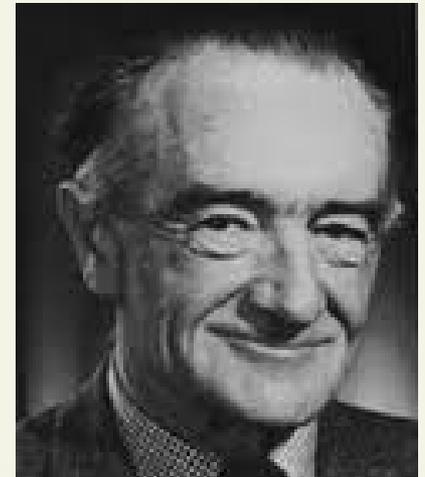


# The Basic Laws of Systematic Review

Ellen Silbergeld

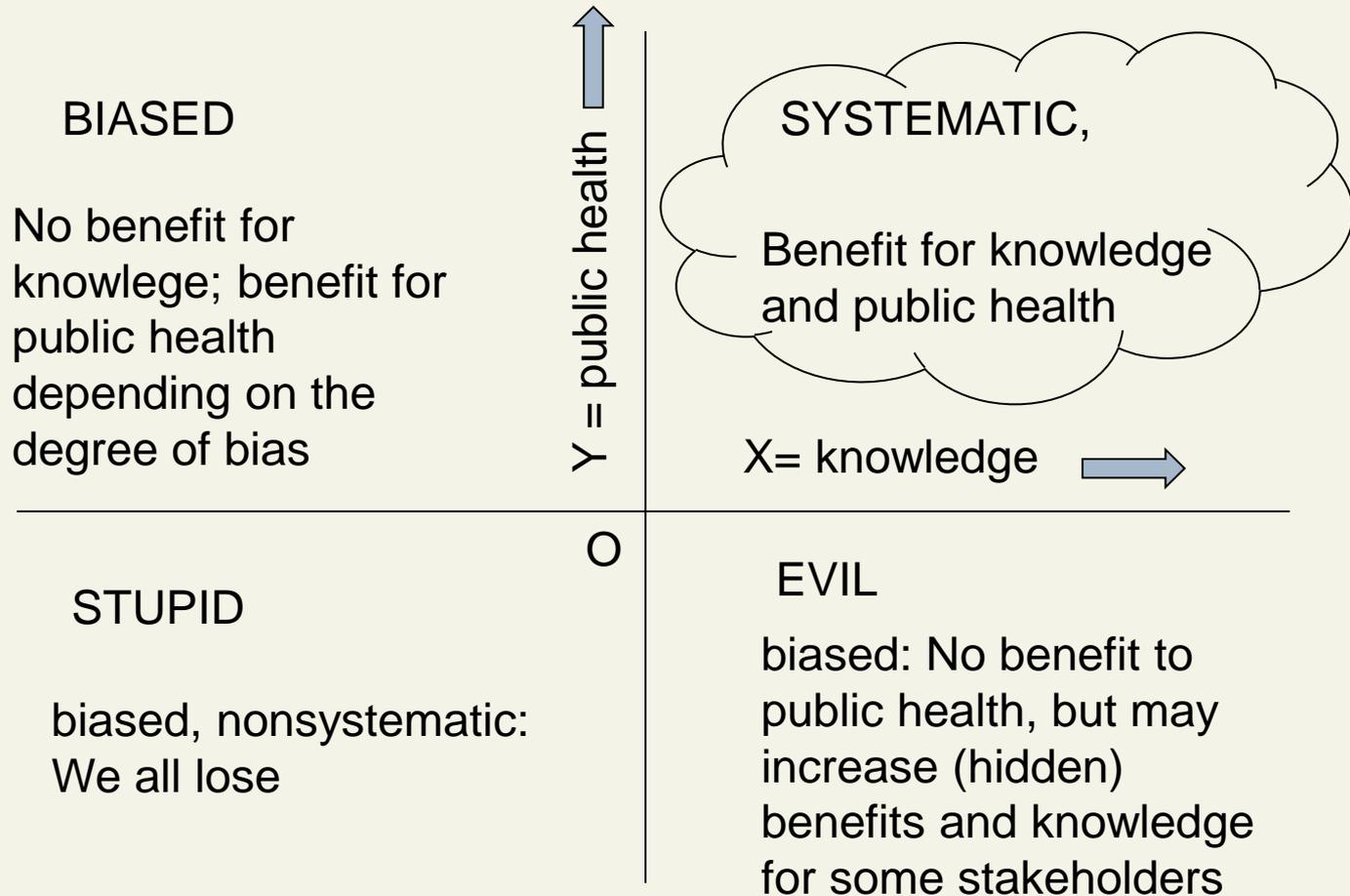
Johns Hopkins Bloomberg School of Public Health



# THE LAWS

- **DON'T BE STUPID** –
  - LEARN FROM OTHERS (COCHRANE)
  - SEEK COMMON PRINCIPLES
- **DON'T BE EVIL** –
  - BE TRANSPARENT [COMPLETELY TRANSPARENT]
  - REVEAL AND AVOID CONFLICTS OF INTEREST
- **AVOID BIAS** – *STUDY DESIGNS, ANALYTIC METHODS, AND DATA INTEGRATION ISSUES THAT INTRODUCE SYSTEMATIC ERROR [NOT COMMON MEANING]*
  - ESTABLISH A PRIORI DEFINITIONS, CRITERIA, AND METHODS
  - VALIDATE EVERYTHING, ANNOTATE EVERYTHING

# CIPOLLA'S SCHEMATIC OF STUPIDITY AND EVIL



# Current methods are not systematic, transparent or replicable (EPA, IARC, WHO, OSHA, etc)

- Problems begin at the beginning
  - How are relevant materials identified?
  - What assurance is there of completeness and lack of selection bias?
- Decision rules are not explicit
  - What are the rules for inclusion/exclusion?
  - are decisions replicable?
- “expert judgment” permeates the process
  - “weight of evidence”, “key study” etc
- **No wonder risk assessment differ!**
  - Endocrine disruptors, lead, dioxins, mercury, etc

# THE FOG OF EVIDENCE: “EXPERT JUDGMENT” aka “WEIGHT OF EVIDENCE”

“The term ‘weight of evidence’ constitutes neither a scientifically well-defined term nor an agreed formalized concept characterized by defined tools and procedures” (Weed, 2005).





# The importance of an evidence based approach in toxicology

- *Increasing the transparency and acceptance of decision making*
- Improving decision making
- Increasing the efficiency of decision making
- Encouraging better use of statistical and other models of inference
- Stimulating innovation in methods and more relevant research

# We can walk in “giant shoes”



- **Evidence based medicine**
  - 70 years of success in supporting improved research protocols and decision making in resource allocation in health care
- **The Cochrane Collaboration**
  - An international consortium working to develop, validate, and apply evidence based methods to clinical diagnosis and treatment



## Stepping outside the giant's shoes

- Generating the international community
  - What are the obstacles to agreement on goals
  - Who is our community?
  - What are our priorities?
- Adhering to the principles of Cochrane
  - Transparency, consistency, replicability, continuous improvement
- Developing evidence based methods for toxicology
  - Is there any precedent or prototype?

# Common Principles and Special Needs

## **Common Principles**

Ethical values

Validation of methods

Transparency at all stages in systematic review

Identification of factors affecting the risk of bias of the studies

Disclosure of Conflict of Interest

## **Toxicology has special needs**

Issues of external validity [nonhuman data for human risk assessment]  
heterogeneity of data sources

Criterion for mechanism as part of SR

Developing effective strategies for information searches