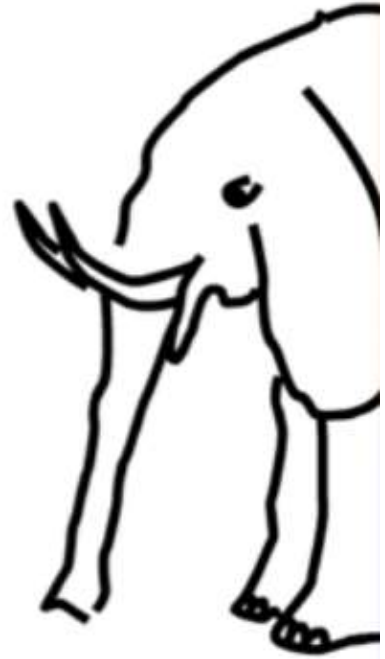
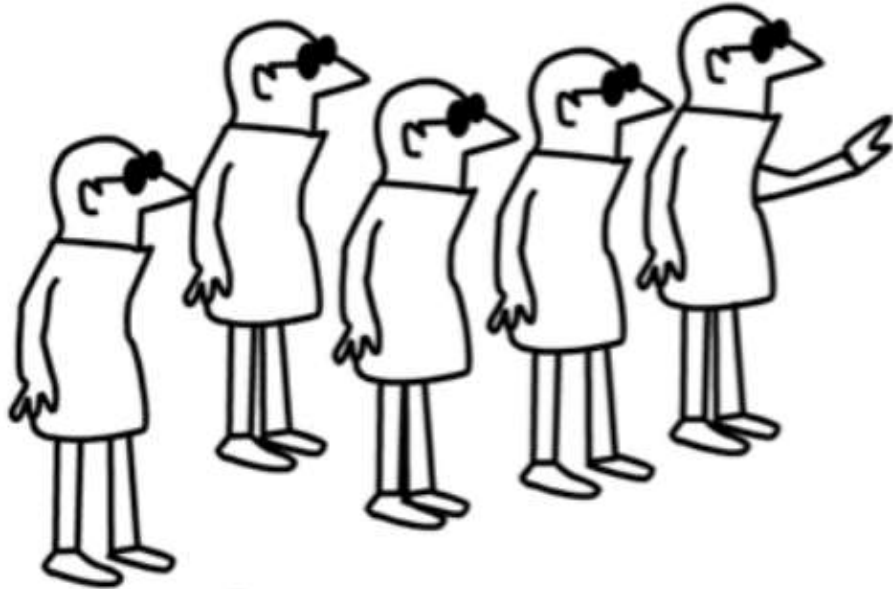


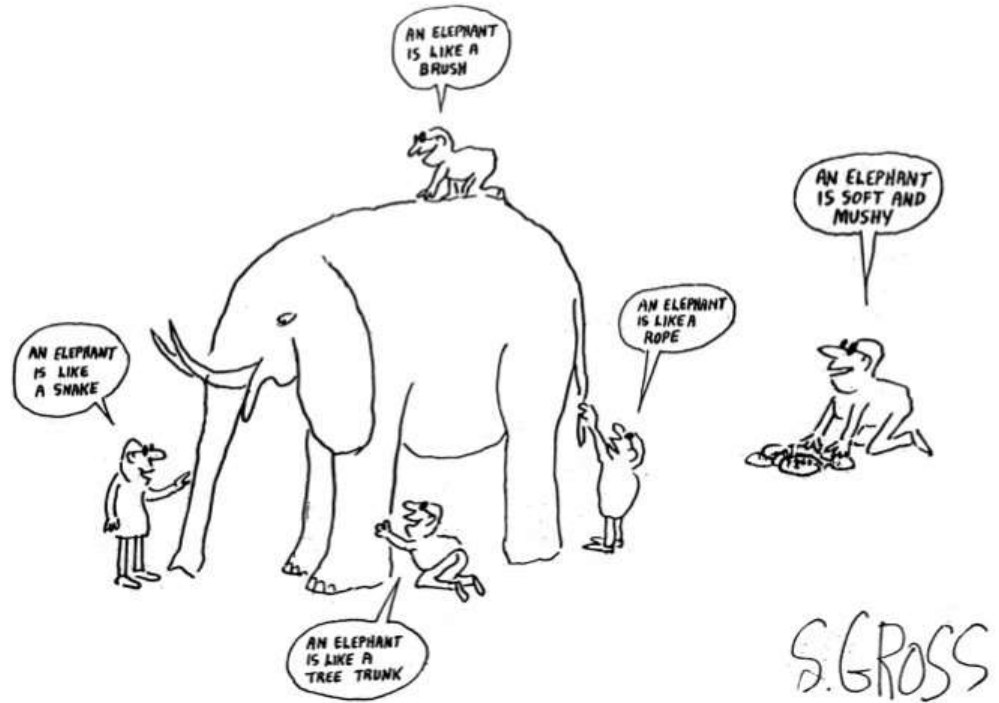
# Intervening on Cumulative Environmental Neurodevelopmental Risks: Introducing a Complex Systems Approach

*Devon Payne-Sturges, DrPH*  
*MAKING THE CONNECTION CONFERENCE 2020*  
*Wisconsin Environmental Health Network*  
*University of Wisconsin – Madison, WI*  
*March 7, 2020*

In public health we work to address problems in complex systems...



But how do we know what the problem is?



# Hallmarks of Complex Problems

- Feedback loops linking factors
- Path dependence
- Heterogeneity
- Dynamics/Changes over time
- Nonlinear effects
- Time delays between action and response
- Counterintuitive
- Policy resistant

# Project TENDR: Targeting Environmental Neurodevelopment Risks

- Protect pregnant women and children from toxic chemicals and pollutants that harm brain development
- Eliminate disproportionate exposures of these harmful chemicals to children of color and low-income children.





## Project TENDR: Targeting Environmental Neuro-Developmental Risks. The TENDR Consensus Statement

<http://dx.doi.org/10.1371/journal.pmed.1001958>

**Summary:** Children in America today are at an unacceptably high risk of developing neurodevelopmental disorders that affect the brain and nervous system including autism, attention deficit hyperactivity disorder, intellectual disability, and other learning and behavioral disabilities. These are complex disorders with multiple causes—genetic, social, and environmental. The contribution of toxic chemicals to these disorders can be prevented. **Approach:** Leading scientific and medical experts, along with children's health advocates, came together in 2013 under the auspices of Project TENDR: Targeting Environmental Neuro-Developmental Risks to issue a call to action to reduce widespread exposures to chemicals that interfere with fetal and children's brain development. Based on the available scientific evidence, the TENDR authors have identified prime examples of toxic chemicals and pollutants that increase children's risks for neurodevelopmental disorders. These include chemicals that are used extensively in consumer products and that have become widespread in the environment. Some are chemicals to which children and pregnant women are regularly exposed, and they are detected in the bodies of virtually all Americans in national surveys conducted by the U.S. Centers for Disease Control and Prevention. The vast majority of chemicals in industrial and consumer products undergo almost no testing for developmental neurotoxicity or other health effects. **Conclusions:** Based on these findings, we assert that the current system in the United States for evaluating scientific evidence and making health-based decisions about environmental chemicals is fundamentally flawed. To help reduce the unacceptably high prevalence of neurodevelopmental disorders in our children, we must eliminate or significantly reduce exposures to chemicals that contribute to these conditions. We must adopt a new framework for assessing chemicals that have the potential to disrupt brain development and prevent the use of those that may pose a risk. This consensus statement lays the foundation for developing recommendations to regulate, assess, and reduce exposure to neurotoxic chemicals. These measures are urgently needed if we are to protect healthy brain development so that current and future generations can reach their fullest potential.

### A Call to Action

The TENDR Consensus Statement is a call to action to reduce exposures to toxic chemicals that can contribute to the persistence of neurodevelopmental disabilities in America's children. The TENDR authors agree that widespread exposures to toxic chemicals in our air, water, food, soil, and consumer products can increase the risks for cognitive, behavioral, or social impairment, as well as specific neurodevelopmental disorders such as autism and attention deficit hyperactivity disorder (ADHD) [De Rosa et al. 2015; Gao et al. 2015; Lanphear 2015; Council on Environmental Health 2011]. This preventable threat results from a failure of our industrial and consumer markets and regulatory systems to protect the developing brain from toxic chemicals. To lower children's risks for developing neurodevelopmental disorders, policies and actions are urgently needed to eliminate or significantly reduce exposures to these chemicals. Further, if we are to protect children, we must overhaul how government agencies and business assess risks to human health from chemical exposures, how chemicals in consumer are regulated, and how scientific evidence informs decision making by government and the private sector.

### Trends in Neurodevelopmental Disorders

We are witnessing an alarming increase in learning and behavioral problems in children. Parents report that 1 in 6 children in the United States, 17% more than a decade ago, have a developmental disability,

including learning disabilities, ADHD, autism, and other developmental delays (Boyle et al. 2011). As of 2012, 1 in 10 (4–5.9 million) children in the United States are estimated to have ADHD (Bloom et al. 2013). As of 2014, 1 in 68 children in the United States has an autism spectrum disorder (based on 2010 reporting data) (CDC 2014).

