Environmental Chemicals and the Development of Cancer: a Public Health Perspective

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No financial relationships to disclose

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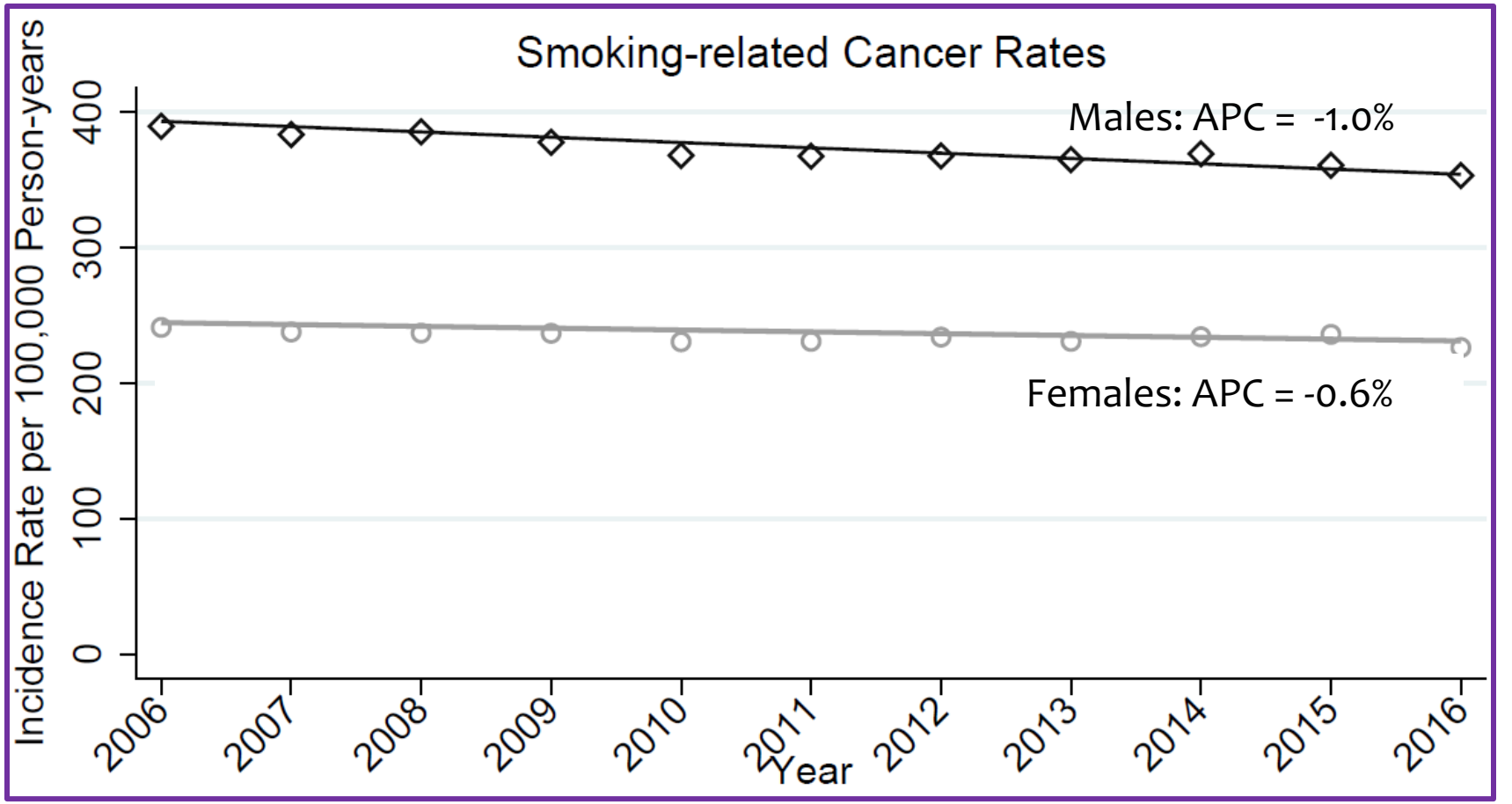
Cancer prevention: how are we doing?

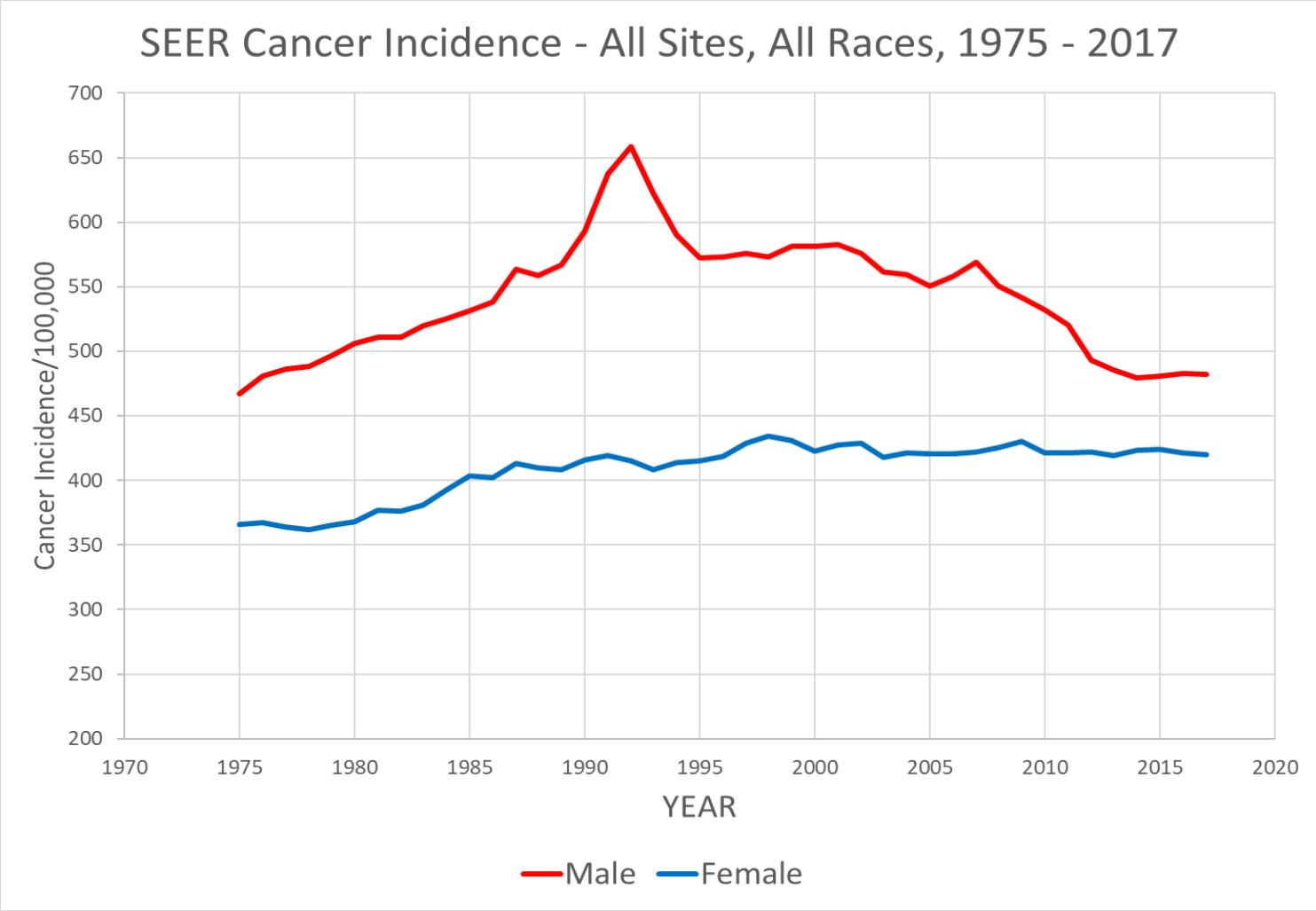
- There has been important progress on several fronts:
  - Tobacco control
  - UV radiation education and prevention
  - Radon monitoring and control
  - Cancer screening programs
    - (secondary prevention)

There has been a decrease in incidence of 12 types of cancer thanks to the decline in smoking

