

# DNTP Strategic Realignment Update

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NTP Board of Scientific Counselors Meeting  
December 12, 2018

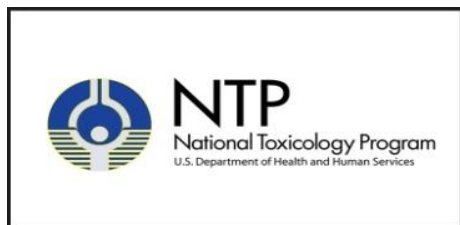




- Previous conversation
- Your feedback
- A refined Vision and Mission
- Taking the bait
- Health Effects Innovation
- Summary



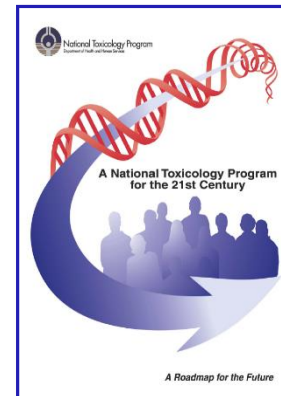
# Aspirational Vision



## Mission

To evaluate agents of public health concern, by developing and applying tools of modern toxicology and molecular biology.

<http://ntp.niehs.nih.gov>; April 2015



## 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.

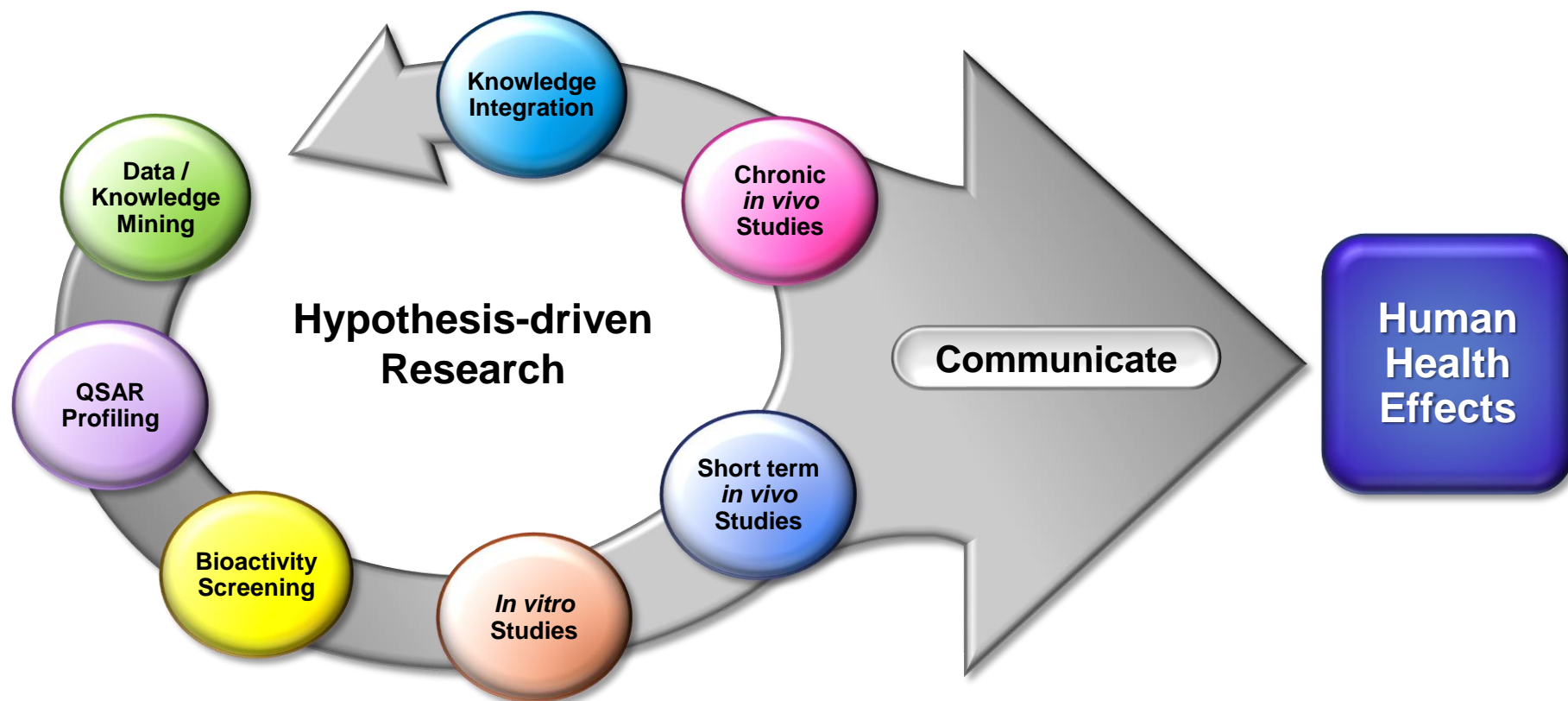


- Rapid pace of chemical development
- Growing concerns about non-chemical agents
- Broad stakeholder group with varying needs, concerns, perspectives and constraints (e.g. regulators vs. policy makers vs. toxicologists vs. advocacy groups vs. general public)
- A decision-making community largely still entrenched in low-throughput assays and modeling platforms for which we have some confidence in human relevance
- Significant and growing societal interest in decreasing animal use
- Gap in our ability to 'predict' human outcomes in a meaningful way



# Strategic Pipeline of Capabilities

Applying our capabilities in deliberate, integrated and complementary ways.



## Translational Toxicology Pipeline



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- Recent WebEx engagement to gain your input on our strategic direction
  - October 9 NTP BSC meeting
  - WebEx with targeted strategic and rapid response questions
- Targeted strategic questions
  - What are NTP's unique strengths?
  - What does it mean to be “human relevant”?
  - How do we build confidence in novel approaches?
- Rapid response questions
  - 3D systems
  - Machine/Deep learning
  - Carcinogenicity testing



- 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



- Rapid responses
  - Opportunity for 3D systems
    - Link between high throughput systems and in vivo studies
    - Build a better comparative understanding of animal and human outcomes
    - Unique role for NTP to demonstrate usefulness
  - Machine/deep learning
    - Not new
    - Deep learning approaches may provide opportunity
    - Concern about the 'black box' nature of proprietary deep learning algorithms
  - Carcinogenicity testing
    - Comfort with current approach even with limitations
    - Need to conduct at more human-relevant exposures
    - NTP should play a role in coordinating efforts to reinvent



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# Refining the Vision and Mission

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- Vision

- To improve public health through the development of **data** and **knowledge** that are **translatable, predictive and timely**.

- Mission

- **Collaborate** with public stakeholders and global partners to identify and address public health issues.
- Generate and **communicate** trusted scientific information to support decision making on environmental hazards of public interest.
- **Lead** the transformation of toxicology through the development and application of innovative tools and strategies.

