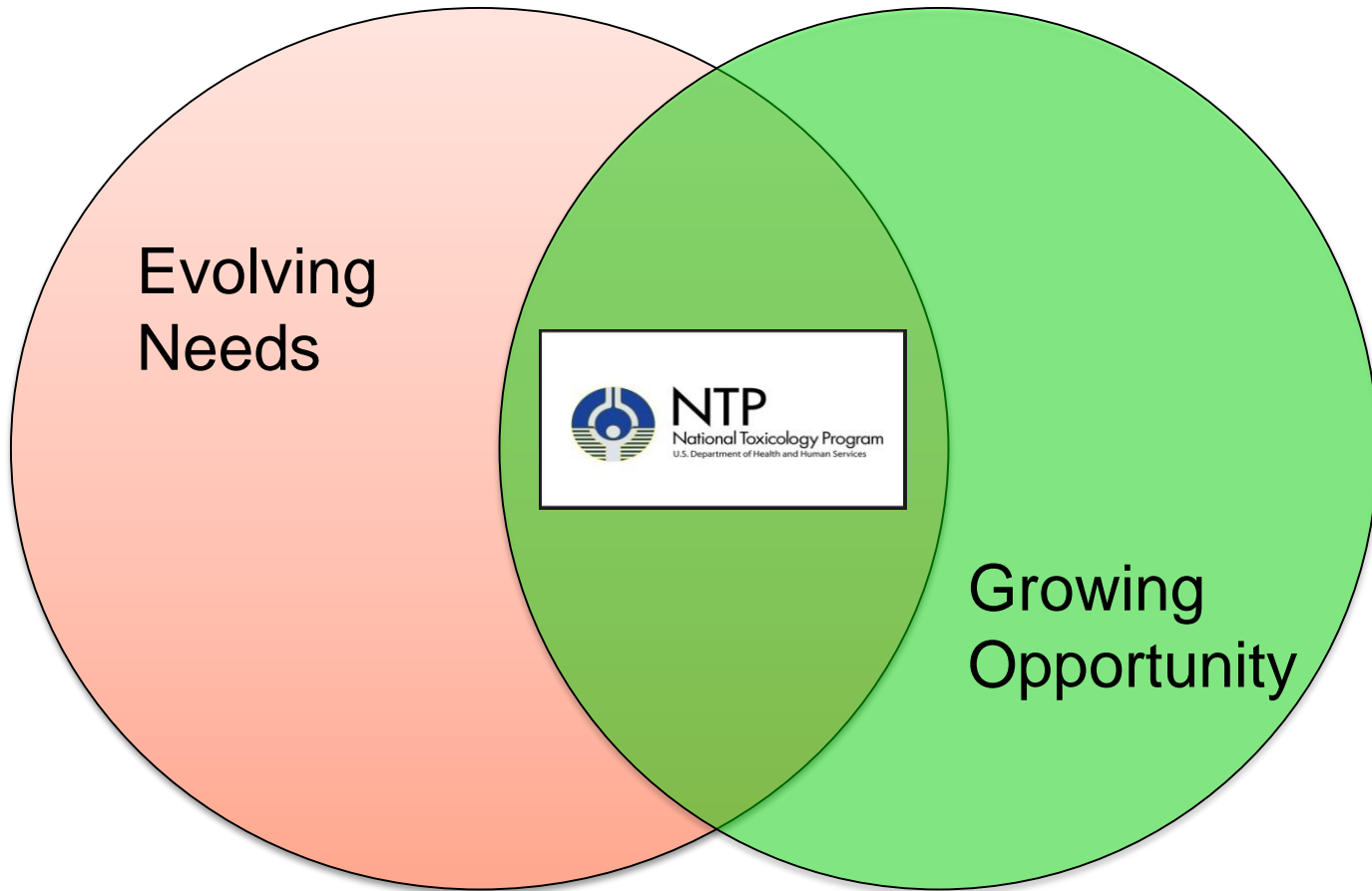


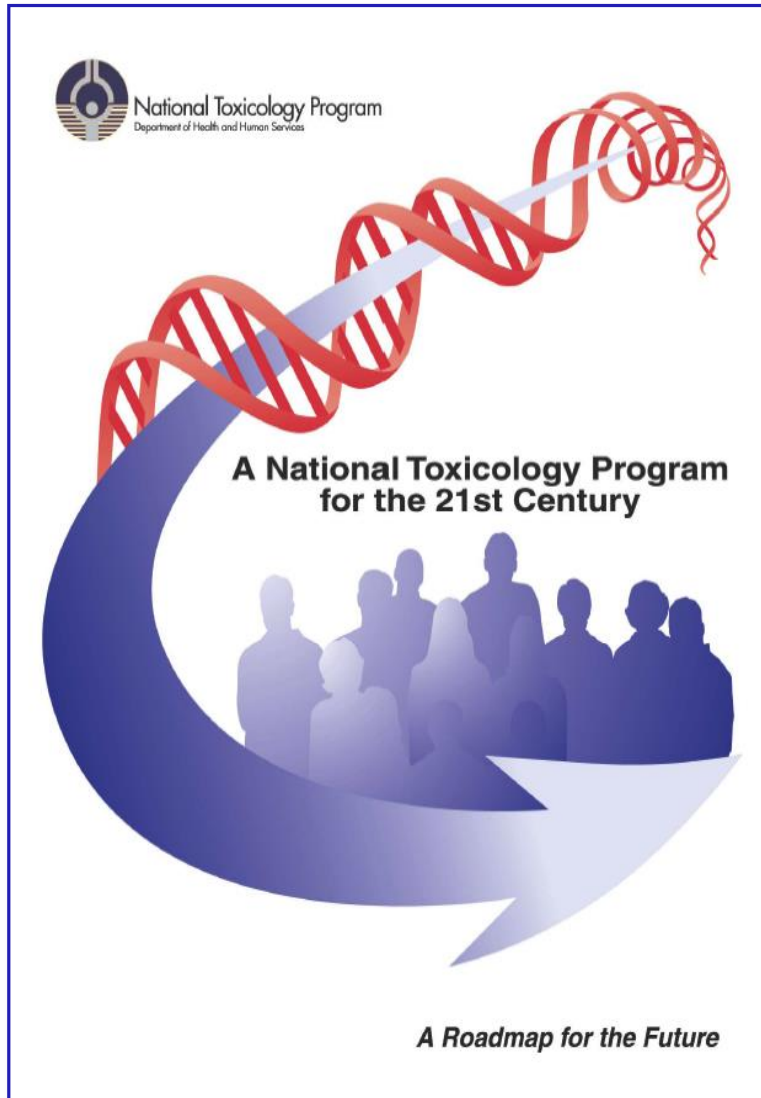
# The Changing Toxicology Landscape: Challenges and the Future of Risk Assessment

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## 21<sup>st</sup> Century Vision

To support the **evolution of toxicology from a predominately observational science** at the level of disease-specific models **to a predominately predictive science** focused upon a broad inclusion of target-specific, mechanism-based, biological observations.



- We have a need to address a rapidly increasing list of concerns.
- We have a need to respond to a broad stakeholder group with changing expectations.
- We have a need to bring more human relevance and individual precision to our hazard characterizations.
- We have a need to build confidence in a different approach to assessing hazards.
- We have a need to decrease our dependence on animals as a primary modeling platform.



- Aspiration
- Advances in technology
  - Machine learning/Artificial intelligence
  - iPSC
  - Complex in vitro microphysiological systems
  - Computer vision and holistic physiologic monitoring in animal studies
  - Biomonitoring patients/people
- Willingness to innovate
- An ability to leverage our experiences
  - NTP
  - Tox21



