(Measurement) Errors in Academic Publications: Statistical Discussion

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Conflicts of Interest

- GlaxoSmithKline
  - Statistical Consultant
- StatReviewer
  - Chief Scientist
- *Anesthesiology*
  - Statistical Editor

Overview

- Statistical/Methodological Errors in Observational Research
  - Most recent
- Measurement Error In Statistical Models
  - 5 myths about error

van Smeden M, Lash TL, Groenwold RH, van Smeden M. Five myths about measurement error in epidemiologic research.

Common Errors in Academic Publications: Reporting

- Propensity
  - Model specification
  - Model diagnostics
    - Calibration
    - Overlap

- Matching
  - Methods (probability, exact, etc.)
  - Algorithm (random, greedy)
  - Software

- Model
  - Specification
  - Distribution, Link
  - Interaction
  - Calibration

Common Errors in Academic Publications

- Typographical errors or copy-paste errors
  - “OR 1.75, 95%(CI: 0.45 to 0.95)”
- Data-driven confounder selection
  - Stepwise variable selection
- Underdeveloped multiple imputation models
  - “We used MI to replace missing data”

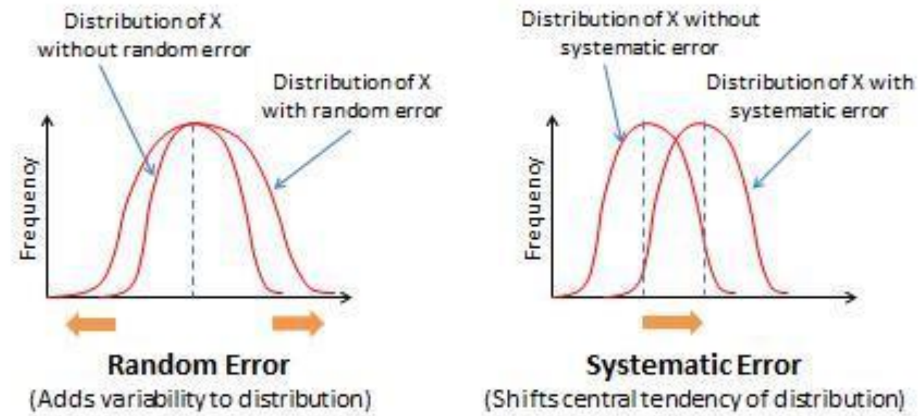
Measurement Error

- Mismeasurements and misclassifications of all kinds
  - Mistaken entries
  - Inaccurate recordings
  - Imperfectly reliable measurements

- Observed = True + Error

Types of Measurement Error

- Classical error
  - ~ N(0,σ2)
- Systematic error
  - ~N(bias, σ2)
- Differential
  - Error dependent on outcome
- Berkson
  - True + ~N(0, constant)



Measurement error is often neglected in medical literature: a systematic review

- Original research published in 2016 in high-impact medical and epidemiology journals
  - Main exposure or confounder

- Search strings related to “measurement error”

Brakenhoff TB, et al. Measurement error is often neglected in medical literature: a systematic review. Journal of clinical epidemiology. 2018 Jun 1;98:89-97.

Measurement error is often neglected in medical literature: a systematic review

- 1178 articles found, 565 met inclusion criteria
  - 337 Epidemiology
  - 228 High Impact Medical
- 247/565 (44%) directly addressed measurement error
  - 70% ONLY in the Discussion section

Table 1 General Characteristics of the 247 Publications That Explicitly Report on Measurement Error (ME) in Some Form.

Characteristic	**No. of Studies**	**% of 247**
ME in which variable		
Exposure	195	79
Confounder	44	18
Outcome	115	47
Exposure & Confounder	35	14
ME discussed in which section		
Abstract	8	3
Introduction	22	9
Methods	49	20
Results	9	4
Discussion[a]	219	89
ME in previous study[b]	88	36
ME prevented by design[c]	60	24

ME = Measurement error

[a] 174 (70%) publications considered ME **only** in the discussion section

[b] Mentions made of ME pertained to previously published research and not to the study presented in the published paper.