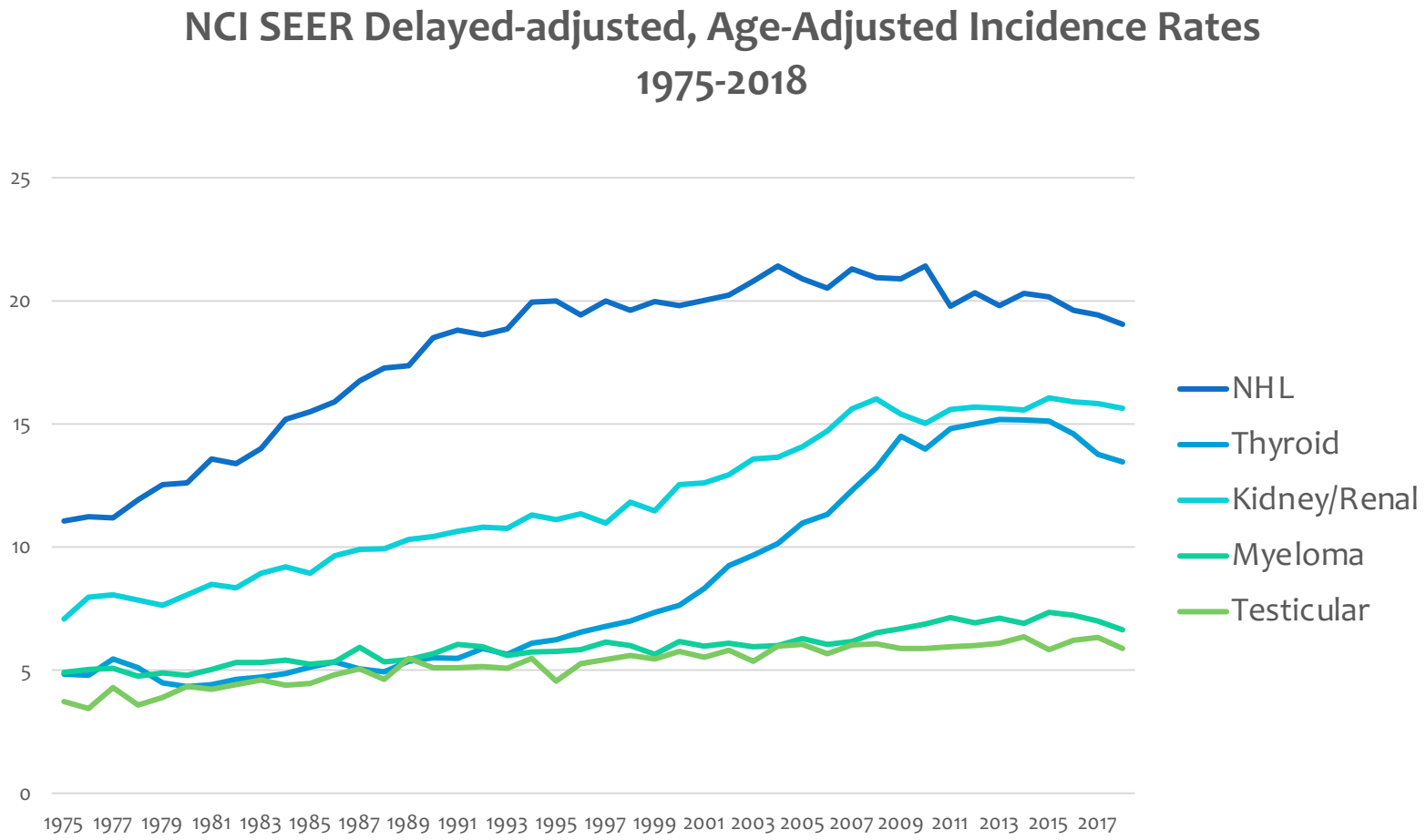


Source: Myers et al. Environmental Health (2020) 19:64 https://doi.org/10.1186/s12940-020-00613-x

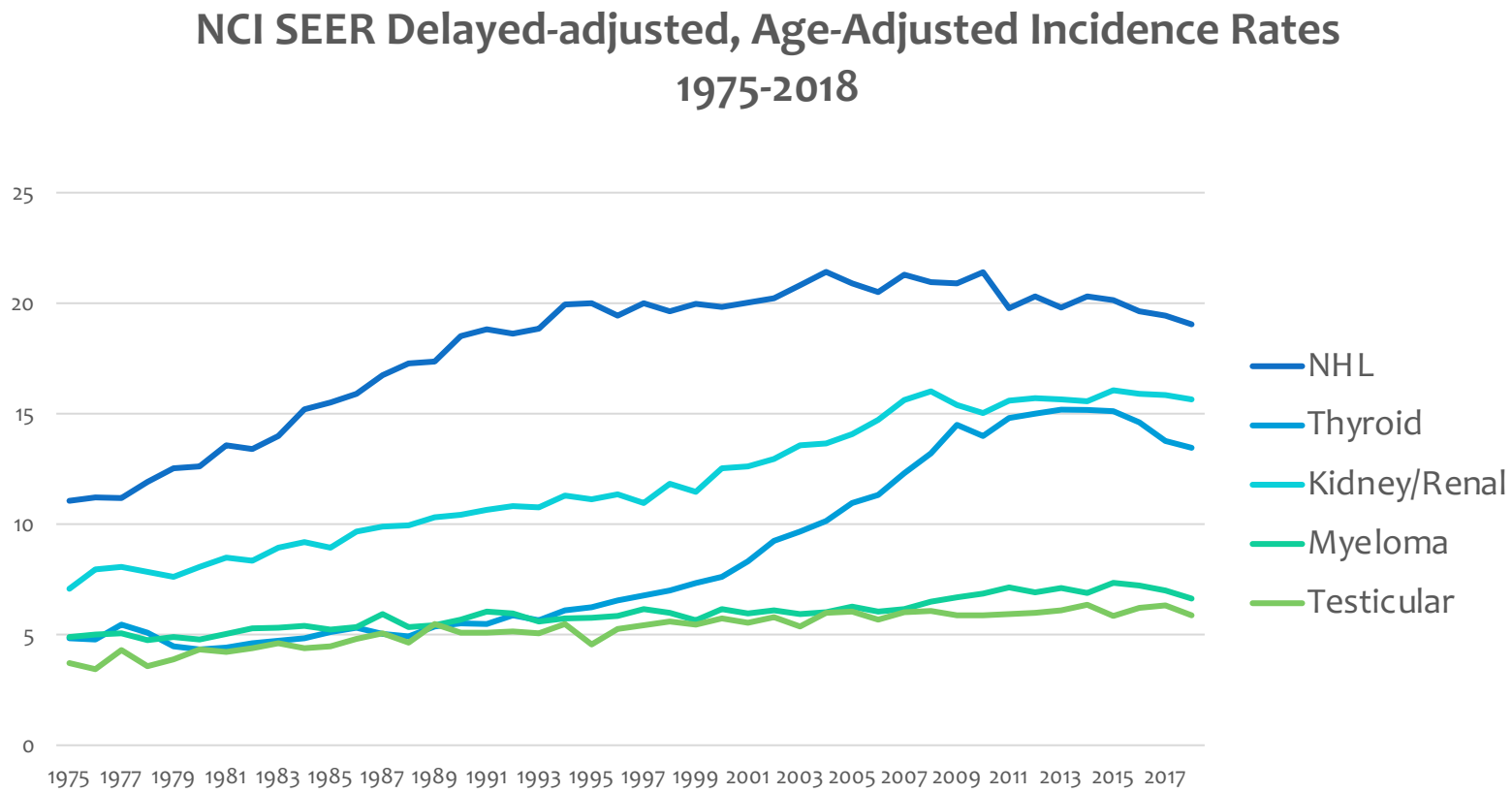
But long-term trends for cancer overall suggest we still have much work to do



There are concerning trends for a number of different types of cancer



These 5 types of cancer all show rising long-term incidence trends, and all have well-established environmental causes

