Recent Contributions of STRATOS Topic Group 4: Measurement Error and Misclassification

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Slide deck available at: `mpwallace.github.io`

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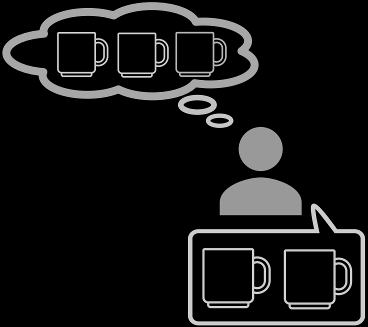
Topic Group 4: Measurement Error and Misclassification

- Measurement error: When what we observe differs from what we want to observe.
- Impact unpredictable, and requires specialist methodology.



STRATOS Topic Group 4: Dedicated to exploration and education for all things measurement error.

Highlight: Two comprehensive ‘guidance papers’ published in Statistics in Medicine (2020).

TG4's recent work includes:

- Categorization of continuous error-prone observations.
- Post-prediction inference and Berkson error.
- Education through our website, R Shiny app, and videos.

Categorization of continuous variables occurs for various reasons:

- ‘Real-world’ interpretations: e.g., blood pressure (hypertensive vs. not); BMI (obese, overweight, etc.).
- Analytical decisions: e.g., to use more familiar methods, simplify assumptions.

Categorization: Not without caveats, but a common practice.

Categorization of error-prone variables can lead to *misclassification*:

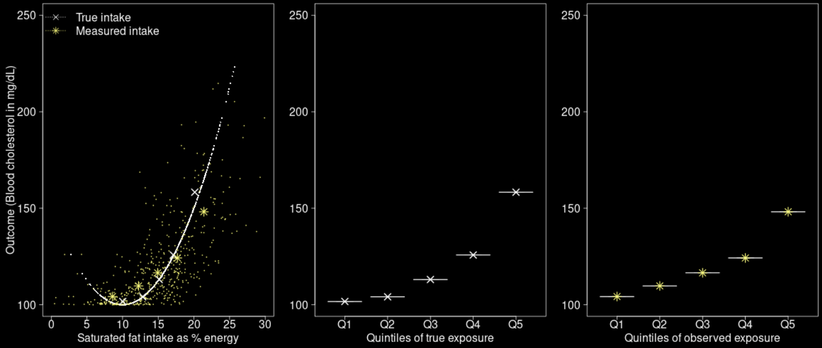
- Truth: Average long-term blood pressure (X):
  - Not hypertensive: $X \leq 130; X_c = 0$
  - Hypertensive: $X > 130; X_c = 1$
- Observed: Single blood pressure measurement (X^*):
  - Not hypertensive: $X^* \leq 130; X_c^* = 0$
  - Hypertensive: $X^* > 130; X_c^* = 1$
- Possibility:
  - True $X = 125 \implies$ not hypertensive ($X_c = 0$)
  - Observed $X^* = 135 \implies$ hypertensive ($X_c^* = 1$)
- **Question**: What are the implications for analysis?

Project 1: Misconceptions

Led by Anne Thiébaut (Inserm, France).

- Many myths, misconceptions, and misunderstandings surround categorization.
- Measurement error adds to the list.
- Goal: Explore, explain (and dispel!) five common misconceptions.

"Categorizing a mismeasured exposure can help with finding the shape of the exposure-outcome relationship"



- Measurement error in X^*: *non-differential* w.r.t. outcome Y if

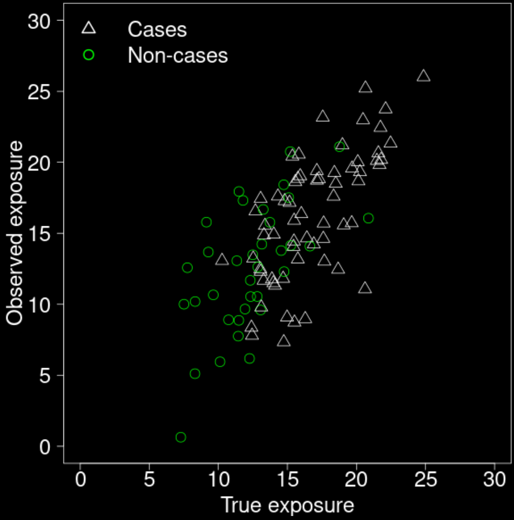
$$X^* \perp Y|X$$

- Differential error example: patients diagnosed with lung cancer report their smoking history with a different level of accuracy to those without lung cancer.
- **Question**: If X subject to non-differential error, will the misclassification in X_c^* also be non-differential?[1]