The economic costs associated with neurodevelopmental disorders are staggering. On average, it costs twice as much in the United States to educate a child who has a learning or developmental disability as it costs for a child who does not (Charlton et al. 2004). A recent study in the European Union found that costs associated with low IQ points and intellectual disability arising from two categories of chemicals—polybrominated diphenyl ether flame retardants (PBDEs) and organophosphate (OP) pesticides—are estimated at 159.44 billion euros (169.45 billion dollars) annually (Hollinger et al. 2015). A 2009 analysis in the United States found that for every \$1 spent to reduce exposures to lead, a public transportation, society would benefit by \$17–\$23 (Gould 2009).

### Vulnerability of the Developing Brain to Chemicals

Many toxic chemicals can interfere with healthy brain development, even at extremely low levels of exposure (Adzinski et al. 2011; Bellinger 2008; Committee on Improving Analytic Approaches Used by the U.S. EPA 2009; Zooler et al. 2012). Research in the neurosciences has identified “critical windows of vulnerability” during embryonic and fetal development, infancy, early childhood and adolescence (Lanphear 2015; Lyall et al. 2014; Rice and Barone 2000). During these windows of development, toxic chemical exposures may cause lasting harm to the brain that interferes with a child's ability to reach his or her full potential.

The developing fetus is continuously exposed to a mixture of environmental chemicals (Mito et al. 2013). A 2011 analysis of the U.S. Centers for Disease Control and Prevention's (CDC) bio-monitoring data found that 99% of pregnant women in the United States have detectable levels of 62 chemicals in their bodies, out of 163 chemicals for which the women were screened (Woodruff et al. 2011). Among the chemicals found in the vast majority of pregnant women are PBDEs, polycyclic aromatic hydrocarbons (PAHs), phthalates, perfluorinated compounds, polychlorinated biphenyls (PCBs), pesticides, lead and mercury (Woodruff et al. 2011). Many of these chemicals cross the placenta during pregnancy and are routinely detected in cord blood or other fetal tissues (ATSDR 2011; Breen 2010; Chen et al. 2015; Lee et al. 2011).

### Prime Examples of Neurodevelopmentally Toxic Chemicals

The following list provides prime examples of toxic chemicals that can contribute to learning, behavioral, or intellectual impairment, as well as specific neurodevelopmental disorders such as ADHD or autism spectrum disorder:

- Organophosphate (OP) pesticides (Eskenski et al. 2007; Foutschery et al. 2014; Pauling et al. 2014; Marks et al. 2010; Reath et al. 2006; Shadish et al. 2014).
- PBDE flame retardants (Chen et al. 2014; Cowell et al. 2015; Ekstrand et al. 2013; Heberman et al. 2010).
- Combustion-related air pollutants, which generally include PM<sub>10</sub>, nitrogen dioxide and particulate matter, and other air pollutants for which nitrogen dioxide and particulate matter are markers (Boorman et al. 2013; Clifford et al. 2016; Judyshvilk

### POLICY FORUM

## Organophosphate exposures during pregnancy and child neurodevelopment: Recommendations for essential policy reforms

Irva Hertz-Picciotto<sup>1,2\*</sup>, Jennifer B. Saas<sup>2,3</sup>, Stephanie Engel<sup>4</sup>, Deborah H. Bennett<sup>1</sup>, Aaa Bradman<sup>5</sup>, Brenda Eskenazi<sup>1</sup>, Bruce Lanphear<sup>6</sup>, Robin Whyatt<sup>1</sup>

Optima

### VIEWPOINT

## Establishing and Achieving National Goals for Preventing Lead Toxicity and Exposure in Children

David C. Bellinger,  
M.D., M.P.H.

Children are exposed to chemicals in consumer products, household dust, food, air, water, and soil that at cohort of children under 6 years of age), a cost-benefit ratio comparable to that of childhood vaccines.<sup>6</sup> An

### COMMENTARY

## Healthy Air, Healthy Brains: Advancing Air Pollution Policy to Protect Children's Health

Evidence is growing on the adverse neurodevelopmental effects of exposure to combustion-related air pollution.

Project TENDR (Targeting Environmental Neurodevelopmental Risks), a unique collaboration of leading scientists, health professionals, and children's and envi-

ronmental health experts, including Dr. David C. Bellinger, M.D., M.P.H., and Dr. Brenda Eskenazi, M.D., M.P.H., are working to advance policy reforms to protect children's health from air pollution. This commentary is part of a special issue of *PLOS Medicine* on air pollution and children's health, edited by Dr. David C. Bellinger, M.D., M.P.H., and Dr. Brenda Eskenazi, M.D., M.P.H.

Children are exposed prenatally and in early childhood to multiple environmental stressors that can adversely af-

fect neurodevelopmental outcomes, including ultrafine particulate matter (PM<sub>2.5</sub>), polycyclic aromatic hydrocarbons, nitrogen dioxide, and fine particulate matter (PM<sub>10-2.5</sub>).

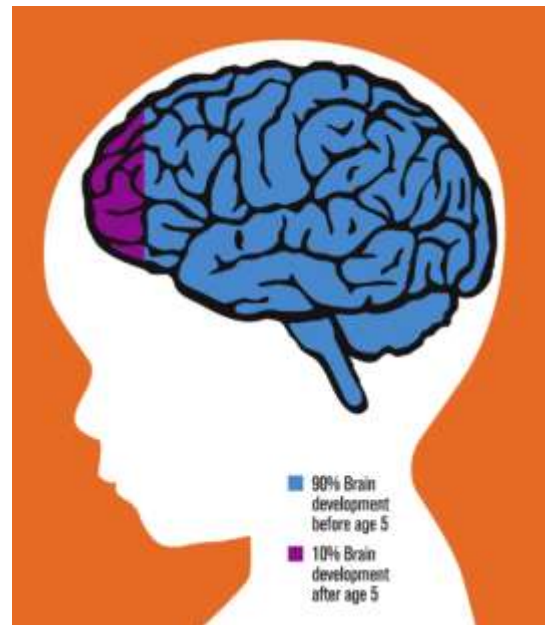
Children are also exposed to neurodevelopmental disorders in children.<sup>1,2</sup> A growing body of human studies associate exposure to combustion-related air pol-

# Project TENDR: Education and Outreach

- **Congressional briefings**
- **Comment letters** on federal, state and international policies & proposed rules.
- **Grand rounds** and **professional presentations**
- **Op-eds**
- Providing **Expert Testimony** on the science
  - Federal agency rulings on PBDEs, lead
  - State bills on toxic chemicals in children's products, and on neurotoxic pesticides
  - Amicus brief in case on federal phthalates rule

## Multiple environmental neurodevelopmental stressors

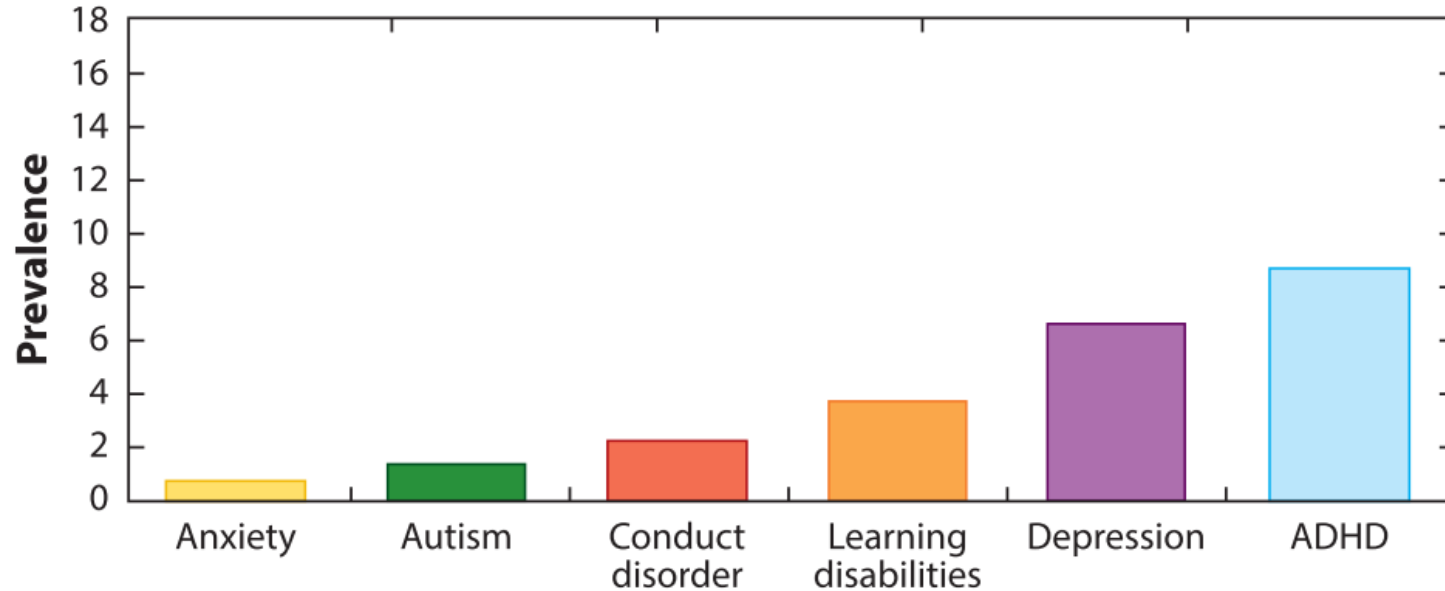
A wide range of prenatal and early childhood environmental conditions, along with physical and psychosocial factors, can affect children's cognitive abilities and academic performance.