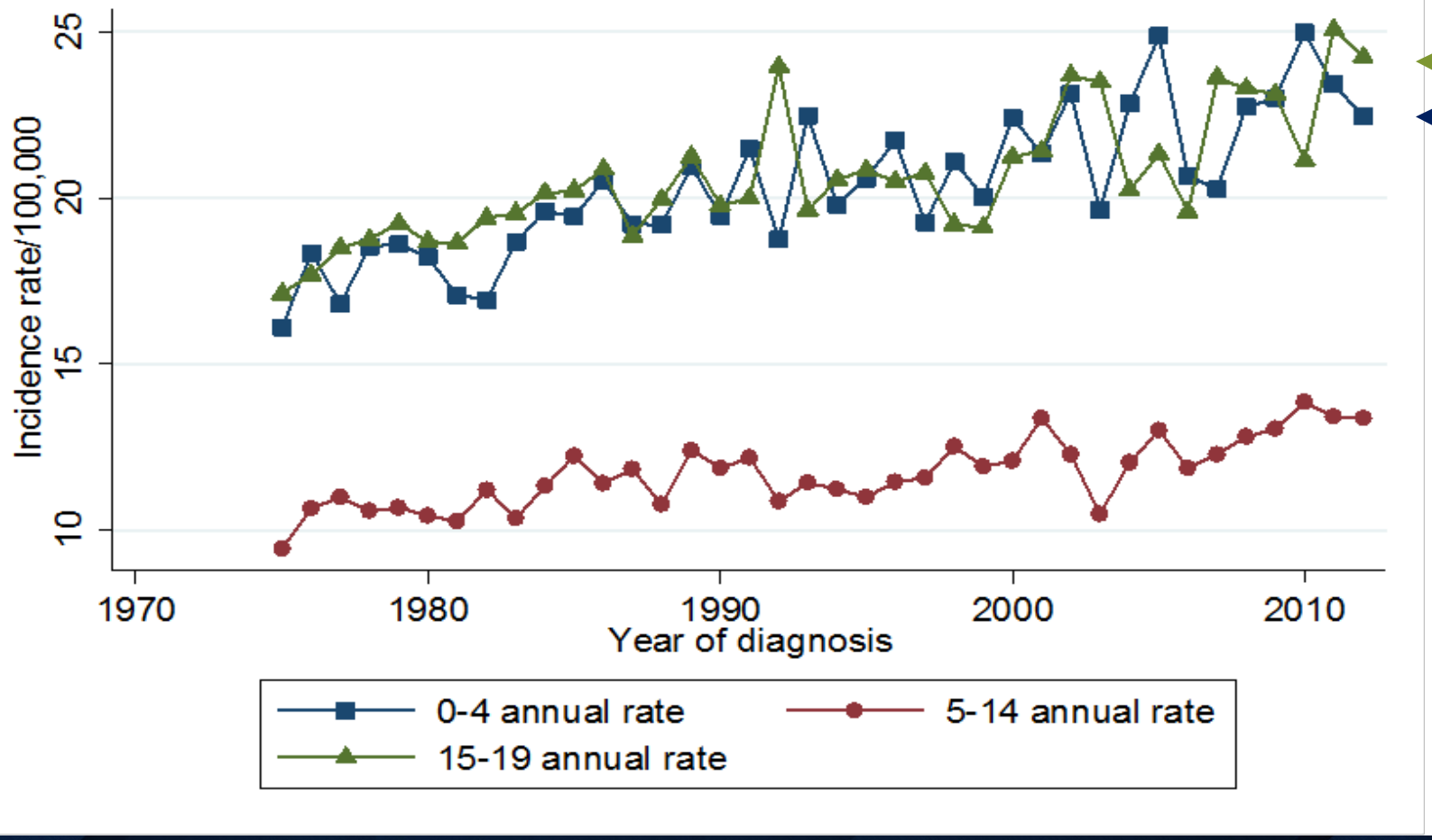


And, while tobacco is a very important preventable cause of cancer, there are many type of cancer not affected by smoking

- Taken as a group, all cancers NOT affected by smoking increased in incidence by 25% between 1975 – 2004

Han Y-Y, et al. Cancer Causes Control. 2010;21(8):1227–36.

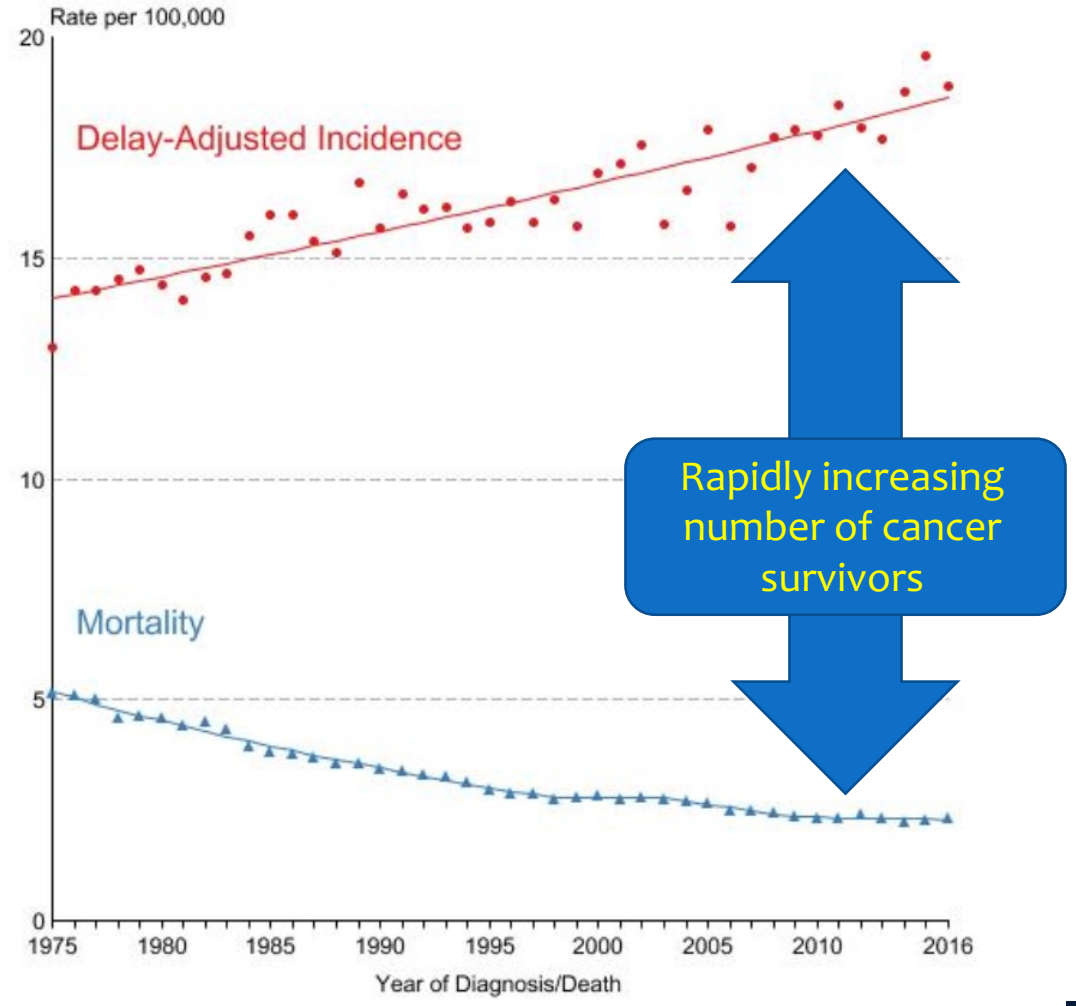
Among U.S. children the incidence of all types of cancer has risen 26% since 1975.



The trend is particularly strong in infants and teenagers

Childhood cancer deaths have been falling for 35 years…

But the numbers of kids getting the disease rises steadily



Source: SEER 9 areas and US Mortality Files (National Center for Health Statistics, CDC).
Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).
Regression lines are calculated using the Joinpoint Regression Program Version 4.7, February 2019, National Cancer Institute.

All cancers, <20 years old

7 most common cancer sites in teenagers

- Non-Hodgkin's lymphoma (NHL) - **Increasing**
- Acute lymphoblastic leukemia (ALL) - **Increasing**
- Thyroid - **Increasing**
- Testicular - **Increasing**
- Brain and other central nervous system (CNS) tumors – Increasing (marginally)
- Ovarian - **Steady**
- Hodgkin's disease (HD) - **DECREASING**

The reasons for rising cancer incidence trends are uncertain and complex. But in the broadest sense, they are "environmental"

- 10 – 30% of all cancers may be due solely to genetic factors
  - that is, they would not be preventable by any exogenous factors
- 70 – 90% are the result of environmental factors
  - radiation, chemical exposures, diet and other aspects of personal "lifestyles"

There is also evidence of environmental role in prognosis, recurrence, morbidity

- Prognosis/Survival
  - bisphenol A may increase aggressiveness of breast cancer tumors Cancer Res. 2008 Apr 1;68(7):2076-80
  - reduced survival of lung cancer patients with higher air pollution exposures Thorax. 2016 Oct; 71(10): 891–898.
  - reduced survival of stage 1 breast cancer patients exposed to PM air pollution Cancer Epidemiol Biomarkers Prev. 2019 Apr;28(4):751-759
- Morbidity
  - Chemotherapy-treated childhood cancer survivors have higher rates of respiratory hospitalizations Int J Environ Res Public Health. 2019 Mar 26;16(6):1081.

