

Re-envisioning Carcinogenicity Assessment @ NTP

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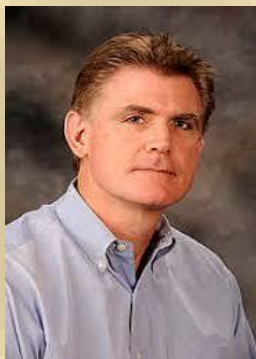
NTP Board of Scientific Counselors

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“To improve public health through the development of data and knowledge that is *translatable, predictive and timely.*”



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Human Relevant & Impactful



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Types of Breast Cancer

- [Ductal Carcinoma In Situ \(DCIS\)](#)
- [Invasive Ductal Carcinoma \(IDC\)](#)
- [IDC Type: Tubular Carcinoma of the Breast](#)
- [IDC Type: Medullary Carcinoma of the Breast](#)
- [IDC Type: Mucinous Carcinoma of the Breast](#)
- [IDC Type: Papillary Carcinoma of the Breast](#)
- [IDC Type: Cribriform Carcinoma of the Breast](#)
- [Invasive Lobular Carcinoma \(ILC\)](#)
- [Inflammatory Breast Cancer](#)
- [Lobular Carcinoma In Situ \(LCIS\)](#)
- [Male Breast Cancer](#)
- [Molecular Subtypes of Breast Cancer](#)
- [Paget's Disease of the Nipple](#)
- [Phyllodes Tumors of the Breast](#)
- [Metastatic Breast Cancer](#)





How many cancers are caused by exposure to carcinogens in the environment?

~4-20%

But the precise causes of most cancers are not known

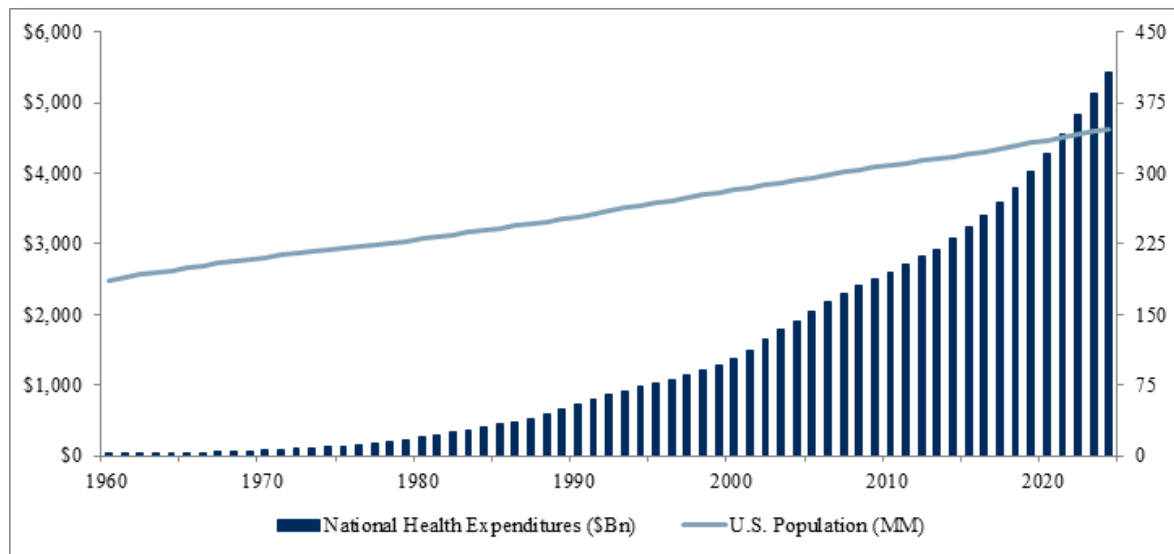




What Are the Costs of Cancer?

The Agency for Healthcare Research and Quality estimates that the direct medical costs (total of all health care expenditures) for cancer in the US in 2015 were **\$80.2 billion**.

According to a recent study by American Cancer Society epidemiologists, at least **42%** of newly diagnosed cancers in the US – about 729,000 cases in 2018 – **are potentially avoidable**





Bill Gates ✓

@BillGates

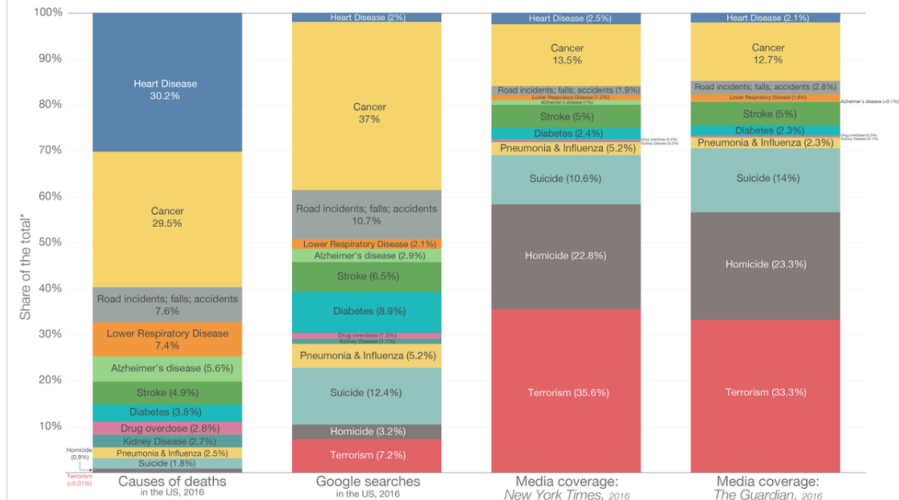


I'm always amazed by the disconnect between what we see in the news and the reality of the world around us. As my late friend Hans Rosling would say, we must fight the fear instinct that distorts our perspective:

