Links Between Cancer and Early Life Exposures to Environmental Pollutants

A Webinar on the Latest Science, and its Implications for Health Professionals

December 8, 2016

Speakers

DR. PHIL LANDRIGAN
Mt. Sinai School of Medicine

DR. RICHARD CLAPP
Boston University School of Public Health/ University of Massachusetts Lowell

DR. JIM FABISIAK
University of Pittsburgh School of Public Health

Respondents

DR. MARSHA HALEY
Magee Women's Hospital – University of Pittsburgh Medical Center

DR. EDWARD KETYER
Pediatric Alliance

DR. MATT MEHALIK
Air Quality Collaborative

Moderator

DR. POLLY HOPPIN
University of Massachusetts Lowell – Lowell Center for Sustainable Production

All presenters and respondents report no disclosures or conflicts of interests related to the topics discussed during this webinar

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EXPLORING THE ENVIRONMENTAL CONTRIBUTION

to

CHILDHOOD CANCER

Philip J. Landrigan, MD, MSc, FAAP
Dean for Global Health
Professor of Environmental Medicine and Pediatrics
Icahn School of Medicine at Mount Sinai

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December 8, 2016

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Childhood Cancer in the US
An Overview

- Beyond infancy, cancer is the leading cause of death by disease among children in the United States. Only injuries kill more children.
- In 2014, an estimated 15,780 children and adolescents ages 0 to 19 years in the US were diagnosed with cancer
- In 2014, an estimated 1,960 American children died of cancer

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First Recognition of Environmental Cancer - 1776

Scrotal Skin Cancer in London Chimney Sweeps
Sir Percival Pott

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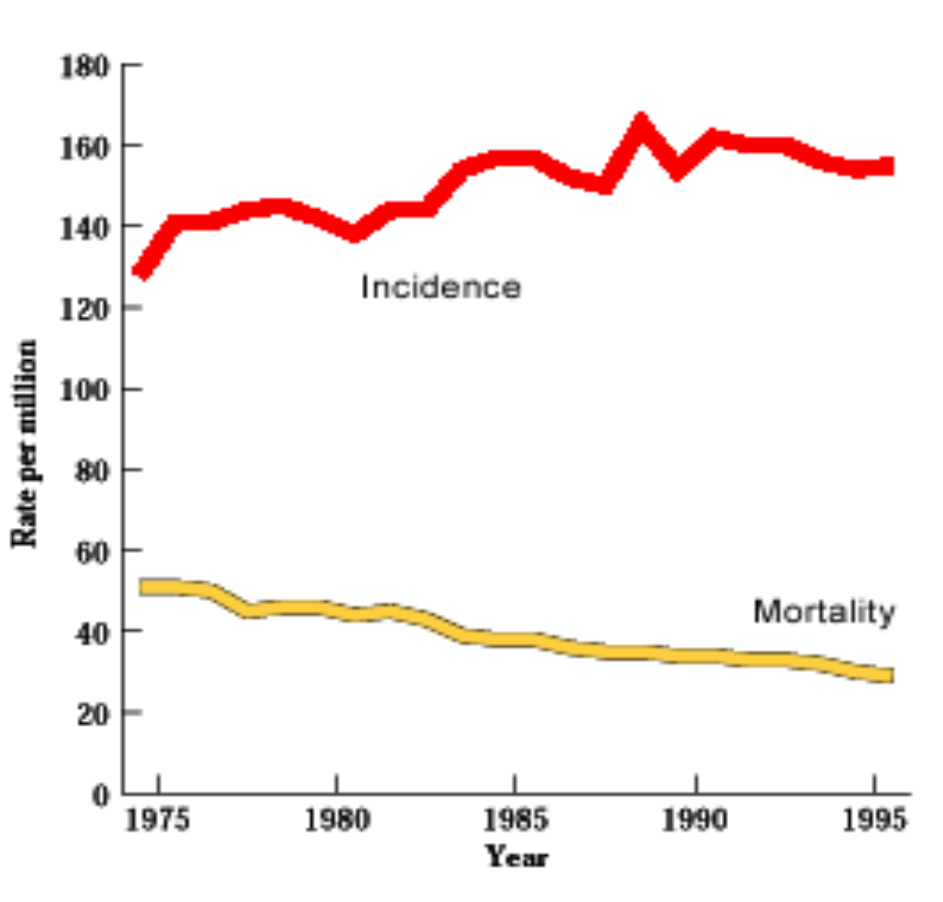
Childhood Cancer (Age 0-19) Age-Adjusted Incidence and Death Rates United States, 1975-1996



Source: Pediatric Monograph 1999, Surveillance, Epidemiology, and End Results Program Division of Cancer Control and Population Sciences, National Cancer Institute. American Cancer Society, Surveillance Research

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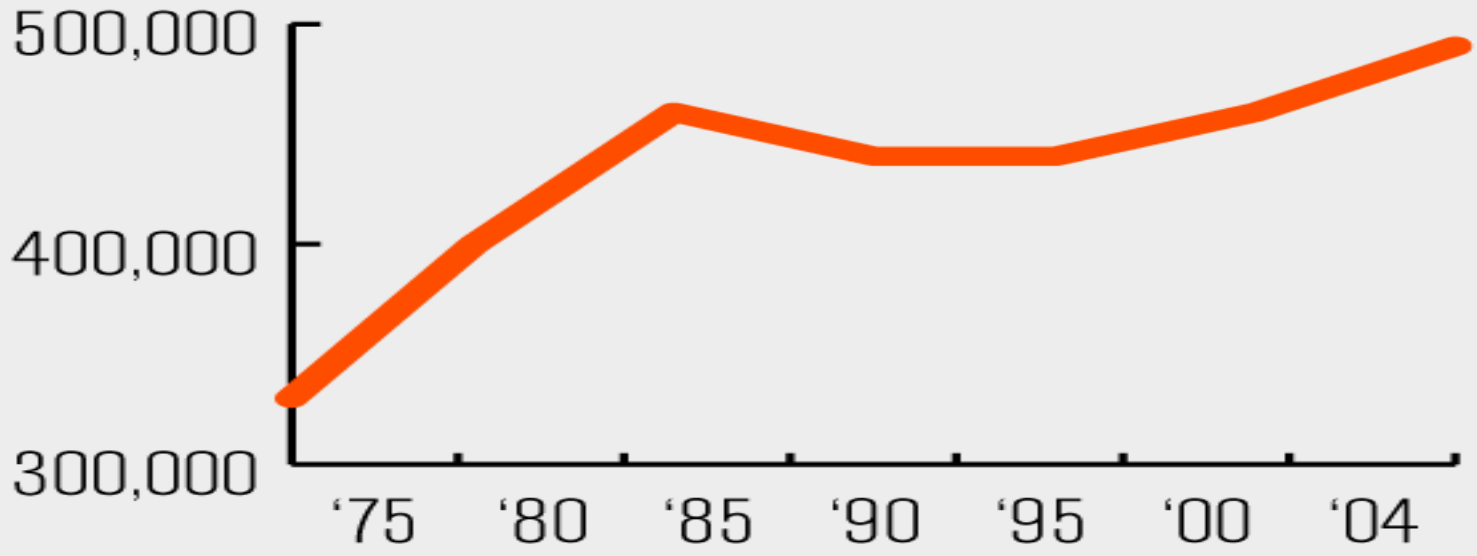
Incidence of Childhood Leukemia 1975–2004