Parkin estimated that 45% of cancers in men, 40% in women in the U.K. could be prevented by altering known risk factors

- Including:
  - tobacco,
  - alcohol,
  - diet,
  - overweight,
  - lack of physical exercise,
  - occupation,
  - infections,
  - radiation,
  - reproductive history

Parkin DM, et al. British Journal of Cancer (2011) 105, S77 – S81

What we do know about the identity of environmental chemical carcinogens?

- Animal studies, in vitro toxicology, human epidemiology all contribute evidence

- National & international expert panels evaluate evidence and classify chemicals
  - National Toxicology Program (NTP)
  - International Agency for Research on Cancer (IARC)

The International Agency for Research on Cancer (IARC) has evaluated nearly 1,000 chemicals/processes for carcinogenicity:

IARC Carcinogen Assessments

• Carcinogenic to humans	121
• Probably carcinogenic to humans	89
• Possibly carcinogenic to humans	319
• Not classifiable	500

Source: https://monographs.iarc.who.int/agents-classified-by-the-iarc/

We are exposed to many of these – legally and routinely

IARC Carcinogen Assessments

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About 40% are industrial chemicals – moving through the economy with varying and sometimes complex points of exposure to humans

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Source: https://monographs.iarc.who.int/agents-classified-by-the-iarc/

There is good evidence that certain chemicals cause specific cancer types

- **Kidney cancer**
  - Trichloroethylene (TCE), cadmium
- **Leukemia**
  - Styrene, formaldehyde, 1,3-butadiene, TCE, benzene, ethylene oxide, traffic pollution
- **Liver cancer**
  - Methylene chloride, nickel compounds, PCBs, TCE
- **Non Hodgkin's Lymphoma**
  - Dioxin, 1,3-butadiene, benzene, formaldehyde, PCBs, TCE, PCE

Sources: President's Cancer Panel Report (Appendix F), 2008-2009; Cogliano, et al. JNCI 2011;103:1827-1839; Siemiatycki et al. Environ Health Perspect 2004;112:1447-1457.

But this list is not fixed!

Only a fraction of all chemicals in widespread use have been tested – even in animals

IARC Carcinogen Assessments

- Carcinogenic to humans 121
- Probably carcinogenic to humans 89
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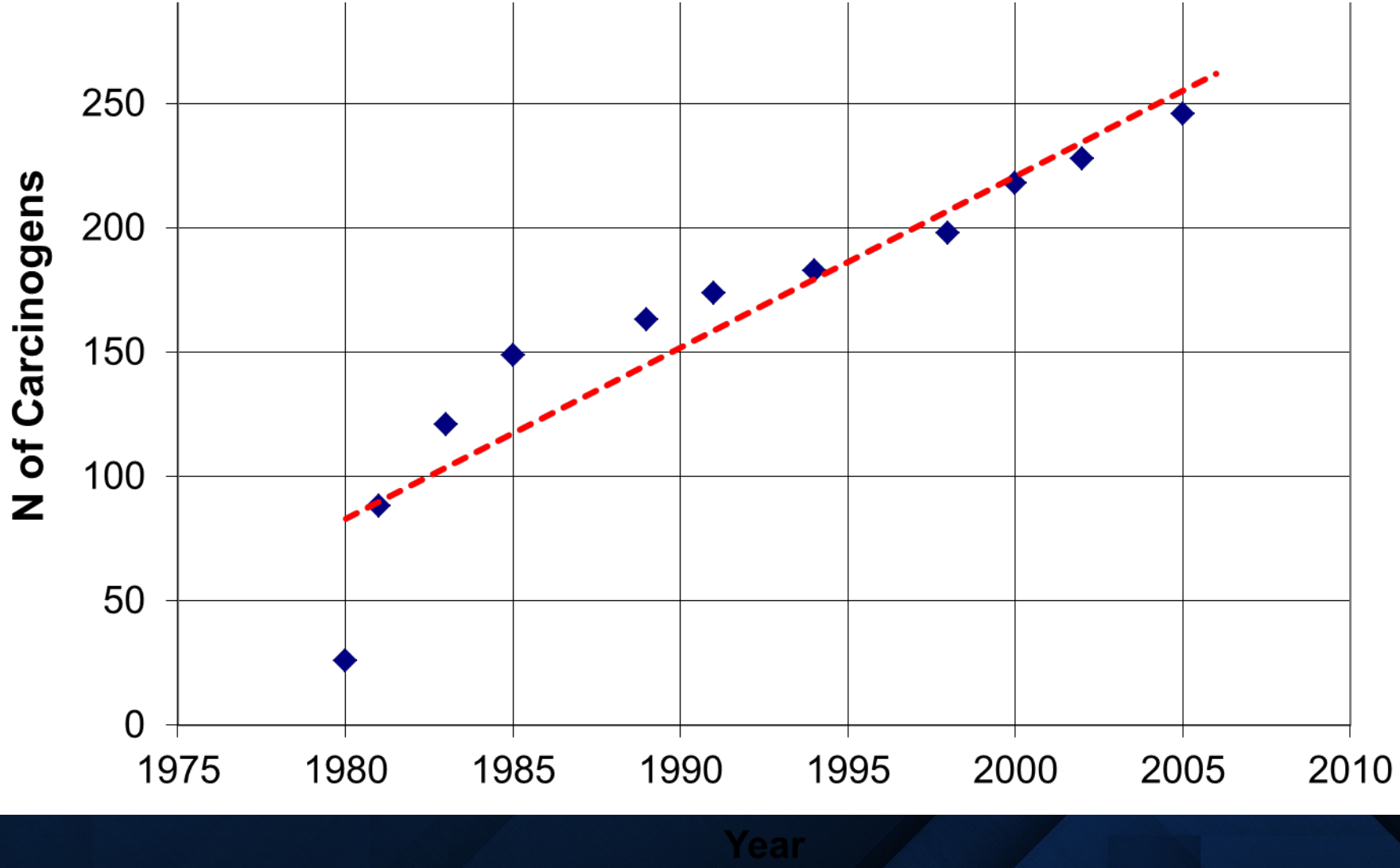
Only a few percent of the ~85,000 chemicals in use have been tested for carcinogenicity

- Of these ~85,000 chemicals on the market:
  - there are approximately ~2,500 considered “high production volume” – more than 1 million pounds/year
  - even among these, only a small fraction have been thoroughly evaluated for carcinogenicity

There are certainly many more carcinogens yet to be identified. The NTP identifies about 7 “new” carcinogens/year



More challenges to identifying carcinogens: complex mixtures and "Deconstructed Carcinogens"

- We are all exposed to a constantly varying complex mixture of synthetic chemicals
  - Our "Exposomes"

Exposome: some examples

- Oxybenzone
  - widely used sunscreen ingredient
  - reproductive toxin, endocrine disruptor, possibly carcinogenic
  - 98% of US population has detectable urinary concentrations
  - found in amniotic fluid, cord blood, semen, breast milk

Exposome: some examples

- Perfluorinated compounds: PFOS, PFOA
  - “forever chemicals”
  - waterproof clothing, food wrappers, firefighting foam
  - contaminant in aquifers, municipal water supplies
  - reproductive and developmental toxins, endocrine disruptors
  - ubiquitous in human tissues