Causes of death in the US

What Americans die from, what they search on Google, and what the media reports on

Our World in Data



*This represents each cause's share of the top ten causes of death in the US plus homicides, drug overdoses and terrorism. Collectively these 13 causes accounted for approximately 88% of deaths in the US in 2016. Full breakdown of causes of death can be found at the CDC's WONDER public health database: <https://wonder.cdc.gov/>

Based on data from Shen et al (2018) - Death: reality vs. reported. All data available at: <https://oversher24.github.io/charting-death>

All data refers to 2016.

Not all causes of death are shown: Shown is the data on the ten leading causes of death in the United States plus drug overdoses, homicides and terrorism.

All values are normalized to 100% so they represent their relative share of the top causes, rather than absolute counts (e.g. 'deaths' represents each cause's share of deaths within the 13 categories shown rather than total deaths). The causes of death shown here account for approximately 88% of total deaths in the United States in 2016.

This is a visualization from OurWorldInData.org, where you find data and research on how the world is changing.

Licensed under CC-BY by the authors Hannah Ritchie and Max Roser.

June 11, 2019

Causes of death in the US

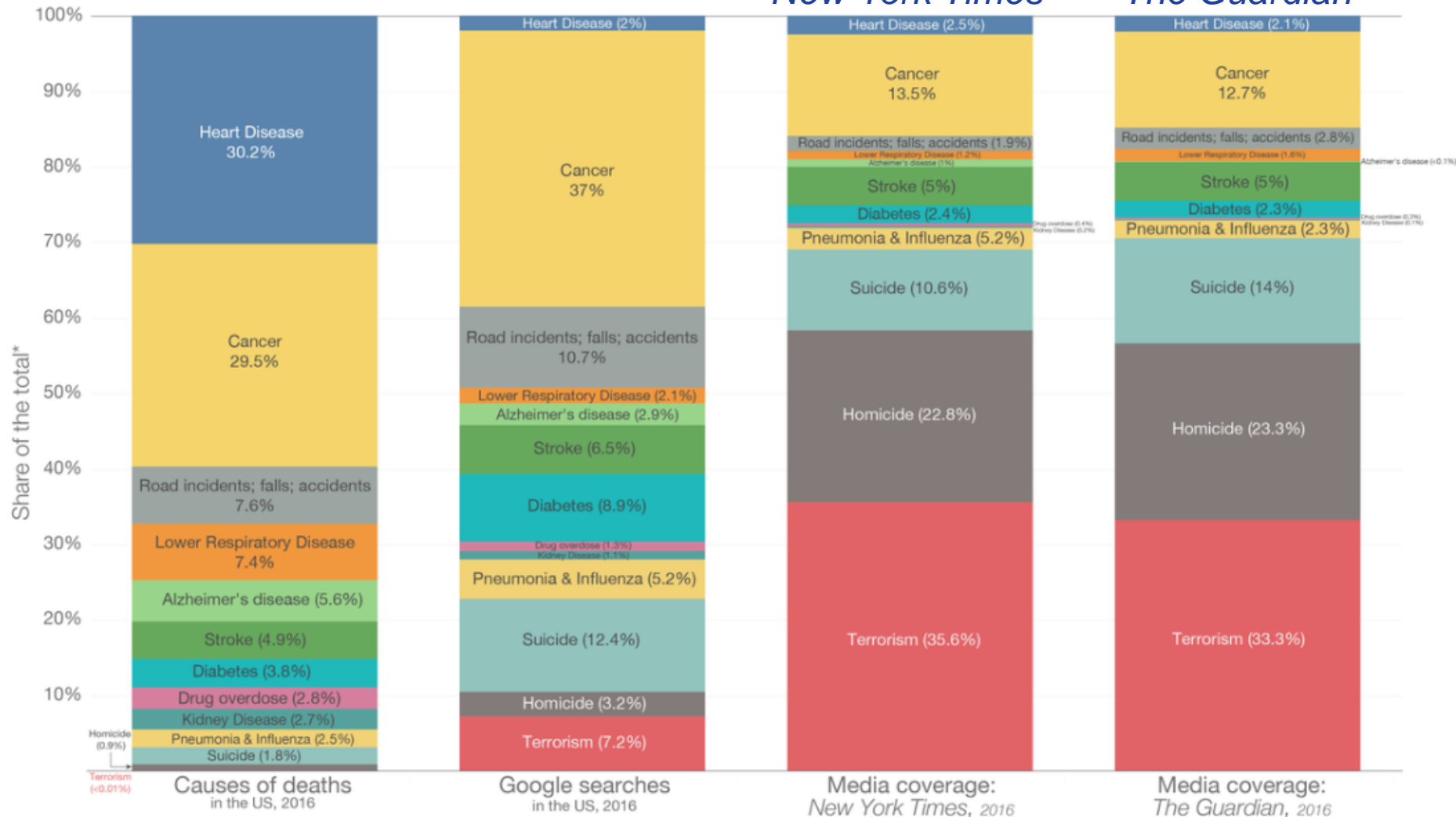
All data for year 2016

Causes of deaths

Google searches

Media coverage:
New York Times

Media coverage:
The Guardian



*This represents each cause's share of the top ten causes of death in the US plus homicides, drug overdoses and terrorism. Collectively these 13 causes accounted for approximately 88% of deaths in the US in 2016. Full breakdown of causes of death can be found at the CDC's WONDER public health database: <https://wonder.cdc.gov/>

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“Does [*Agent*] cause cancer?”

2 year Bioassay



“Cancer”
(Hazard ID)



Agent X

Rodent Carcinogen: Yes, No, Maybe

Human Carcinogen: ?



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Agent X

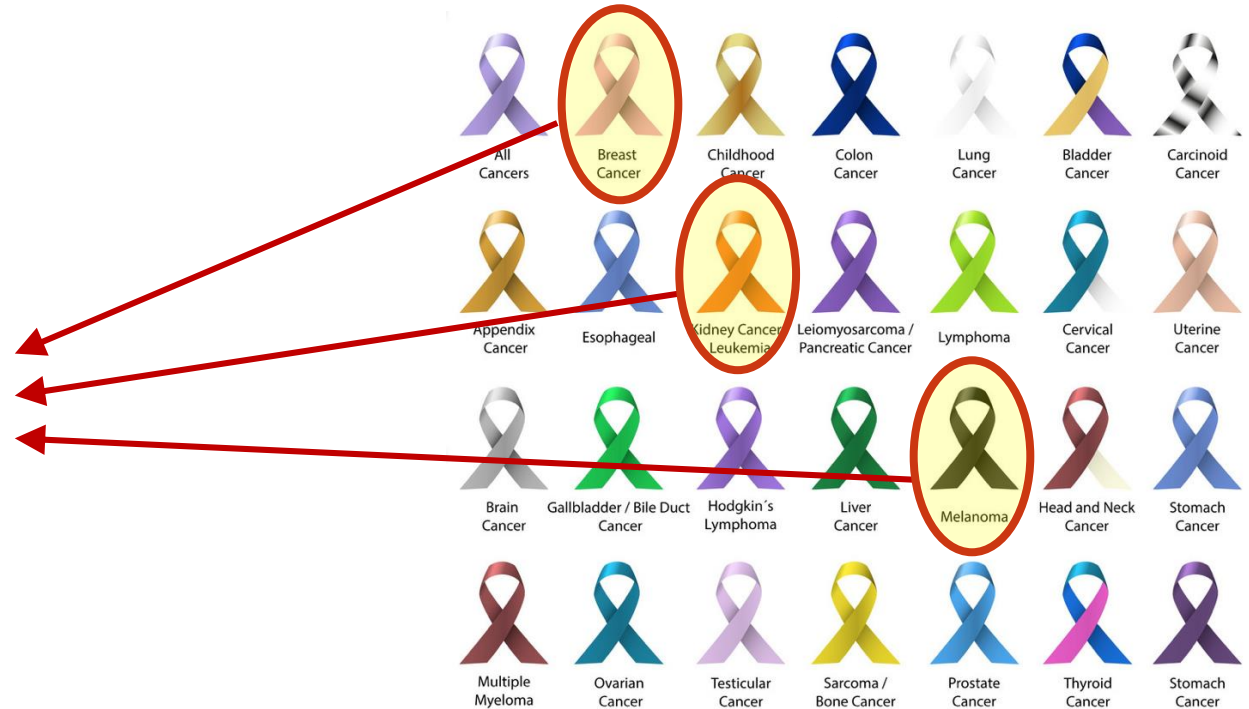
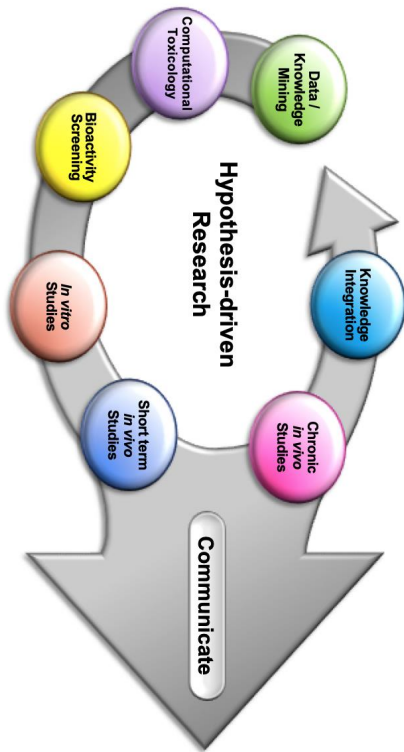
How do we make this more
translatable, predictive and timely?