Graphic adapted from Harvard Center for the Developing Child



# Prevalence of learning disabilities and mental disorders in US children



Boyle CA, Boulet S, Schieve LA, Cohen RA, Blumberg SJ, Yeargin-Allsopp M, Visser S, Kogan MD: **Trends in the prevalence of developmental disabilities in US children, 1997-2008.** *Pediatrics* 2011, **127**:1034-1042.  
Lanphear BP: **The impact of toxins on the developing brain.** *Annu Rev Public Health* 2015, **36**:211-230.

# CHEMICALS KNOWN TO DISRUPT BRAIN DEVELOPMENT

**90%**  
OF PREGNANT U.S. WOMEN:

have detectable levels of **62 chemicals**  
in their bodies out of 163 screened

SOURCE: DOI-10.1289/ehp.11021



Lead



Mercury



Organophosphate  
pesticides



Phthalates

Polybrominated  
diphenyl ethers  
(PBDEs)



Polychlorinated  
biphenyls (PCBs)

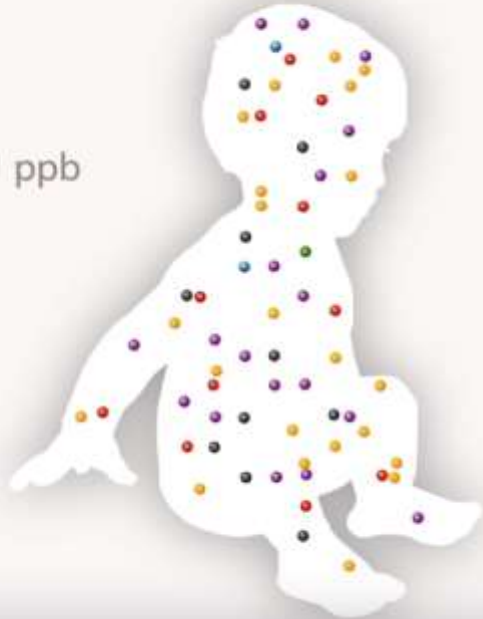


Polycyclic  
aromatic  
hydrocarbons  
(PAHs)



PROJECT TENDR:  
TARGETING ENVIRONMENTAL NEURODEVELOPMENTAL RISKS

1 Marble = 1 ppb



## Body Burden

● Lead.....	11.7 ppb
● Mercury.....	0.6 ppb
● PCBs.....	19.6 ppb
● PBDEs.....	10.4 ppb
● OP Pesticides..	17.0 ppb
● BPA.....	2.5 ppb

# Multiple social and psychosocial factors have independent and substantial impacts on neurodevelopment, cognitive and behavioral functioning

- substandard housing, crowding and noise
- family turmoil, violence, poverty and household food insecurity



# Social conditions make environmental exposures worse

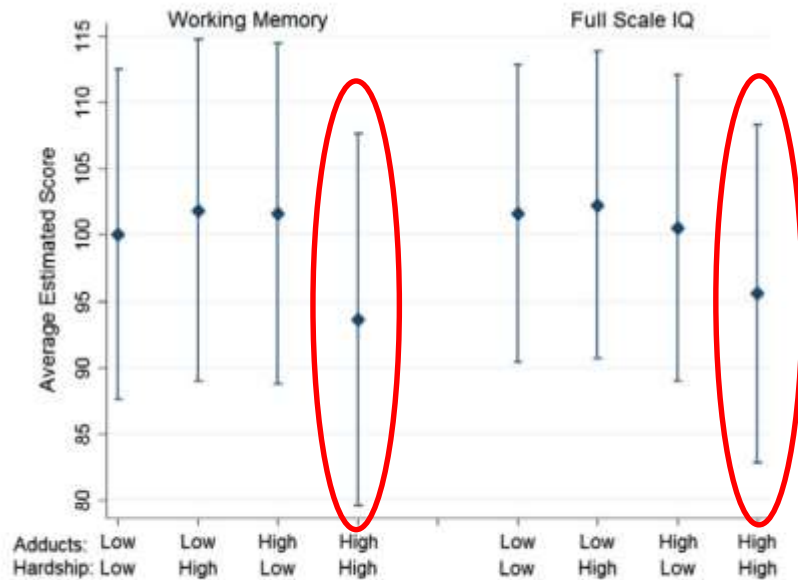
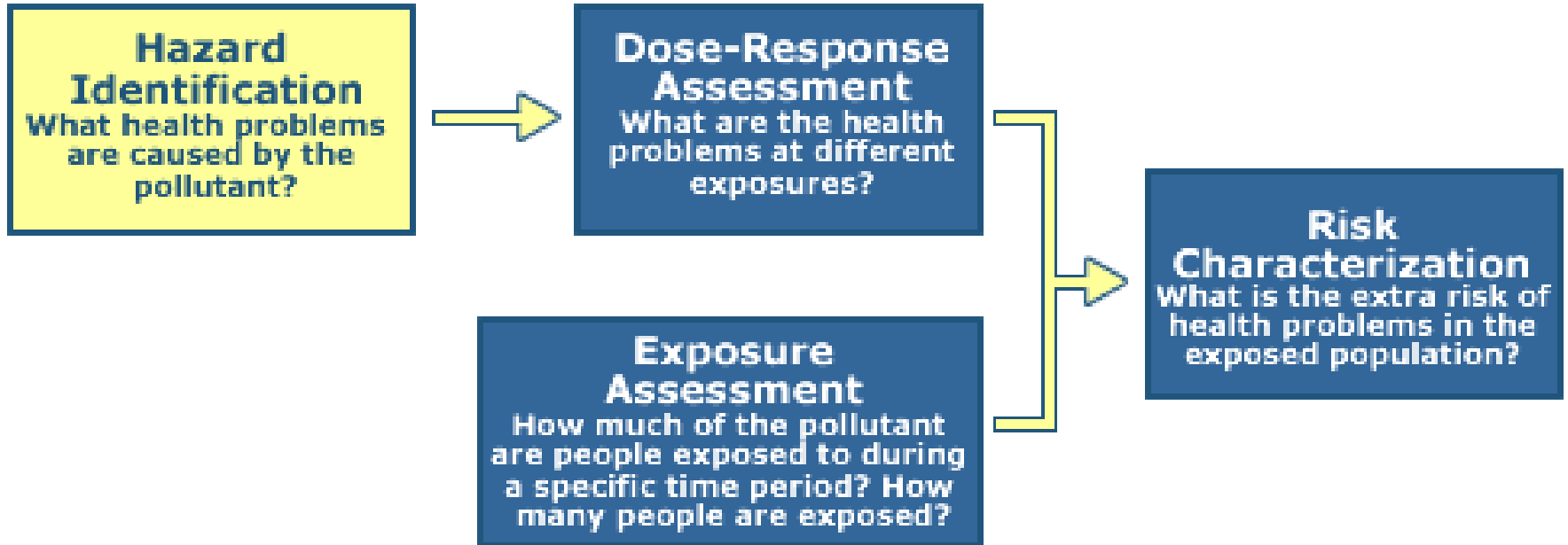


Fig. 2. Full Scale IQ and Working Memory Scores in the low and high cord PAH-DNA adduct groups stratified by recurrent hardship ( $n = 276$ ).