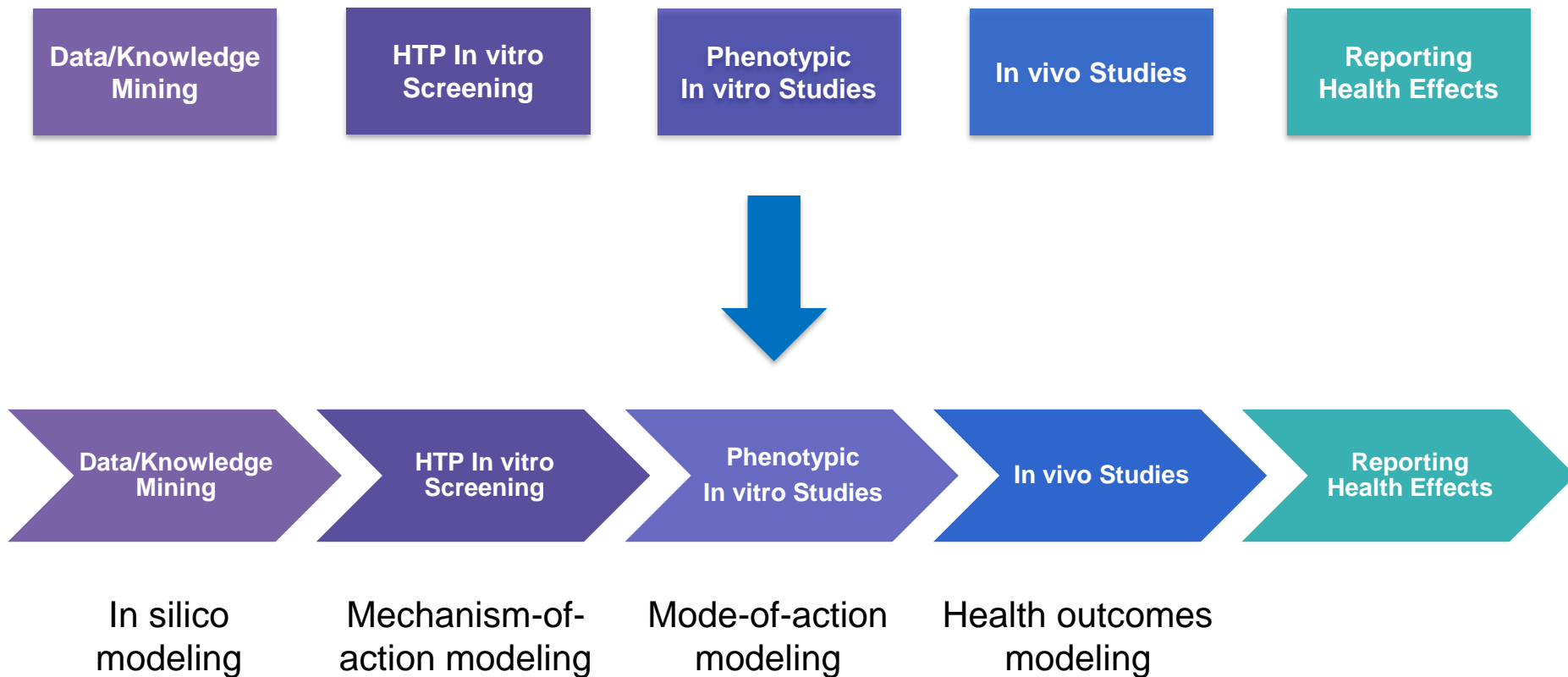


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Why are we struggling to become more predictive and how can NTP facilitate getting there?