The intergenerational exposome

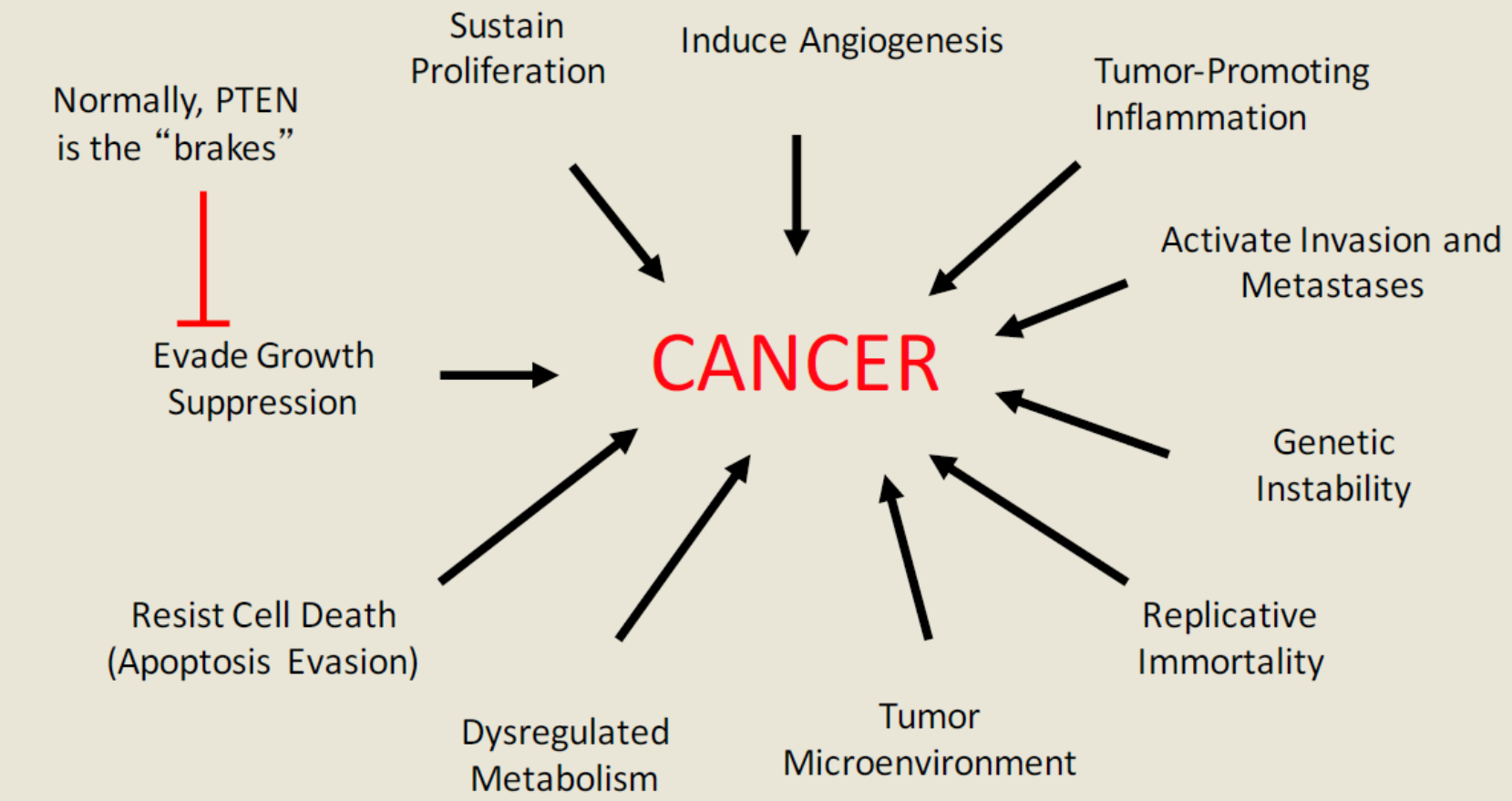
- Pregnant women in U.S. have at least 43 environmental chemicals in their bodies
  - babies are born, “pre-contaminated”

Deconstructed carcinogens

- Many of the synthetic organic chemicals in our exposomes are carcinogens

- But there is another complexity:
  - chemicals which are not themselves “complete” carcinogens can contribute to cancer by triggering one step in the multi-stage process of transforming a normal cell into a cancerous one

Hallmarks of Cancer *or* Cancer is not a One-Step Process



Slide courtesy William H. Goodson III, MD

Drawn from Weinberg and Hanahan, 2011

The exposome can be carcinogenic

- Mixtures of chemicals may act collectively and synergistically to affect cancer development
  - how often do “deconstructed carcinogens” cause cancer?
    - we don’t know
  - but eliminating exposure to noncarcinogens may also reduce the cancer burden

The exposome can be carcinogenic

- 85 chemicals not currently classified as carcinogens were active towards one or more cancer hallmarks
- Review by the Halifax Project
  - *Carcinogenesis*, 2015, Vol. 36, Supplement 1, S254–S296 doi:10.1093/carcin/bgv039

How important are toxic chemicals in the cancer epidemic?

- We don't know for certain
  - How could we know when thousands have never been tested?
  - We know even less about combinations of risk factors
- Less than 10% of National Cancer Institute's budget is focused on primary prevention
  - majority of funding focused on treatment

How important are toxic chemicals in the cancer epidemic?

- At least 5% of cancer in the U.K. due to workplace carcinogens (Rushton 2008)
  - counting known carcinogens only (of course)
  - considering only high exposure scenarios

- Air pollution? Certainly important -
  - Diesel exhaust alone may account for 5% of lung cancer

How important are toxic chemicals in the cancer epidemic?

- Beware of calculations of "attributable fractions" of cancer due to different causes
  - these are often little more than guesses
  - all cancers have multiple causes
  - any single case of cancer could probably have been prevented by removing several different causal factors (Hallmarks)

  - some carcinogens are well-studied, many are not

We think there is good evidence that toxic chemicals are contributing to the rising incidence of many types of cancer.

- Rising incidence trends over the past 30 years
  - too rapid to be explained by genetics
- An ever-growing list of cancer causing chemicals in air, water, food and products
- Epidemiologic evidence that populations with high exposures to many carcinogens have increased cancer risk

But how important are environmental carcinogens compared to the well-established unhealthy behaviors?

- American Cancer Society recently estimated the contributions to total cancer incidence from unhealthy behaviors
  - tobacco smoking: 19%
    - 46% of incidence of 12 smoking-related types
  - excess body weight: 7.8%
  - alcohol: 5.6%
  - physical inactivity: 2.9%

Islami F, et al. CA Cancer J Clin. 2018;68(1):31–54.

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In other words, completely eliminating smoking would reduce the incidence of the 12 smoking-related cancer types by less than half

- We recently analyzed the cancer incidence data for these 12 cancer types, 2006 – 2016 in 612 counties reporting to the SEER registries
  - we simulated total smoking cessation
  - we found the same overall reduction in cancer incidence as the ACS

Myers et al. Environmental Health (2020) 19:64 https://doi.org/10.1186/s12940-020-00613-x

But not all counties would benefit equally from smoking cessation

- Counties with high smoking prevalence would benefit a lot from eliminating smoking
  - And counties that already have low smoking rates have less "room for improvement"
- But some counties with average smoking rates would benefit very little from eliminating smoking
  - why?

Myers et al. Environmental Health (2020) 19:64 https://doi.org/10.1186/s12940-020-00613-x

But not all counties would benefit equally from smoking cessation

- 5 counties with high predicted cancer rates even after eliminating smoking were all in the metropolitan areas of large cities:
  - Jefferson County KY (Louisville)
  - Wayne and Macomb counties MI (Detroit)
  - Campbell County KY (Cincinnati)
  - Jefferson Parish LA (New Orleans)

- These 5 counties would see only an approximate 8% reduction in their rates of smoking-related cancers
  - far less than the overall average of about 40%, after total smoking elimination.

But not all counties would benefit equally from smoking cessation

- We hypothesize that environmental chemicals play a more important role in carcinogenesis in these urban counties
  - These toxic exposures would “off-set” the benefits that should come from smoking cessation, according to the simulation

In summary:

- Rates of many types of cancer are rising
- There is a long and growing list of chemicals that may be contributing to cancer
- Eliminating chemical carcinogens would prevent cancer
  - there is uncertainty about how big the benefit would be

If cancer rates are rising, and there are chemicals we know cause cancer, why not get rid of them?

- We have good examples of cases in which cancer chemicals are removed and cancer risk falls –
  - workplaces,
  - air pollution,
  - smoking (active & passive)

Opportunities for cancer prevention

- Removing carcinogens and other toxic chemicals from the environment – look for synergies and additional benefits
  - improved building ventilation
    - reduces COVID-19 risk, and radon exposure
  - reduce household use of organic solvents
    - eliminates fire hazard and carcinogen exposures
  - support all-electric new home construction
    - reduces green house gases and indoor air pollution

How shall we set priorities for prevention?