Start incorporating human data



Identify those cancers likely associated with environmental exposures

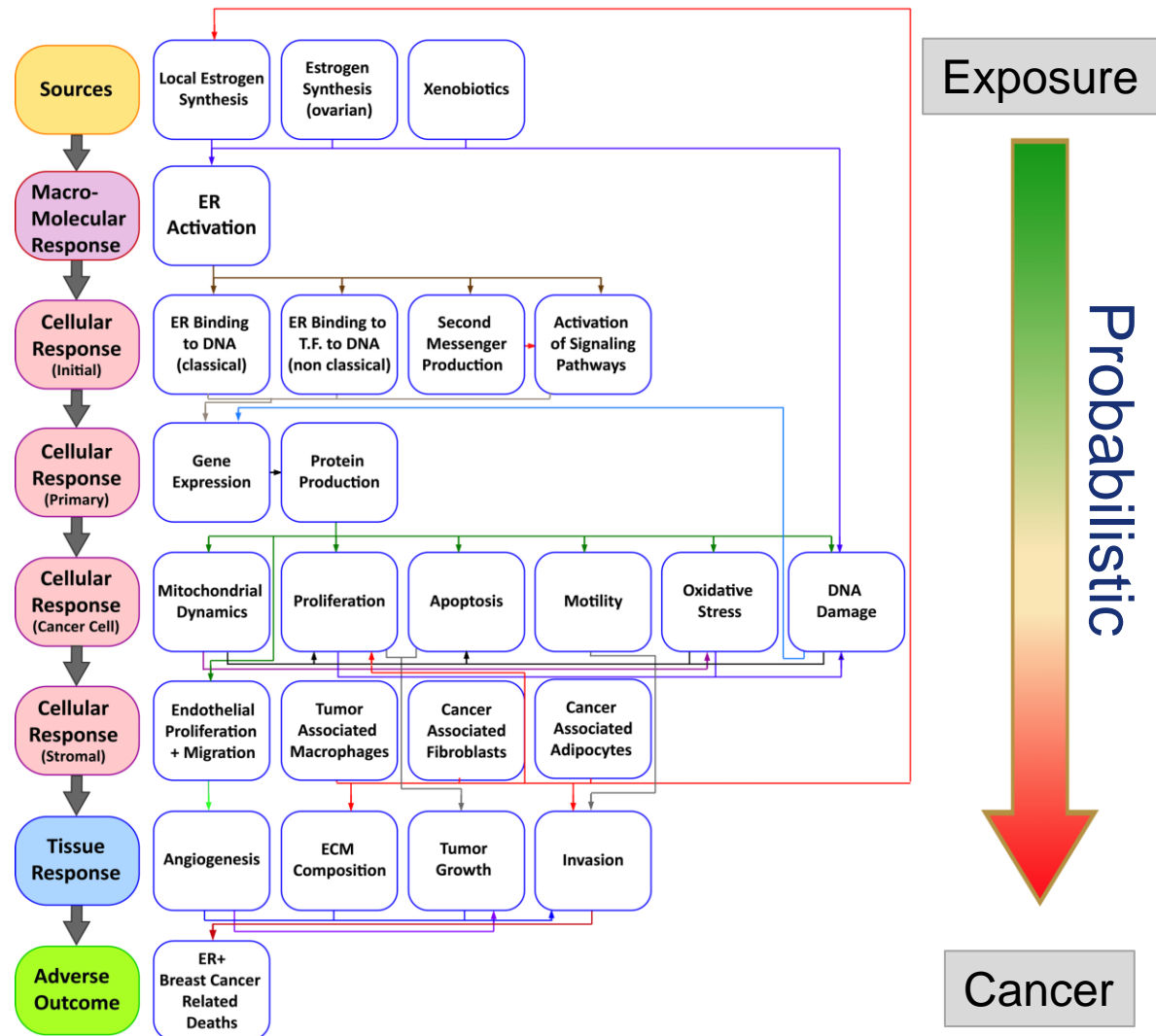


“[Quantitative contribution] of
Agent X
to [cancer type Y] in
[population Z]”