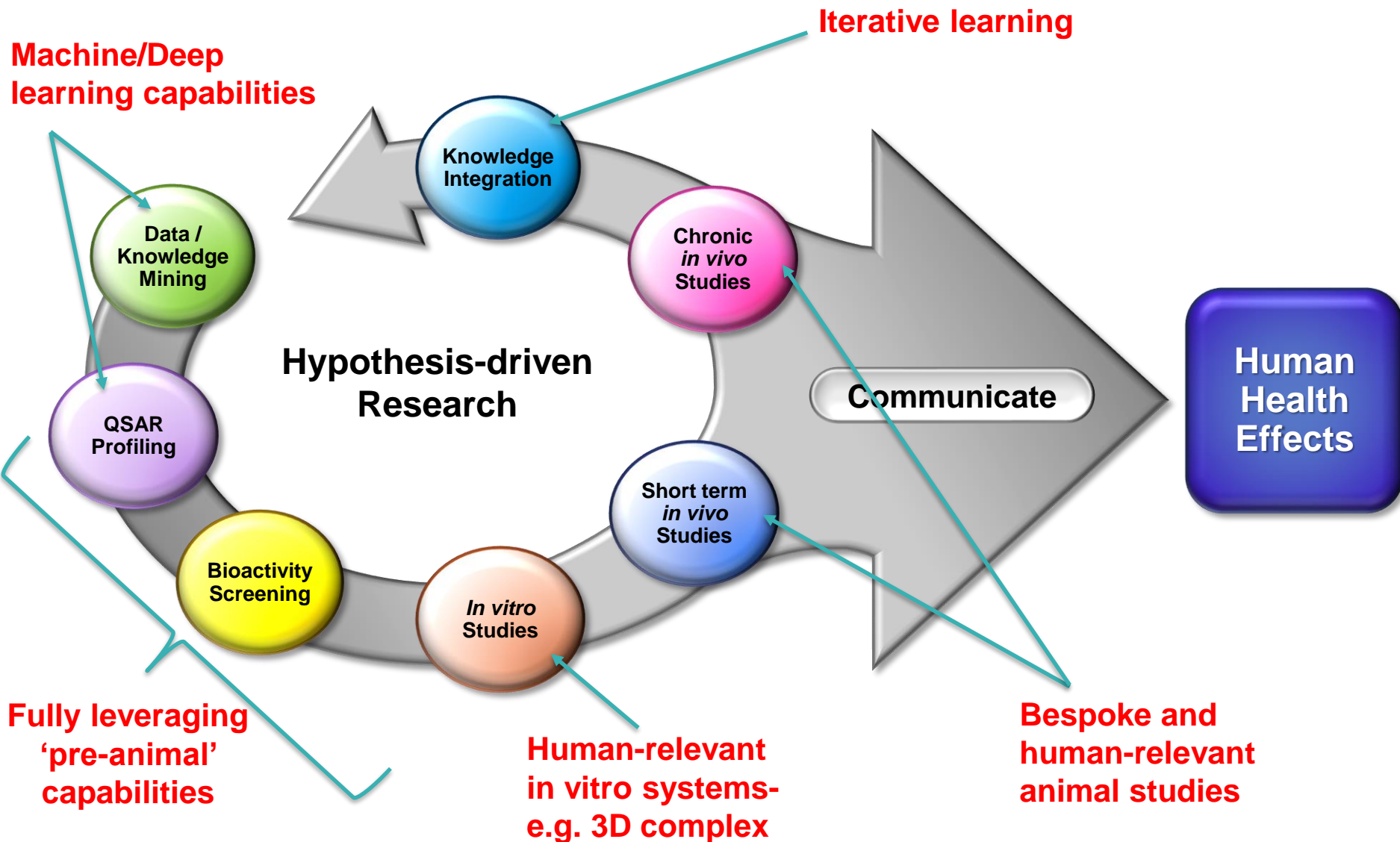


# Progressing the Paradigm





# Innovating the Paradigm

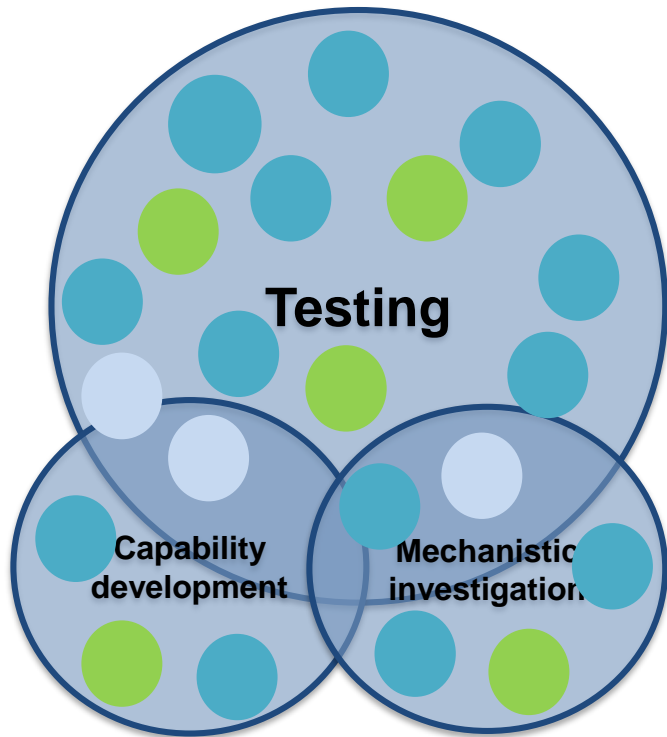






# Evolving Our Portfolio

## Agents/Projects



## Programs



- Studies
- Projects
- Programs

### Goals

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



# Current Programmatic Research

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- Mixtures
- Botanical Dietary Supplements
- Polycyclic Aromatic Compounds
- Radiofrequency radiation
- PFAS
- AIDS-related research
- Flame retardants



# Increasing DNTP Portfolio Impact: Flagship Initiatives in 'Health Effects Innovation'



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

## Goals

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



# Aims of Health Effects Innovation

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- Define and build a strategic assessment pipeline for key environmental health effects
- Understand the mechanism of action, mode of action, health effect continuum for these areas
- Increase confidence in the predictivity of MOA assessments
- Align our capability development to problems we're trying to solve
- Maximize the collective strength of the NTP organization
- Build novel partnerships in and outside NIH