Vishnevetsky, J. et al. *Neurotoxicol Teratol* 2015, 49, 74-80,

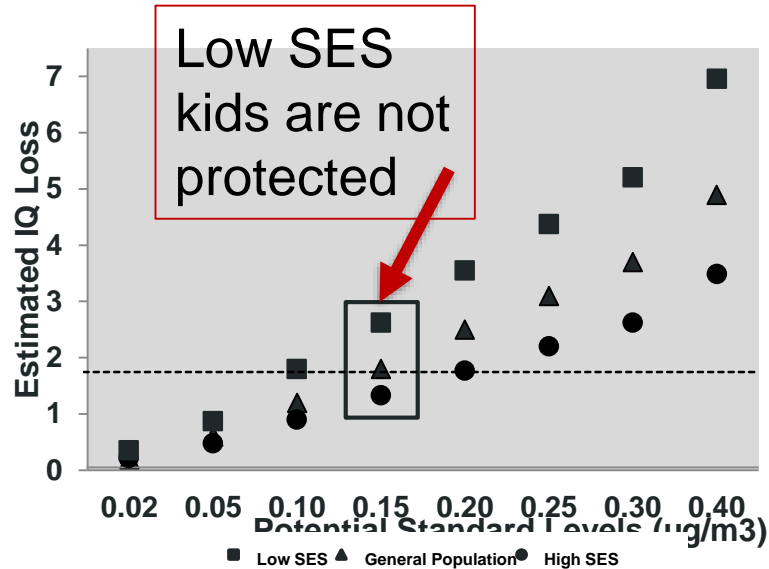
- Vishnevetsky et al. 2015 - Prenatal PAH exposures combined with poverty lowers IQ in kids
- Rauh et al. 2004 - combined ETS and material hardship (e.g poverty) resulted in lower cognitive functioning in kids
- Cory-Slechta et al. 2005– lab studies on lead and prenatal stress and neurological outcomes in offspring

# The 4 Step Risk Assessment Process





# Expected mean IQ loss estimates for children exposed at the level of the NAAQS lead in air standard

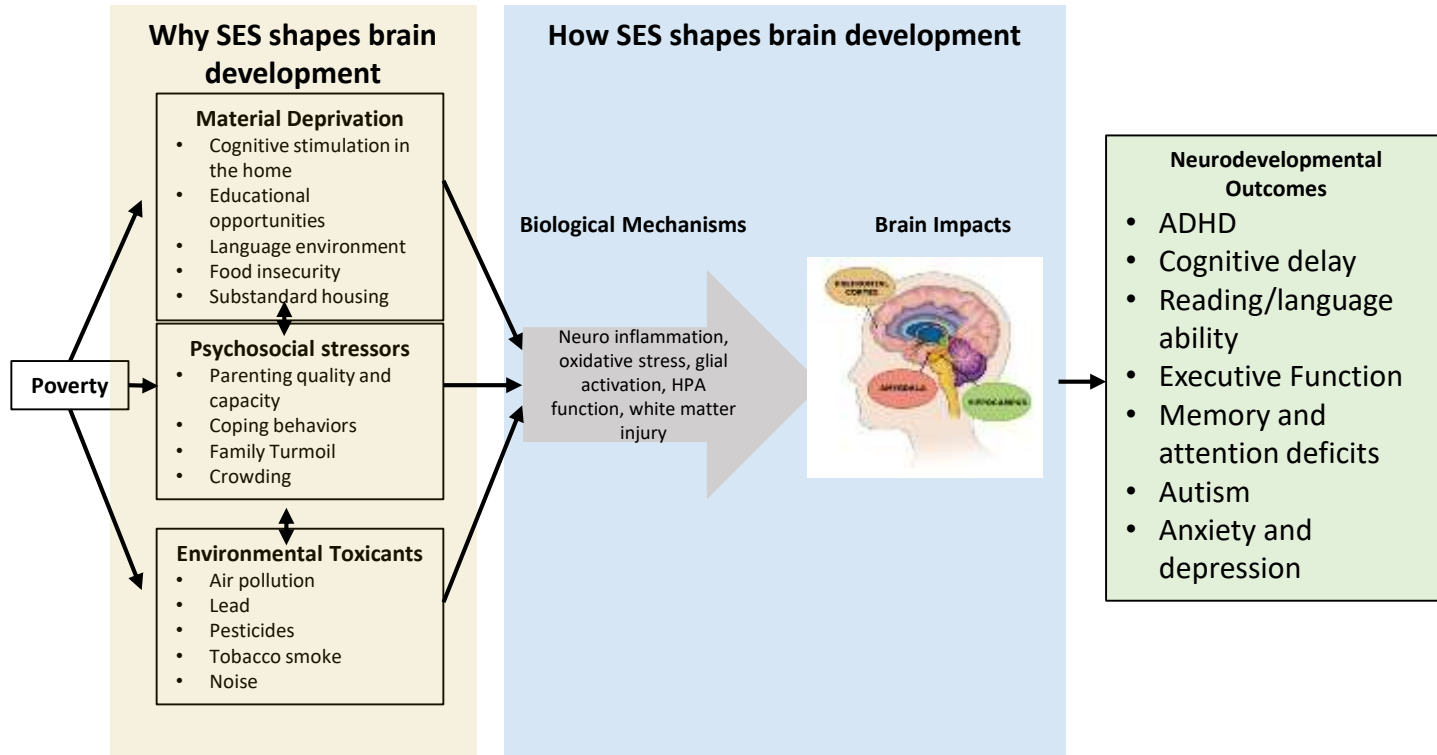


Comparison of population mean IQ loss estimates derived from general population and susceptible groups. Dotted line at 2 IQ points represents the acceptable risk level defined by EPA. A box surrounds estimates associated with the final chosen air lead standard

# Longer-term cognitive consequences of childhood lead exposure

- Impairment in brain development in one domain could alter the trajectory of development in other domains.
- Set in motion a process that results in a child who is
  - poorly equipped to make good, future-oriented decisions and
  - has poor academic success, faces restricted employment opportunities, material hardship, and other socio-economic stresses

# Environments of poverty and combined effects



# Hallmarks of Complex Problems : Lead Exposures

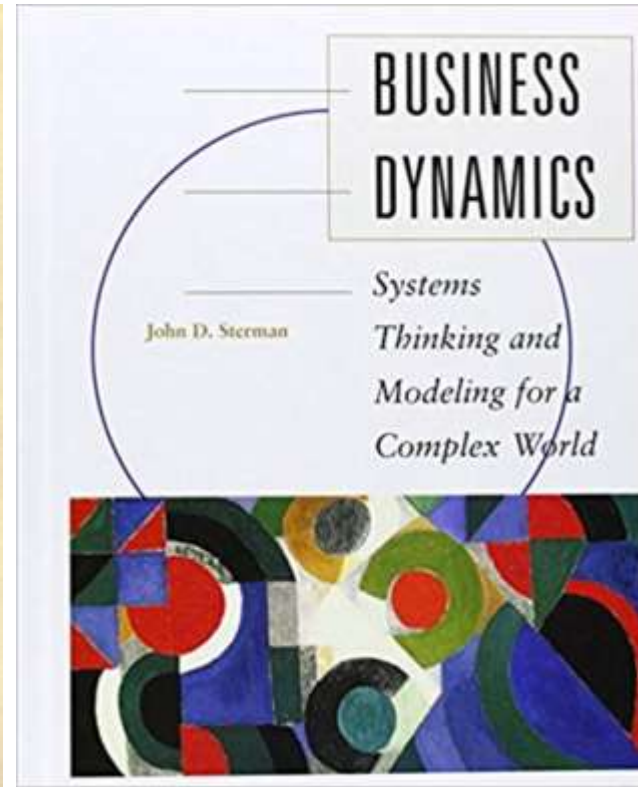
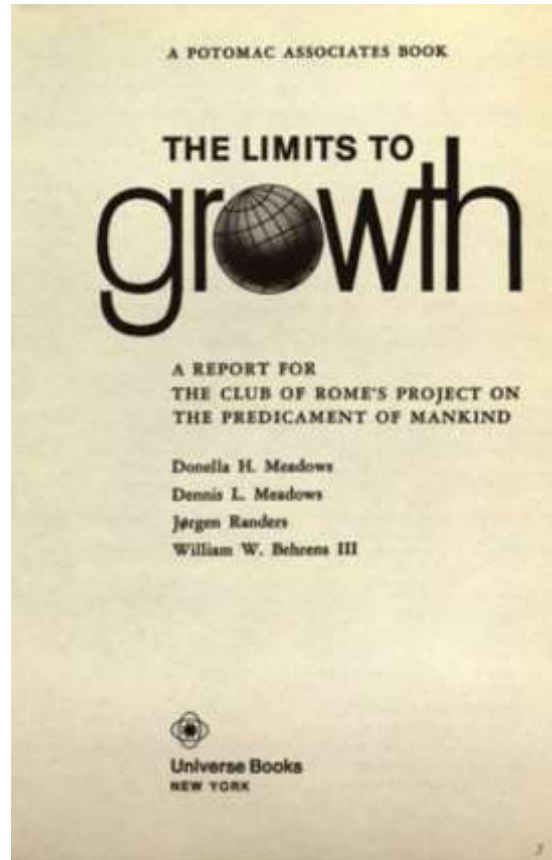
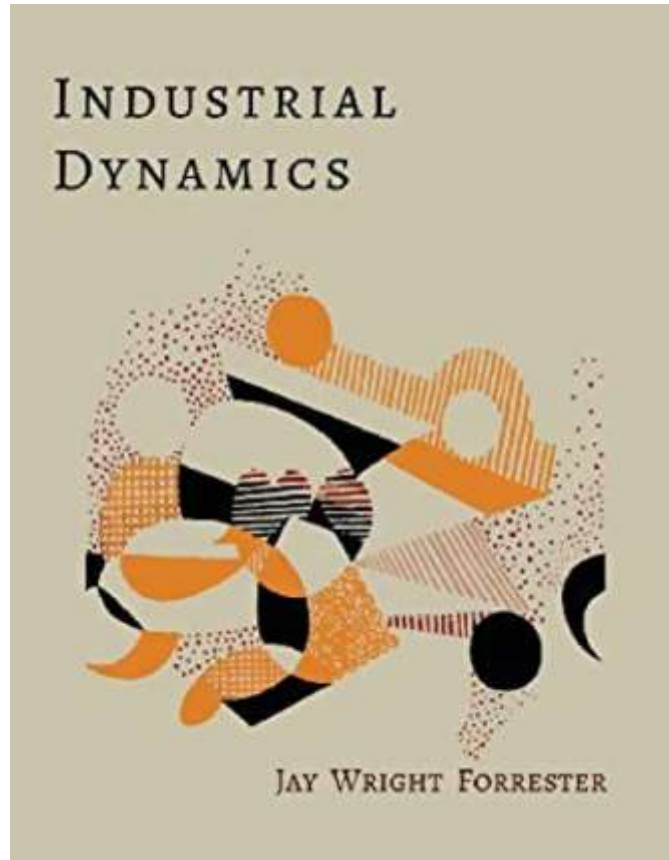
- Intergenerational effects /vicious cycles (Feedbacks)
- Trends in prevalence of neurodevelopmental disorders (Dynamics/temporal effects)
- Intervening early can lead to greater reduction in negative effects (Path dependence)
- Inequities by race/ethnicity/class (Heterogeneity)
- Despite knowing it's bad we have not removed lead from housing (Time delays)