Develop a deep knowledge of
specific cancer pathways

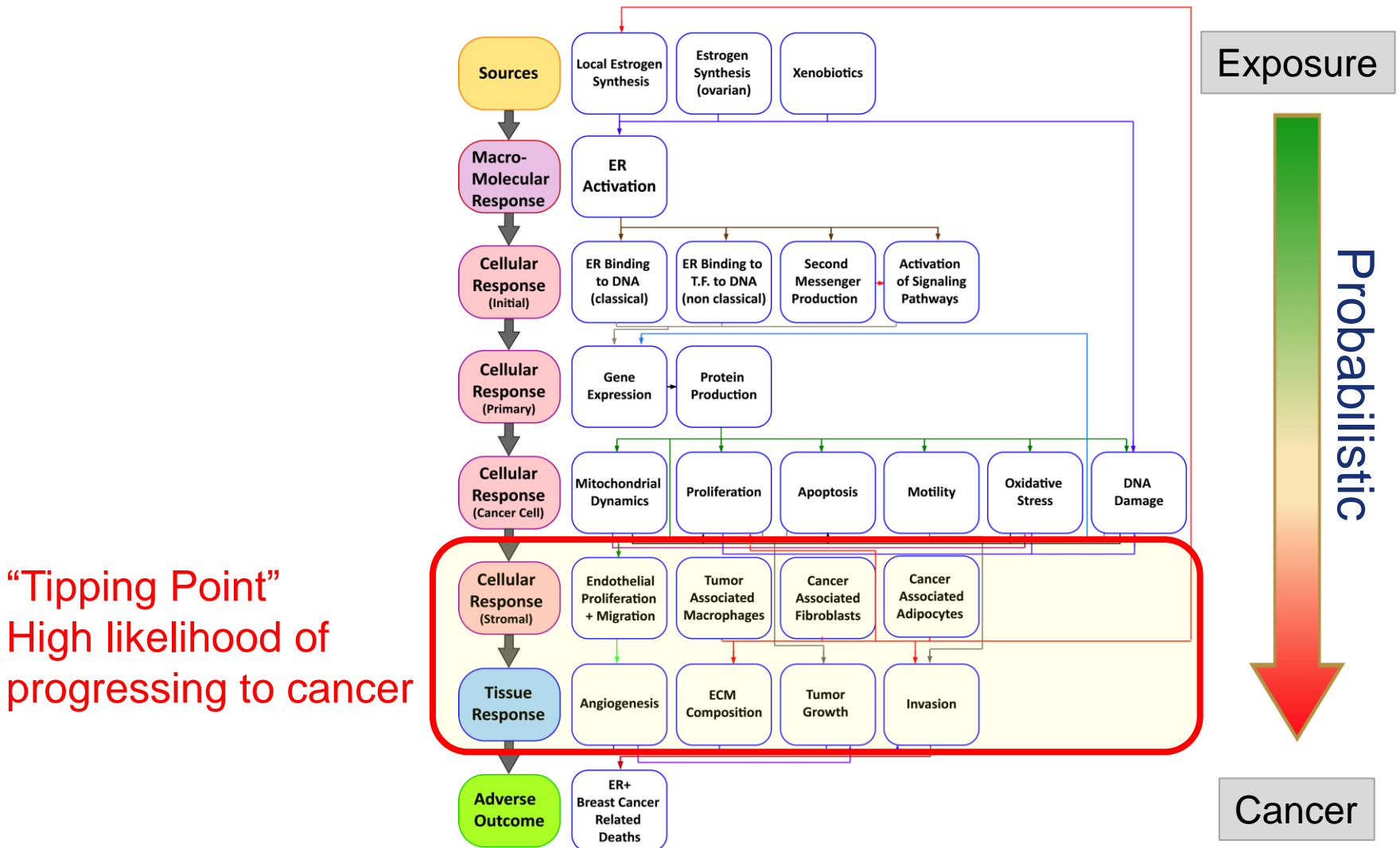


ER Pathway to Breast Cancer



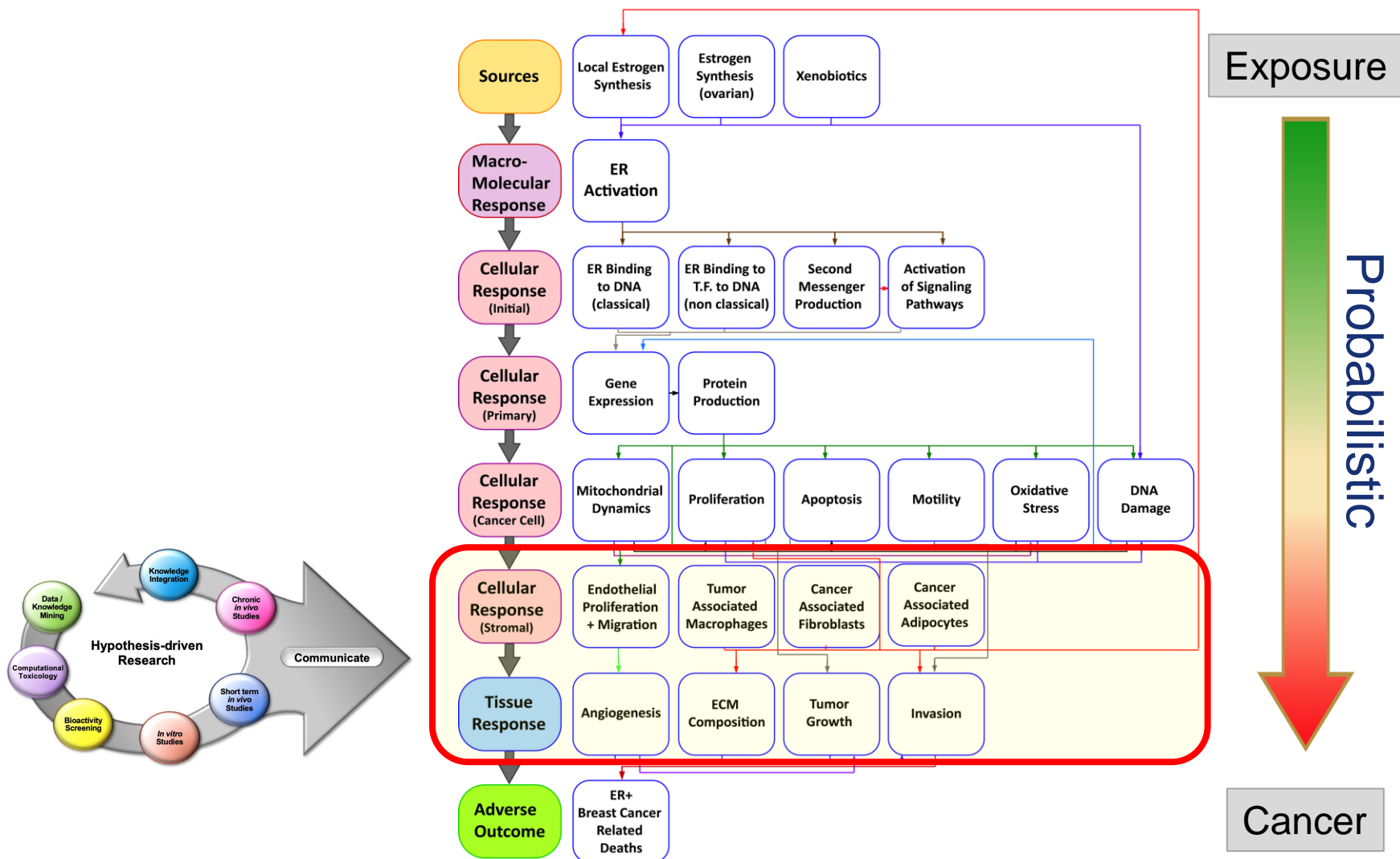