[1] Yes, but only in highly improbable scenarios: Flegal et al. (1991) Differential misclassification arising from non-differential errors in exposure measurement. doi:10.1093/oxfordjournals.aje.a116026

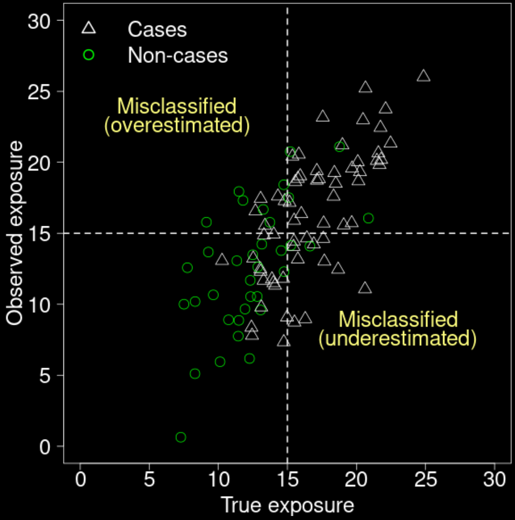
"Categorization of a continuous variable with non-differential error will produce non-differential misclassification"

- Suppose: Binary outcome Y denoting presence/absence of disease, with an exposure positively associated with the outcome.



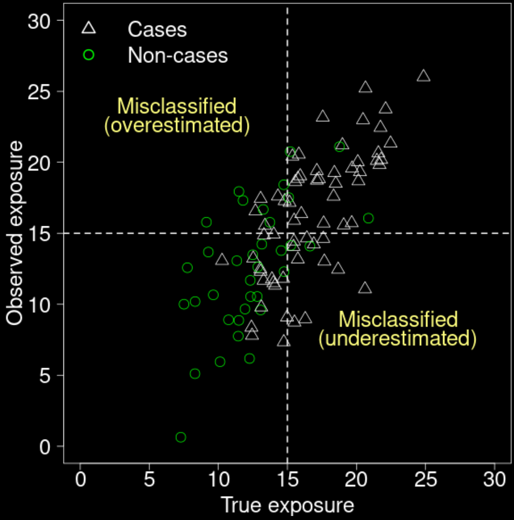
"Categorization of a continuous variable with non-differential error will produce non-differential misclassification"

- Probability of misclassification when categorizing X^* higher around boundary, so depends on true exposure X



"Categorization of a continuous variable with non-differential error will produce non-differential misclassification"

- In this example: sensitivity is higher amongst cases (75%) than amongst non-cases (67%).



Other misconceptions covered:

- Categorizing an error-prone continuous exposure mitigates bias due to measurement error.
- The comparison of extreme quantiles involves less misclassification and therefore results in smaller bias.
- Misclassification of exposure always results in attenuated association.

Led by Hendriek Boshuizen (Wageningen University & Research, Netherlands).

A categorized error-prone continuous variable causes various problems:

- Biases effect estimates (both attenuation and not).
- Obfuscates shapes of relationships.
- Differential misclassification (even if the continuous variable error is non-differential).
- Goal: Develop a new approach to measurement error correction in this setting.

We propose a correction method using regression calibration (RC)[2]:

- Principle of RC: Estimate X using X^* and confounders Z:

$$\hat{X} = E[X|X^*, Z]$$

  and use $\hat{X}$ in place of X in standard analysis.
- Exact for linear models, good for many GLMs.
- Could be applied to categorical models by replacing X_c with $E[X_c|X^*, Z]$...
- ...but categorization of a non-differential errorred X results in differential misclassification, which violates RC.

[2]We extend MacMahon et al. Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. Lancet. 335(8692) 765-774

- Assume non-differential error: $X^* \perp Y|X, Z$
- Define C_k: set of values for category k (e.g. the k^{th} quintile).
- Define $\hat{X} = E[X|X^*, Z]$, then

$$E[\hat{X}|\hat{X} \in C_k, Z] = E[X|\hat{X} \in C_k, Z]$$

- Thus: $E[\hat{X}|\hat{X} \in C_k, Z]$ in category k can be interpreted as the mean exposure in the category defined by $\hat{X} \in C_k$.
- We can link $E[\hat{X}|\hat{X} \in C_k, Z]$ to the mean of Y in category k.

