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EPIDEMIOLOGY AND RISK ASSESSMENT:

REFLECTIONS ON WORKING TOGETHER TO IMPROVE PUBLIC HEALTH

Judy S. LaKind, Ph.D.

International Conference on Using Epidemiological Studies in Health Risk Assessments: Relevance, Reliability and Causality

9 November 2023

Outline

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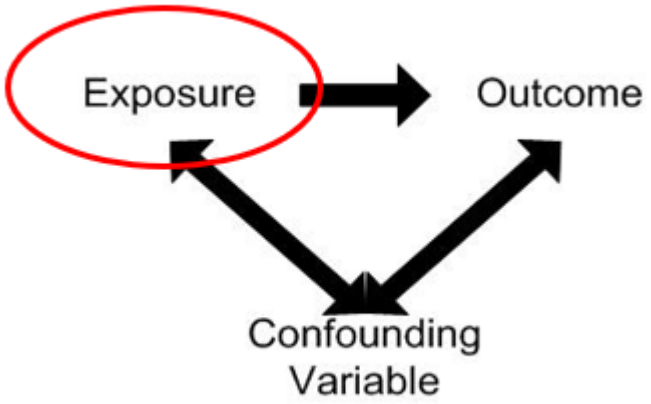
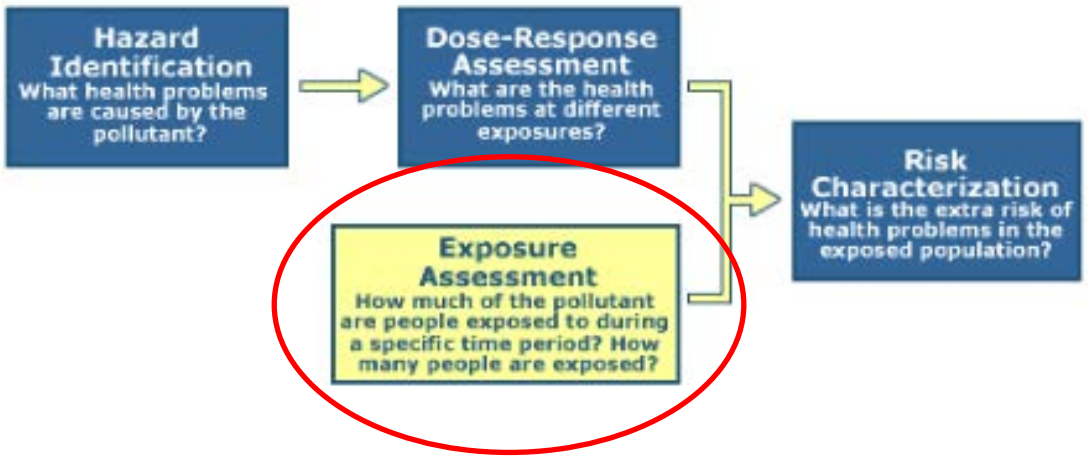
- Disclaimer
- Background
- Barriers
- Tools