Source: National Cancer Institute

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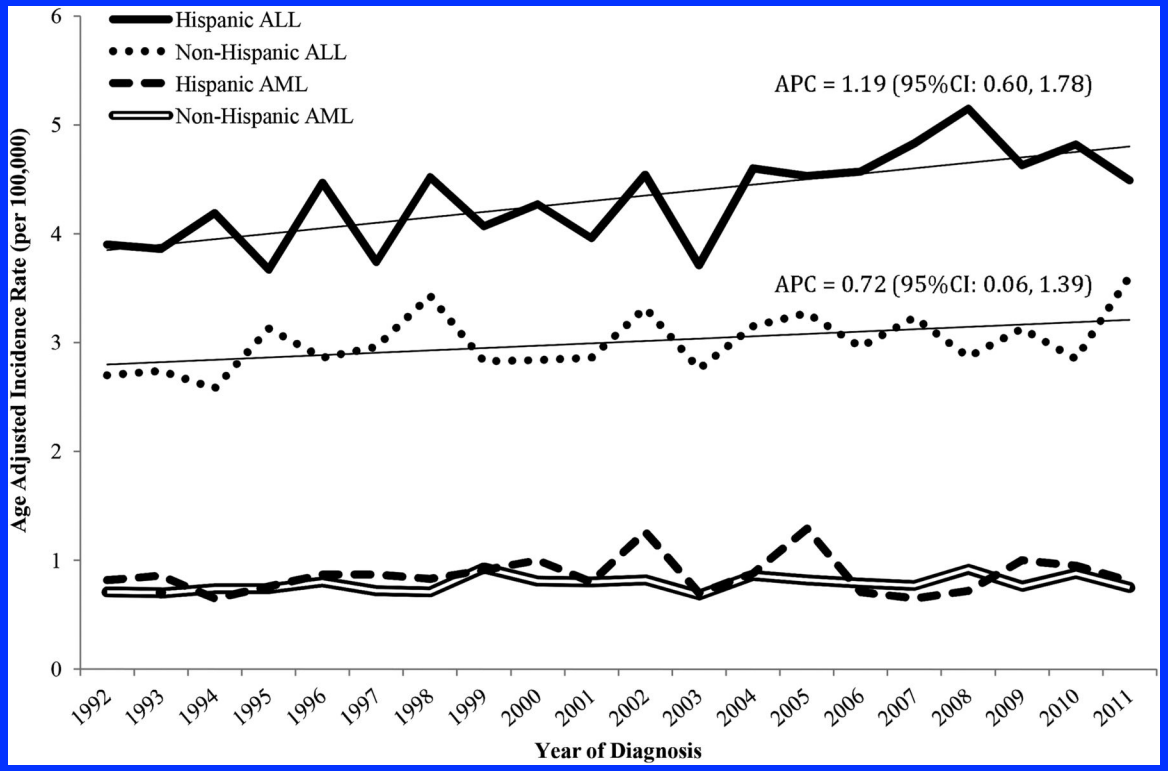
Increasing Incidence of Childhood Leukemia, USA, 1992-2011



Jessica L. Barrington-Trimis et al. *Blood* 2015;125:3033-3034

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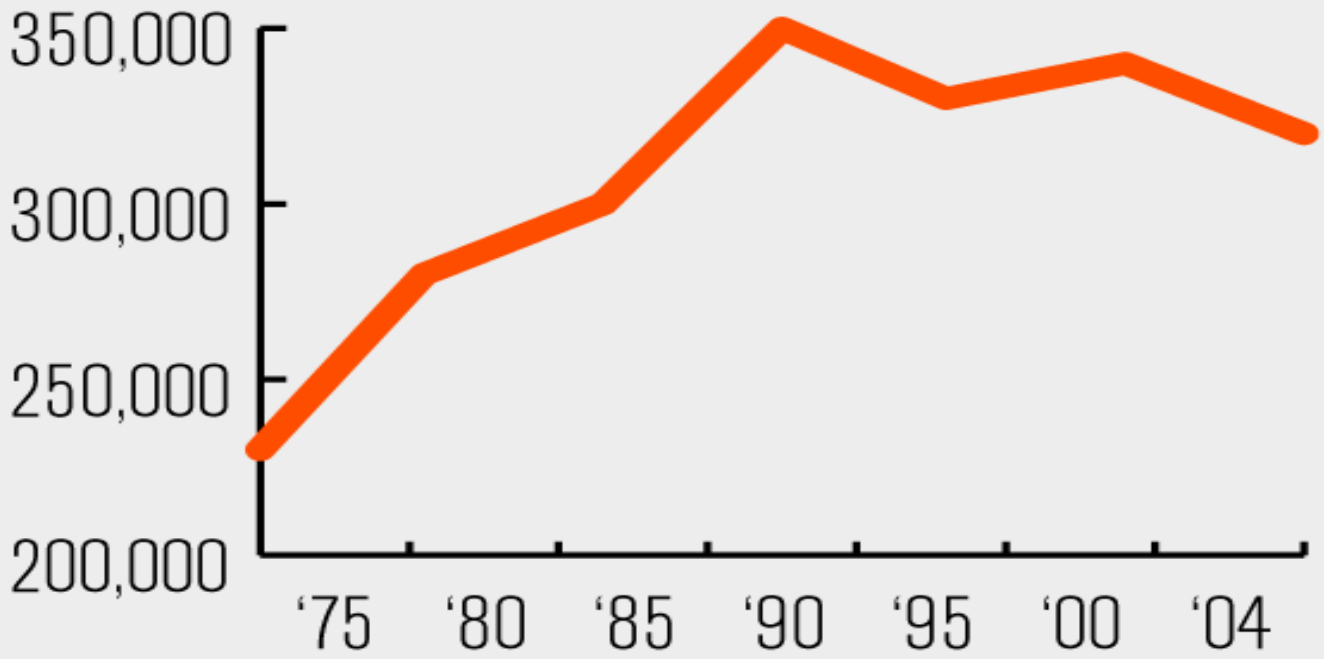
Incidence of Childhood Brain Cancer 1975–2004



Source: National Cancer Institute

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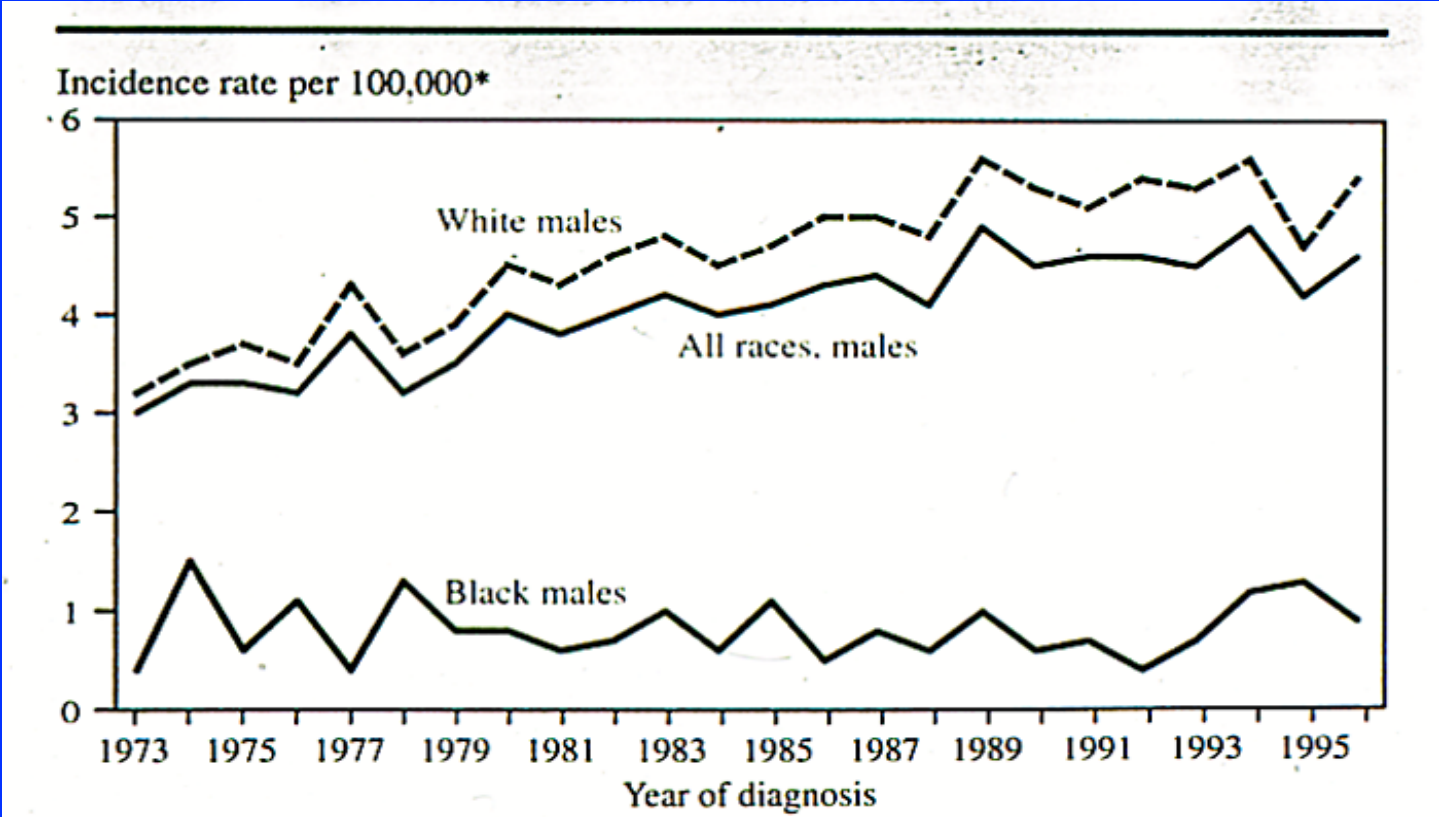
Increasing Incidence of Testicular Cancer, USA, 1973-2003



