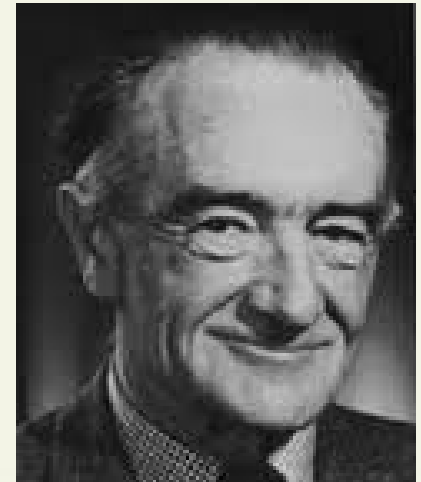


The Basic Laws of Systematic Review

Ellen Silbergeld

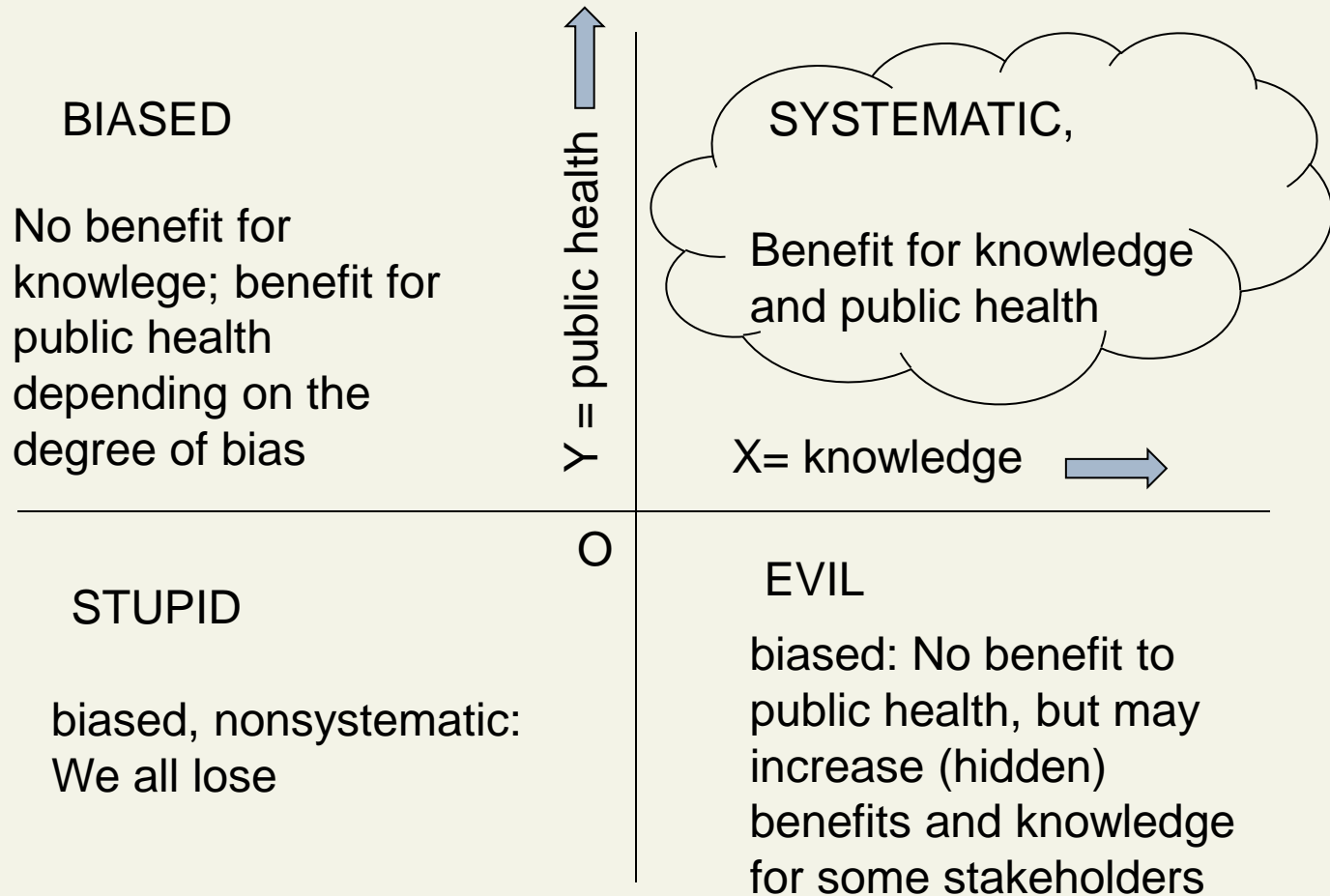
Johns Hopkins Bloomberg School of Public Health



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