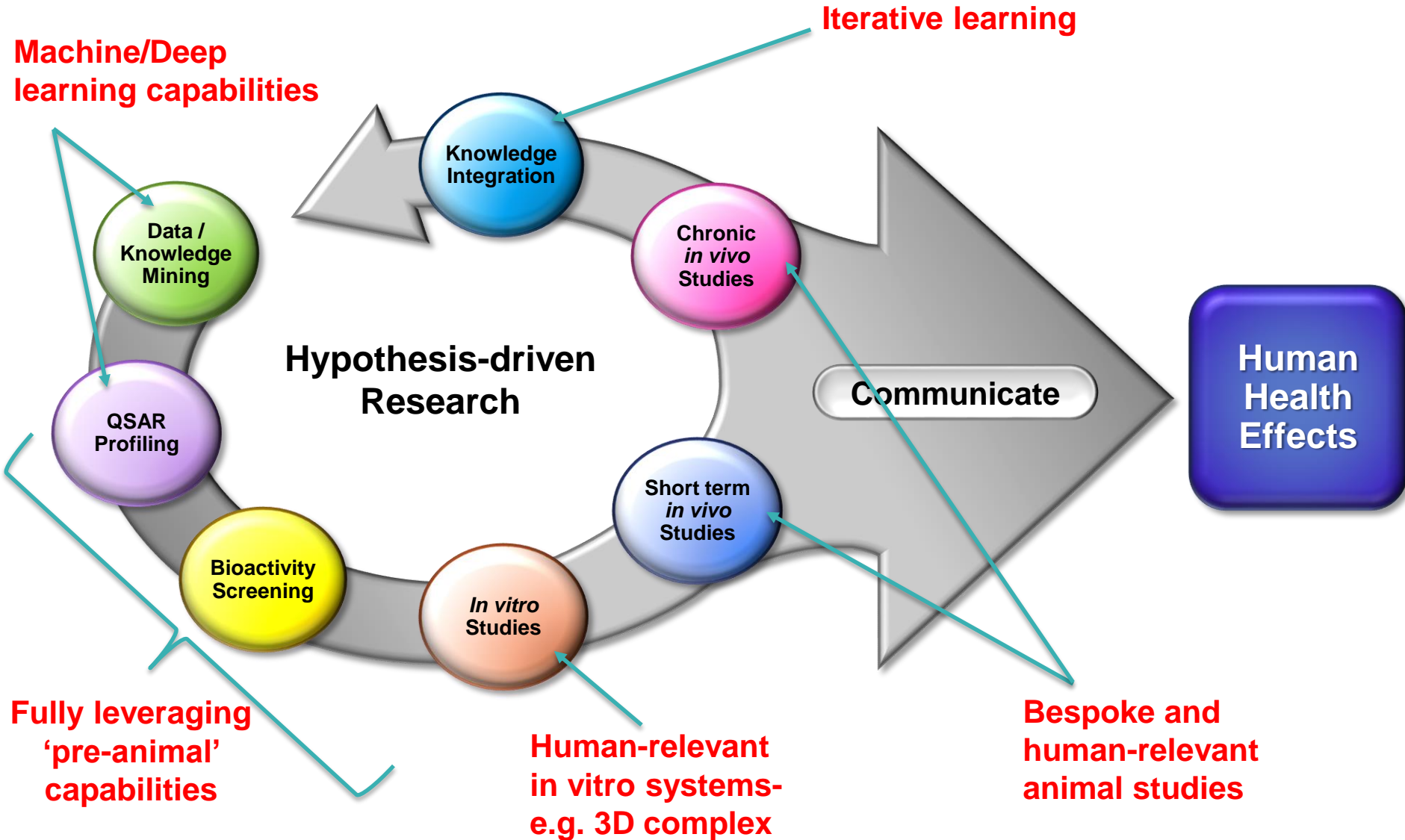
- What is NTP's unique value?
  - Ability to focus on complex challenges for prolonged periods of time
  - Impactful science supporting policy and regulation
  - Opportunity to address chronic health effects
  - Build predictive capabilities
- What does it mean to be human-relevant?
  - Studying things of contemporary human concern/importance
  - Studying things in a relevant human context
    - Modeling human exposure context- quantity, route
    - Demonstrating exposure/outcomes relationships
  - Addressing public confusion



- How do we build confidence in non-traditional evidence?
  - Demonstrating human relevance
  - Understanding mechanisms
    - Toxicologists and pathologists working together



# Innovating the Paradigm

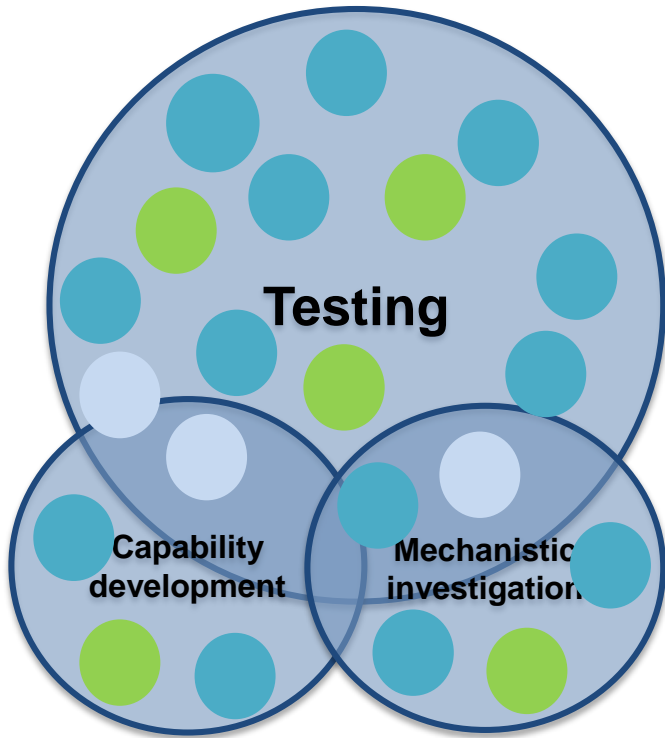







# Evolving Our Portfolio

## Agents/Projects



## Programs



-  Studies
-  Projects
-  Programs

### Goals

- Increase impact
- Improve sustainability
- Increase visibility
- Improve complementarity



