Berkson measurement error in epidemiology

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STRATOS Task Group 4
Measurement Error and Misclassification

Aim

To increase:

(i) awareness of measurement error issues in observational epidemiology and

(ii) use of statistical methods to adjust for such error

STRATOS Task Group 4
Measurement Error and Misclassification

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STRATOS Task Group 4
Publications

Shaw et al 2018
Epidemiologic analyses with error-prone exposures: review of current practice and recommendations.
Ann Epidemiol 2018, in press.

Freedman & Kipnis
Introducing TG4
Biometric Bulletin 2018 Vol 35, Issue 1

Submitted (in two parts):
STRATOS TG4 membership:
STRATOS Guidance Paper on measurement error and misclassification

Impact of Measurement Error on Study Results

Depends on:

- The amount of error
- The nature of the error –

  measurement error model
- What is being estimated

Content of this talk

Focus on the Berkson error model:

- Its definition
- Examples of when it occurs
- Impact on various estimates
- How to adjust for Berkson error
- Examples in epidemiology

To put all this in context, I will contrast it with the classical measurement error model

Classical Measurement Error Definition

$$X^* = X + e$$

X^* is the measurement that has error

X is the true (unknown) value

e is the (additive) error in measurement X^*

e has mean zero (X^* is unbiased)

e is independent of X

Classical Measurement Error Examples

- Average short term blood pressure
- Average short term serum cholesterol

In each of the above, error is due to:

- ❖ laboratory error
- ❖ biological variation and
- ❖ fluctuations over time

Berkson Measurement Error Definition

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Berkson Measurement Error
Some history

Joseph Berkson (1899-1982)

- Physicist, Physician and Biostatistician
- Headed the Biometry Unit at the Mayo Clinic from 1934-64
- Discussed “Berkson” measurement error in a 1950 paper in “Are there two regressions?”

J Am Stat Assoc 1950; 45:164–180.
doi:10.2307/2280676. JSTOR 2280676

Berkson Measurement Error Examples

- Berkson's example:

  Volume of preparation pipetted into a test tube in a laboratory experiment

- Exposure level in occupational medicine studies: groups of individuals classified according to average exposure

- Values obtained from a prediction equation:

  e.g. Schofield's equation for resting energy expenditure based on age, sex and weight

Berkson Measurement Error Prediction Equations

Table 2 Predictive equations for basal metabolic r

Age (years)	Schofield n^{**}	Schofield Equations
Men	4809	
0–2.9	162	0.249 × Wt − 0.127
3.0–9.9	338	0.095 × Wt + 2.110
10.0–17.9	734	0.074 × Wt + 2.754
18.0–29.9	2879	0.063 × Wt + 2.896
30.0–59.9	646	0.048 × Wt + 3.653
≥ 60.0	50	0.049 × Wt + 2.459
60.0–69.9		
≥ 70.0		
Women	2364	
0–2.9	137	0.244 × Wt − 0.130
3.0–9.9	413	0.085 × Wt + 2.033
10.0–17.9	575	0.056 × Wt + 2.898
18.0–29.9	829	0.062 × Wt + 2.036
30.0–59.9	372	0.034 × Wt + 3.538
≥ 60.0	38	0.038 × Wt + 2.755
60.0–69.9		
≥ 70.0		

Each age group prediction equation is a regression of the form:

$REE = b_0 + b_1 \times Wt + e$, with e independent of predicted value

Impact on estimates

Types of Estimate:

- ❑ Percentiles of X: observe X*

- ❑ Coefficient of X in regression of Y on X

  Y is measured exactly, but observe X*, not X
- ❑ Coefficient of X in regression of Y on X