[c] ME in the presented study was prevented due to decisions made during the design of the study.

Brakenhoff TB, et al. Measurement error is often neglected in medical literature: a systematic review. Journal of clinical epidemiology. 2018 Jun 1;98:89-97.

Myth 1:

Measurement error can be compensated by large number of observations

- Increased N causes estimates to approach the measurement error mechanism, not their true value

- With unreliable measurements, sample size needs to increase ~ 50 fold to compensate (Devine, 1998)

- “Triple Whammy” (Carroll, 2006)
  - Covariate-outcome relationship biased
  - Statistical power diminished
  - Relational features masked
    - Non-linearity difficult to detect

Devine et al. Estimating sample size for epidemiologic studies: the impact of ignoring exposure measurement uncertainty. Stat Med 1998;17:1375-1389.

Carroll et al.. Measurement Error in Nonlinear Models: A Modern Perspective. Chapmann & Hall/CRC; 2006.

Myth 2:

The exposure effect is *underestimated* when variables are measured with error

- An exposure can be *over* or *under* estimated in the presence of measurement error

- Spearman error attenuation formula
  - Regression dilution bias
  - Attenuation to the null
  - Hausman's iron law

$$\text{"True" association}_{xy} = \frac{\text{Observed Association}_{xy}}{\text{Reliability}_x * \text{Reliability}_y}$$

$$r_{x'y'} = \frac{r_{xy}}{\sqrt{r_{xx} * r_{yy}}}$$

Spearman C. The proof and measurement of association between two things. Am J Psychol 1904;15:72-101.

RESEARCH ARTICLE

Random measurement error: Why worry? An example of cardiovascular risk factors

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Table 1. Baseline characteristics of the example dataset of patients with manifest vascular disease.

Baseline characteristic	N = 7395
Age in years (mean (sd))	60.5 (9.7)
Male (%)	5474 (74)
SBP in mmHg (mean (sd))	140 (21)
DBP in mmHg (mean (sd))	81 (11)
CIMT in mm (mean (sd))	0.92 (0.27)
ABI (mean (sd))	1.09 (0.19)
Follow up in days (median [IQR])	2510 [1293–3827]
Cardiovascular events* during follow up (%)	1309 (18)

SBP = systolic blood pressure; DBP = diastolic blood pressure; CIMT = carotid intima media thickness; ABI = ankle-brachial index at rest; IQR = interquartile range.

*Defined as the composite of myocardial infarction, stroke, and cardiovascular death (whichever came first) developed over a minimum of three years of follow up time.

https://doi.org/10.1371/journal.pone.0192298.t001

Observed Associations

Table 2. Crude and adjusted hazard ratios for the relation of the exposures (SBP and CIMT) and main confounders (DBP, ABI, and SBP) with the outcome (cardiovascular events).