- Carcinogenicity Testing for the 21<sup>st</sup> Century
- Developmental Neurotoxicity Modeling
- Cardiovascular Hazard Assessment in Environmental Toxicology

## **Aims**

- Fill a gap in current capabilities
- Build on existing effort
- Align to NIH model
- Leverage our key strengths and value

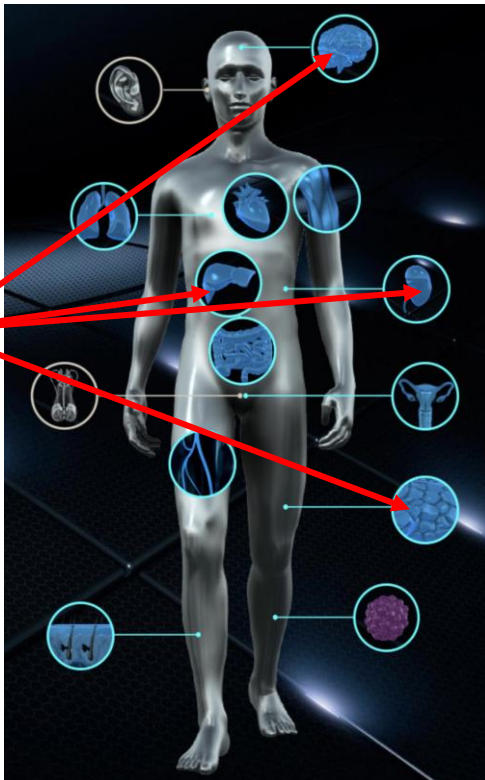


# Fundamental Shift

X lbs./yr. commercial production



Agent Y



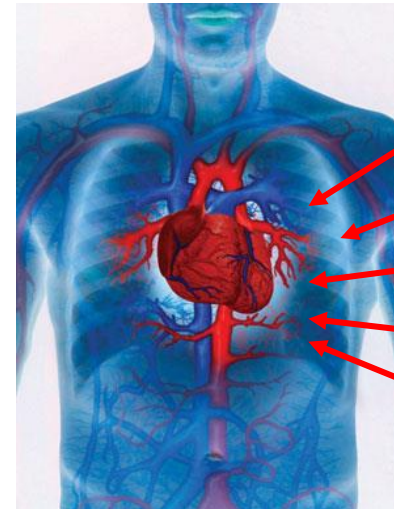
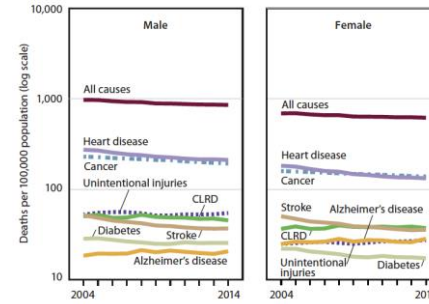
<https://ncats.nih.gov/tissuechip/chip>



## Mortality

Selected Causes of Death

Figure 2. Age-adjusted death rates for selected causes of death for all ages, by sex: United States, 2004–2014