# System Dynamics

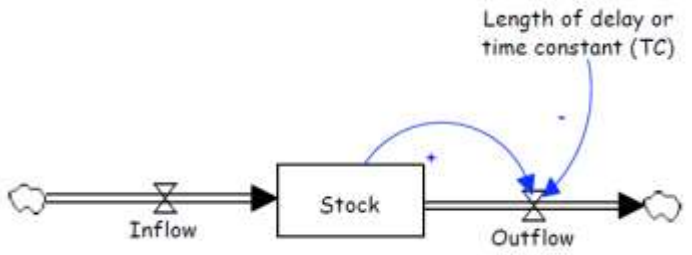
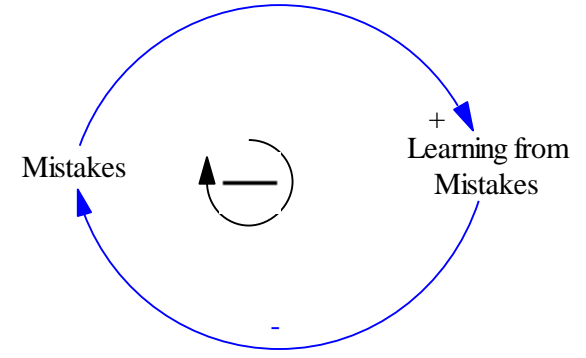
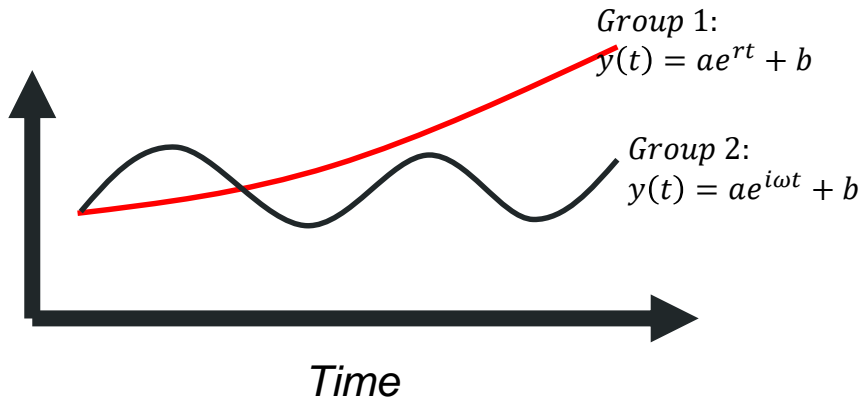
*System dynamics (SD) is the use of informal maps and formal models with computer simulation to uncover and understand endogenous sources of system behavior.*

Richardson, G.P. (2011). Reflections on the foundations of system dynamics. *System Dynamics Review*, 27(3), 219-243.

