</td>
</tr>
<tr>
<td>ultrafine particles 5.6-99.5 nm, /10^{12}</td>
<td>( 3.99 \pm 0.60 )</td>
<td>( 0.639 \pm 0.188 )</td>
</tr>
<tr>
<td>total particles 5.6-560 nm, /10^{12}</td>
<td>( 4.38 \pm 0.66 )</td>
<td>( 1.68 \pm 0.27 )</td>
</tr>
<tr>
<td>count median diameter, nm</td>
<td>( 37.9 \pm 4.1 )</td>
<td>( 130 \pm 8 )</td>
</tr>
<tr>
<td>Volatile aldehydes, ug</td>
<td>( N = 6 )</td>
<td>( N = 5 )</td>
</tr>
<tr>
<td>Total aldehydes</td>
<td>( 12000 \pm 1610 )</td>
<td>( 2954 \pm 416 )</td>
</tr>
</tbody>
</table>

Observational studies in WP cafés

Hammal et al., 2013

PM2.5 Exposure Inside

Venues:
- Casino 1
- Casino 2
- WP1
- WP2
- WP3
- WP4
- WP5

* 1-Hour PM2.5 exposure Guideline-Alberta
Observational studies in WP cafés

Zhang et al., 2013
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