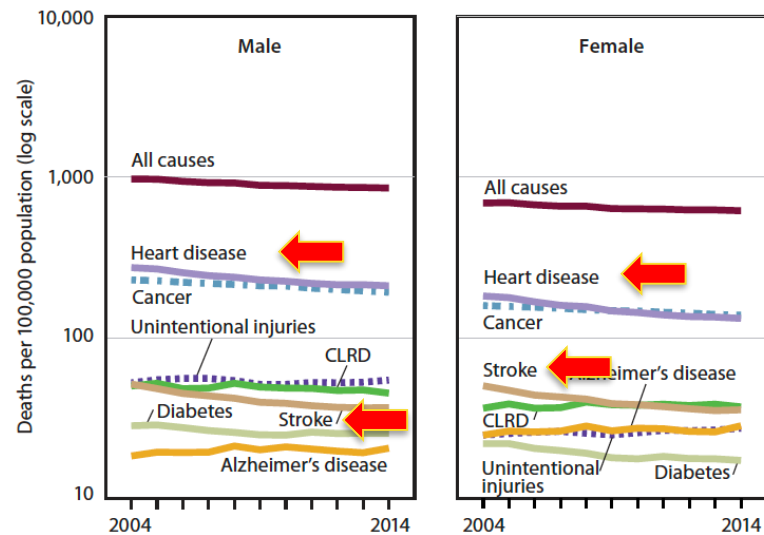


# E.g. Impact of CV Morbidity and Mortality

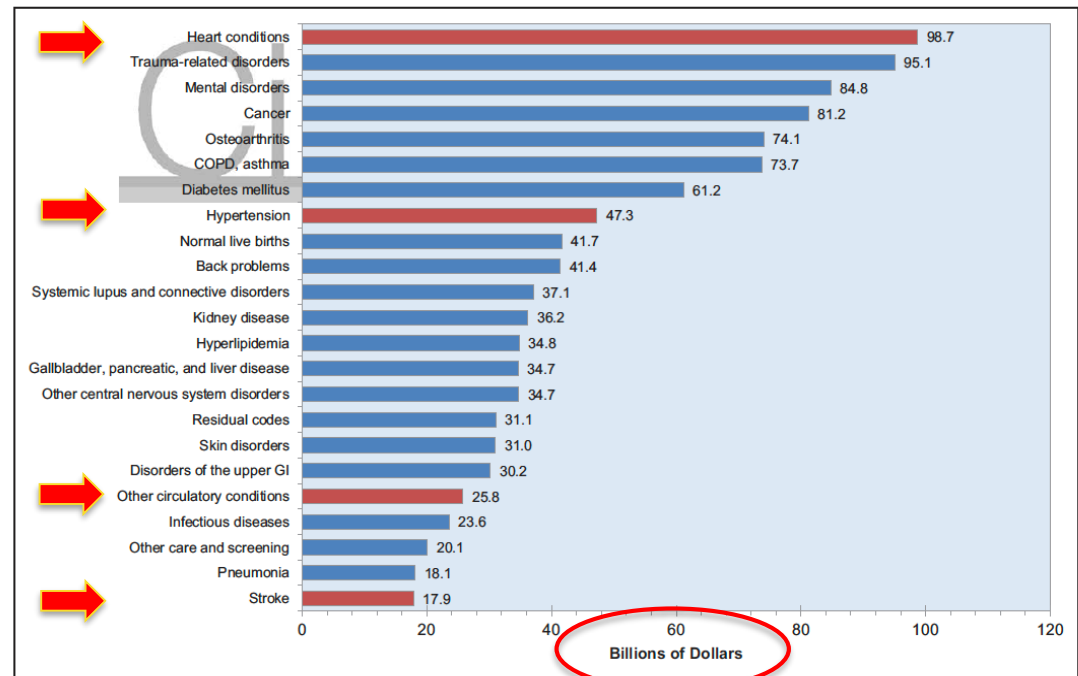
## Mortality

### 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.



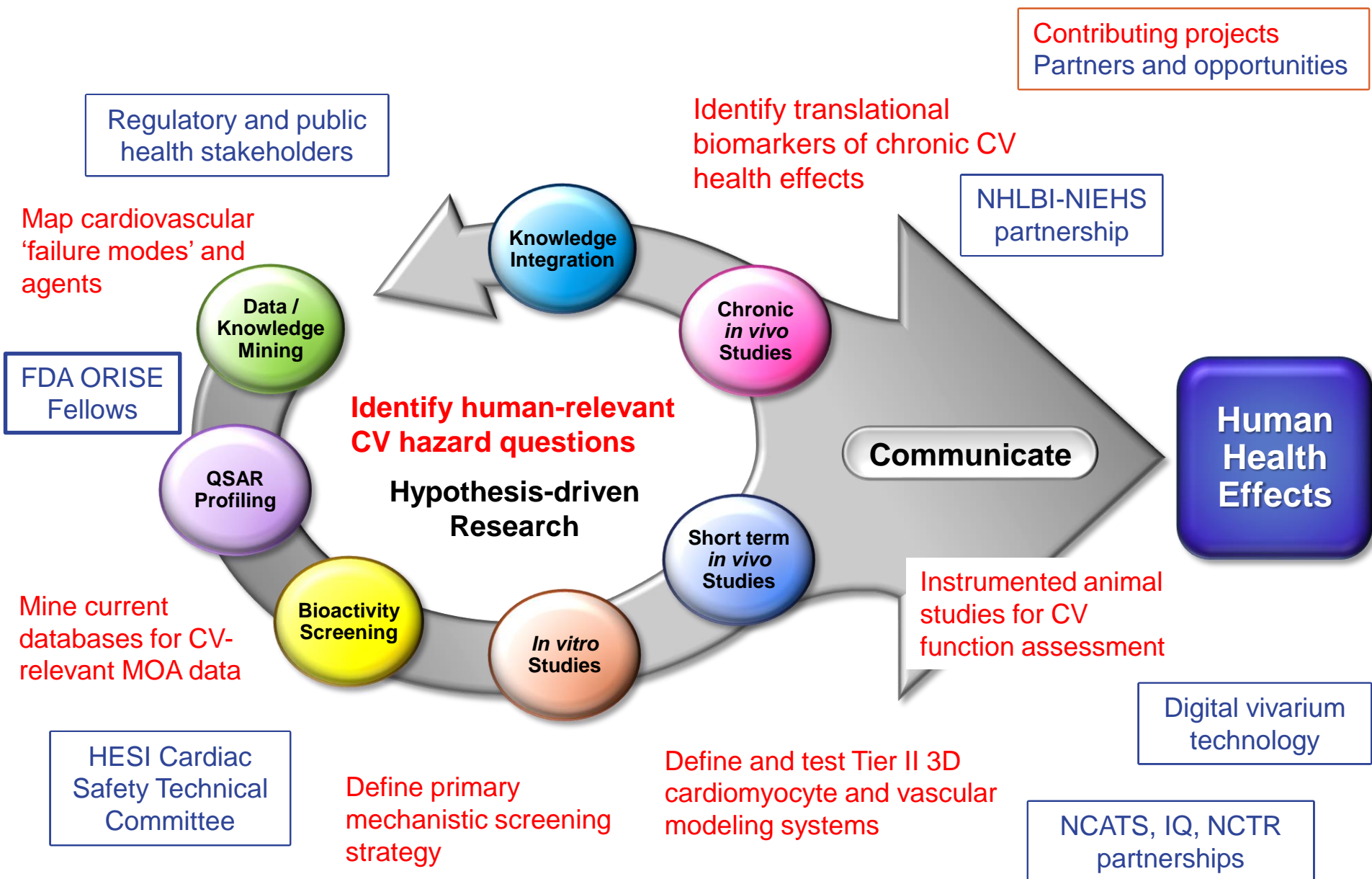
**Chart 27-2. The 23 leading diagnoses for direct health expenditures, United States, average annual 2012 to 2013 (in billions of dollars).**

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 Healthcare Research and Quality, and exclude nursing home costs.



# E.g. Cardiovascular Health Effects Strategy





- Your feedback has been important to us and is being integrated into our strategic realignment.
- We believe a more deliberate and integrated application of our 'pipeline' of capabilities will enable us to improve our rate of progress in reaching our 'predictive' aspiration.
- Focus on discrete areas of 'health effect innovation' will increase our visibility and impact in biomedical science as well as increase the value of NTP's efforts to lead a strategic transformation of toxicology.





# Acknowledgements





# Thank You!