Sources: *SEER Cancer Statistics Review, 1973-1996* (NCI 1999) and *Cancer Rates and Risks, 4th edition* (NCI 1996); access at http://www-seer.ims.nci.nih.gov

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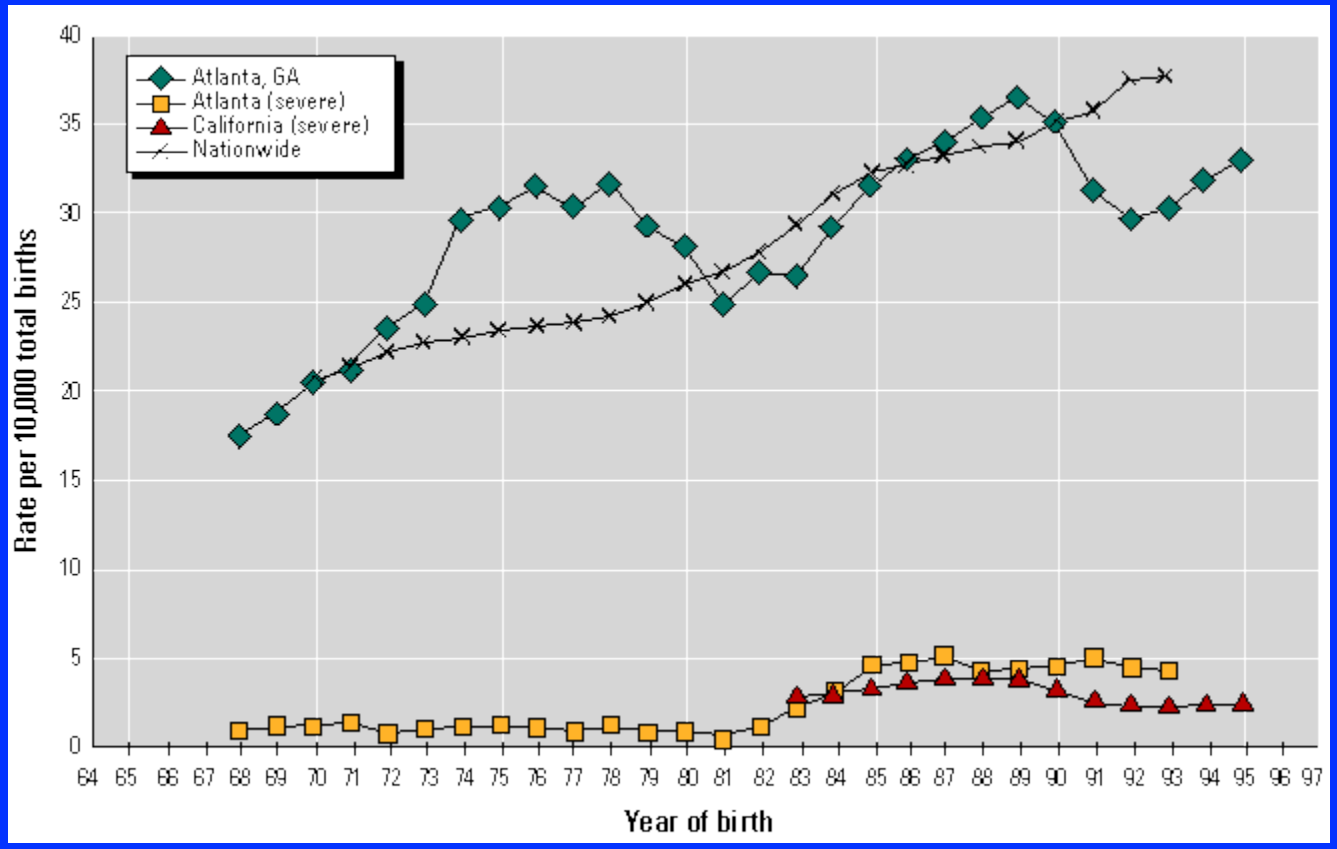
Increasing Incidence of Hypospadias/Cryptorrchidism, 1968-95



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Possible Causes of Increasing Incidence of Childhood Cancer

- Genetics – too rapid
- Diagnostic artefact – would have explained a one-time “bump”, but not a consistent rise of several different cancers over several decades
- Environmental exposures

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Children's Exposures to Chemicals in the Environment

- 85,000 + chemicals in commerce today
- 3,000 synthetic chemicals are produced in quantities of 1 million pounds or more per year – High Production Volume chemicals
- Widespread exposure – documented in CDC national surveys
- No basic toxicity information is available for fewer than half of HPV chemicals
- Information on developmental toxicity is available for fewer than 20% of HPV chemicals
- Almost nothing is known about synergistic effects of simultaneous exposures to multiple chemicals

Children are Uniquely Vulnerable to Toxic Chemicals

- Greater exposure Kg-per-Kg
- Diminished ability to detoxify and excrete many chemical toxins
- Heightened biological vulnerability
- More years of future life

"Children are not Little Adults"

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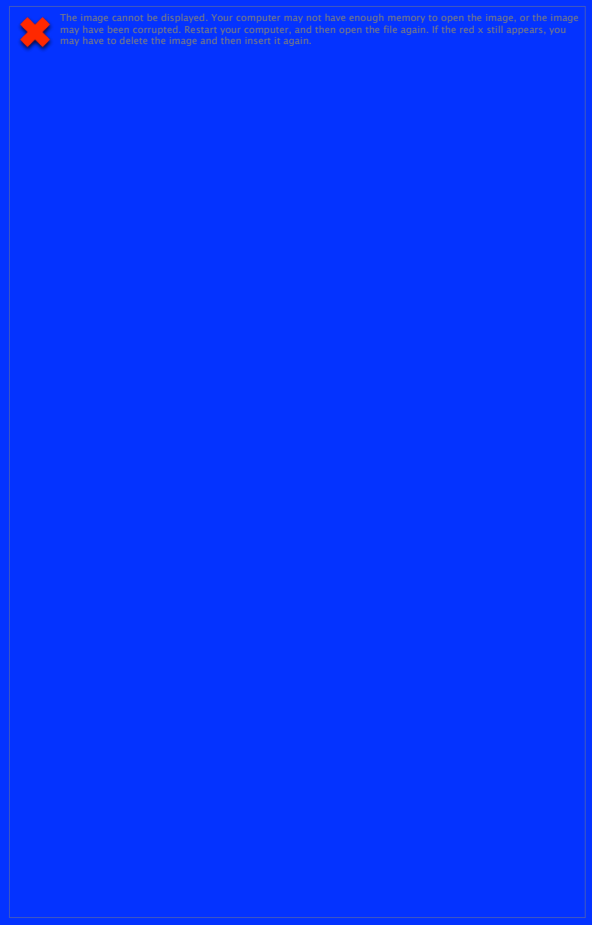
Infants and Children are Exquisitely Sensitive to Toxic Chemicals in the Environment

Examples:

- Phocomelia in infants exposed *in utero* to thalidomide.
- Epidemic of neurobehavioral disease in Minamata Japan caused by *in utero* exposure to methylmercury
- Adenocarcinoma of the vagina in girls exposed in the womb to di-ethylstilbestrol (DES)

Phocomelia following *in utero* Exposure to Thalidomide



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A Child Massively Exposed to Mercury
Minamata, Japan, 1960

No visible damage to the mother

Growing Evidence for Environmental Causation of Childhood Cancer

- Radiation – post Hiroshima and Nagasaki and Alice Stewart's studies
- DES and adenocarcinoma of vagina
- Solvents, especially benzene – and parental employment in industries that use solvents – painting and printing
- Pesticide exposure, especially prenatally
- Air pollution
- Aspartame – experimental evidence
- Protective effects of folic acid and breast feeding

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Key Elements of a Research Strategy to Discover the Environmental Causes of Childhood Cancer

- *Toxicology*. Independent, publicly funded testing of chemicals to discover developmental carcinogens

- *Epidemiology*. Independent, publicly funded epidemiologic studies of children – especially large, multi-year prospective birth cohort studies that incorporate careful measures of chemical exposures and of genetic susceptibility

- *Research translation*. Translation of research findings into evidence-based prevention

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The Good News: Progress is Possible

Examples of evidence- based prevention:

- Removal of lead from gasoline
- Reduction in use of X-rays during pregnancy
- Decline in exports of toxic pesticides
- Global control of asbestos

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Challenges Remain

- Rising global levels of air pollution
- Increasing use of carcinogenic pesticides, e.g., glyphosate
- Migration of polluting industries to the world's least developed countries
- Persistent global trade in asbestos – 2 million tons of new asbestos enter global trade each year

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A Final Thought for Those Who Provide Clinical Care for Children

- Cancers of environmental origin in children have no distinctive clinical features
- Therefore a careful history of environmental exposure is in most cases the way to diagnose environmental causation
- A careful history is also the only way to discover new environmental causes of cancer
- Pioneering pediatrician and cancer epidemiologist Robert W. Miller spoke of "*The Critical Importance of the Alert Clinician*"

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Thank You

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Childhood cancer and environmental exposures – a focus on air pollutants

Richard W. Clapp, D.Sc., MPH
B.U. School of Public Health and
U. of Mass.- Lowell

Outline

- Additional information on environmental risk factors for childhood cancer
  - Two recent meta-analyses of air pollution and leukemia
- Cancer in teenagers
- Conclusions and recommendations

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Additional information on environmental risk factors

- Evidence of “windows of vulnerability” for breast cancer following early life exposure
- Two examples:
  - Cohn, et al., 2007 found risk of breast cancer before age 50 was significantly higher in those exposed to DDT before age 14.
  - Cohn, et al., 2015 found increased risk of breast cancer in young women whose mothers had elevated maternal DDT levels.