Proposed method: Residuals

- If there is confounding, categorization means effect of confounder is not estimated correctly.
- Mitigation: use a residual exposure model:

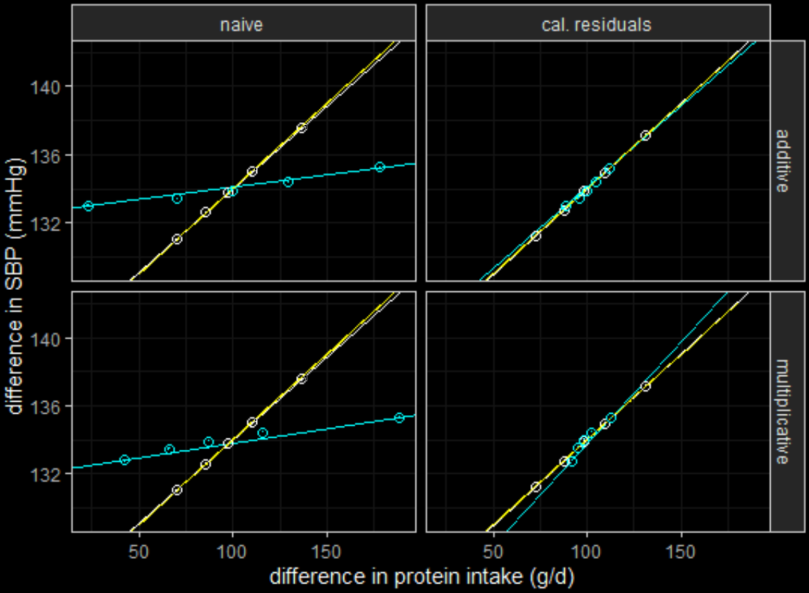
$$R = X - E[X|Z] \qquad R^* = X^* - E[X^*|Z]$$

- Like RC estimates of X, we have RC estimates of R:

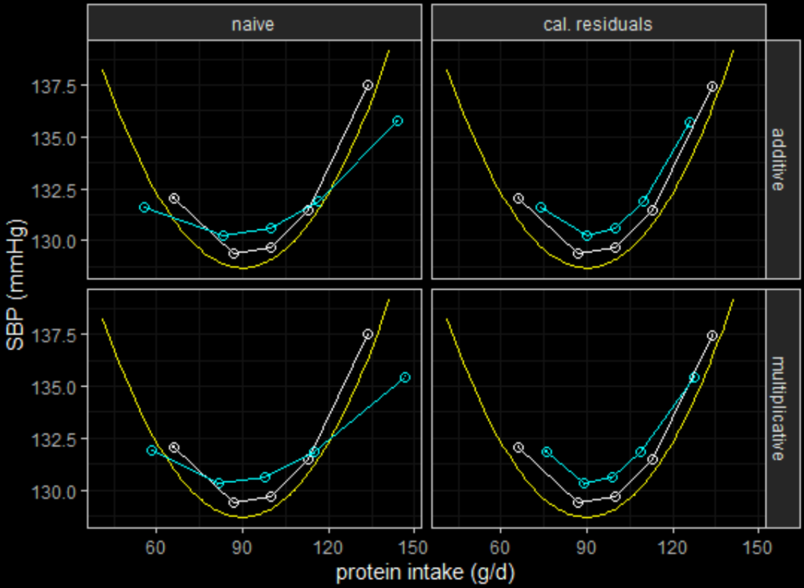
$$\hat{R} = \hat{E}[R|R^*, Z]$$

- We can then define $\hat{R}_c$ derived from sets C_k based on $\hat{R}$ and use these in our analysis.