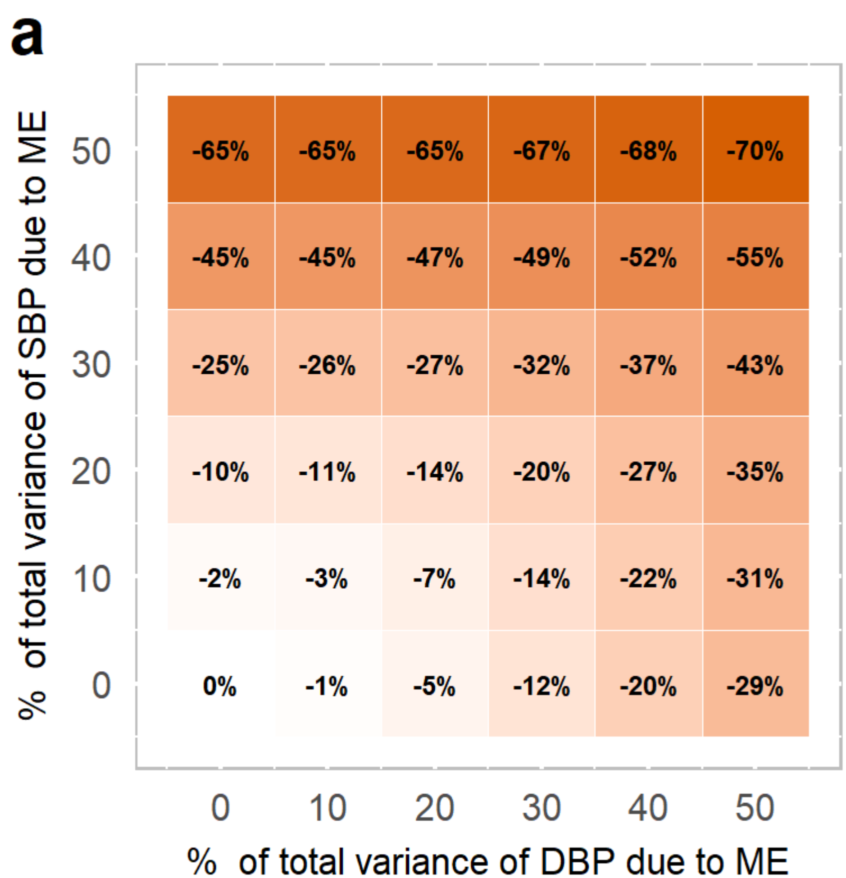
Model	Variable	Crude HR (95% CI)	Adjusted HR* (95% CI)
1	Exposure: SBP per 10 mmHg	1.11 (1.09, 1.14)	1.10 (1.07, 1.14)
	Confounder: DBP per 10 mmHg	0.99 (0.94, 1.04)	0.88 (0.83, 0.94)
2	Exposure: SBP per 10 mmHg	1.11 (1.09, 1.14)	1.03 (1.00, 1.06)
	Confounder: ABI	0.20 (0.16, 0.26)	0.22 (0.18, 0.29)
3	Exposure: CIMT per mm	2.82 (2.48, 3.20)	2.10 (1.79, 2.47)
	Confounder: SBP per 10 mmHg	1.11 (1.09, 1.14)	1.04 (1.01, 1.06)

HR = hazard ratio; SBP = systolic blood pressure; CIMT = carotid intima media thickness; DBP = diastolic blood pressure; ABI = ankle-brachial index at rest.

*Besides the exposure and main confounder shown in the table, each model was further adjusted for the variables age and sex.

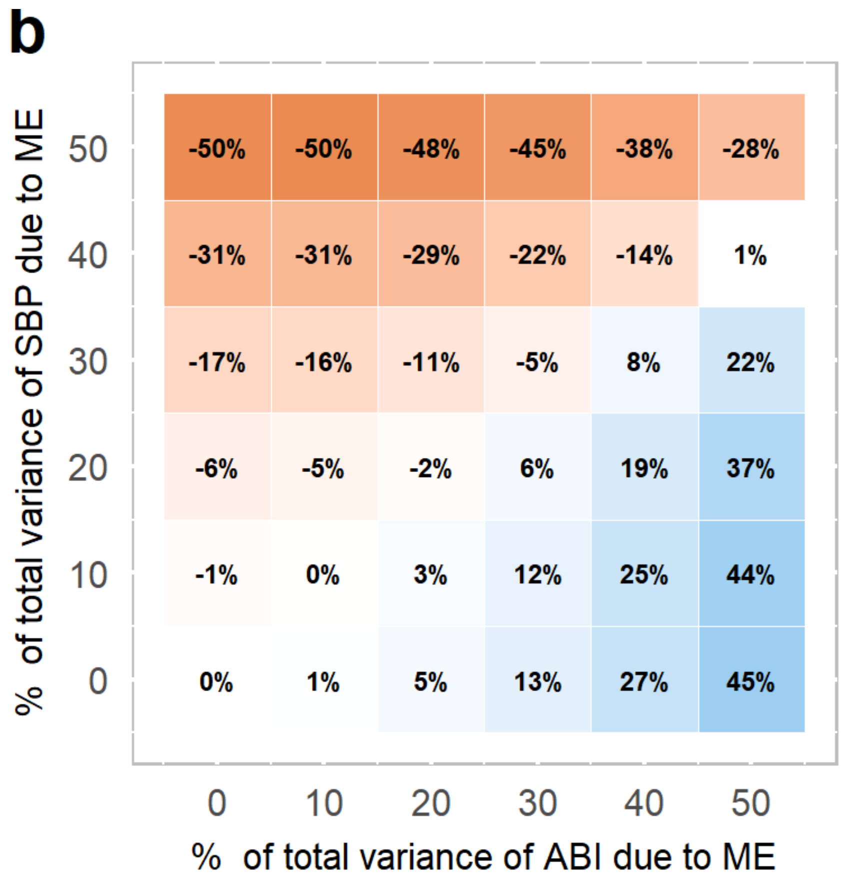
https://doi.org/10.1371/journal.pone.0192298.t002