ER Pathway to Breast Cancer



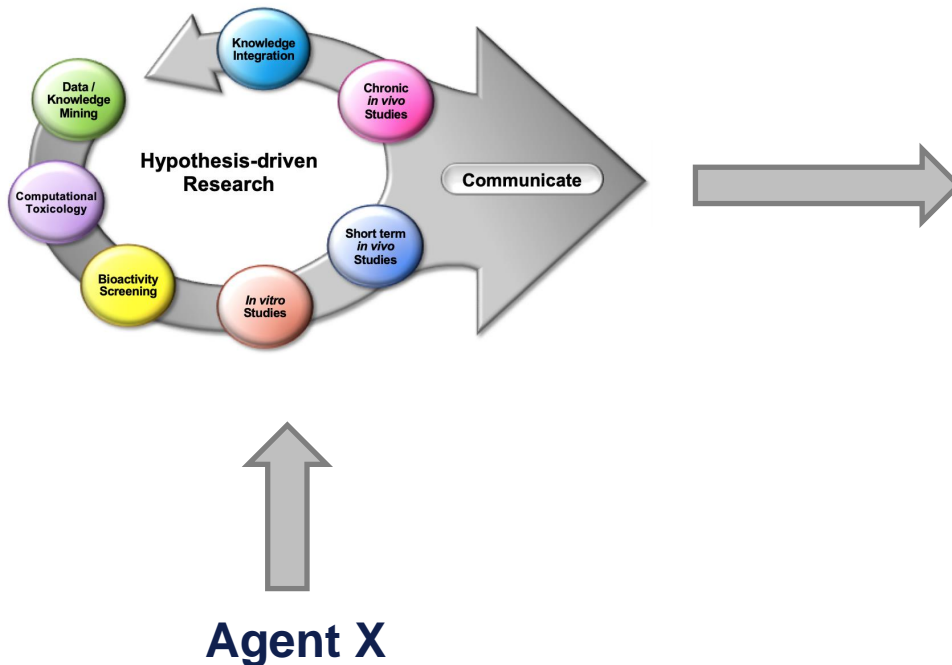


ER Pathway to Breast Cancer



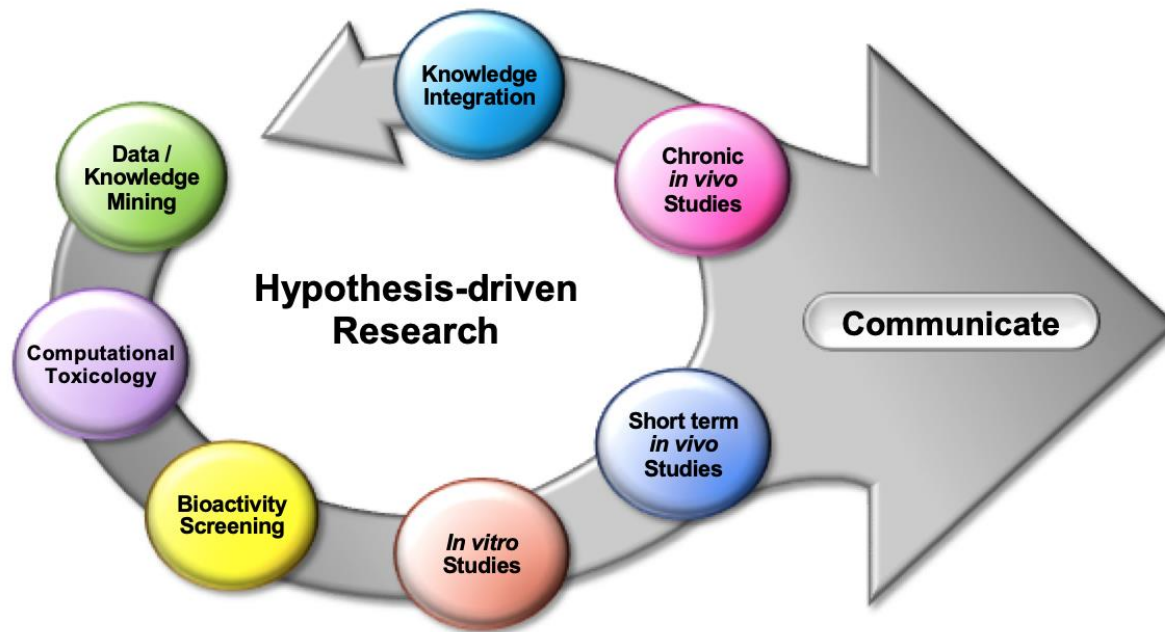


