National Cancer Institute

NIH Support of International Tobacco Control Research

Mark Parascandola, PhD, MPH
Epidemiologist
Tobacco Control Research Branch

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

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.

COMMENTARY

POLICY

Addressing the Growing International Challenge of Cancer: A Multinational Perspective

Harold Varmus[1]* and Harpal S. Kumar[2]*

Leaders in cancer research and policy from 15 economically diverse countries met at the U.S. National Institutes of Health in November 2012 to discuss opportunities to reduce cancer incidence and mortality, improve cancer care, and increase our understanding of disease pathophysiology. Here, we present recommendations that the participants believe will enable faster progress in addressing the growing international challenge of cancer.

INTRODUCTION

The diseases grouped together as cancers are among the major liabilities of human life. The global burden of cancer includes 12.7 million newly diagnosed cases per year, of which more than half occur in less developed regions of the world (1). Cancers now account for more than 15% of the world's annual deaths (>7.5 million per year), and that number is rising, especially in less affluent countries (2). Moreover, cancers are among the most feared medical conditions, often causing prolonged periods of suffering, requiring substantial health-care expenditures for advanced care, and being fought with medical tools that are relatively ineffective and themselves frequently disabling. [In this Commentary, the authors represent the views of participants at an international meeting of leaders in cancer research (complete list shown in Table 1).]

Leaders of institutions and organizations that fund and perform cancer research came from 15 countries to the U.S. National Institutes of Health (NIH) in November 2012 to discuss opportunities to reduce cancer incidence and mortality, improve cancer care, and increase our understanding of the many forms of the disease. Here, we present recommendations supported by the meeting participants, who represented more than half of the world's population, including citizens in low- and middle-income countries. We address several areas that the group believes to be of great importance, such as development of cancer registries and national cancer-control plans; implementation of better methods to prevent, detect, and treat cancers; and ways to expand and improve research on a wide range of cancer-relevant topics.

To address the growing international challenge of cancer, our "reach should exceed [our] grasp" (26).

AN EXPANDING PERSPECTIVE

Until recently, efforts to improve the world's capacity to combat cancers have not often been addressed in a globally coordinated way. Notwithstanding critical work by professional societies and by many international and national nongovernmental organizations (NGOs) to improve care, increase awareness of cancer, and provide basic infrastructure and equipment, most countries—and those responsible for the support and conduct of cancer care and research within them—have focused on cancers that most commonly afflict their own citizens, using a variety of approaches and resources.

There are several possible explanations for this heterogeneity. First, countries differ substantially with respect to the kinds of cancers that are prevalent locally and the underlying environmental, behavioral, and genetic factors that predispose to those cancers. Second, countries have different fiscal, professional, and political capacities to confront disease. Efforts in each national context may also be influenced by competing health concerns, such as infectious diseases (for example, HIV/AIDS or malaria) or chronic conditions (such as diabetes or cardiovascular diseases), and by varying abilities to help address the plights of citizens of other nations. Finally, countries have distinct traditions—and individual citizens have different perspectives—that affect the way their governments approach cancers. These views may date to a time when malignant diseases were relatively rare and tools for controlling them and their complications were usually ineffective.