SBP exposure and DBP confounder



r = 0.65

SBP exposure and ABI confounder

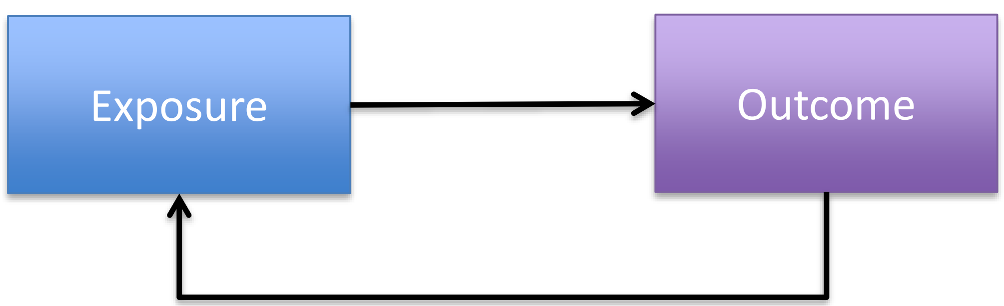


r = -0.17

Myth 3:

Exposure measurement error is nondifferentiable if measurements are made without knowledge of outcome

Example: Case-control study where cases attend more to the existence of
an exposure



Myth 4:
Measurement error can be prevented but not mitigated in observational data analysis

- Statistical methods for error bias adjustments are available
  - Knowledge of error structure
  - Knowledge of error variance

- Greatly facilitated by a validation sample
  - Observed data can be contrasted with ‘true’ data
  - Repeated measures
  - Surrogate measures (latent dimensions)

Measurement Error Correction Methods

- Regression calibration (Rosner et al., 1989)
  - Error prone covariate replaced by expected true score
- Simulation-extrapolation (SIMEX; Cook et al., 1994)
  - Simulate dataset through adding MORE error to the covariates
  - Extrapolate predictions back to original situation
- Latent variable models
  - Replicate measures used to estimate ‘true’ value of a more reliable latent construct
- Bayesian approaches
- Multiple Imputation

Myth 5:

Certain types of observational research are unaffected by measurement error

- Single exposure and set of confounders
- Time-series analysis
- Diagnostic accuracy studies
- Randomized controlled trials
- Many others…

Recommendations

- Measurement error is nearly ubiquitous in observational data analysis
  - Let's stop neglecting it
- Measurement error can have a counter-intuitive impact on observed associations
  - Must consider its structure AND degree
  - Be cautious when applying general claims about the direction of the error
- Strongly consider the use of formal strategies to mitigate error
  - Conduct validation efforts
  - Utilize formal statistical methods

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Thank you!

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