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Environmental risks (cont.)

- Multiple air pollution and childhood leukemia studies published between 1989 and 2014.
- Recent meta-analyses suggest associations between traffic density, specific air pollutants and childhood leukemia, especially acute myelogenous leukemia.
  - Boothe, et al., 2014 found 50% excess childhood leukemia with post-natal exposure to residential traffic in seven studies.

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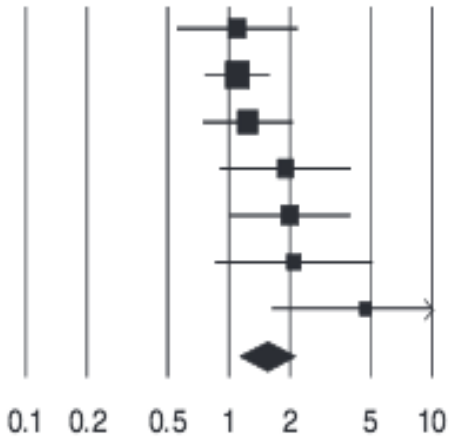
Studies of Air Pollution and Childhood Leukemia

Boothe et al / Am J Prev Med 2014;46(4):413–422

Study name	Statistics for each study[b]			
	Odds ratio	Lower limit	Upper limit	Relative weight
Raaschou-Nielsen, 2001	1.10	0.55	2.20	13.5
Steffen, 2004	1.10	0.76	1.60	25.3
Von Behren, 2008	1.24	0.74	2.08	19.1
Langholtz, 2002	1.90	0.90	4.01	12.2
Amigou, 2010	2.00	1.00	4.00	13.5
Crosignani, 2004	2.09	0.85	5.13	9.3
Savitz, 1989	4.70	1.62	13.65	7.1
Summary weighted OR	1.53	1.12	2.10	



Bottom line: 53% elevated risk of childhood leukemia based on post-natal exposure to traffic-related pollutants

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Environmental risks (cont.)

- Filippini, et al., 2015 included review of studies published through 2014.
  - Results suggest modest increase in leukemia risk associated with traffic density in multiple studies.
  - Four studies which estimated benzene exposure found 64% increased risk of leukemia; two studies found greater than two-fold risk of acute myelogenous leukemia.
  - Authors discuss benzene leukemogenic mechanisms and suggest motorized traffic increases risk.

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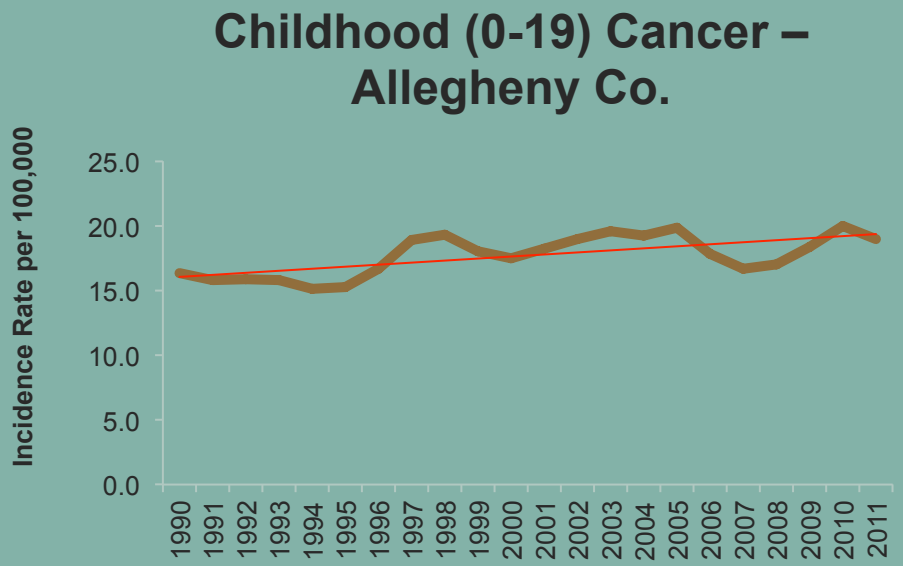
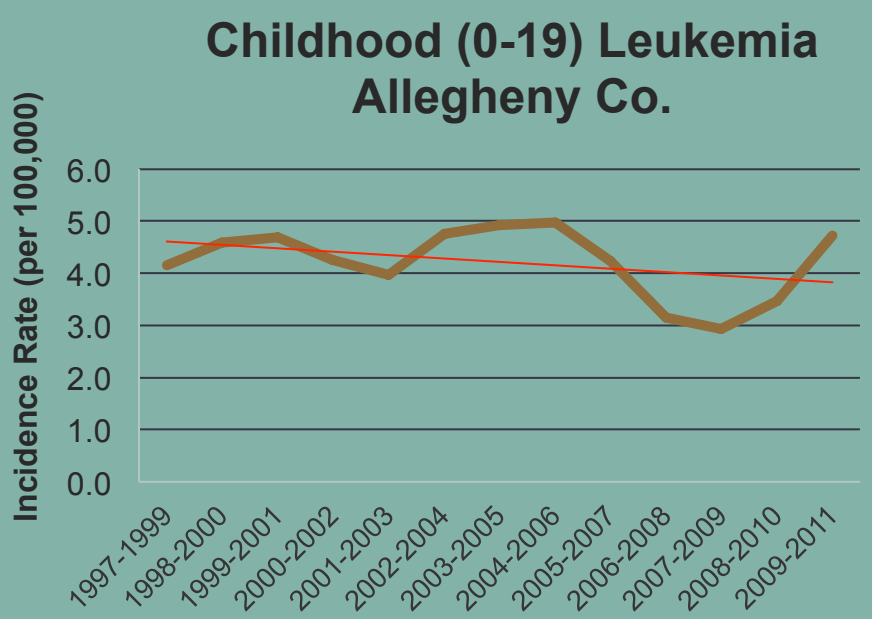
Childhood Cancer Trends in Allegheny County





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Pennsylvania Department of Public Health's Epidemiologic Query and Mapping System (EpiQMS) [cancer incidence: https://apps.health.pa.gov/EpiQMS/asp/ChooseDataset.asp.

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Trends in teenage cancer incidence

- Most common cancers in teenagers age 15-19 are Hodgkin lymphoma (15%), thyroid cancer (11%), brain and central nervous system (10%), testicular germ cell cancer (8%)
  - There were an estimated 5,330 cases in 2014 in the U.S.
  - Source: American Cancer Society, 2014

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Age-specific Childhood Cancer Rates