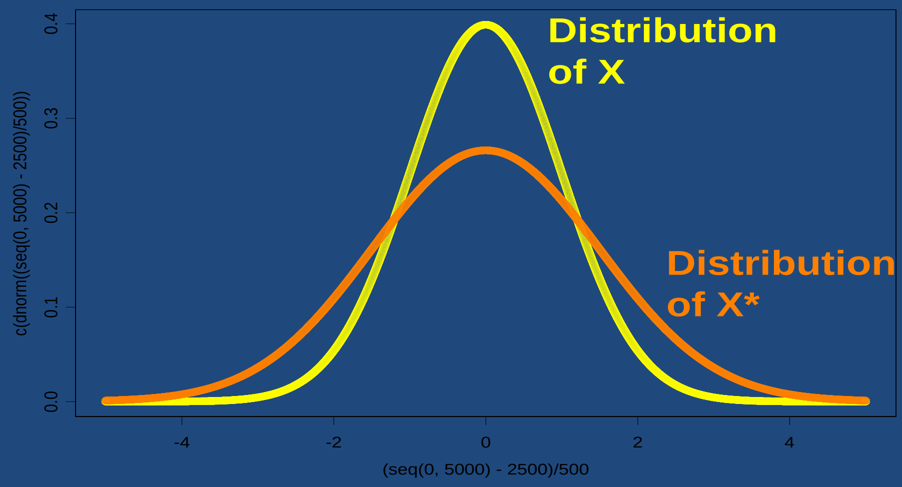
  X is measured exactly, but observe Y*, not Y

Impact on Estimates

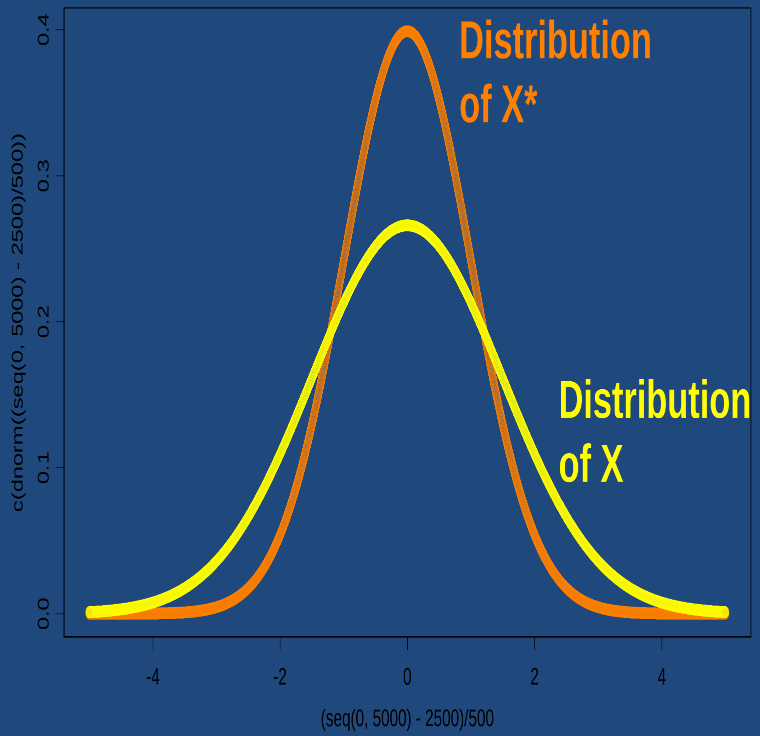
The impacts of classical and Berkson errors on these estimates are opposite!

Percentiles of X

Classical error



Berkson error



Percentiles of X

Estimate	Classical	Berkson
Upper percentile	Overestimate	Underestimate
Lower percentile	Underestimate	Overestimate

Method of Adjustment for Berkson Error

Berkson error: $X = X^* + e$

- The unadjusted estimate forms a distribution of the X^* values

- Instead, use moment reconstruction (MR):
- Form a new variable X_{MR}

  $X_{MR} = (1\text{-}w)\overline{X^*} + wX^*$, where

  $w = \mathrm{SD}(X)/\mathrm{SD}(X^*)$: note that $w > 1$

  $\mathrm{E}(X_{MR}) = \mathrm{E}(X)$; $\mathrm{var}(X_{MR}) = \mathrm{var}(X)$

- w is estimated from external information
- Form the distribution using the X_{MR} values

Example from the OPEN dietary reporting validation study

Potassium intake (K)