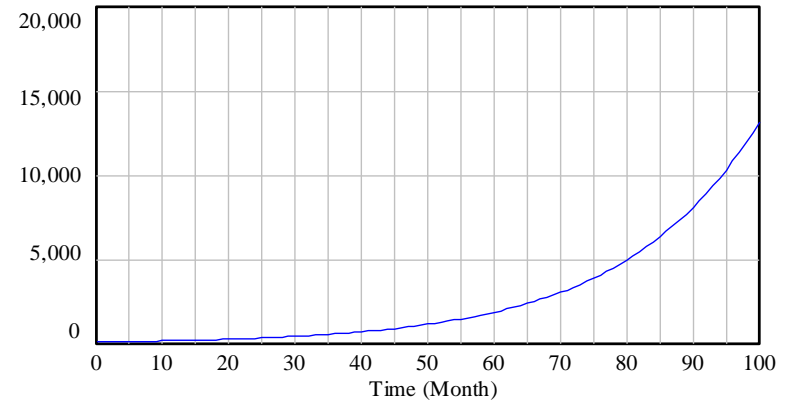
# Canonical System Dynamics Texts





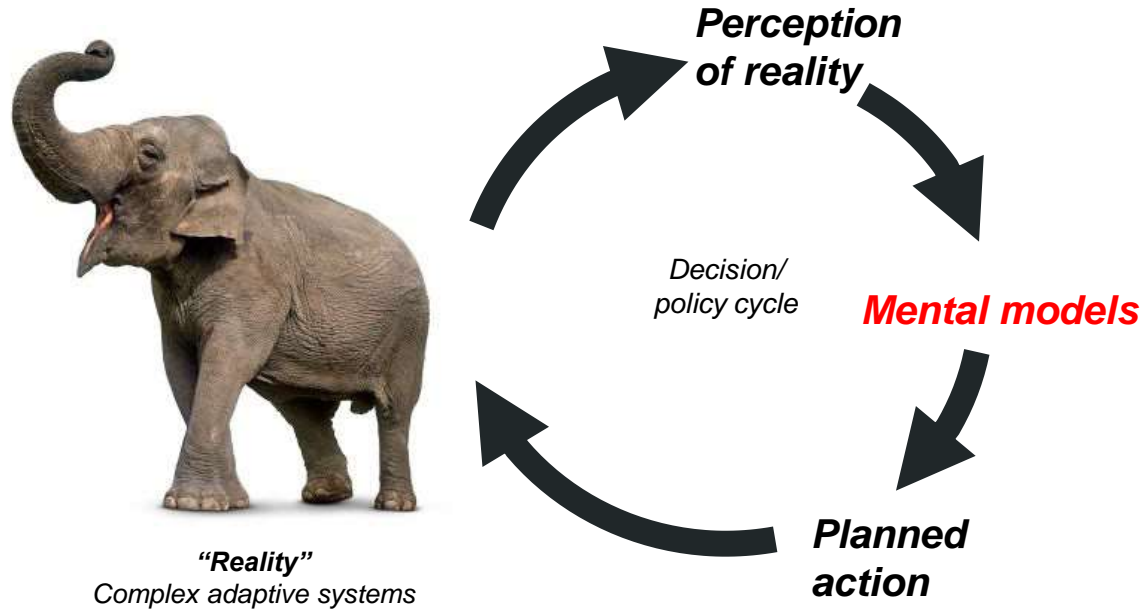


Graph for Stock

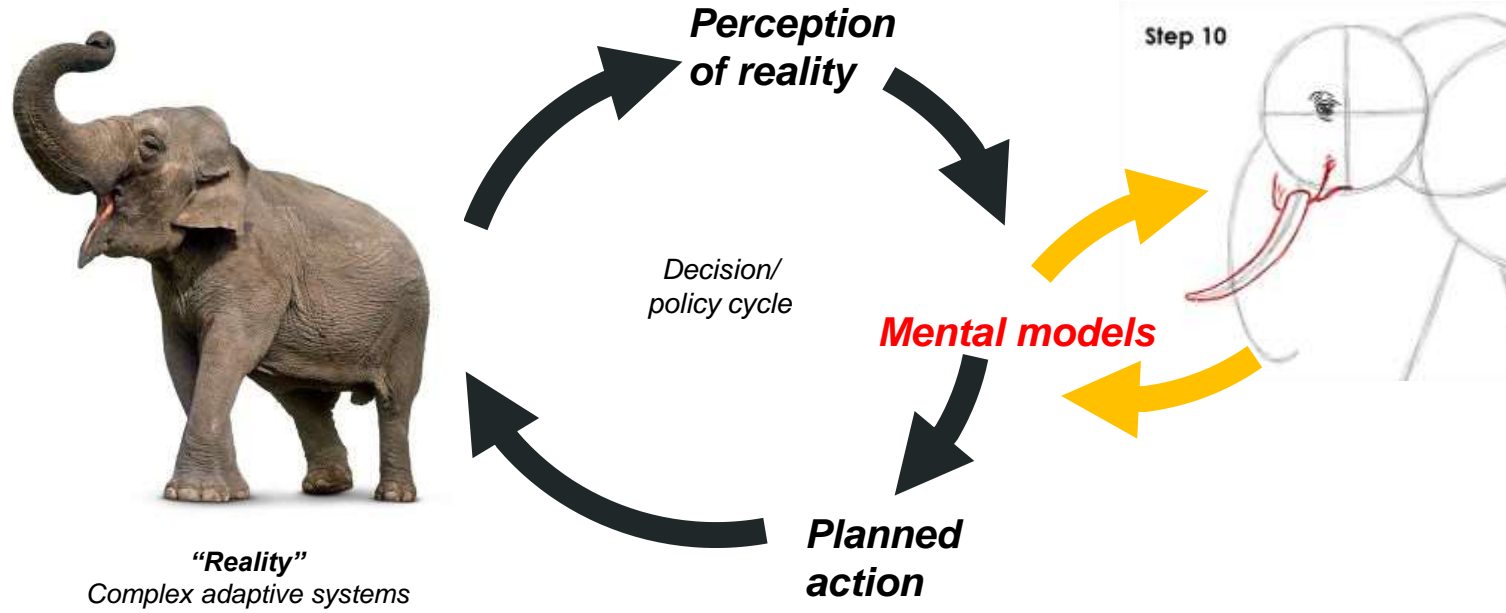


Stock : Current

# Mental models help us understand complex problems & systems



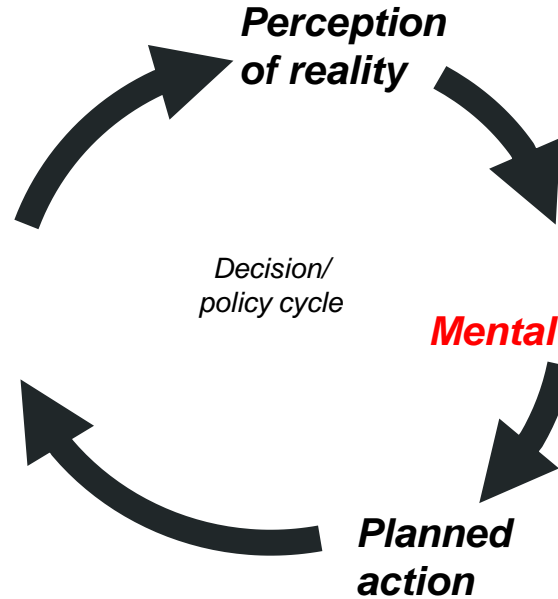
# Use of SD models to improve mental models



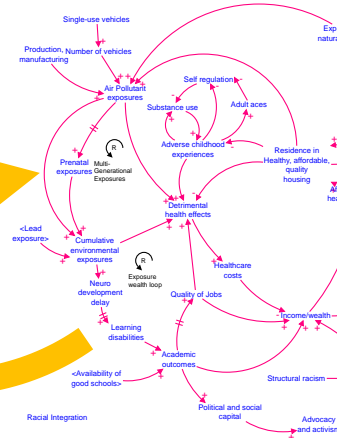
# We use SD models to refine & improve our mental models



**“Reality”**  
Complex adaptive systems



**Mental models**



# Critical questions to consider

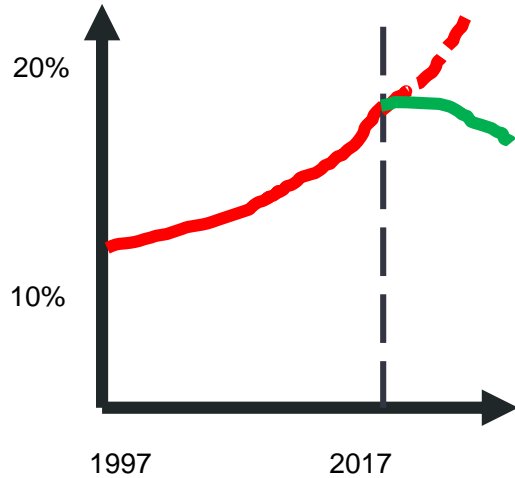
Question	How is this answered
What is the problem? Is the problem dynamic?	Drawing a BOT graph with the desired and feared behaviors over time over a defined period of time
What kind of problem is it?	Primary diagnosis as a learning, coordination analysis or restructuring problem or a combination
Does the system involve feedback mechanisms?	Drawing a diagram of the system that involved one or more feedback loops
What kind of insights would help solve the problem?	Identifying the types of model-based insights such as visualizing the system of identifying leverage points that will help solve the problem
What is the purpose of the model?	Writing a description of the problem, explaining why it is dynamic and involves feedback and clearly stating the purpose in terms of insights that will help solve the problem
What would be the added value of the model?	Identifying how the approach being considered would offer something above the existing tools

# Is it dynamic?

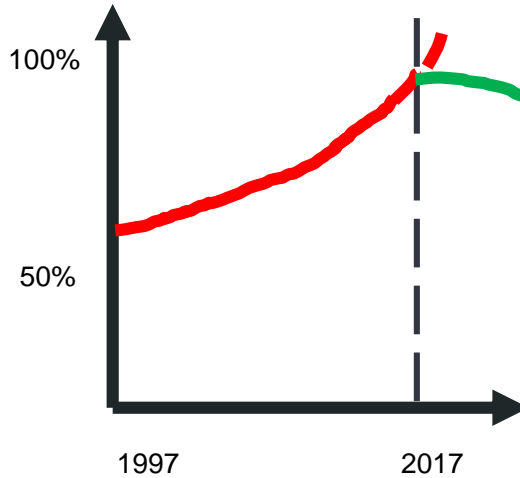
- What is the reference mode?
  - What do you know about the behavior of the system over time?
  - Stagnant patterns of behavior are still dynamic
- What is/are the key variable(s) of interest or importance?
  - Not restricted to variables for which numeric data exists
- What is the time horizon of your model?
  - How long has it taken for dynamics to emerge?
  - How soon might you expect to see change?



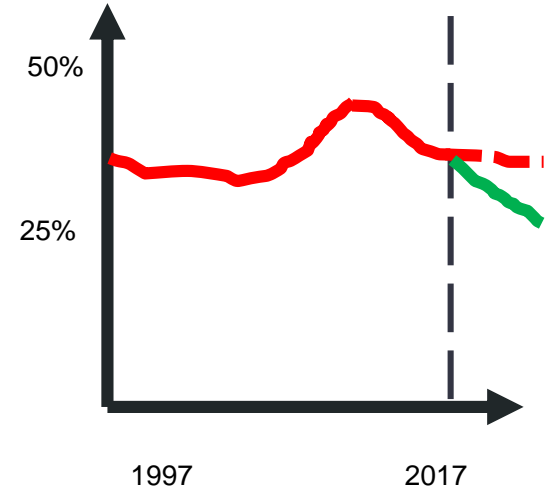
# Example: Targeting Environmental Neurodevelopmental Risks Reference Modes



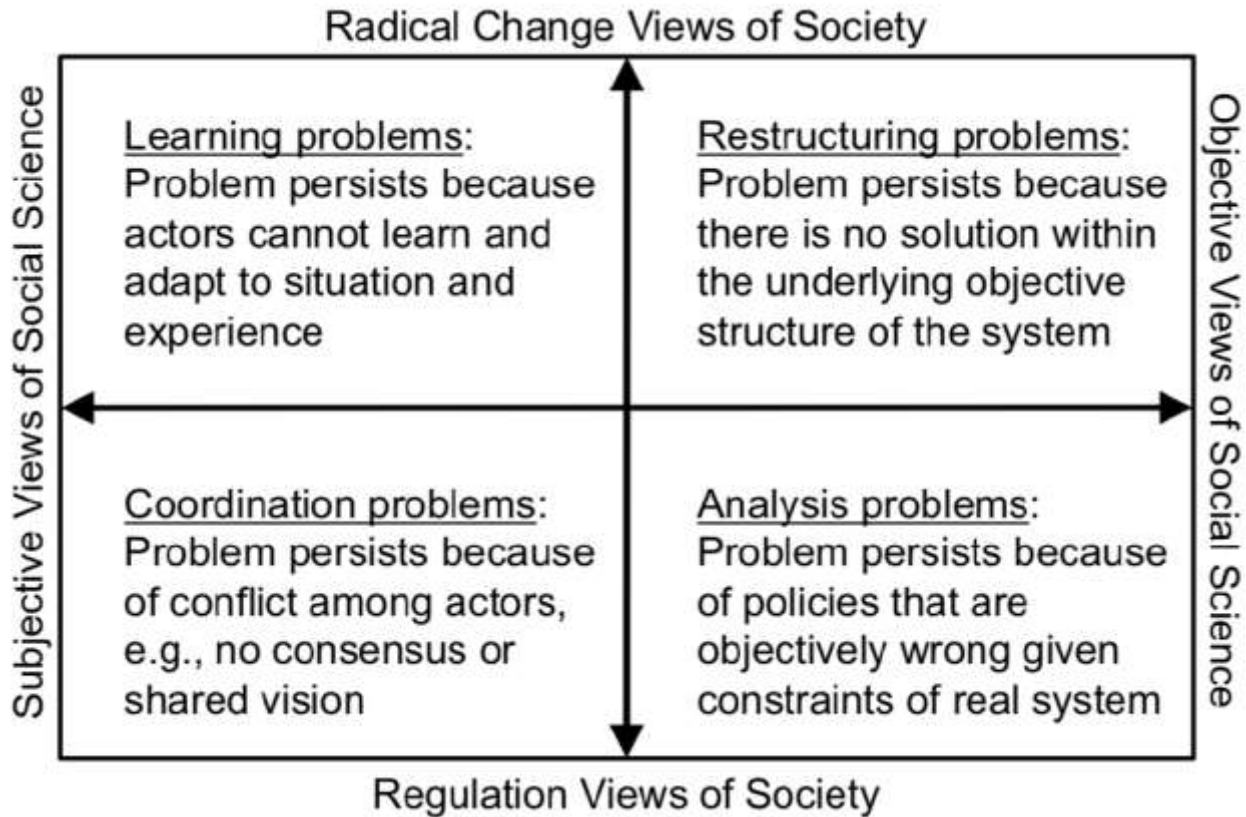
Prevalence of developmental disability among US children