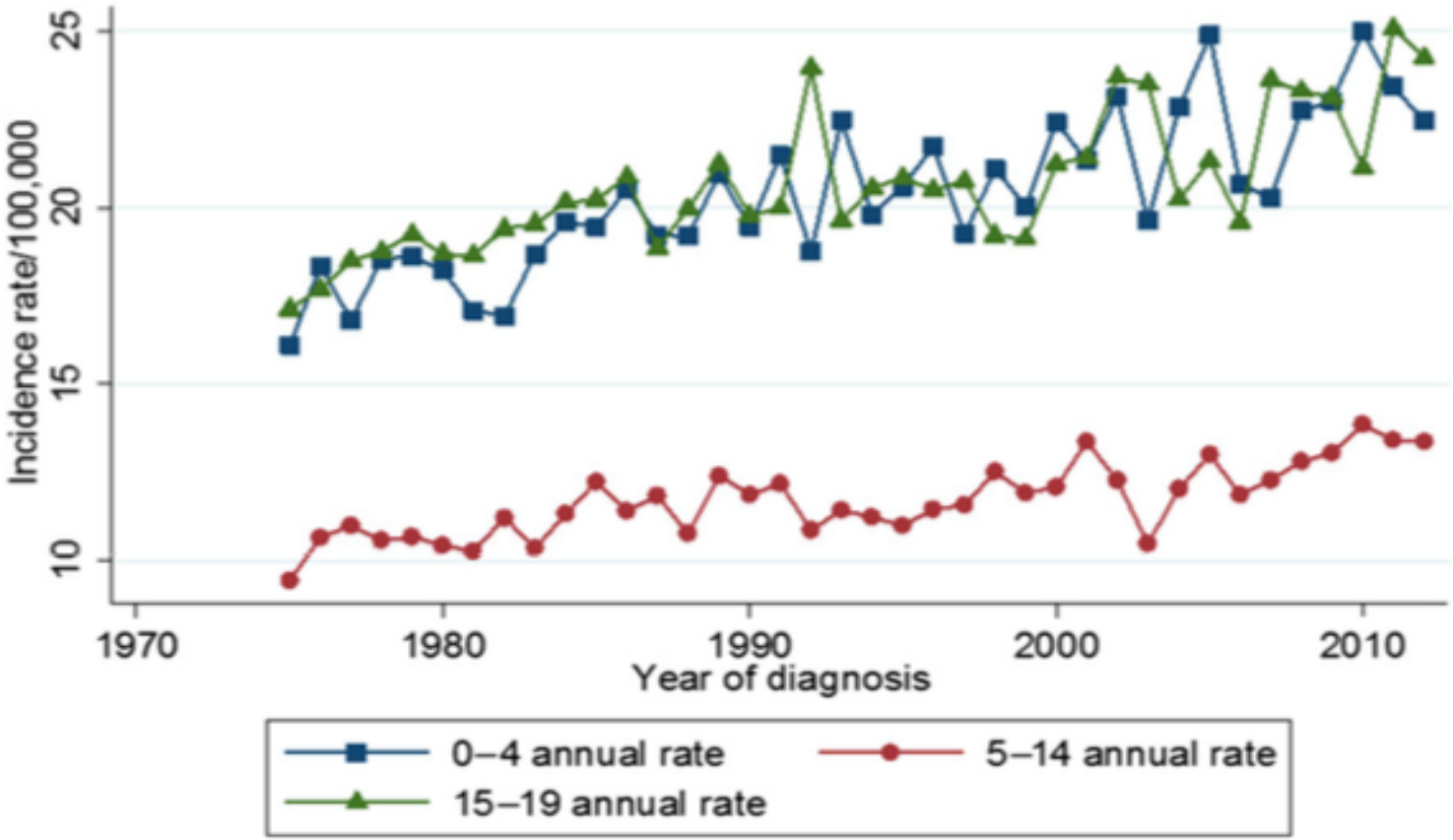

FIGURE 1
Childhood cancer incidence in the United States. Surveillance, Epidemiology, and End Results data for all cancer sites combined, both sexes, in 3 age groups, 1975–2012.

Cancer in teenagers

- Overall incidence rates are similar to those in children under age 5, and are increasing over time.
- Fastest rising cancer types are non-Hodgkin lymphoma, thyroid cancer, acute myeloid leukemia and testicular cancer.
- Increased screening and medical radiation does not explain entire pattern.
- Source: Kriebel, et al., *Pediatrics*, 2016.

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Conclusions and recommendations

- Childhood cancer incidence is steadily increasing, as are numbers of early adult survivors of childhood cancer.
- One in 285 children will be diagnosed with cancer before age 20.
  - One in 530 adults age 20 to 39 are childhood cancer survivors.
- Source: American Cancer Society, 2014

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Conclusions and Recommendations

- Reduction of carcinogenic exposures to parents, the developing fetus, newborns and young children will prevent some childhood and teen cancers.
  - Green chemistry and alternatives assessment provide a way forward for many companies.
  - Health care providers can join efforts to reduce childhood cancer incidence.

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Links Between Cancer and Early Life Exposures to Environmental Pollutants
Webinar
December 8, 2016

Exposure to air toxics from mobile and point sources in Southwest PA

Jim Fabisiak, Ph.D.

Dept. of Environmental & Occupational Health

University of Pittsburgh

What are air toxics?

- The Clean Air Act amendments of 1990 listed 188 hazardous air pollutants (HAPs) known or highly suspected to cause cancer or other serious non-cancer health effects (usually respiratory, neurological, or reproductive/development effects).
- Contrast to NAAQS criteria pollutants (PM, O_3, NO_x, SO_2, CO, Pb)

Not all hazardous air pollutants are created equal, and they can produce differing health effects from varying chemical properties. Some produce cancer in regions of the body; others are respiratory irritants, while others may affect the nervous system, reproduction, or neurological development.

About 50% of HAPs have been classified as "known", "probable", or "possible" human carcinogens. Each has a unique estimate of its potency to induce cancer.

URE = risk of cancer per million people / (µg/m^3 in air).

EPA uses a threshold of "one-in-a-million" probability of lifetime (70 yrs) cancer risk above which is unacceptable or cause for concern.

US EPA periodically conducts the National Air Toxics Assessment (NATA) that tries to characterize cancer and non-cancer risk based on estimations HAP concentrations at the census tract level throughout the U.S.

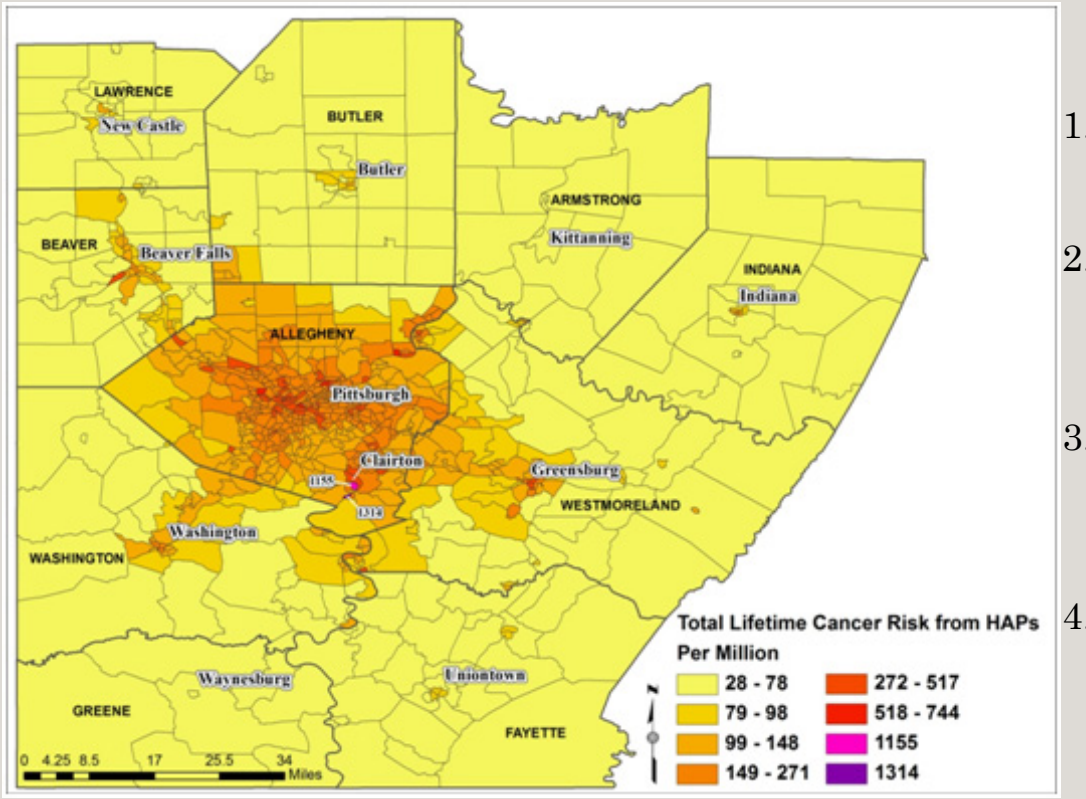
We conducted an analysis of NATA (2005) specifically within the 10 county region of Southwest PA in a form relateable to the non-technical community.