- A systems approach – set priorities based on:
  - cancers with elevated incidence
  - elevated exposures to known carcinogens
  - communities already suffering other health impacts
  - availability of alternatives to the toxic substance
- And most importantly:
  - get all the relevant communities around the table

Acknowledgments

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- Doug Myers, ScD, Boise State University

The Garfield Foundation
The Heinz Endowments

MANUFACTURED CHEMICALS TODAY

- There are currently 235,000 chemicals in commerce
- Mostly are new materials invented since 1950. Never before existed on earth
- Used in millions of consumer products
- Widely disseminated in the environment – from the high Arctic to the ocean depths.
- Nearly universal human exposure – including pregnant women and newborn infants
- Disproportionately heavy exposure of the poor and minorities – environmental injustice
- Global chemical production is increasing by 3.5% annually. Doubling time of 25-30 yrs
- **The great majority – 80-90% - of chemicals in commerce have never been tested for safety or toxicity**

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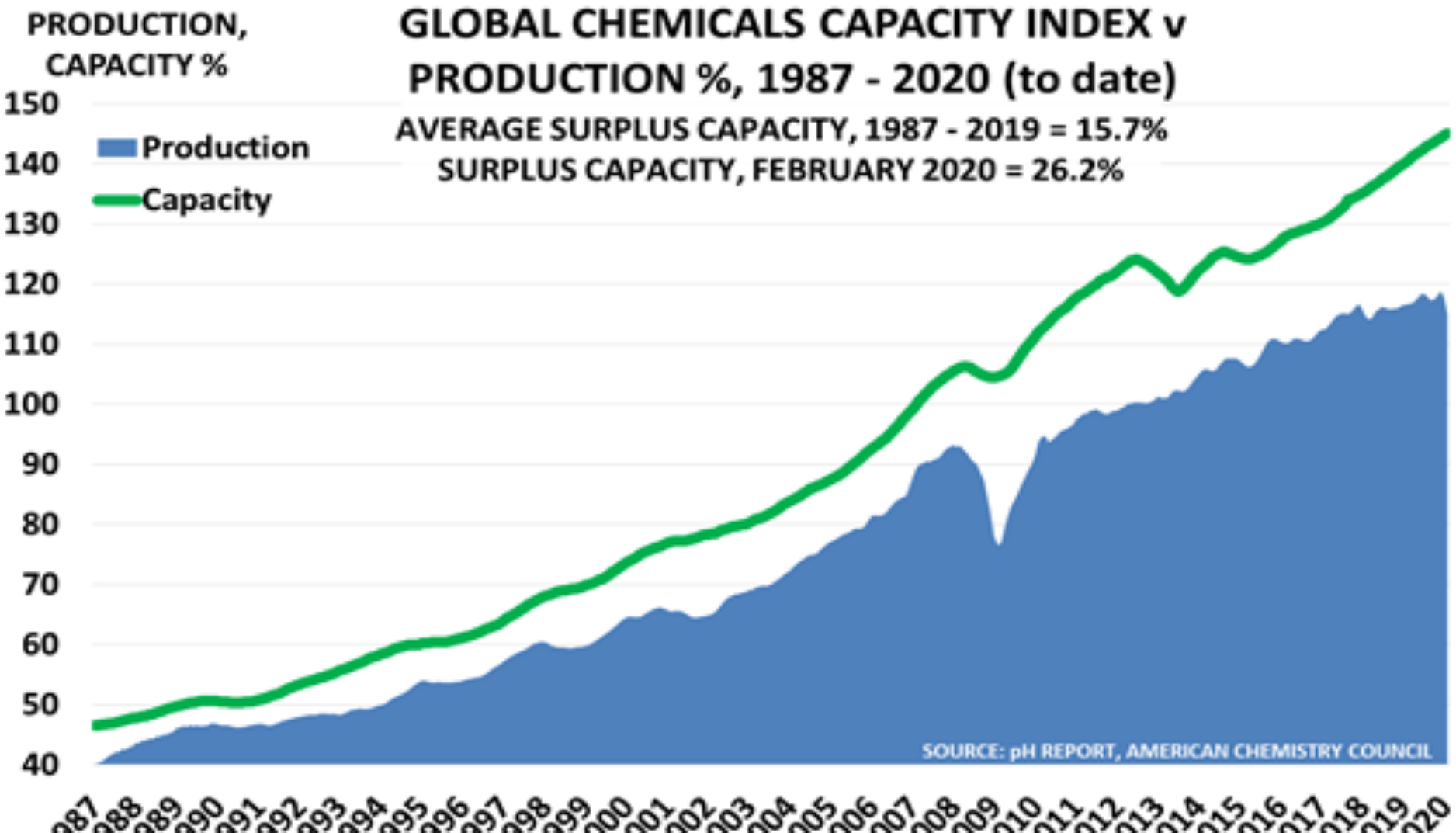
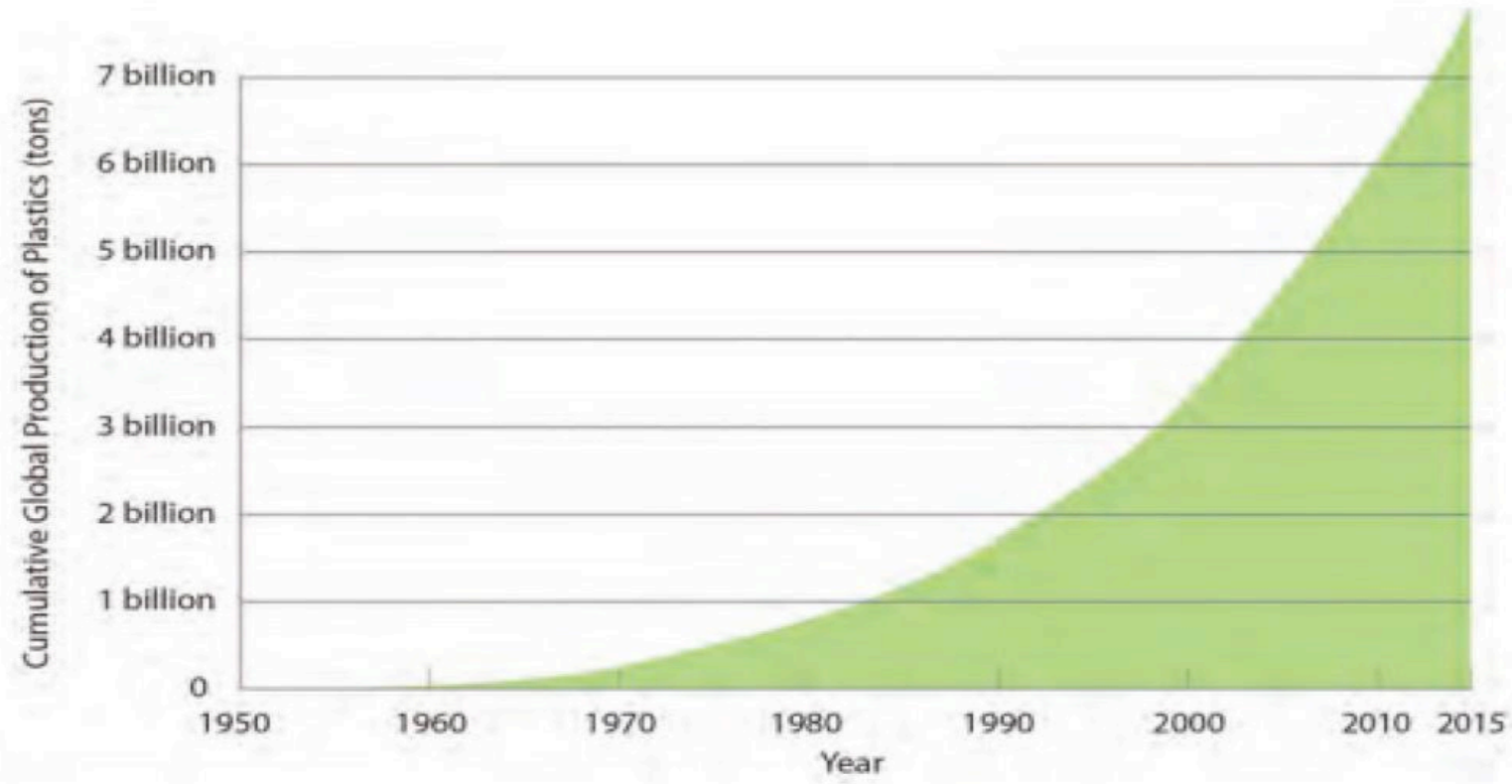
GLOBAL PRODUCTION OF MANUFACTURED CHEMICALS



GLOBAL PRODUCTION OF PLASTIC



NEW CHEMICALS ARE INTRODUCED WITH GREAT ENTHUSIASM BUT LITTLE DUE DILIGENCE…

…AND THEN BELATEDLY ARE FOUND TIME AND AGAIN TO CAUSE GREAT HARM TO THE ENVIRONMENT AND TO HUMAN HEALTH

NEED FOR A NATIONAL CANCER PREVENTION PLAN

- Require testing of all consumer chemicals for carcinogenicity before they come to market
- Conduct research to discover the environmental causes of cancer in children. Research is essential for evidence-based prevention
- Deploy a risk assessment paradigm for cancer prevention that explicitly recognizes the unique vulnerability of fetuses, infants and children.
- Act on what we know. Deploy the precautionary principle because we cannot test our way out of the current mess.
- Avoid use of manufactured chemicals and plastics wherever possible

A SECOND FRONT IN THE WAR ON CANCER

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THE GOOD NEWS: PREVENTION IS POSSIBLE