Prevalence of pregnant women with detectable levels of 62 neurotoxic chemicals



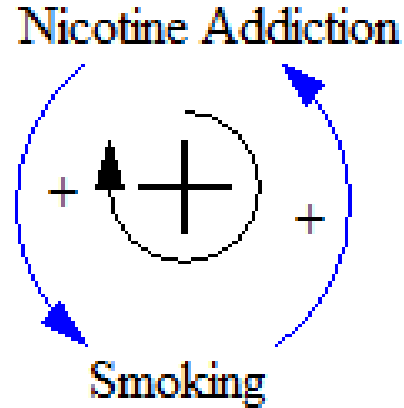
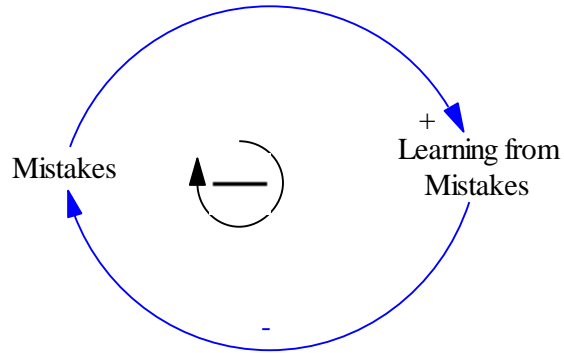
Prevalence of US children living below 200% poverty line



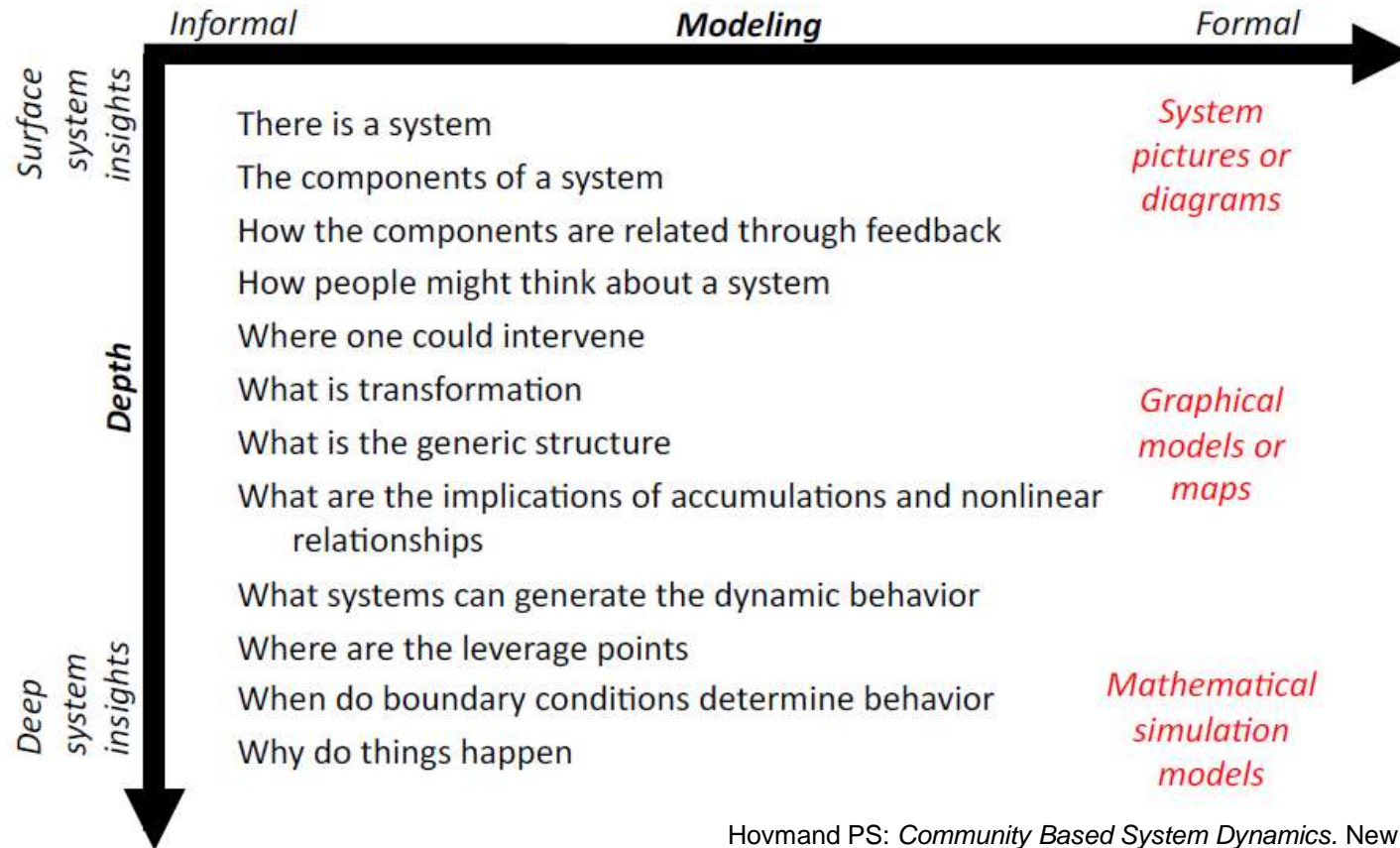
Adapted from Hovmand (2014)

# Does it involve feedbacks?

- Take time to sketch out some hypothesized loops
- Are there important delays?
- Nonlinear relationships?



# What kinds of insights would solve the problem?



# What is the value added?

- Examples of value added: learning, shared understanding, dialogue, developing policies, policy evaluation, and more...
- What is the value added for your community partners?
- What is the value added for researchers/outsideers?
- How does this fit into a larger plan of work?

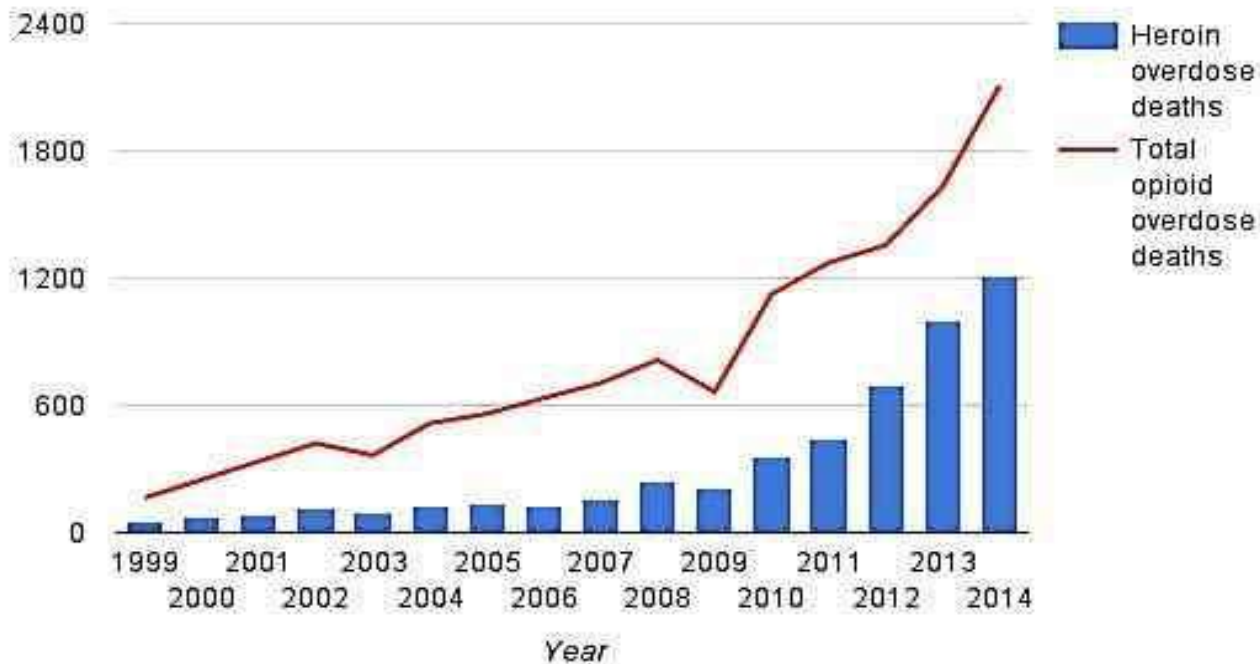
**Shifting the Burden of Asthma Management to Fundamental Issues**