Allegheny, Armstrong, Beaver, Butler, Fayette, Greene, Indiana, Lawrence, Washington, Westmoreland

Risk ≠ Rate

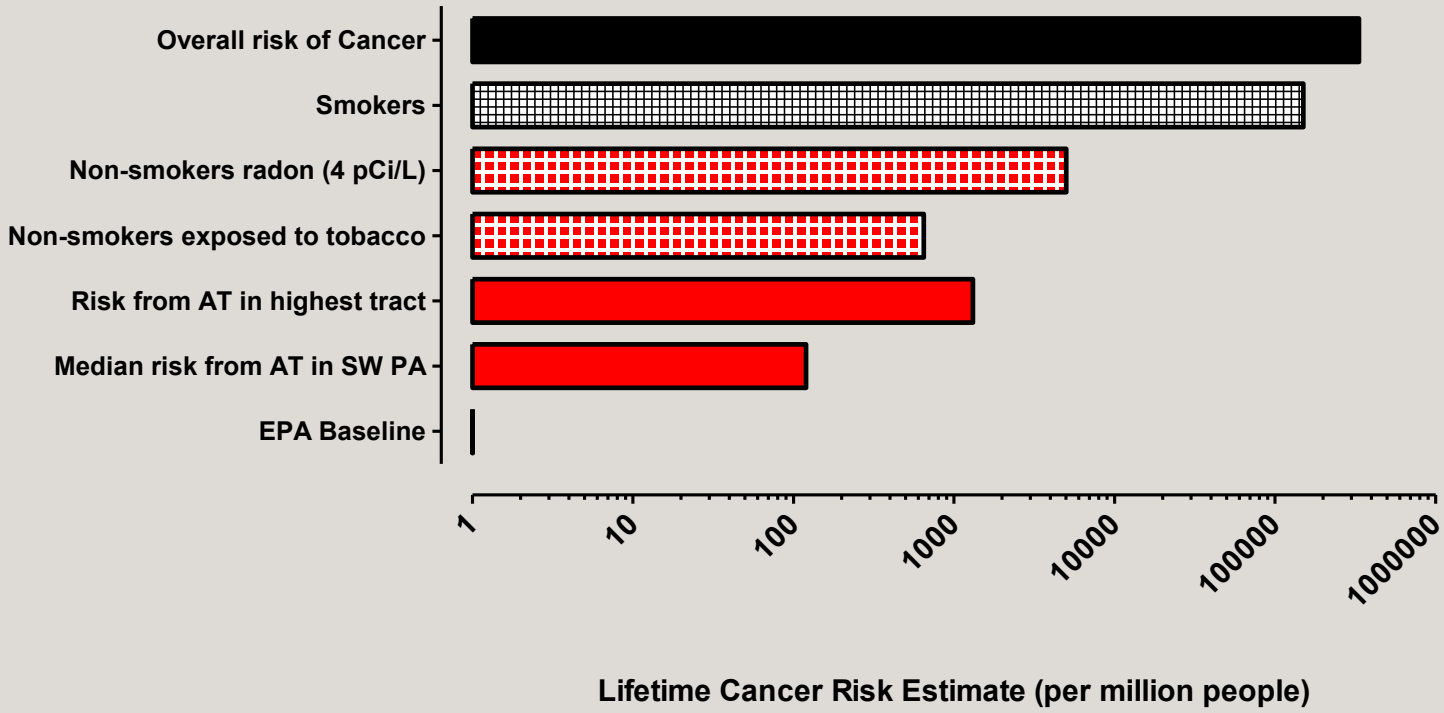
http://www.chec.pitt.edu/documents/PRETA/CHEC%20PRETA%20HAPs%20Report.pdf

Total lifetime cancer risk from all HAPs Southwest PA ten county area as predicted by NATA (2005)



1. Median cancer risk across entire 10-county area > 120 per million.
2. Residents of Allegheny County are at least twice as much risk as rural areas.
3. Allegheny County ranks 63rd out of 3,225 U.S. counties ranking it in the top 2% nationally.
4. Some areas reach risk levels in excess of 1,000 per million by proximity to various point sources.

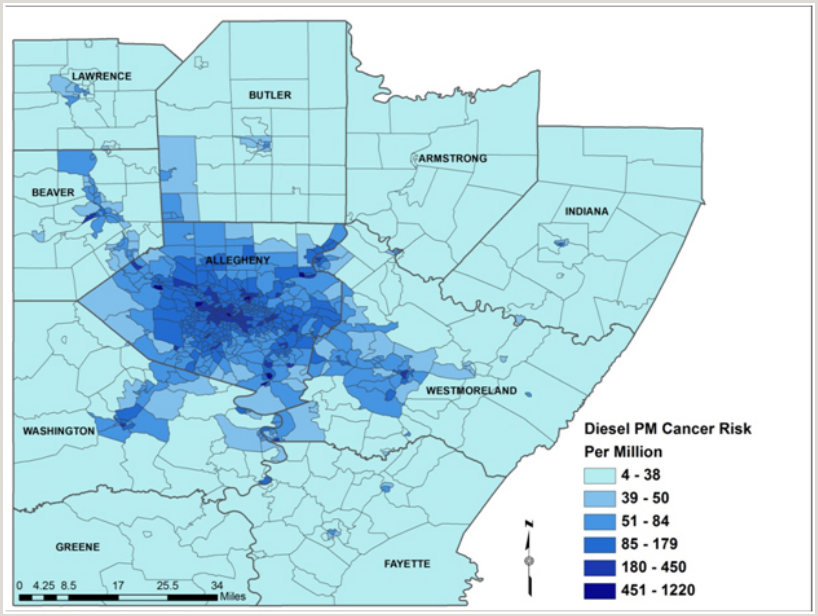
Comparison of cancer risk estimates for various environmental exposures



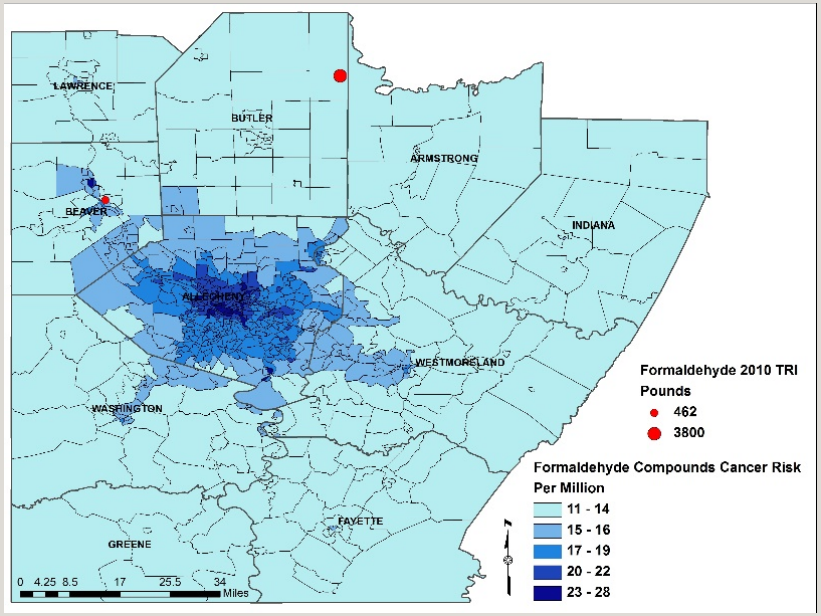
Top HAP Drivers of Cancer Risk in the Southwest PA 10 County Area

Rank within PRETA	Air Toxic Name	Cancer Risk (lifetime risk, in a million)[a]
1	**DIESEL PARTICULATE MATTER**	93.43
2	**FORMALDEHYDE**	16.37
3	**BENZENE (INCLUDING BENZENE FROM GASOLINE)**	7.49
4	**COKE OVEN EMISSIONS**	7.05
5	**CARBON TETRACHLORIDE**	2.86
6	**ACETALDEHYDE**	2.75
7	**ARSENIC COMPOUNDS(INORGANIC INCLUDING ARSINE)**	2.71
8	**CHROMIUM COMPOUNDS**	2.13
9	**1,3-BUTADIENE**	1.99
10	**NAPHTHALENE**	1.44
11	**POLYCYCLIC AROMATIC HYDROCARBONS**	1.30
Median	**All HAPs**	122