Studies showing environmental harm to children are powerful drivers of progress

REMOVAL OF LEAD FROM GASOLINE AS A CASE STUDY

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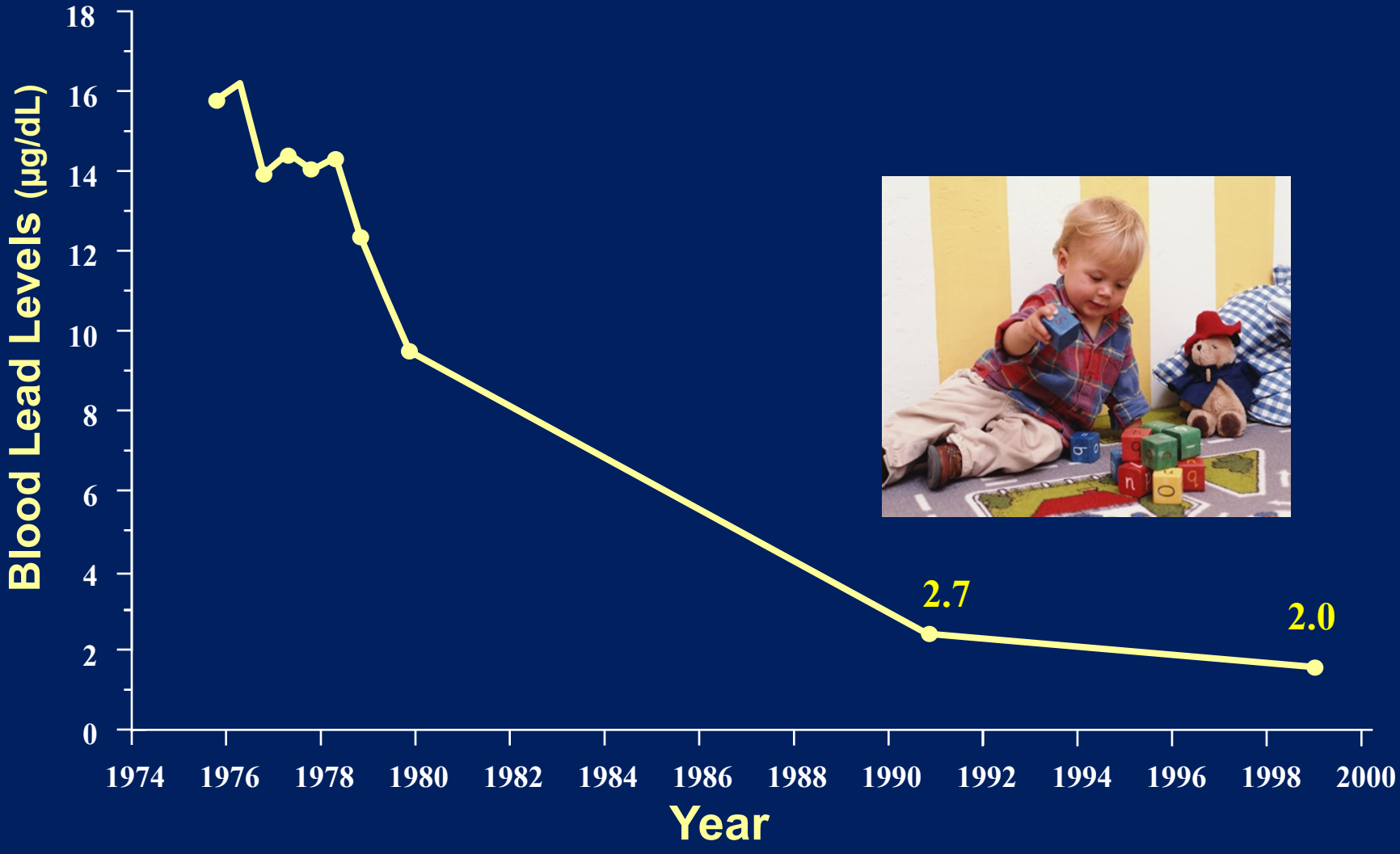
RAPID FALL IN BLOOD LEAD LEVELS FOLLOWING REMOVAL OF LEAD FROM GASOLINE



A FINAL THOUGHT FOR THOSE WHO PROVIDE CLINICAL CARE

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

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Environmental Chemicals and Impact on Cancer Prevention

This webinar will be archived at: https://chronicdisease.org/page/cancerprograms/cancer-prevention-across-the-lifespan/

- Lowell Center for Sustainable Production: https://www.uml.edu/research/lowell-center/
- Global Public Health and the Common Good: https://www.bc.edu/bc-web/centers/schiller-institute/programs/global-public-health.html
- CDC Cancer Prevention Across the Lifespan: https://www.cdc.gov/cancer/dcpc/prevention/lifetime.htm

Integrating Environmental Chemicals into Cancer Prevention

Polly Hoppin, ScD

Lowell Center for Sustainable Production/U. Mass. Lowell

Cancer Free Economy Network

October 20, 2021

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NACDD Survey of State Cancer Programs

Environmental Health Questions
Spring, 2020

- Have you included environmental chemicals in state cancer plans?
  - 74% yes; 26% no
- Which sources of environmental carcinogens are most important?
  - Radon, IAQ, air pollution, pesticides, water, point sources, climate-related, hazardous wastes, consumer products, household chemicals and others
- Resources needed to move beyond environmental risk management to a focus on prevention
  - Improved knowledge of evidence-based and/or promising interventions
  - Dedicated program and data staff
  - Support from partners
  - Support of admin leadership
- Webinar topics of interest
  - Identifying key environmental problems
  - Knowledge about evidence-based interventions, including specific risk factors
  - How to engage important partners and stakeholders

Webinar Series

- Webinar #1
  - Grounding in systems change
  - Key foundational information and concepts
- Webinar #2
  - Identifying priority environmental chemicals-related risk factors
  - Evidence-informed interventions
- Webinar #3
  - Policies and partnerships
- Webinar #4
  - Social determinants
  - Centering equity in knowledge creation and leadership

Lowell Center for Sustainable Production

Sustainability Solutions Science

Collaboration with Toxics Use Reduction Institute

Public Health Framework +

- Surveillance – Who is at risk?
- Risk and protective factors—What are causes?
- Interventions on modifiable risk factors—What works for whom?
- Implementation—Scale up effective interventions

+ Strategic engagement for systems change

National/regional/local systems change initiatives

GROWING CONSENSUS ON CONTRIBUTION OF ENVIRONMENTAL CHEMICALS TO CANCER

International Federation of Gynecology and Obstetrics (FIGO) Opinion on Reproductive Health Impacts of Exposure to Toxic Environmental Chemicals

Gian Carlo Di Renzo[1], Jeanne A. Conry[2], Jennifer Blake[3], Mark S. DeFrancesco[2], Nathaniel DeNicola[2], James N Martin Jr.[2], Kelly A. McCue[2], David Richmond[4], Abid Shah[4], Patrice Sutton[5], Tracey J. Woodruff[5], Sheryl Ziemin van der Poel[6], Linda C. Giudice[7]

[1]International Federation of Gynecology and Obstetrics

[2]American College of Obstetricians and Gynecologists

[3]Society of Obstetricians and Gynaecologists of Canada

[4]Royal College of Obstetricians and Gynaecologists

[5]University of California San Francisco, Program on Reproductive Health and the Environment

[6]World Health Organization

[7]American Society for Reproductive Medicine

AACR Conference Features Latest Research on Impact of Environmental Carcinogens and Potential Pathways to Cancer Prevention

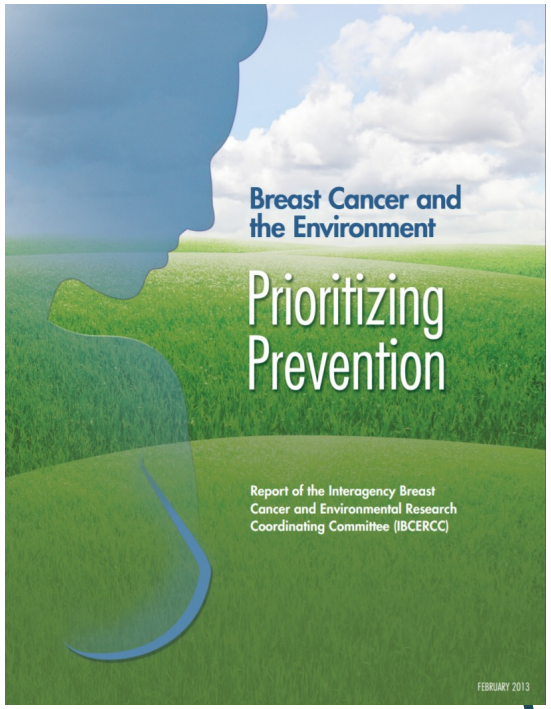
June 21, 2019

AACR American Association for Cancer Research VIRTUAL ANNUAL MEETING II JUNE 22-24, 2020