Simulations: Linear, Log-Normal X, confounding



Simulations: Quadratic, Log-Normal X, no confounding



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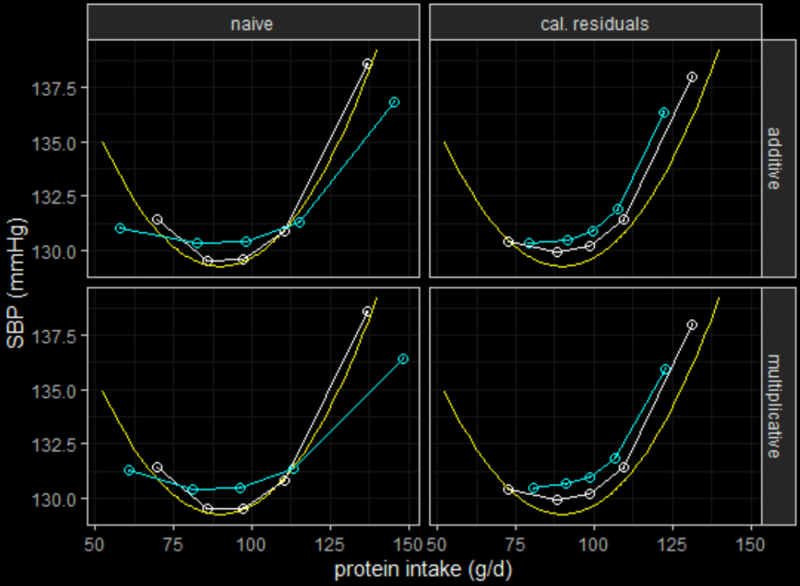


Overall, our proposed method:

- Accurate for linear relationships, but in such cases using the continuous exposure variable would seem prudent.
- Less effective for strongly non-linear relationships the approach does not, but still an improvement over naive analysis.
- Could be used to help determine whether linear modelling is appropriate.

Preceding projects focused on *classical* measurement error.

e.g., Reported usual daily calorie intake X^* equals true intake X plus some random error U:

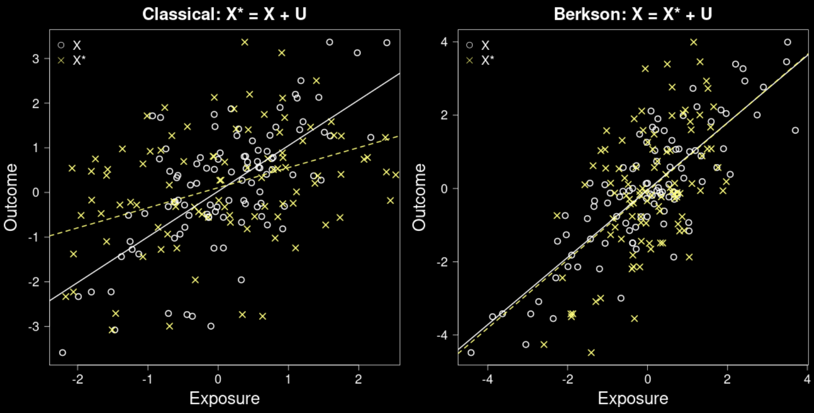
$$X^* = X + U; \qquad U \perp X$$

In contrast, there is *Berkson* error.

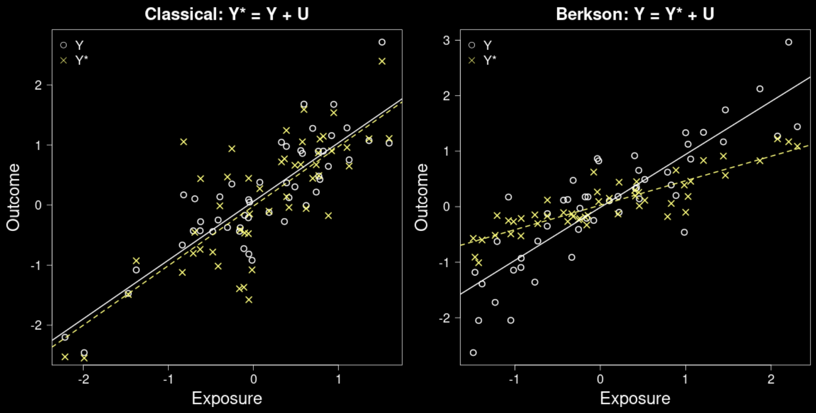
e.g., True nutrient absorption X equals nutrient intake X^* plus some random error U:

$$X = X^* + U; \qquad U \perp X^*$$

Classical vs. Berkson: Exposure



Classical vs. Berkson: Outcome



TG4 has three projects on Berkson error, addressing:

- An introduction to Berkson error in exposure and outcome variables variables.
- The impact of Berkson error on estimating distributional measures and a correction approach.
- The relationship between Berkson error and regression calibration.