Cancer-driving HAPs from mobile sources

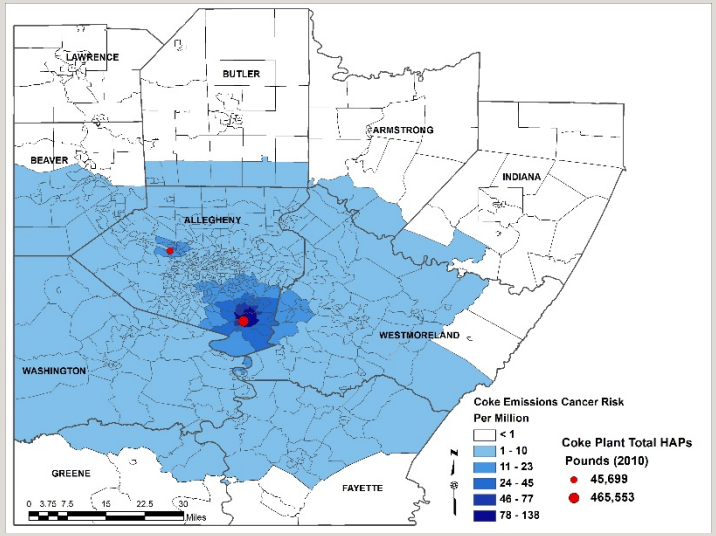


Diesel Particulate Matter

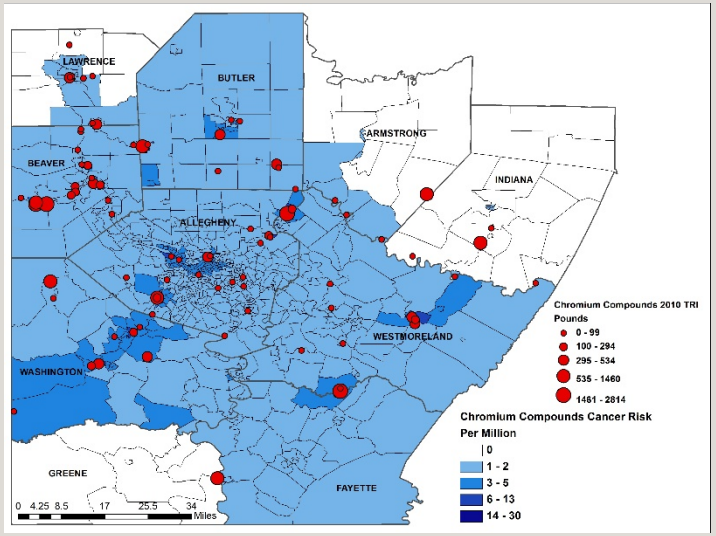


Formaldehyde

Cancer-driving HAPs from stationary sources



Coke Oven Emissions

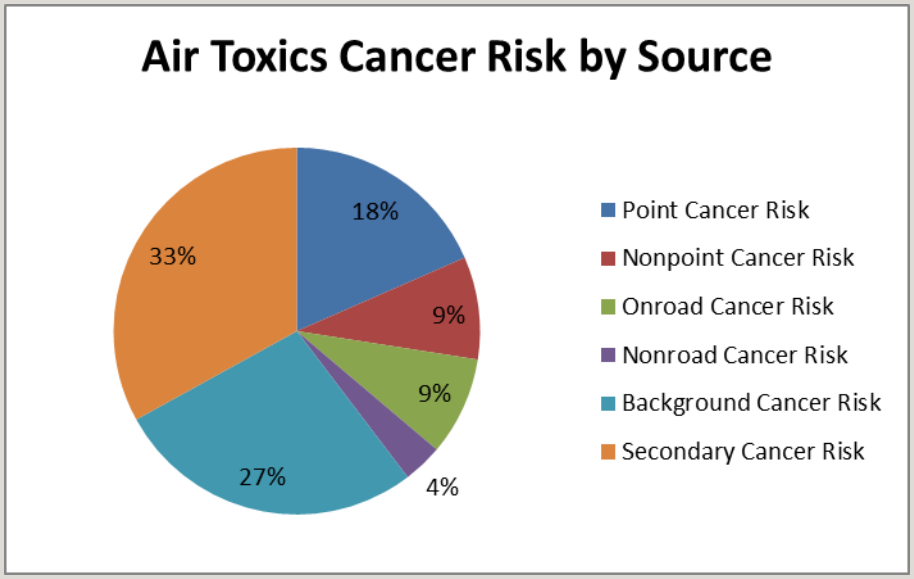


Chromium

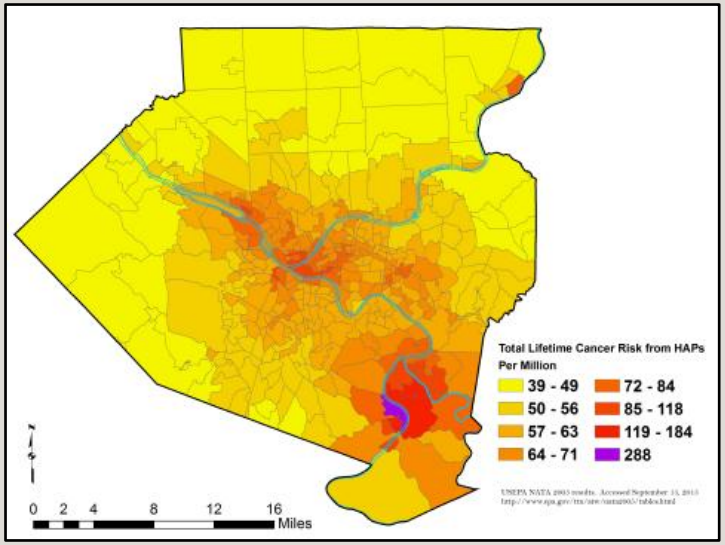
Five out of the 10 census tracts with the highest cancer risk (excluding DPM) in PA, MD, OH, WV are in Allegheny county

Rank	State	County	Tract Number	Total Cancer per Million	Major Contributing Source Type	Location
1	PA	Allegheny	4927	289	Point	Clairton
2	WV	Brooke	0312	243	Point	Follansbee (Weirton-Steubenville)
3	OH	Hamilton	0007	199	Non-point	Cincinnati (Central Business Dist.)
4	PA	Allegheny	4928	184	Point	Clairton
5	PA	Allegheny	4970	156	Point	Lincoln
6	PA	Allegheny	4980	143	Point	Liberty
7	PA	Allegheny	4994	142	Point	Glassport
8	OH	Cuyahoga	1024.1	142	Point	West Boulevard (Cleveland)
9	OH	Cuyahoga	1132	128	Non-point	Fairfax (Cleveland)
10	OH	Hamilton	0006	125	On-road	Cincinnati (Central Business Dist.)

Sources of HAPs (excluding DPM)



Source Type	Definition
Point (stationary)	Large industrial stacks, power plants, incinerators, factories
Nonpoint (stationary)	Smaller facilities – dry cleaners, gas stations, minor manufacturing (less than 10 TPY of one HAP or < 25 of total HAPs)
On-road (mobile)	Vehicles including cars and trucks that travel along roadways
Non-road (mobile)	Construction machinery, marine vessels, trains, etc.
Background	Anthropogenic and natural sources that persist in the environment or sources that are emitted from distances greater than 50 km
Secondary (formation)	Point-, non-point, and mobile-source types that emit compounds that are readily transformed in the atmosphere into HAP compounds



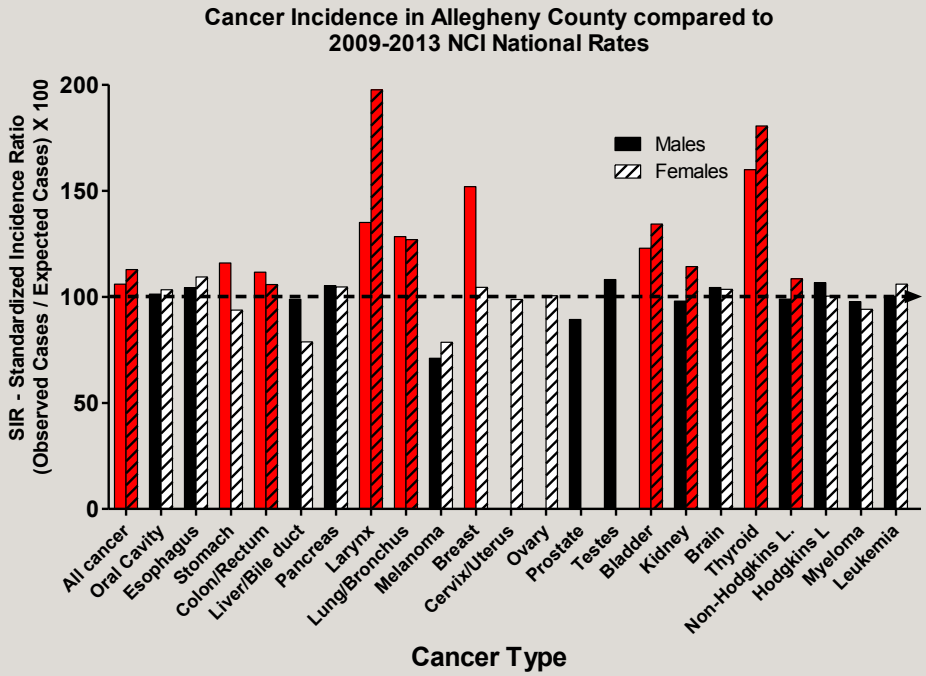
Similar analysis using 2011 NATA data for Allegheny County. (Excluding DPM)

John Graham
Boston, MA

- Allegheny county ranked 21st out of 3,200 US counties (top 1%) for cancer risk from HAPs (57 per million people).
- Only 0.2% of ≈78,000 census tracts in the US had HAP cancer risk > 100 per million people, but 12% of those were located in Allegheny county.
- Almost 40% of that risk was attributed to **point source** emissions, which is nearly 20X greater that of urban counties in general.
- Amongst **all** US counties, Allegheny County ranks third in cancer risk from **point source** emissions.