Agent A

Agent B

Agent C

Agent Y

Agent Z



# Human Value for Cancer Testing

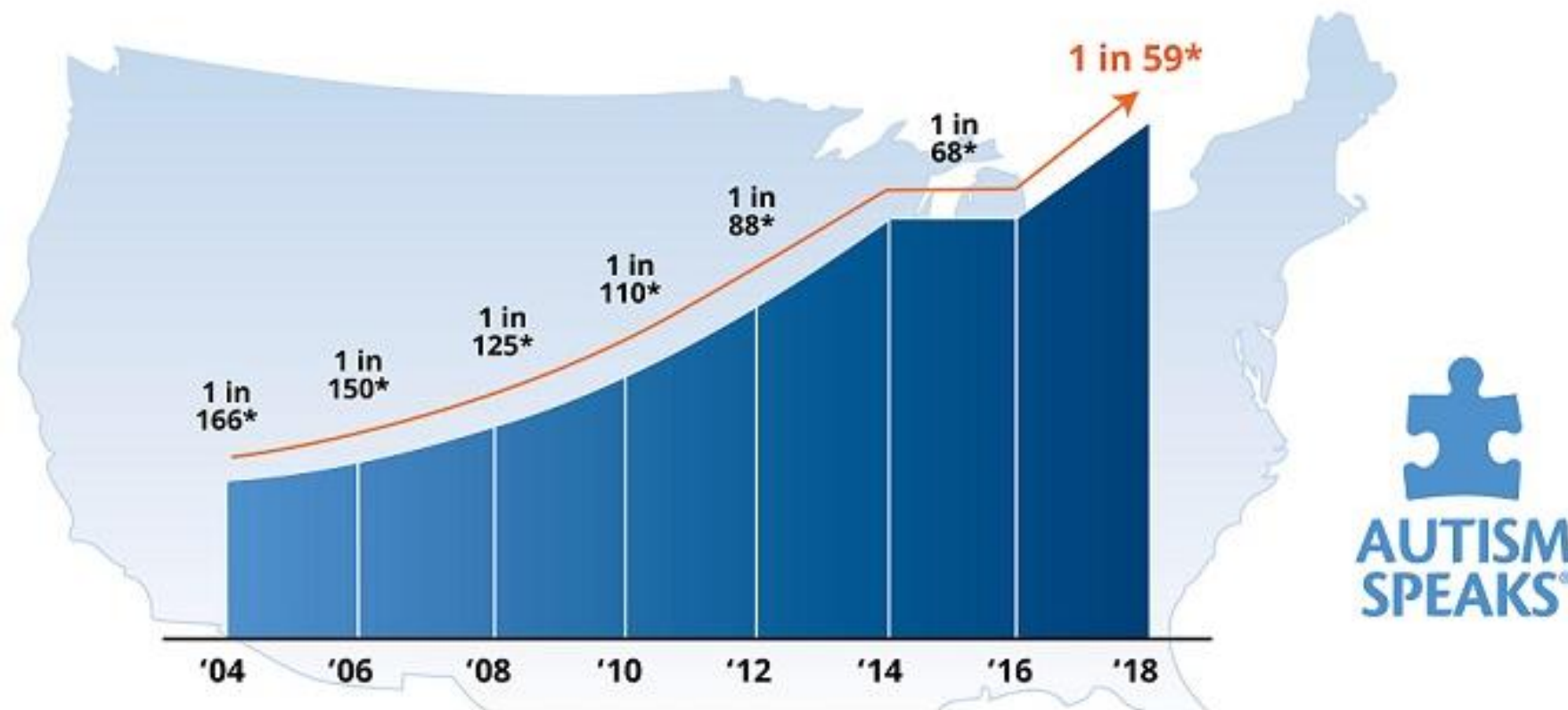
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- In 2018, an estimated 1,735,350 new cases of cancer will be diagnosed in the United States and 609,640 people will die from the disease.
- Approximately 38.4% of men and women will be diagnosed with cancer at some point during their lifetimes (based on 2013–2015 data).
- In 2017, an estimated 15,270 children and adolescents ages 0 to 19 were diagnosed with cancer and 1,790 died of the disease.
- The number of cancer deaths (cancer mortality) is 163.5 per 100,000 men and women per year (based on 2011–2015 deaths).



## Autism Spectrum Disorder

### Estimated Autism Prevalence 2018



\* Centers for Disease Control and Prevention (CDC) prevalence estimates are for 4 years prior to the report date (e.g. 2018 figures are from 2014)

Source: autismspeaks.org, "CDC increases estimate of autism's prevalence by 15 percent, to 1 in 59 children"

