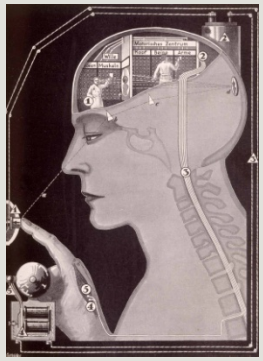

“Risk of Bias” and Causality Assessments

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USEPA, CRYSTAL CITY, VA

WORKSHOP ON ADVANCING SYSTEMATIC REVIEWS

Questions for the day

"Does 'risk of bias' as currently conceptualized and used, adequately encompass the breadth of issues needed for evaluation of studies of chemical exposures in observational epidemiology studies? If not, what approaches can be used to appropriately expand the focus?"

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How can we improve upon the current approaches used to assess risk of bias?

Is ACROBAT-NRSI a good candidate for moving that effort forward?

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Is ACROBAT-NRSI a good candidate for moving that effort forward?

"If not, what approaches can be used to appropriately expand the focus?"

How does any reasonable approach to assessing 'risk of bias' fit into the broader activity of assessing causality (i.e. "hazard")?

Methods for Interpreting Evidence*

General Scientific Method

Study Design & Statistical (Analytic) Methods

Research Synthesis Methods

- **Systematic Narrative Review**
- **Meta-Analysis and Pooled Analysis**
- **Criteria-based Methods**

*** Note: each of these has an extensive discussion in the peer-reviewed literature and textbooks; each has its "theory" and its "practice."**

WEED DL. RISK ANALYSIS 2005;25:1545-57; WEED DL. JECH 2001;55:104-110.

Sanderson et al. “Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography.” IJE 2007;36:666-76

“Assessing quality and susceptibility to bias is essential when interpreting primary research and conducting systematic reviews and meta-analyses. Tools for assessing quality in clinical trials are well-described but much less attention has been given to similar tools for observational epidemiological studies.”

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"Assessing quality and susceptibility to bias is essential when interpreting primary research and conducting systematic reviews and meta-analyses. Tools for assessing quality in clinical trials are well-described but much less attention has been given to similar tools for observational epidemiological studies." **(Sanderson et al. 2007, p. 666)**

Authors identified 86 such tools for evaluating bias (and more broadly, the quality) of observational epidemiology studies (1979-2006).

Other More Recent Examples

Vlaanderen et al. "Guidelines to evaluate human observational studies for quantitative risk assessment." EHP 2008;116:1700-5.

Money et al. "A systematic approach for evaluating and scoring human data." Reg Tox Pharm 2013;66:241-7.

Sterne et al. "A Cochrane Risk of Bias assessment tool: for non-randomized studies of interventions (ACROBAT-NRSI)." September 2014.

NTP RoC Handbook for Preparing Report on Carcinogens Monograph: "Assessment of the utility of the individual epidemiologic studies." 2015:25-40.

More from Sanderson et al. IJE 2007;36:666-76 (Table 1, p. 668)

Description and evaluation of each tool (n = 86) used the following "domains and criteria:"

1. Methods for selecting study participants
2. Methods for measuring exposure and outcome variables
3. Design specific sources of bias (excluding confounding)
4. Methods for control of confounding
5. Statistical methods
6. Conflict of interest

More from Sanderson et al. IJE 2007;36:666-76 (Table 1, p. 668)

"STRONGLY INFLUENCED by the STROBE guidelines"

Description and evaluation of each tool (n = 86) used the following "domains and criteria:"

1. Methods for selecting study participants **(> 75%)**
2. Methods for measuring exposure and outcome variables **(> 75%)**
3. Design specific sources of bias (excluding confounding) **(>75%)**
4. Methods for control of confounding **(> 75%)**
5. Statistical methods **(> 75%)**
6. Conflict of interest **(approximately 4%)**

Recommendations (Sanderson et al. 2007) re Tools for Evaluating Quality and Susceptibility to Bias (Epidemiology)

(1) Tools should include a small number of key domains

(2) Tools should be as specific as possible (taking into account study designs and topic area)

(3) Tools should employ simple checklists (rather than a numeric scale)

(4) Tools should show evidence of development, validity, and reliability

ACROBAT-NRSI

Domain	Related Terms	Distinct from RCTs?
PRE-INTERVENTION		
Bias due to Confounding	Selection bias; Allocation bias; Case-mix bias; Channeling bias	Y
Bias in Selection of Study Participants	Selection bias; Inception bias; Lead-time bias; Immortal time bias	Y
AT INTERVENTION		
Bias in Measuring Interventions	Misclassification bias; Information bias; Recall bias; Measurement bias; Observer bias	Y
POST-INTERVENTION		
Bias due to Departures from Intended Interventions	Performance bias; Time-varying confounding	N
Bias due to Missing Data	Attrition bias; Selection bias	N
Bias in Measuring Outcomes	Misclassification bias; Observer bias; Measurement bias	N
Bias in Selecting Reported Result	Outcome reporting bias; Analysis reporting bias	N

ACROBAT-NRSI

"is concerned with evaluating the risk of bias (ROB) in the results of non-randomized studies that compare the health effects of 2 or more interventions." (p. 3)

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Recommendations (Sanderson et al. 2007) re Tools for Evaluating Quality and Susceptibility to Bias (Epidemiology)

How does ACROBAT-NRSI fare?