K_{FFQ} = Food Frequency Questionnaire report of K

The study also included a urinary determination of K

Calibration (prediction) equation:

$$\ln(K) = 5.895 + 0.271*\ln(K_{FFQ}) - 0.193*\text{sex} + 0.00035*\text{age}$$

This equation for ln(K) has Berkson error

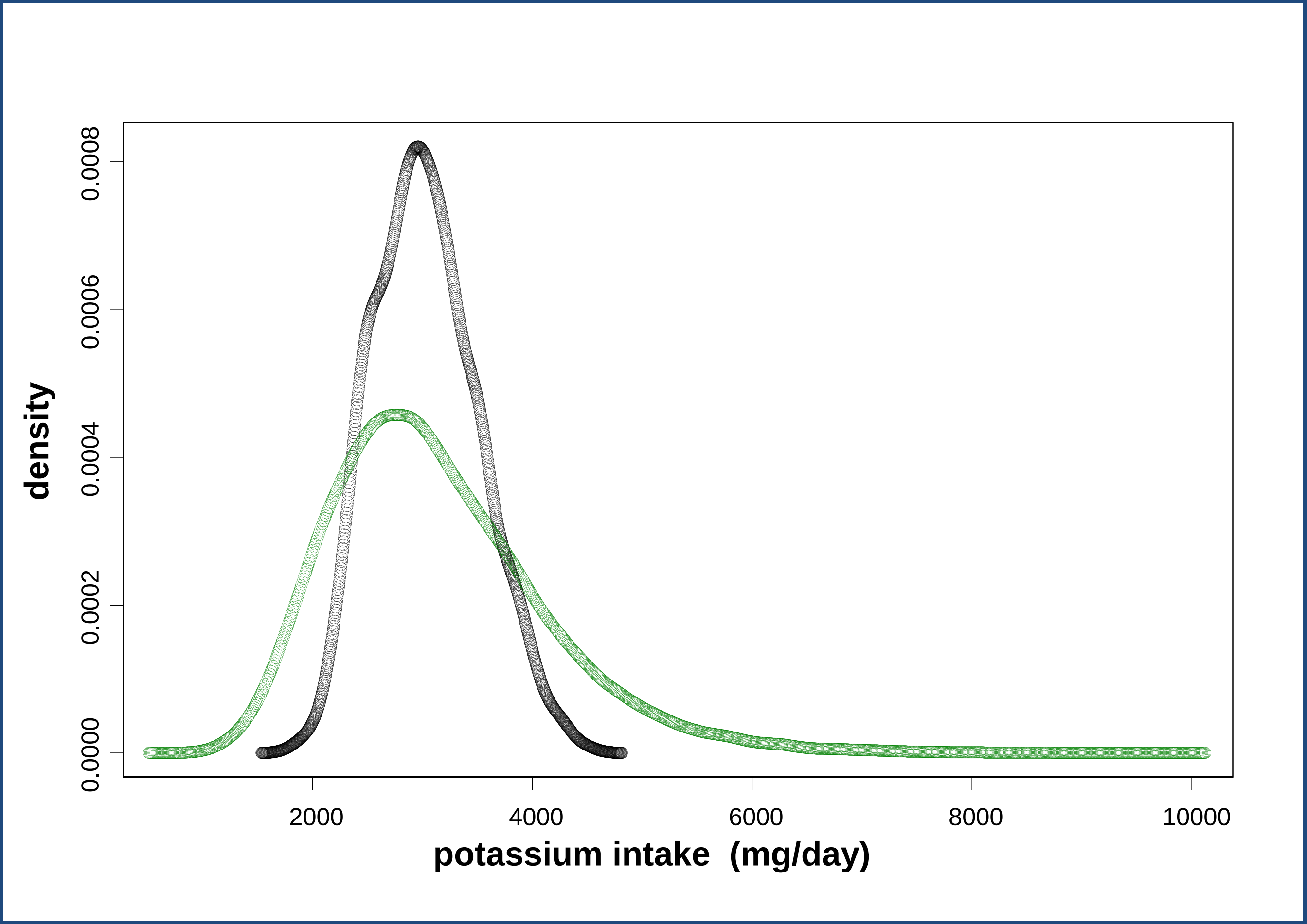
Var(predicted ln(K)) = 0.0239

Var(prediction residual) = 0.0682

MR method: $w = \sqrt{\{(0.0239+0.0682)/0.0239\}} = 1.96$

Results

Black = Empirical distribution of predicted potassium intake
Green = Adjusted for Berkson error