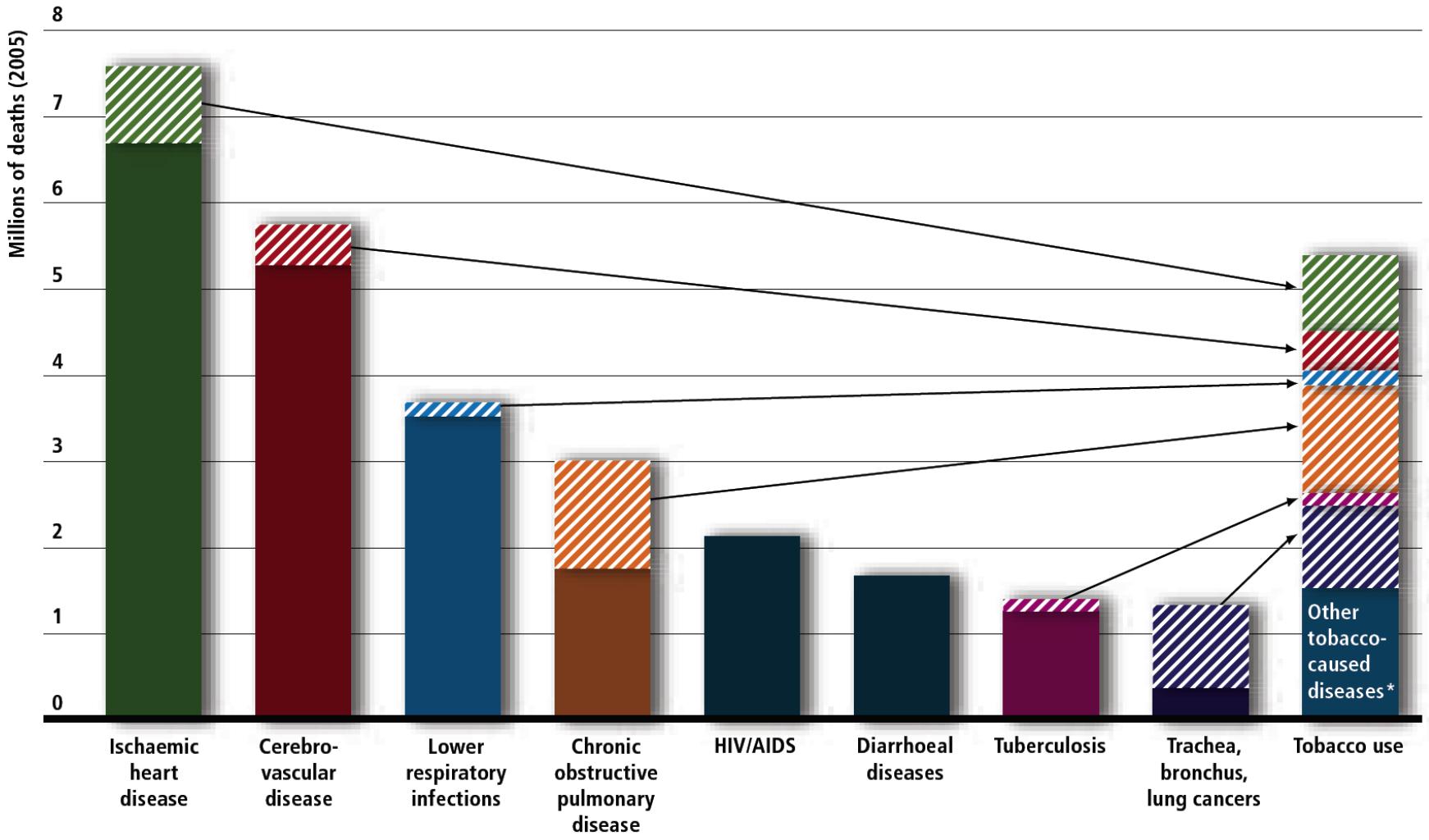
The signatories to this article are individuals with influential positions at agencies and institutions that perform or support research on various kinds of cancer in several countries. The November 2012 meeting followed an initial gathering of a similar group at Cancer Research UK in London in 2011. Participants at the two meetings discussed how we can augment our individual efforts: (i) by promoting the application and expansion of existing knowledge to prevent, detect, and treat cancers in many nations, and (ii) by seeking opportunities to foster pioneering research in laboratories and clinics on all aspects of these diseases, including cancers that take their greatest toll in the developing world.

We have been encouraged in our deliberations by a variety of factors. These include a greater appreciation of epidemiological evidence for the large and growing burden of cancers, especially in developing countries; major advances in the understanding of can-

Downloaded from stm.sciencemag.org on June 18, 2013

Source: H. Varmus, H. S. Kumar, Addressing the growing international challenge of cancer: A multinational perspective. Sci. Transl. Med. 5, 175cm2 (2013).

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



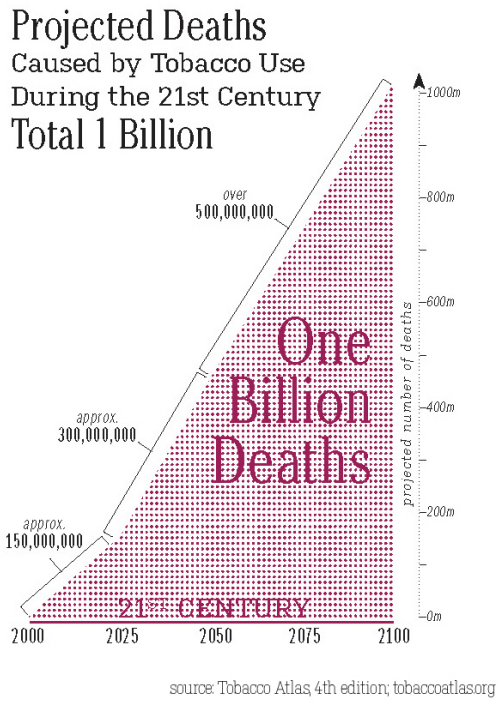
Source: Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Medicine, 2006, 3(11):e442.

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.