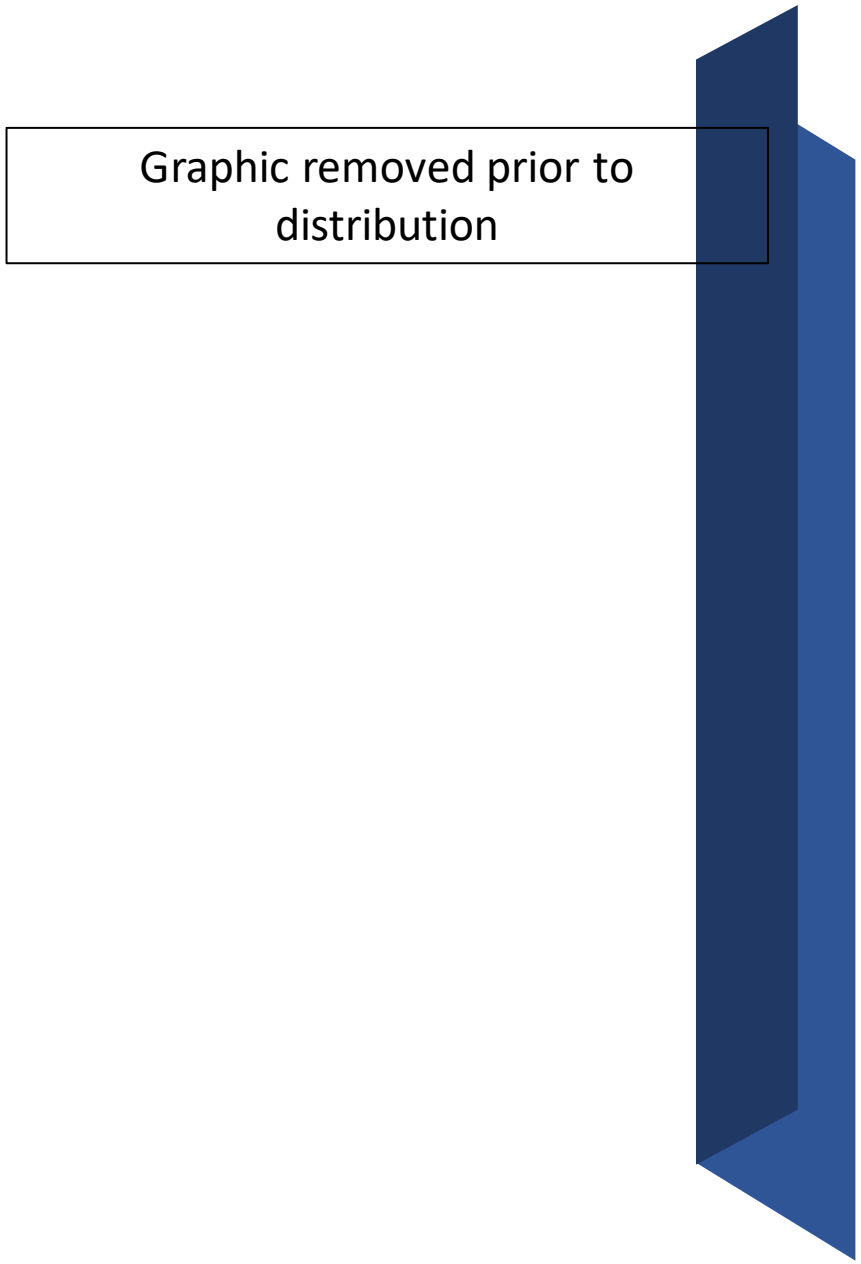
Disclaimer





- Not an epidemiologist
- Am an exposure scientist and risk assessor
- American exposure scientist and risk assessor

https://www.epa.gov/risk/conducting-human-health-risk-assessment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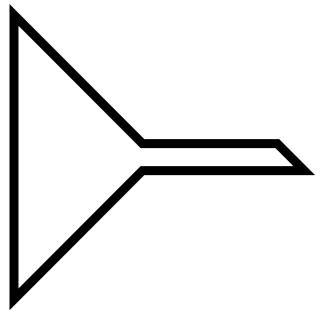
Background

Chemistry
Geology
Biology
Hydrology
Toxicology
Epidemiology
NAMS (e.g., in vitro, in silico)



Risk Assessment

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Early post grad school training in risk assessment in the 1980's

Need for data for quantitative activities

Risk Assessment
Guidance for Superfund
Volume I
Human Health Evaluation Manual
(Part A)

Interim Final

EPA/540/1-89/002
December 1989

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Time went by…..

Use of information for WOE/systematic review/etc.