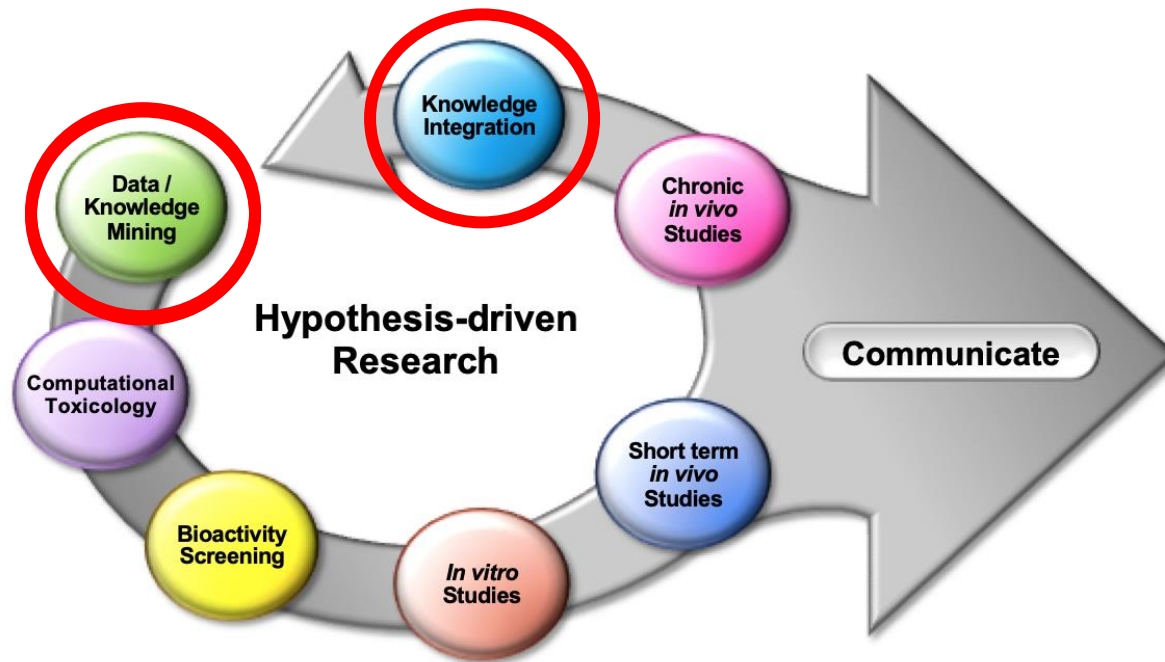
“Does [*Agent*] cause cancer?”



“[Quantitative contribution] of
Agent X
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Or Not