Impact on estimates

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- ❑ Percentiles of X: observe X*

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An extra assumption

- The errors are non-differential

- For the case where X is measured with error, this means:

  X* and Y are independent conditional on X

- For the case where Y is measured with error, this means:

  Y* and X are independent conditional on Y

Impact on Estimates

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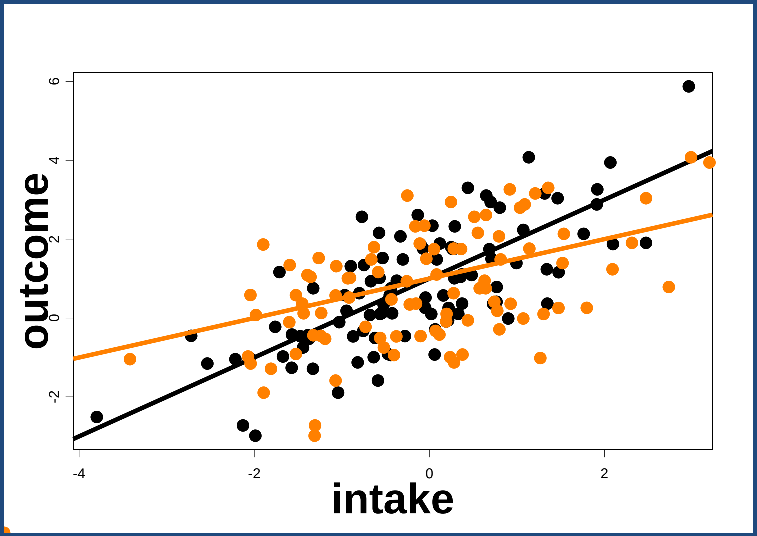
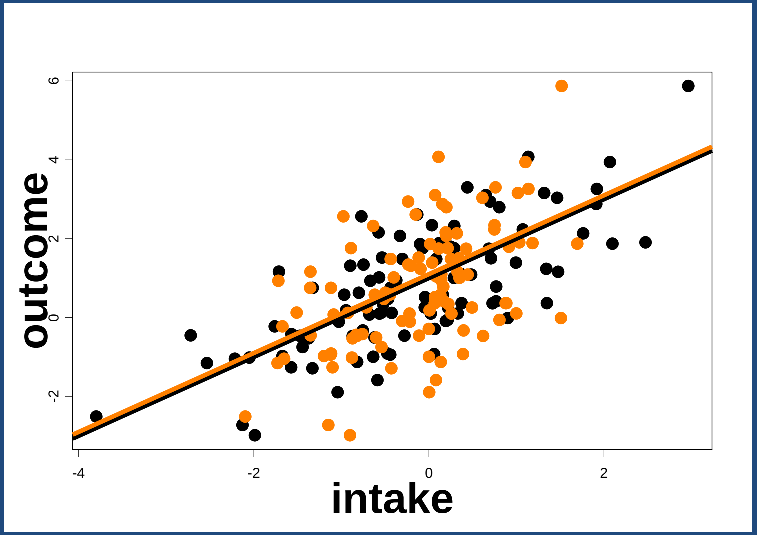
Impact on Estimates of Regression Coefficients