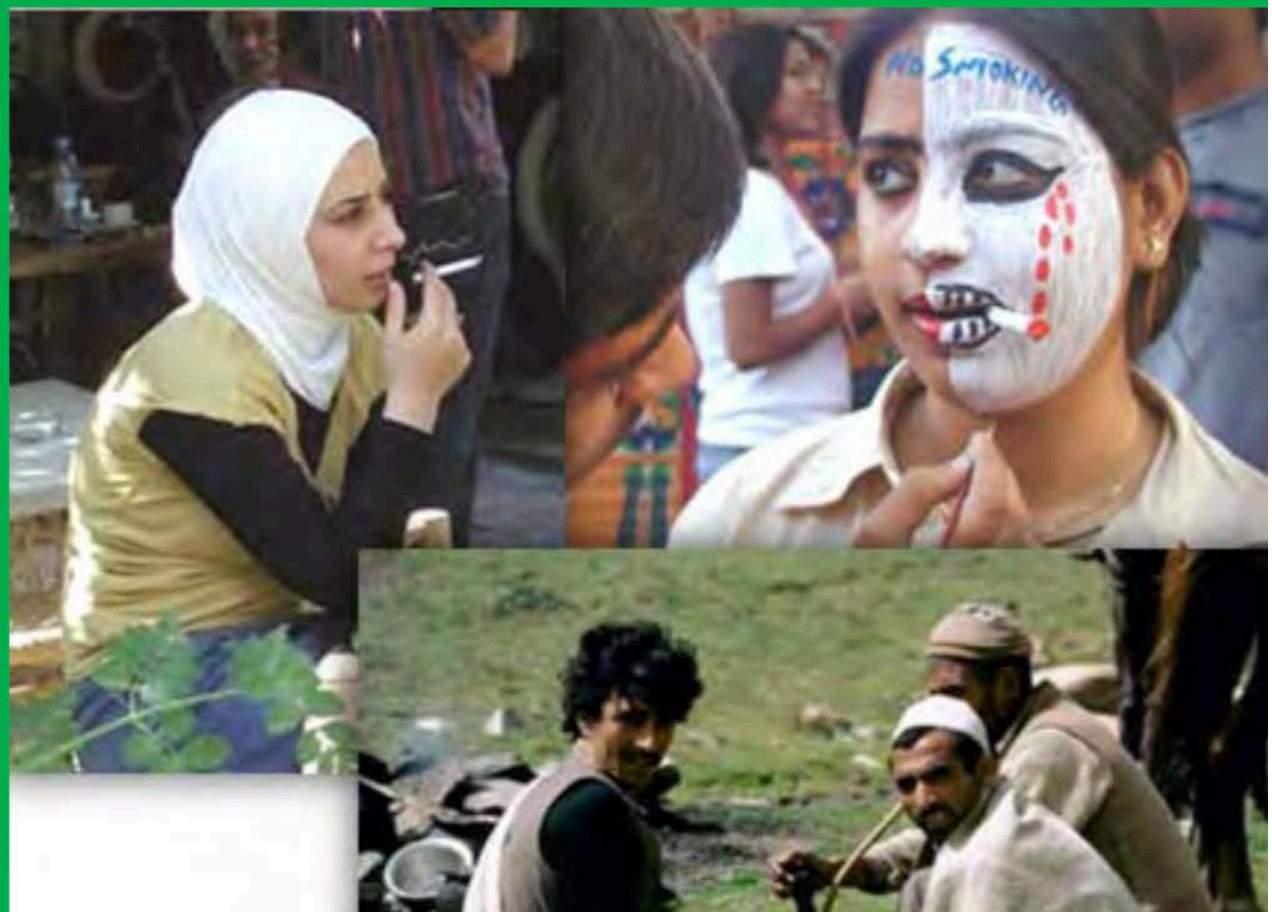


source: Tobacco Atlas, 4th edition; tobaccoatlas.org

- 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 Heath Research and Capacity Building Program (TOBAC) Country Collaborators, 2001-2013

NIH Tobacco or Health Research and Capacity Building Grant Program Review: Policy Outcomes

Hungary

- Tobacco sales tax increase nine-times over from 2007-2011.
- Passage of national clean air laws

Syria

- Supported the first-ever population surveys, toxicity and addiction studies for waterpipe use.
- Information generated by the project has been used to inform the country's health policies, including a ban on public smoking.