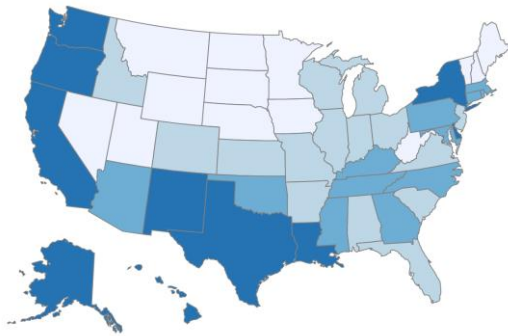




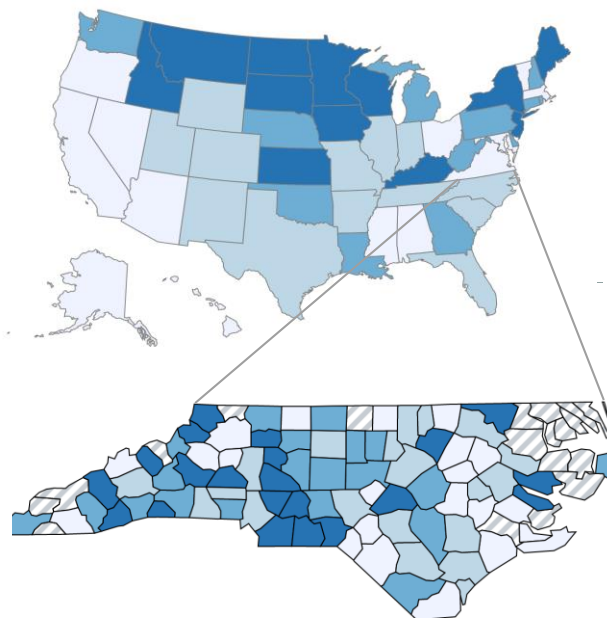
- **Centralized cancer registries** in the United States conduct population-based surveillance of cancer incidence and mortality.
- State health departments (funded by CDC's [National Program of Cancer Registries](#)) and NCI's [Surveillance Epidemiology and End Results Program](#), collect cancer incidence data.

Cancer Incidence

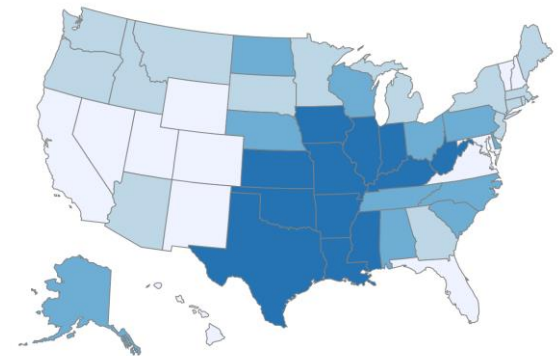
Liver cancer



Leukemia



Kidney cancer

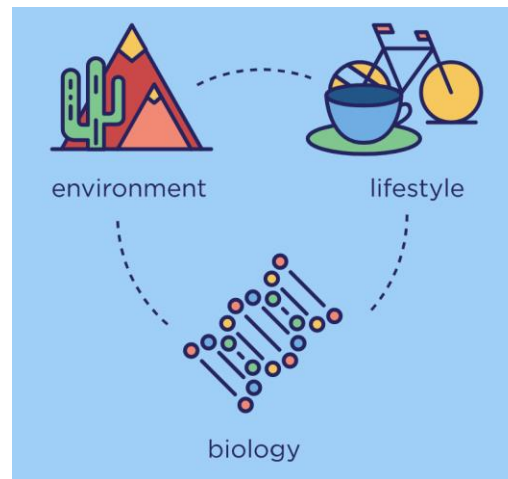




Timely: Expanding resources for population data

NIH All of Us

The *All of Us* Research Program is a historic effort to gather data from one million or more people living in the United States to accelerate research and improve health



Million Veteran Program (MVP)

MVP is a national, voluntary research program funded entirely by the Department of Veterans Affairs Office of Research & Development. The goal of MVP is to partner with Veterans receiving their care in the VA Healthcare System to study how genes affect health.



U.S. Department
of Veterans Affairs



Clinical Pharmacology & Therapeutics

Commentary | [Open Access](#) |

From Discovery to Practice and Survivorship: Building a National Real-World Data Learning Healthcare Framework for Military and Veteran Cancer Patients

Jerry S. H. Lee , Kathleen M. Darcy, Hai Hu, Yovanni Casablanca ... [See all authors](#)

Fir

Cell

A Compendium of Mutational Signatures of Environmental Agents

Kucab et al., 2019, Cell 177, 1–16 May 2, 2019 <https://doi.org/10.1016/j.cell.2019.03.001>

[Cancer Res.](#) 2018 Oct 1;78(19):5527-5537. doi: 10.1158/0008-5472.CAN-18-0362.

Sex Differences in Cancer Driver Genes and Biomarkers.

[Li CH](#)^{1,2}, [Haider S](#)³, [Shiah YJ](#)^{3,2}, [Thai K](#)³, [Boutros PC](#)^{1,2,4}.

[Brief Bioinform.](#) 2019 May 31. pii: bbz046. doi: 10.1093/bib/bbz046. [Epub ahead of print]

A comprehensive overview of oncogenic pathways in human cancer.

[Li F](#)¹, [Wu T](#)¹, [Xu Y](#)¹, [Dong Q](#)¹, [Xiao J](#)¹, [Xu Y](#)¹, [Li Q](#)¹, [Zhang C](#)¹, [Gao J](#)¹, [Liu L](#)¹, [Hu X](#)¹, [Huang J](#)², [Li X](#)¹, [Zhang Y](#)¹.





The European Partnership
for Alternative Approaches to Animal Testing



HESI





- Work with internal and external stakeholders to establish a problem statement and define scope
- Survey available resources
- Identify initial areas of focus
- Develop a strategic plan to set goals and establish timelines
- Develop a communication plan



Thank you

Questions?