PA has high rates of cancer

- PA ranked third highest in overall cancer rate in the US *(CDC, 2013*).
- Rates of lung, laryngeal, bladder, and thyroid cancer in Allegheny County exceed national averages *(PA-DOH, 2009-2013)*

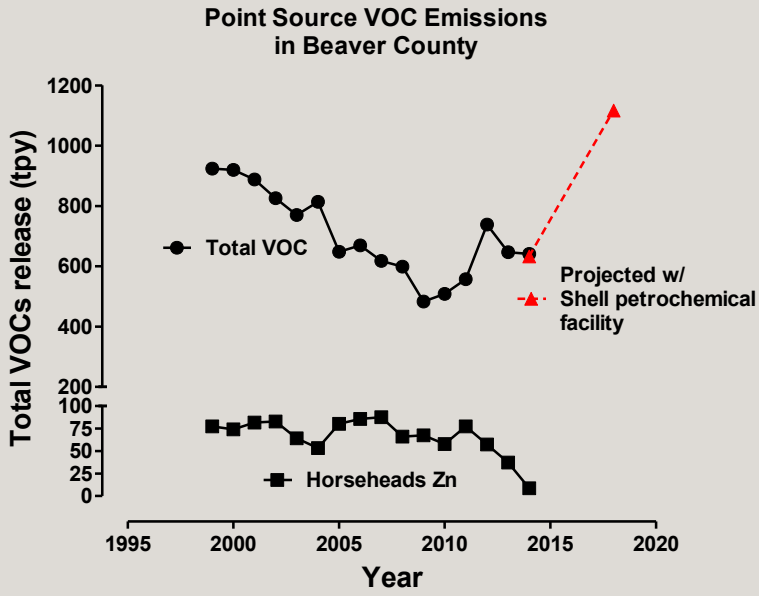


- Mortality from lung cancer, C-V and respiratory disease exceed national averages in 14 SWPA counties **after correcting for smoking**. Between 12 - 13,000 excess deaths during that time period. *(http://scienceblogs.com/thepumphandle/2010/12/15/the-pittsburgh-post-gazette-co/)*

What does the future hold?

- Multiple data sources examined over the last decade highlight:
  - Pervasive, geographic variability, and persistence.
- Emerging and novel potential pollution sources.

Source: Pennsylvania Department of Community and Economic Development



PA-DEP Facility Emission Inventories

- A changing and challenging political landscape.

Respondent

DR. MARSHA HALEY
Magee Women's Hospital – University of Pittsburgh Medical Center

Respondent

DR. EDWARD KETYER
Pediatric Alliance

Respondent

DR. MATT MEHALIK
Air Quality Collaborative

Community Organizations Engaged in Improving Air Quality in Southwestern Pennsylvania

HOMEWOOD CHILDREN'S VILLAGE
http://hcvpgh.org

WOMEN for a Healthy ENVIRONMENT
http://www.womenforahealthyenvironment.org

CLEAN WATER ACTION
http://www.cleanwateraction.org

CREATE Lab
Community Robotics, Education and Technology Empowerment
http://www.cmucreatelab.org

SUSTAINABLE PITTSBURGH
Our Region. Our Resources. Our Future.
http://sustainablepittsburgh.org

go GREEN BUILDING ALLIANCE
https://www.go-gba.org

PennFUTURE
http://www.pennfuture.org

GASP
http://gasp-pgh.org

CLEAN AIR COUNCIL
http://cleanair.org

SOUTHWEST PENNSYLVANIA ENVIRONMENTAL HEALTH PROJECT
http://www.environmentalhealthproject.org

ALLEGHENY COUNTY CLEAN AIR NOW ACCAN
https://www.facebook.com/AghCoCAN/

PennEnvironment
http://www.pennenvironment.org

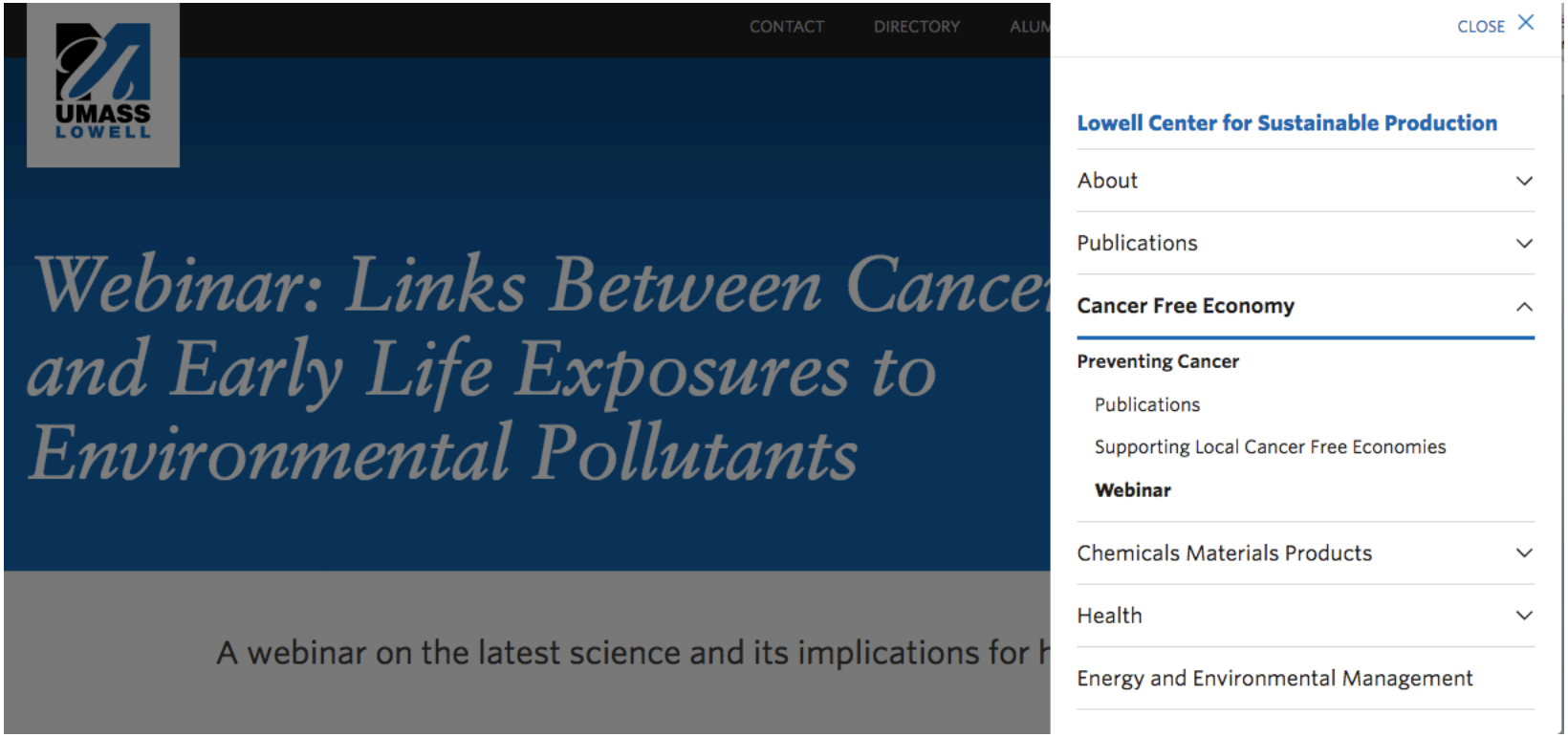
EIP ENVIRONMENTAL INTEGRITY PROJECT
http://www.environmentalintegrity.org

AMERICAN LUNG ASSOCIATION. OF THE MID-ATLANTIC
http://www.lung.org

Webinar Audio & Slides

The audio recording and slides shown during this presentation will be available by next week at:

https://www.uml.edu/Research/Lowell-Center/Cancer-Free-Economy/Preventing-Cancer/webinar.aspx



Thank you for attending!

Evaluation survey to follow by email

Questions? Contact: molly_jacobs@uml.edu