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

USAID FROM THE AMERICAN PEOPLE

NATIONAL INSTITUTES OF HEALTH

Partnerships for Enhanced Engagement in Research (PEER) Health

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

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

*Hoffmann et al, 2001; Hecht 1997

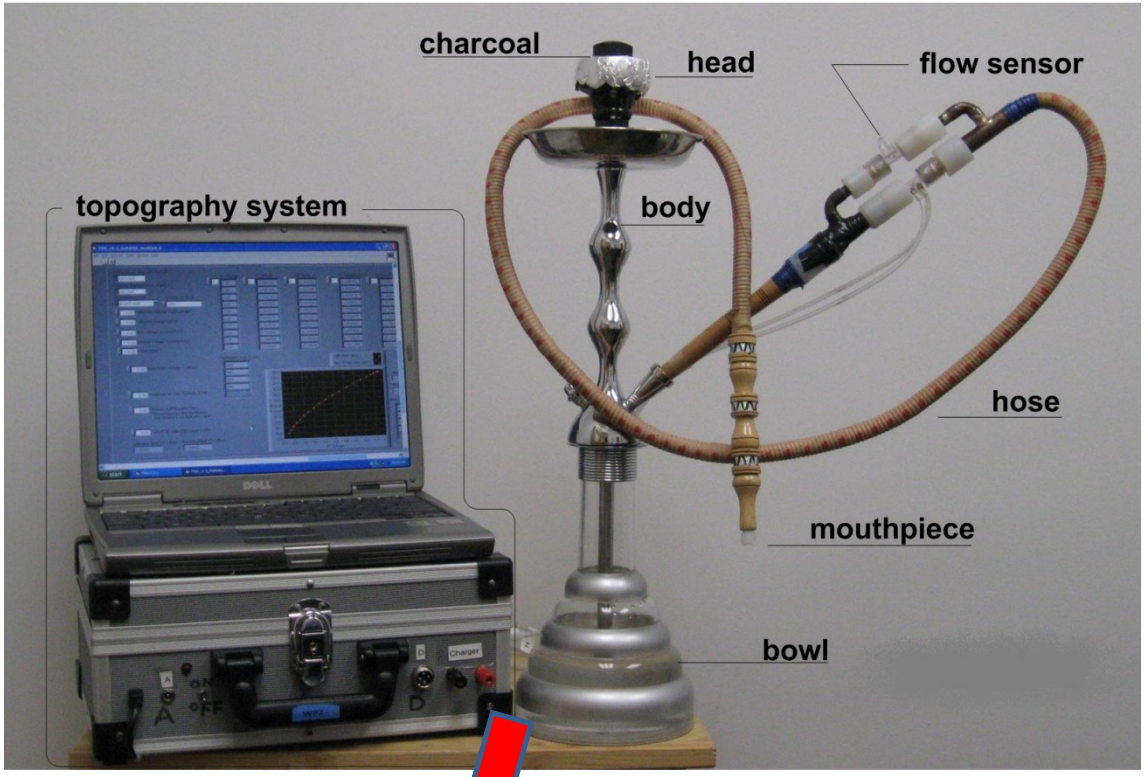
Do waterpipes emit toxicants?