Many important attributes

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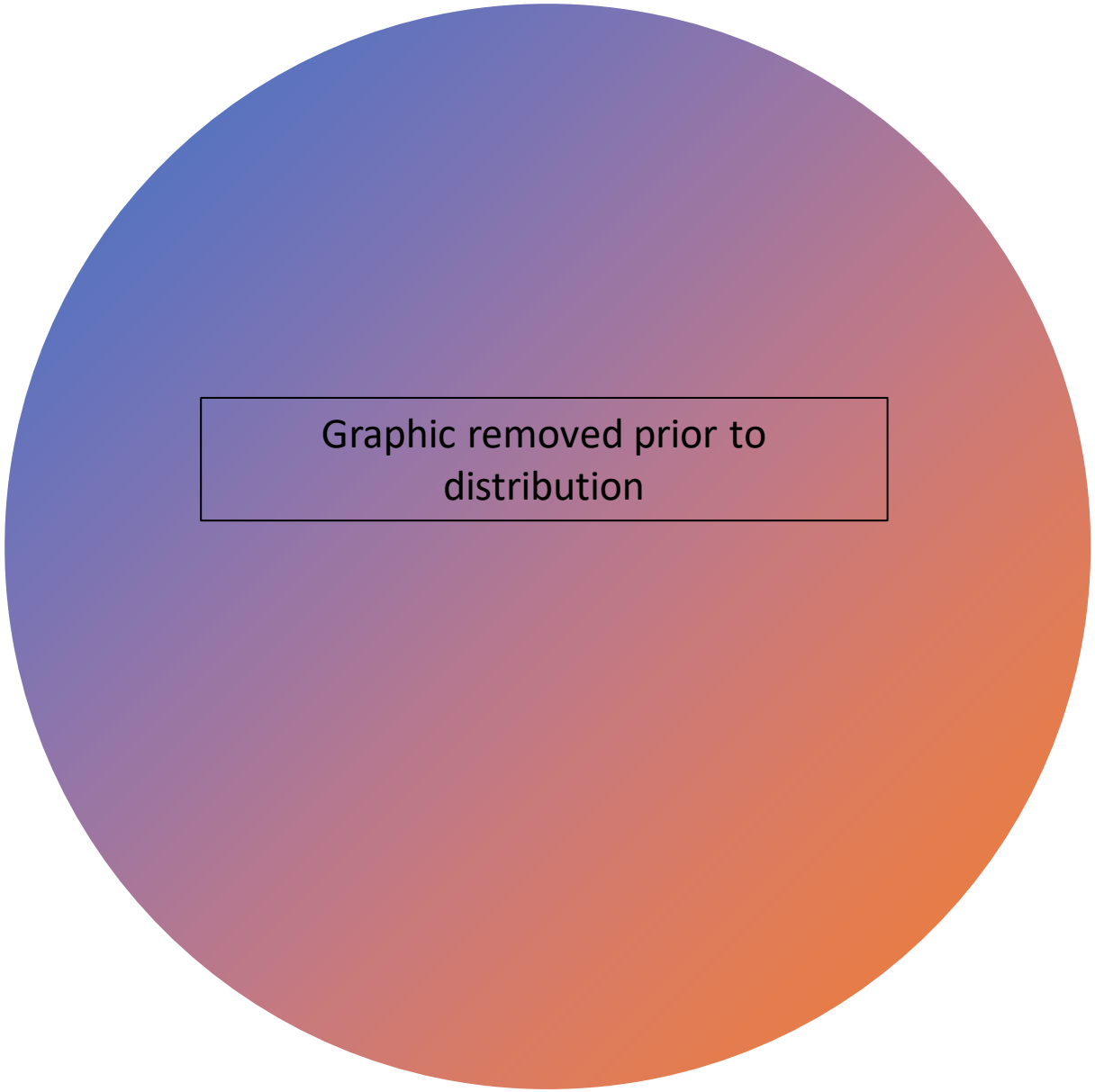
Target species is directly relevant

Reduces need for high-to-low dose extrapolations

No/poor laboratory animal models for some health endpoints

Minimize the use of animals in chemical testing



Barriers to use of epidemiology research in risk assessment

Epi-risk assessment barriers: not a new issue

For decades, calls for improving suitability of epidemiology studies for risk assessment.

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Barriers

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From Conference announcement:

"The presumed inability of observational studies to demonstrate a causal relationship may even lead to their exclusion from the evidence assessment…"

545 health assessments…as of June 2007, ~8% derived non-cancer or cancer risk estimates based on human data.