Courtesy of Robert Sills, Mamta Behl

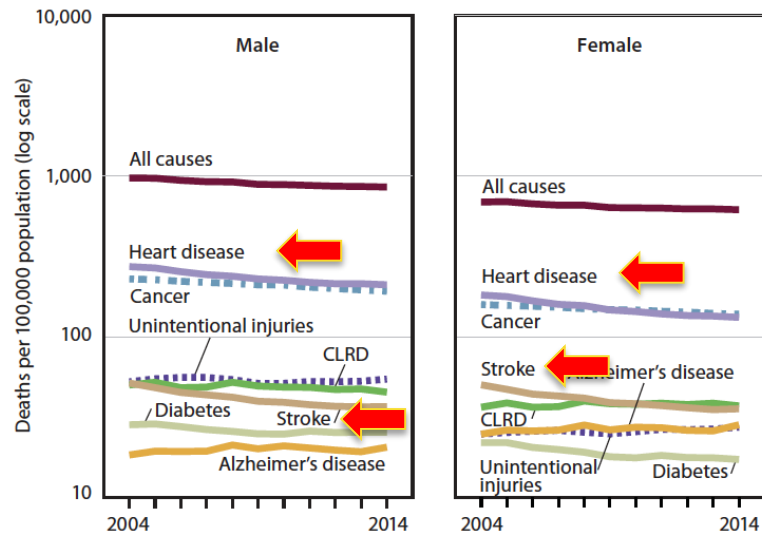


# CV Morbidity and Mortality

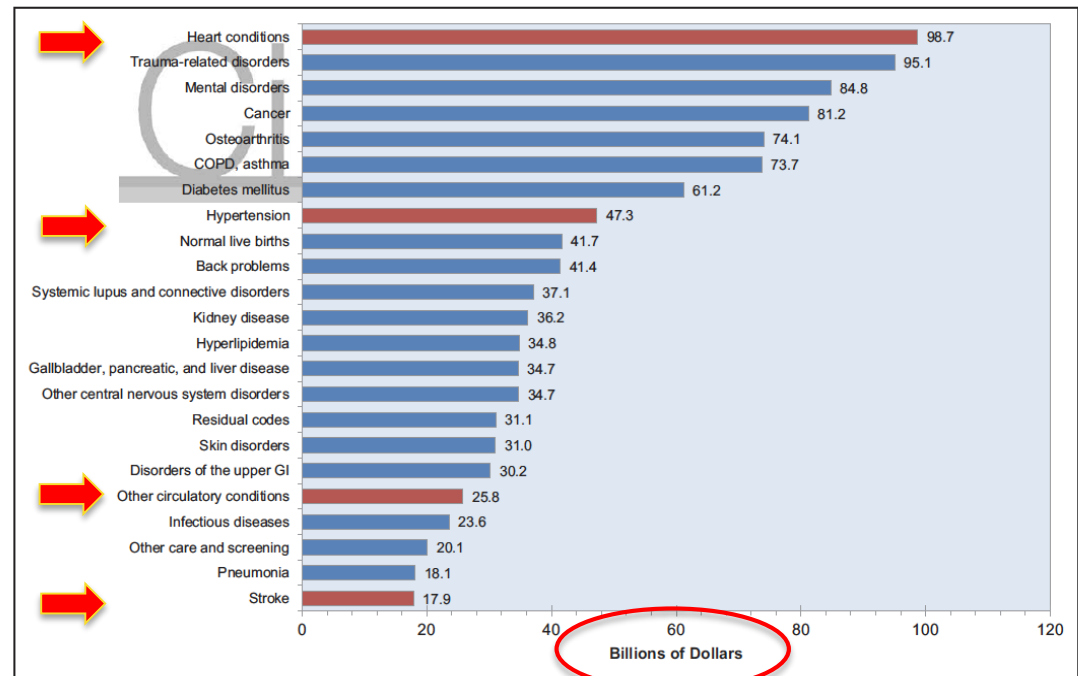
## Mortality

### Selected Causes of Death

Figure 2. Age-adjusted death rates for selected causes of death for all ages, by sex: United States, 2004–2014



National Center for Health Statistics. Health, United States, 2015: With Special Feature on Racial and Ethnic Health Disparities. Hyattsville, MD. 2016.



**Chart 27-2. The 23 leading diagnoses for direct health expenditures, United States, average annual 2012 to 2013 (in billions of dollars).**

COPD indicates chronic obstructive pulmonary disease; and GI, gastrointestinal (tract). Source: National Heart, Lung, and Blood Institute; estimates are from the Medical Expenditure Panel Survey, Agency for Health-care Research and Quality, and exclude nursing home costs.



- Contextualizing hazard
  - How do you make hazards relevant?
  - Where/when does hazard characterization become risk assessment?
- Enabling stakeholders
  - Which stakeholders?
    - Regulatory/Policy
    - Scientific
    - \* • Public
    - Industry



# The Changing Toxicology Landscape

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- How might potential challenges of the future affect the NTP mission?
- How should the NTP position itself to be impactful in the toxicology and risk assessment communities?



**Thank You!**