Berkson Error and Regression Calibration

Led by Lillian Boe (Memorial Sloan Kettering Cancer Center, NY).

- In some settings *predicted* values used to estimate true values.
- Example: Schofield's equation to predict basal metabolic rate as a function of body mass and activity level.
- Such predicted measures often subject to Berkson error.
- In particular: Regression calibration and Berkson error highly related.

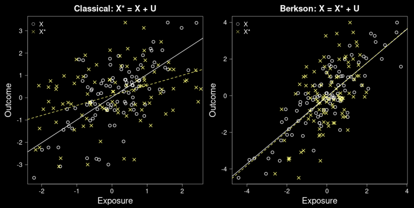
Suppose $X^* = X + U$ (classical error). RC tells us to use

$$\hat{X} = E[X|X^*, Z]$$

in place of X.

But: $\hat{X}$ is itself an error-prone measurement of X. How is this an improvement?

Answer: $\hat{X}$ has Berkson error, and may result in unbiased effect estimates in certain settings.



Viewing RC with a Berkson lens highlights limitations.

e.g., We must estimate $\hat{X} = E[X|X^*, Z]$ using the same variables Z in the calibration equation as in the outcome model.

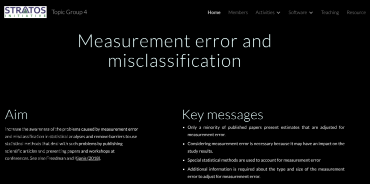
This principle means that, for any given exposure, there is no single calibration equation that is appropriate for all analyses.

Regression Calibration: Guidance

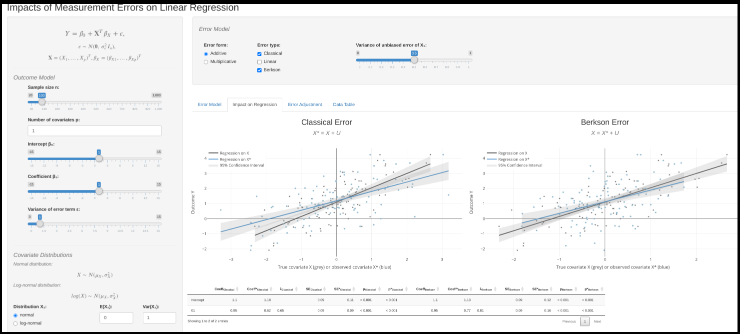
This project provides a checklist when implementing RC, including:

- Further modelling considerations for the outcome model.
- Where and how to source additional data to inform the calibration model.
- Advice on adjusting standard errors to account for calibration uncertainty.

- Website featuring previous presentations and other resources.
- General audience introductory video series.



- An R Shiny app for exploring measurement error.



- **Measurement Error Guidance**: P. A. Shaw et al. (2020). STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: Part 2 - sample size, more complex methods of adjustment and advanced topics. *Statistics in Medicine* **39(16)** 2197-2231.
- **Measurement Error Guidance**: R. H. Keogh et al. (2020). STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: Part 1 - basic theory, validation studies and simple methods of adjustment. *Statistics in Medicine* **39(16)** 2232-2263.
- **Epidemiologic Review Paper**: P. A. Shaw et al. (2018). Epidemiologic analyses with error-prone exposures: Review of current practice and recommendations. *Annals of Epidemiology* **28(11)** 821-828.
- **Misconceptions**: A. C. M. Thiébaut et al. (2025). Five misconceptions about categorizing exposure variables measured with error in epidemiological research. *In review.*
- **Regression Calibration and Berkson Error**: L. A. Boe et al. (2023). Issues in Implementing Regression Calibration Analyses. *Practice of Epidemiology* **192(8)** 1406-1414.
- **General Audience Article**: M. P. Wallace (2020). Analysis in an imperfect world. *Significance* **17(1)**.

- **TG4 website**: `http://www.stratostg4.statistik.uni-muenchen.de`
- **Shiny app**: `https://mem-explorer.shinyapps.io/MEMExplorer-v5`
- **Introductory videos**: `https://youtube.com/@TheSTRATOSinitiative`

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`https://mpwallace.github.io`