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

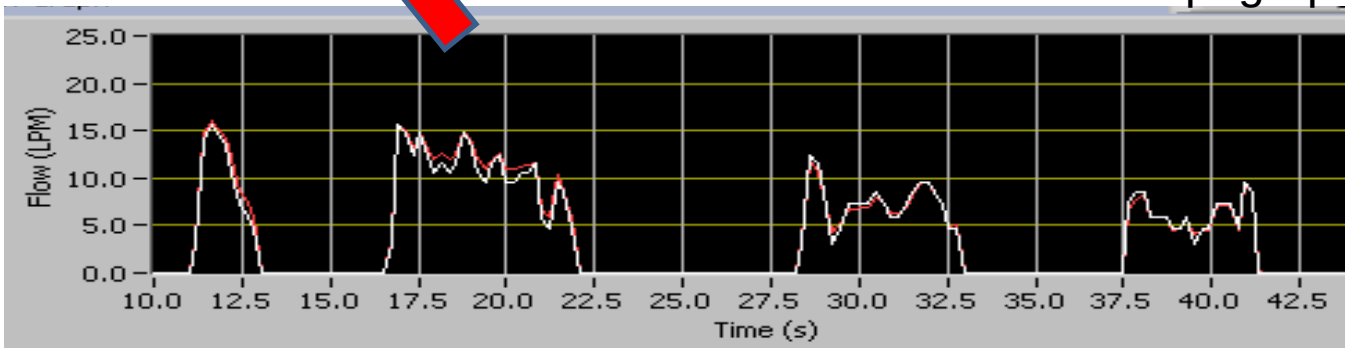
Shihadeh, Antonius, Azar, BRIMC,2005



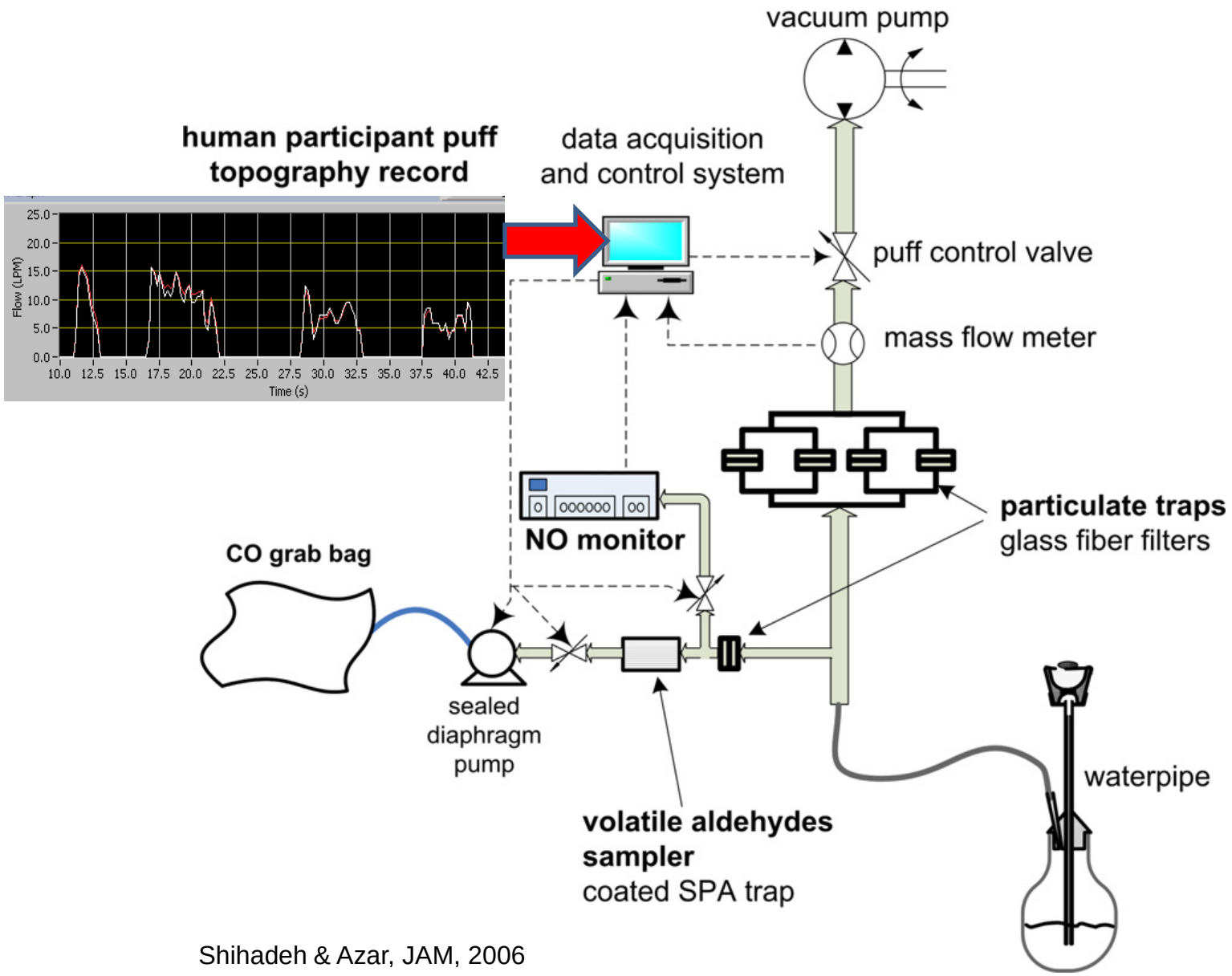
Average puff topography

- Volume
- Duration
- Frequenc
- Number

Puff topography record



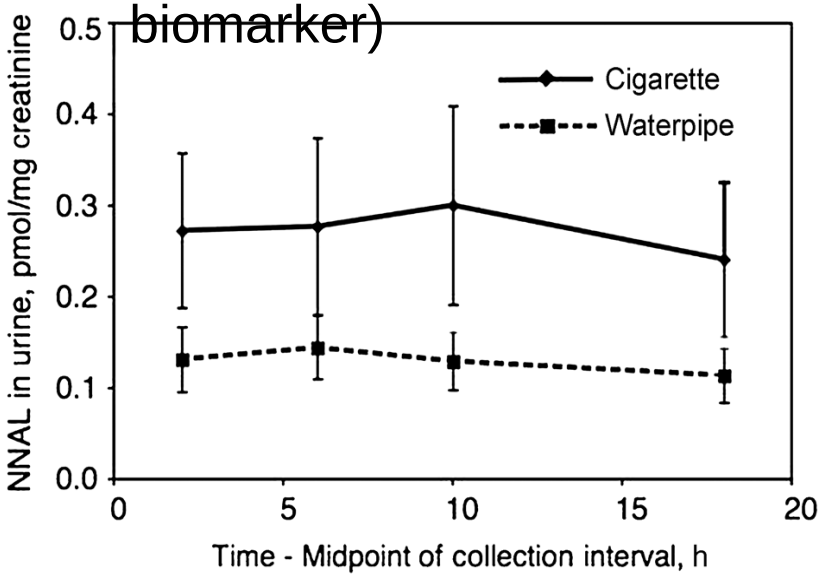
Program smoking robot & sample/analyze smoke