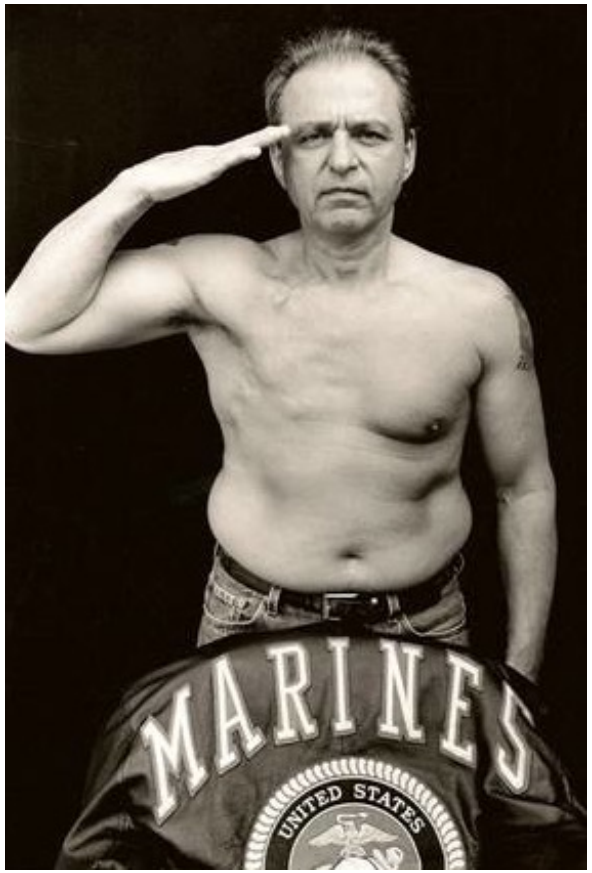
EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals

A. C. Gore, V. A. Chappell, S. E. Fenton, J. A. Flaws, A. Nadal, G. S. Prins, J. Toppari, and R. T. Zoeller

Pharmacology and Toxicology (A.C.G.), College of Pharmacy, The University of Texas at Austin, Austin, Texas 78734; Division of the National Toxicology Program (V.A.C., S.E.F.), National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina 27709; Department of Comparative Biosciences (J.A.F.), University of Illinois at Urbana-Champaign, Urbana, Illinois 61802; Institute of Bioengineering and CIBERDEM (A.N.), Miguel Hernandez University of Elche, 03202 Elche, Alicante, Spain; Departments of Urology, Pathology, and Physiology & Biophysics (G.S.P.), College of Medicine, University of Illinois at Chicago, Chicago, Illinois 60612; Departments of Physiology and Pediatrics (J.T.), University of Turku and Turku University Hospital, 20520 Turku, Finland; and Biology Department (R.T.Z.), University of Massachusetts at Amherst, Amherst, Massachusetts 01003

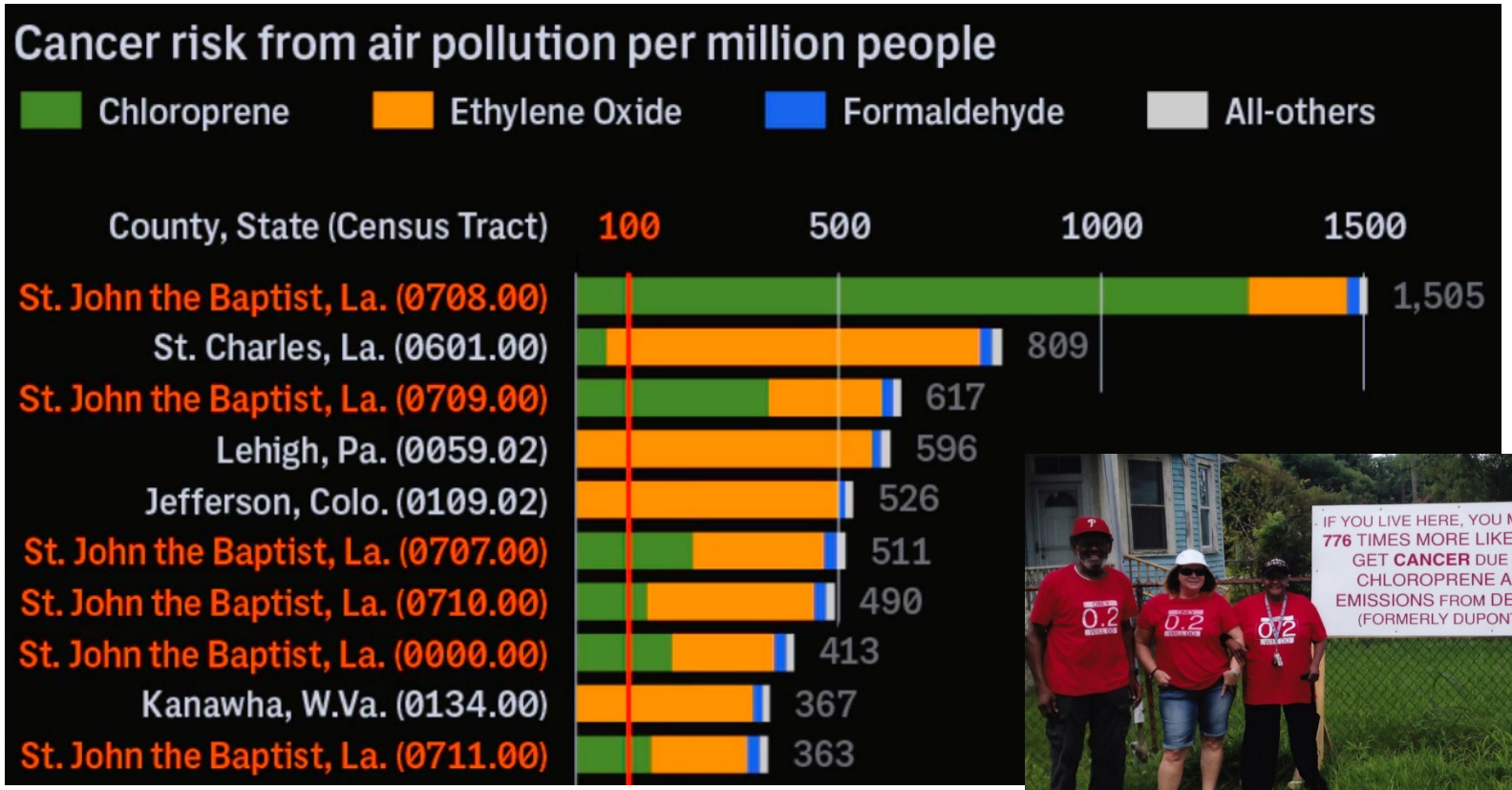


Legacy Exposures: Cancer in Camp Lejeune, NC



- Drinking water contamination (1953-1987)
- Studies have found:
  - Increased risk of bladder and kidney cancer
  - Non-statistically significant increased risk of male breast cancer (strongest association w/ PERC)
  - Non-statistically significant associations for childhood cancer (leukemia and NHL) with maternal exposure during (1st trimester)
- VA established a presumptive service connection for specific cancers (e.g., bladder, leukemia, kidney, liver, NHL and MM) with service at Camp Lejeune (1953 -1987)

Ongoing Exposures:
Cancer in St. John the Baptist Parish, LA



Source: The Intercept, 2014 National Air Toxics Assessment Data, U.S. EPA

Of the top 10 census tracts in counties with the highest cancer risks due to industrial air pollutants, 6 are in St John the Baptist in LA

Cancer risk from toxic chemicals: how can systems thinking help?

US chemicals policy does not require testing before marketing

Minimal investment in understanding health impacts, and limited data

Industry claims lack of scientific evidence; opposes regulation

Scientific norms seek certainty in conclusions about risks

Government and health scientists reinforce dominant narrative of small problem or "no proof"

Public is confused/ accepts health problems as inevitable

Regulation remains weak

Collaborative Networks for Systems Change

- Systems approach
  - Investigate why the system is stuck and opportunities for shifting dynamics
  - Engage people and groups that can influence different parts of the system
- Collaborate to:
  - Share information, learn together
  - Lift up aligned efforts of participating organizations and generate additional support towards common goal
  - Develop strategic initiatives uniquely possible because of particular collection of groups

CANCER FREE ECONOMY NETWORK

Cancer & Environment Network of Southwestern Pennsylvania