\*EPR3 4 Components of Asthma Care



## Ohio heroin and total opioid overdose deaths

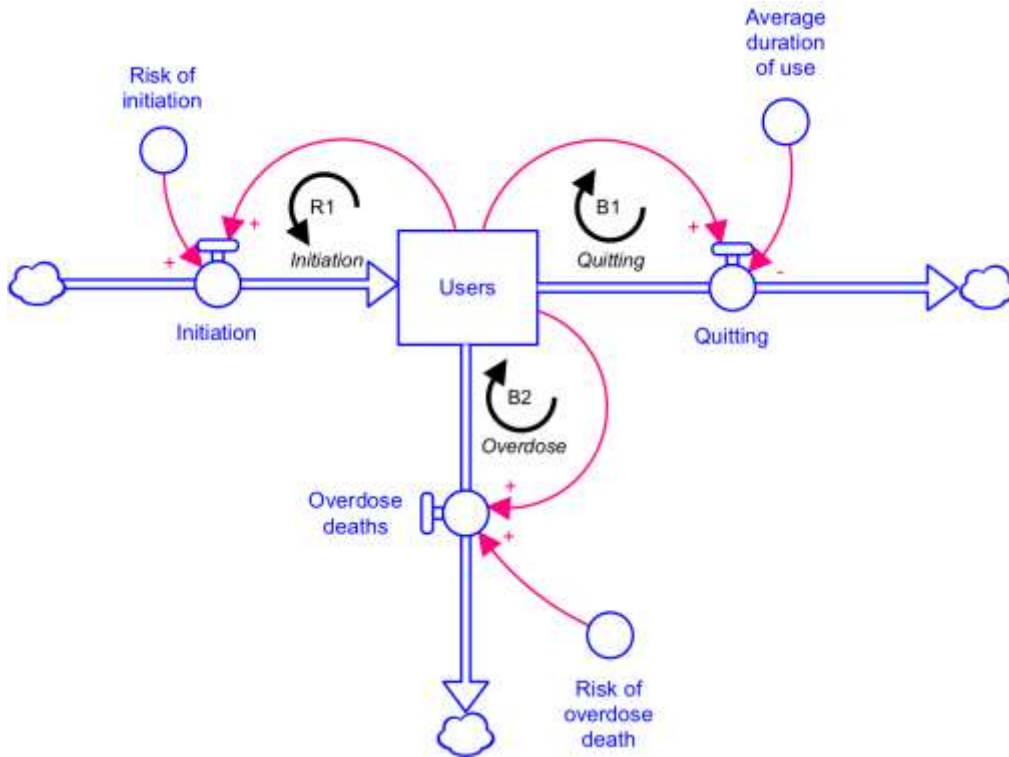


**Source: Henry J. Kaiser Family Foundation**

Hovmand, P. Policy and Sensitivity Analysis using the Opioid Model S65-5660



## Opioid simulation model



## Feedback loops

**R1:** Reinforcing loop of initiation where initiation spreads through social networks at a rate proportional to the number of current users

**B1:** Balancing loop of quitting where users have an average duration of use

**B2:** Balancing loop of overdose deaths associated with the risk of overdose

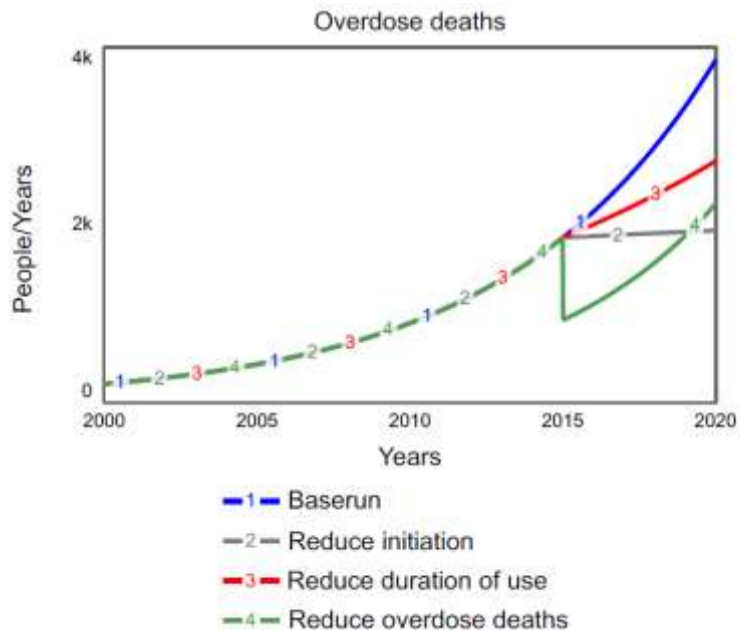
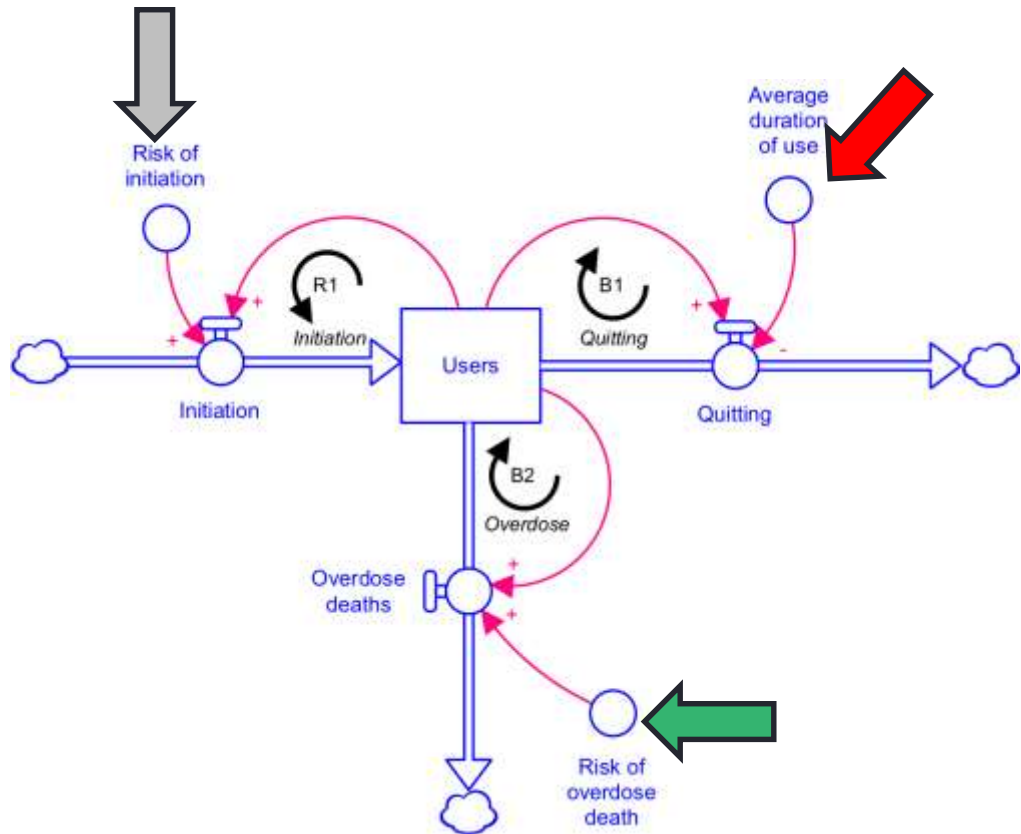
## Equations and initial conditions

$$\text{Initiation}(t) = \text{Risk\_of\_Initiation} \cdot \text{Users}(t),$$

$$\text{Quitting}(t) = \text{Users}(t) / \text{Average\_duration\_of\_use},$$

$$\text{Overdose\_deaths}(t) = \text{Risk\_of\_overdose\_deaths} \cdot \text{Users}(t),$$

$$\text{Users}(t=0) = \text{Init\_users}.$$



Hovmand. P. Policy and Sensitivity Analysis using the Opioid Model S65-5660

# Key Takeaways

- Systems models can help us to develop insights that change our mental models
- SD could be useful tool for research on health inequities – can see feedbacks that are relevant to diverse disciplines
- Systems simulation modeling can be used to help policy makers understand the impact of various policy decisions and how they play out over time before implementation.
- Iterative process; need stakeholder engagement

“All models are wrong, some are useful”

-George Box, 1976

# Thank you!