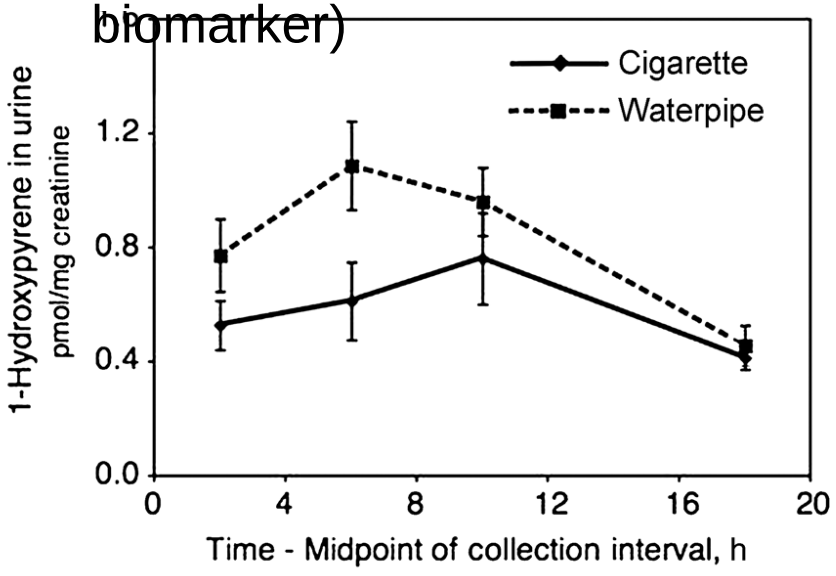
Shihadeh & Azar, JAM, 2006

Carcinogen exposure over 24 hours: waterpipe vs cigarette

Urinary NNAL (TSNA biomarker)



Urinary 1-HOP (PAH biomarker)

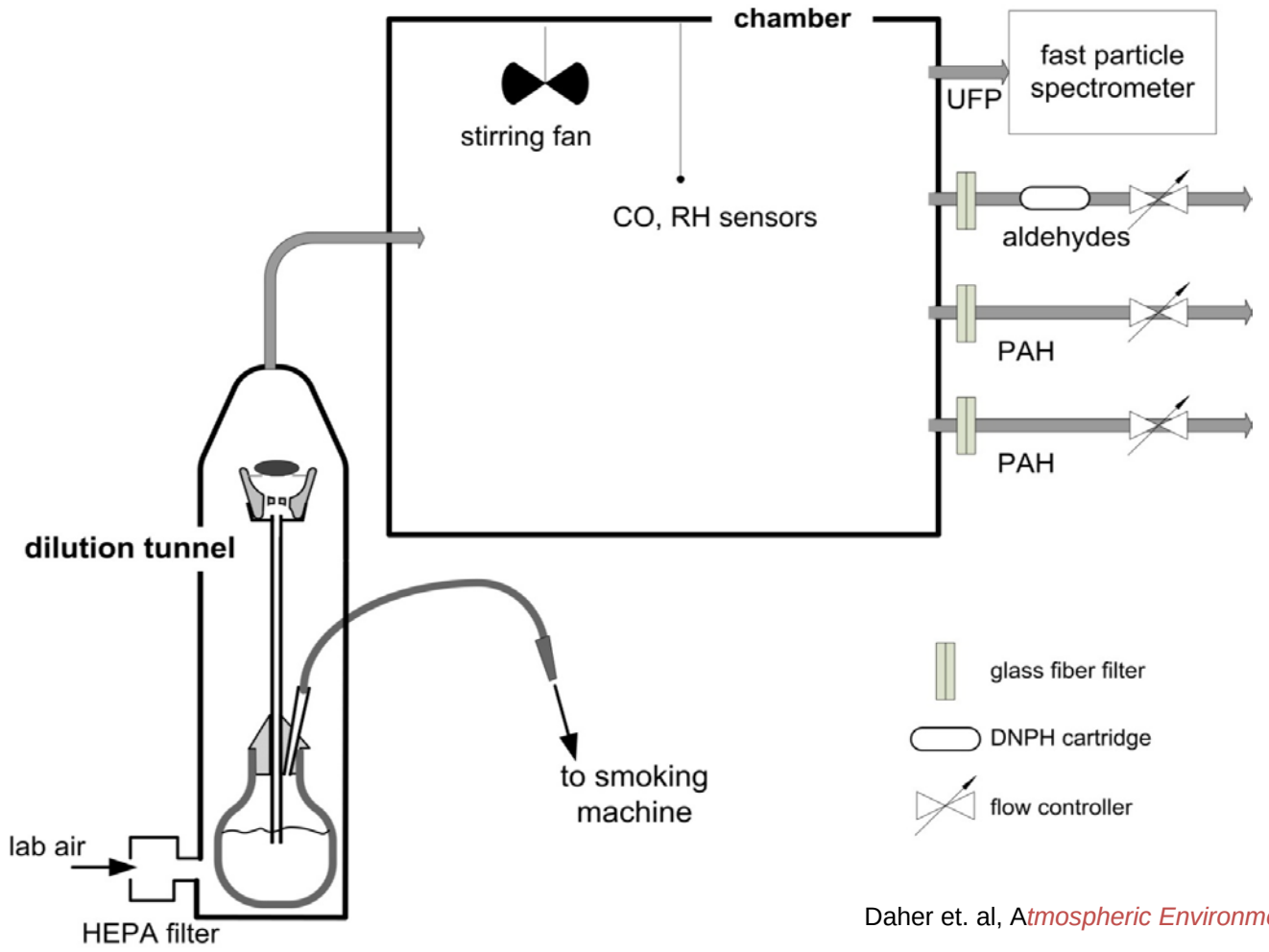


- Hospital setting, cross-over design, N=13 dual users
- All day *ad libitim* cigarette smoking (11 cpd mean) versus 3 WTS use sessions
- Measurements on day 4 of 4-day protocol.