Not just due to no epi studies

Quality of epi studies:

- selection and characterization of comparison groups
- sufficient length of follow-up in prospective studies
- adequate sample size to detect an effect
- accuracy of the exposure characterization

Persad and Cooper. 2008. Toxicol Appl Pharmacol 223:137–145

Assessment of chemicals in IRIS using neurodevelopmental testing in children in a regulatory context was limited by several factors:

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- Adequacy of sample size
- Inconsistent testing methodologies
- Questions about the selection or implementation of testing procedures
- Inadequate consideration of confounding factors
- Uncertainties regarding the exposures
- Reproducibility of the study findings
- Inconsistencies due to timing or life stage of assessment

Makris, Bale, Raffaele. 2010. Presentation.

EPA - National Ambient Air Quality Standards (NAAQS) - Integrated Science Assessments

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Are the air quality, exposure, or dose metrics of adequate quality and are they sufficiently representative of or pertinent to ambient conditions?

US EPA, 2015. Preamble to the Integrated Science Assessments (ISA). U.S. Environmental Protection Agency, Washington, DC vol EPA/600/R-15/067U.S.

LaKind JS, Burns CJ, Johnson GT, Lange SS. Epidemiology for risk assessment: US EPA guidance and the Matrix. *Hygiene and Environmental Health Advances* 106:100059.

Risk assessor attitudes

Not useful but has potential: 16%
Not useful, no potential 19%
Useful but could be more so 39%
Useful as is 20%

Common theme: need for useful exposure measurements

"this needs to be done right for the results to be useful, and it usually is not."

"…multiple calls for epidemiologists to sit down with risk assessors and learn what they need…"

Burstyn et al. (Health and Environmental Sciences Institute). Improving the integration of epidemiological data into human health risk assessment: What risk assessors told us they need

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Road trip –

met with epis from academia, government, business

Epi attitudes

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- Why should *we* sit down with *them?*
- Epi studies are fine – it is the risk assessors who need to change
- We are doing the research the way we want to answer the questions that interest us
- No reward (benefit)
- Funding barriers

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But:

- How can I learn more?
- Where can I get training?
- What is it that risk assessors need?

You can’t always get what you want…

…but if you try sometimes you might find you get what you need

…..Mick Jagger

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Tools are not rocket science – that is the point!!

Two tools have some overlap – that is *also* the point

Focus here on exposure

Tool #1: BEES-C

Environment International 73 (2014) 195–207

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

A proposal for assessing study quality: Biomonitoring, Environmental Epidemiology, and Short-lived Chemicals (BEES-C) instrument

Judy S. LaKind [a,b,c,*], Jon R. Sobus [d], Michael Goodman [e], Dana Boyd Barr [f], Peter Fürst [g], Richard J. Albertini [h], Tye E. Arbuckle [i], Greet Schoeters [j,k], Yu-Mei Tan [d], Justin Teeguarden [l], Rogelio Tornero-Velez [d], Clifford P. Weisel [m]

*any medium or chemical

BEES-C: Exposure Quality Evaluation

STUDY ASSESSMENT COMPONENTS	TIER 1	TIER 2	TIER 3
Biomarker Selection and Measurement			
Biological relevance (parent/surrogate relationship) of exposure biomarker	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.	Evidence exists for a relationship between biomarker in a specified matrix and external exposure, internal dose, or target dose.	Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose.
Biological relevance (parent/surrogate relationship) of effect biomarker	Bioindicator of a key event in an AOP.	Biomarkers of effect shown to have a relationship to health outcomes but the mechanism of action is not understood.	Biomarker has undetermined consequences (e.g., biomarker is not specific to a health outcome).
Specificity	Biomarker is derived from exposure to one parent chemical.	Biomarker is derived from multiple parent chemicals with similar adverse endpoints.	Biomarker is derived from multiple parent chemicals with varying types of adverse endpoints.

- Exposure and biological relevance
- Specificity
- Method sensitivity
- Contamination
- Stability
- Adjust for matrix dilution
- Ability to use data to estimate exposure over window of interest
- Ability to establish that exposure precedes effect

LaKind et al. Environ Int 73C:195-207.