(1) Tools should include a small number of key domains ☺☹

(2) Tools should be as specific as possible (taking into account study designs and topic area) ☺☹

(3) Tools should employ simple checklists (rather than a numeric scale) 😐

(4) Tools should show evidence of development, validity, and reliability ☺☹☹

ACROBAT-NRSI

“It will be rare that a non-randomized study is judged as at low risk of bias due to confounding.” (p. 12)

Methods for Interpreting Evidence*

General Scientific Method

Study Design & Statistical (Analytic) Methods

- **Including "risk of bias" aka "quality"**

Research Synthesis Methods

- **Systematic Narrative Review**
- **Meta-Analysis and Pooled Analysis**
- **Criteria-based Methods**

*** Note: each of these has an extensive discussion in the peer-reviewed literature and textbooks; each has its "theory" and its "practice." Each of these methods have published tools for assessing quality.**

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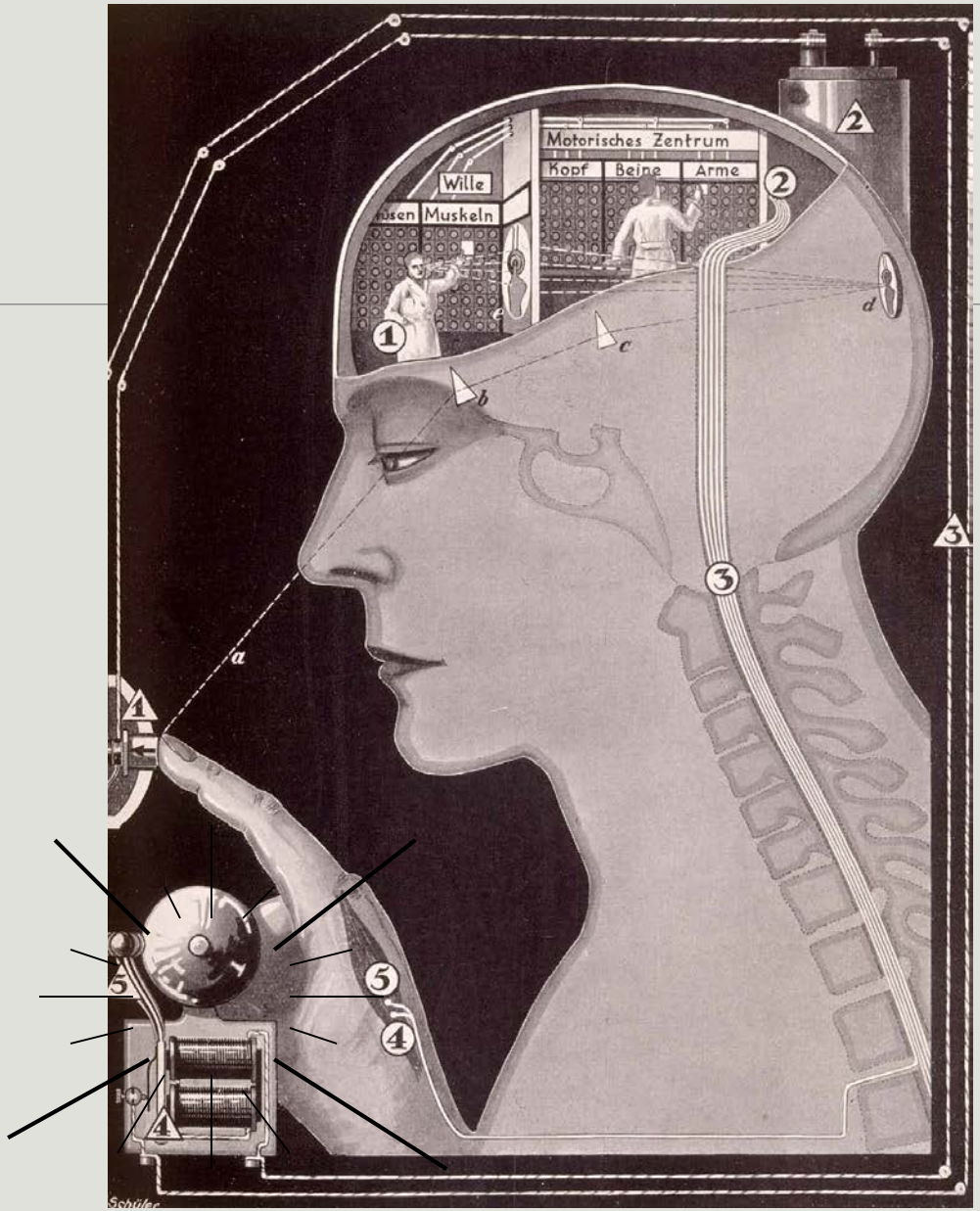

Fritz Lang, circa 1926. Stuttgart, Germany. Courtesy: National Library of Medicine