Jacob et al, 2013. Cancer Epidemiol Biomarkers Prev 2013;22:765-772.

Chamber study of waterpipe environmental emissions

$$\frac{dN_k}{dt} = \frac{1}{2}\sum_{i=1}^{\infty}\beta(v_i, v_j)N_iN_j - N_k\sum_{i=1}^{\infty}\beta(v_i, v_k)N_i - \gamma N_k$$



Daher et. al, A*tmospheric Environment*, 44, 8-14, 2009.

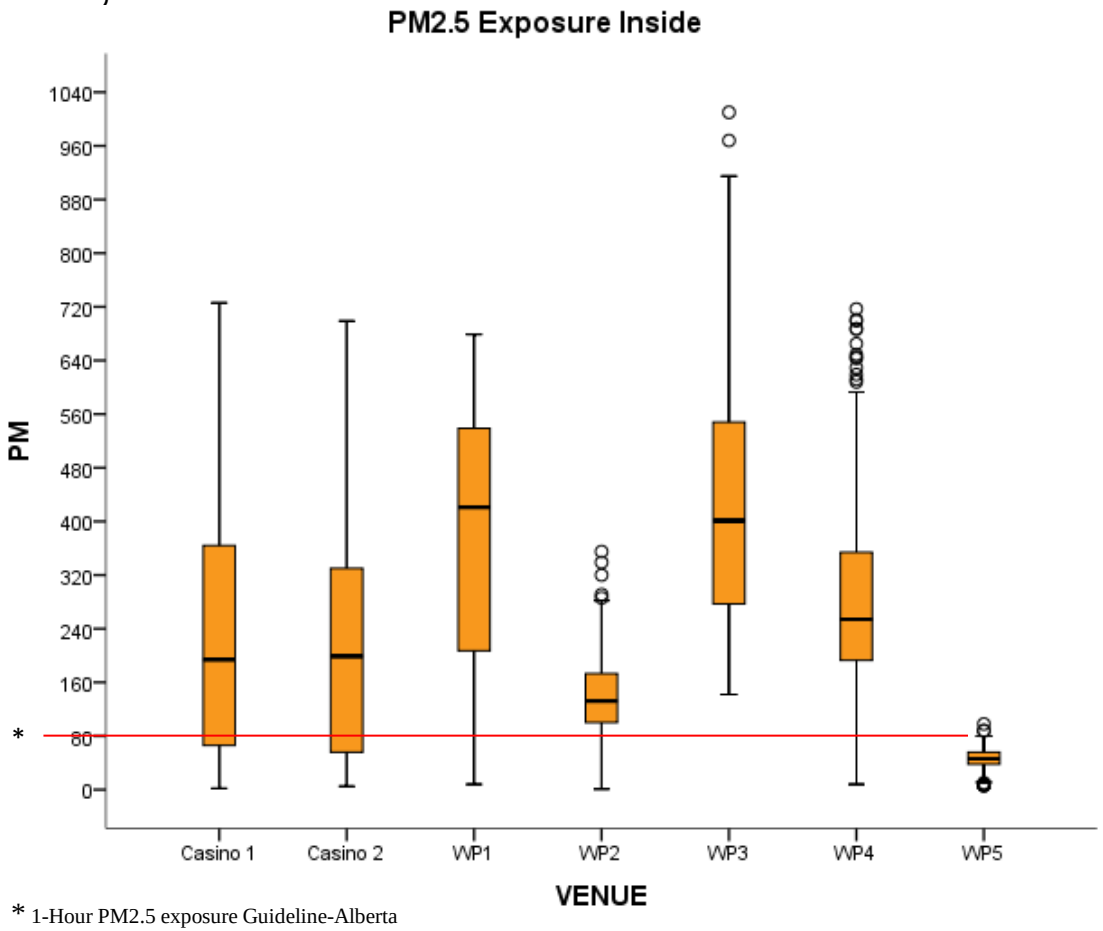
WP emits more of everything measured cf cigarettes

mean±95% CI	*waterpipe SS*	*cigarette SS*
	N = 12	*N=9*
Carbon monoxide, mg	2269 ± 108	65.5 ± 5.5
PAH, ng	*N = 11*	*N = 3*
Total PAH	*1193 ± 226*	*305 ± 49*
Particle number emissions	*N = 4*	*N = 4*
ultrafine particles 5.6-99.5 nm, /10^{12}	3.99 ± 0.60	0.639 ± 0.188
total particles 5.6-560 nm, /10^{12}	4.38 ± 0.66	1.68 ± 0.27
count median diameter, nm	37.9 ± 4.1	130 ± 8
Volatile aldehydes, ug	*N = 6*	*N = 5*
Total aldehydes	*12000 ± 1610*	*2954 ± 416*

Daher et. al, A*tmospheric Environment*, 44, 8-14, 2009.