Documentation of avoidance of sample contamination

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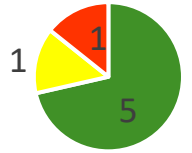
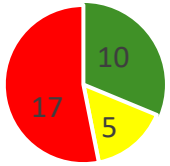
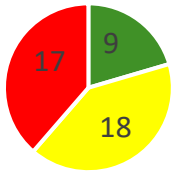
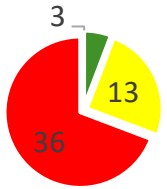
Environmental media and human matrices:

contamination during sample collection, transport, storage, in lab

Tier 1
Documentation that samples are contamination-free from time of collection to time of measurement

Matrix/total number of 2,4-D epi studies	Contamination
Foods/beverages: 7	
Soil and dust: 16	
Air: 32	
Water: 44	
Urine: 52	

LaKind et al. J Toxicol Env Health, B. 2017

Establish that exposure precedes effect:

Can one biomonitoring sample do this?

outcome

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exposure exposure exposure

ICC (intraclass correlation coefficient)

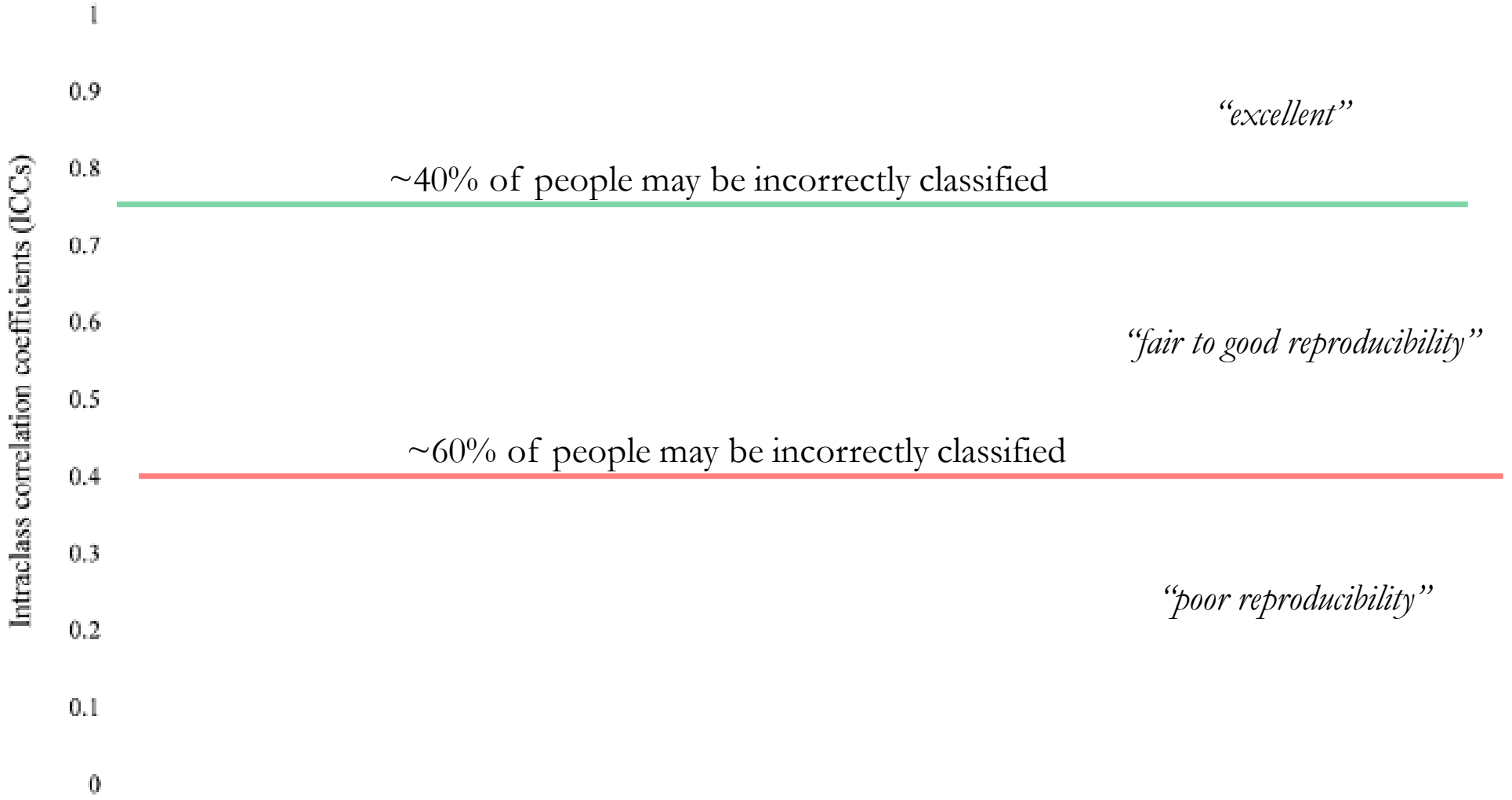
Proportion of variability explained by between subject variation