Observational studies in WP cafés

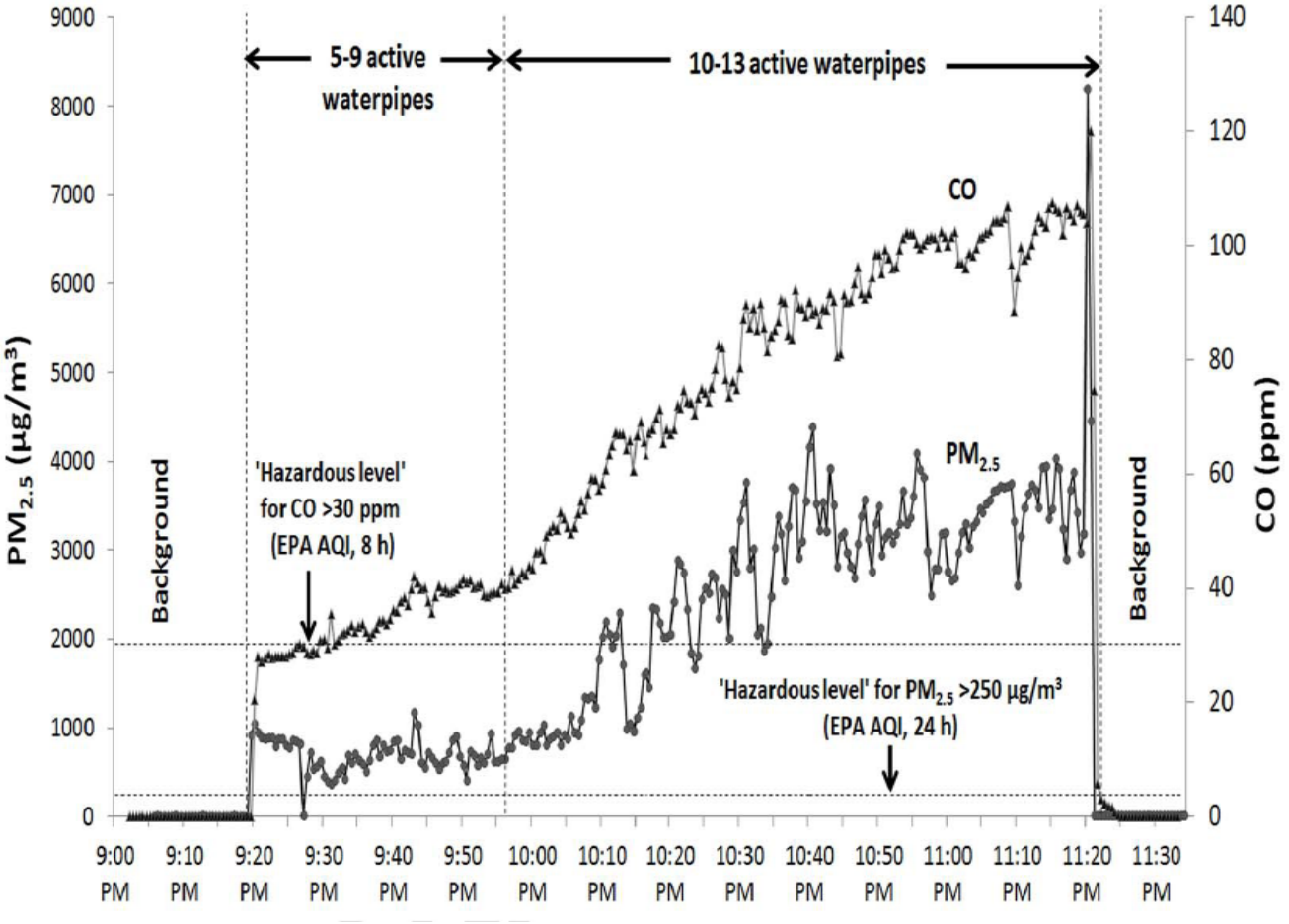
Hammal et al., 2013



* 1-Hour PM2.5 exposure Guideline-Alberta

Observational studies in WP cafés

Zhang et al., 2013



Contact

Mark Parascandola, PhD, MPH

Epidemiologist

Tobacco Control Research Branch
Behavioral Research Program
Division of Cancer Control and Population Sciences
National Cancer Institute
6130 Executive Blvd, MSC 7337
Executive Plaza North, EPN 4032
Bethesda, MD 20892-7337

Email: paramark@mail.nih.gov