ICC<0.4 – poor reproducibility

ICC ≥ 0.40 - fair to good reproducibility

ICC ≥ 0.75 excellent

Rosner B. 2000. Fundamentals of Biostatistics. 5th ed. Pacific Grove (CA):Duxbury.



Goodman et al. 2018. Systematic review of the literature on triclosan and health outcome in humans. Crit Rev Toxicol 48(1):1-51. doi: 10.1080/10408444.2017.1350138.

LaKind JS, Idri F, Naiman DQ, Verner M-A. 2019. Biomonitoring and nonpersistent chemicals – understanding and addressing variability and exposure misclassification. Current Environmental Health Reports 6(1):16-21.

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Take-home

One sample generally not sufficient for properly characterizing exposure

Valuable to have the resources to do serial sampling

Tool #2: Matrix

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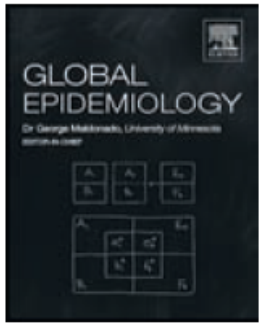
A little more, please!

Global Epidemiology 1 (2019) 100005

Contents lists available at ScienceDirect

Global Epidemiology

journal homepage: https://www.journals.elsevier.com/global-epidemiology



Methodology article

A matrix for bridging the epidemiology and risk assessment gap☆

Carol J. Burns [a,*], Judy S. LaKind 2[b], Donald R. Mattison [c], Cecilia S. Alcala [d], Francesca Branch [e], Juan Castillo [f], April Clark [g], Jane Ellen Clougherty [h], Sally P. Darney [i], Heidi Erickson [j], Michael Goodman [k], Matthias Greiner [l], Anne M. Jurek [m], Aubrey Miller [n], Andrew A. Rooney [o], Angelika Zidek [p]

The Matrix

	Asks for risk assessment		
Hazard ID	Confirm outcome?	Confirm exposure?	Report methods fully and transparently?
Dose Response	Include information on shape of the curve?	Harmonize exposure categories?	Describe direction/ magnitude of error?
Exposure Assessment	Describe source-to-intake pathways?	Provide complete exposure data?	Report on quality assurance/quality control?

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Source to intake pathway?

- Part of study planning
- Multiple media sampling can offer information on main source(s) of exposure
- High impact study
- This allows for ACTION

	Asks for risk assessment		
Hazard ID	Confirm outcome?	Confirm exposure?	Report methods fully and transparently?
Dose Response	Include information on shape of the curve?	Harmonize exposure categories?	Describe direction/ magnitude of error?
Exposure Assessment	Describe source-to-intake pathways?	Provide complete exposure data?	Report on quality assurance/quality control?

- Communication tool

  advance an understanding of risk assessment

  increase the translation of epidemiology data

- Asks for epidemiologists

- Elements that have impact

- Not intended to supplant current best practices

- Forward-looking

Summary

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Risk assessors *want* to use epidemiology data

Epidemiologists *want* to have impact but don't know what is needed

<u>BEES-C and Matrix:</u>

- offer guidance on key aspects of epi studies that can help with translation
- serve as a foundation for inter-disciplinary dialogue

Small changes can have a BIG impact

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Many problems feel overwhelming and insurmountable…

…enhancing epi for risk assessment should not be one of them

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Risk assessors and epidemiologists can be vocal about the need for:

- Training (providing succinct, clear information)
- Funding (support for the additional components/analyses)
- Rewards (promotions, awards)

Danke fürs Zuhören!

For information, contact me at lakindassoc@gmail.com