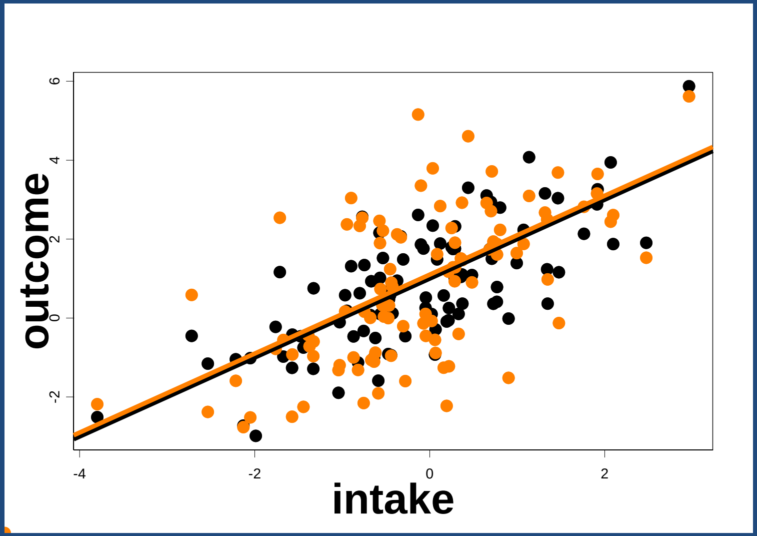
Classical Error in X



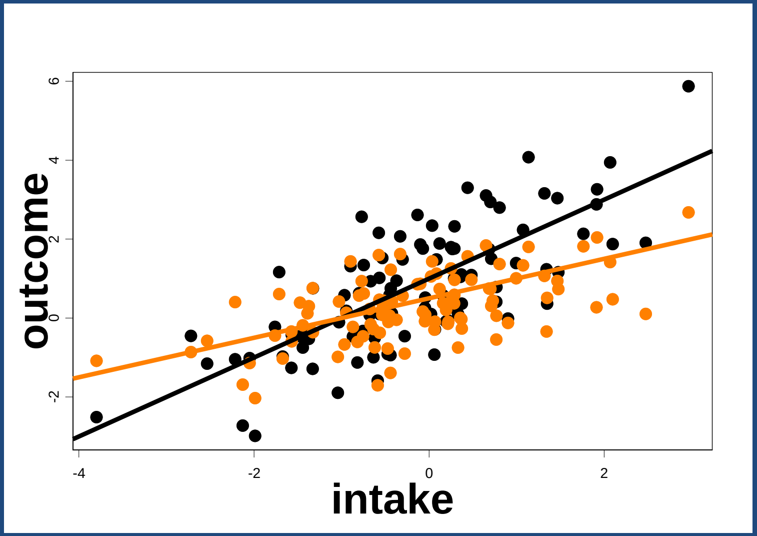
Berkson Error in X



Classical Error in Y



Berkson Error in Y



Regression coefficient of X in regression of Y on X

Variable measured with error	Estimate	Classical	Berkson
X	Regression coefficient	Attenuated	Unbiased
Y	Regression coefficient	Unbiased	Attenuated

How to adjust for classical error in X?

Regression calibration:

- ❑ Obtain a "calibration" equation: E(X|X*)
- ❑ Substitute E(X|X*) for X in regression of Y on X

Why does it work?

E(X|X*) has Berkson error as an estimate of X.

Berkson error in a covariate does not cause bias in estimation.

How to adjust for Berkson error in Y?

"Inverse regression calibration":

- ❑ Invert the Berkson measurement error model $Y=Y^*+U$ to:
  $Y^* = \alpha_0 + \alpha_1 Y + U^*$
- ❑ Form $Y^{est} = (Y^* - \alpha_0)/\alpha_1$ (Buonaccorsi, 1991)
- ❑ Substitute Y^{est} for Y in regression of Y on X

Why does it work?

Y^{est} has classical error as an estimate of Y.

Classical error in Y does not cause bias.

Example from OPEN: does potassium density intake vary with educational level?

Potassium density (mg/kcal)

Calibration (prediction) equation:

$\ln(Kden) = -0.385 + 0.480*\ln(Kden_{FFQ}) - 0.029*sex + 0.00602*age$

This equation for ln(Kden) has Berkson error

Var(predicted ln(Kden)) = 0.0203

Var(prediction residual) = 0.0696

Inverse regression calibration:

Value of Y^{est} to be entered into model of Y on X:

$(\ln(Kden) - 0.124) / 0.226$

Example from OPEN: does potassium density intake vary with educational level?

1. Run regression of ln(Kden) on education, sex and age.
2. Estimate median levels of Kden (mg/1000 kcal) for women, aged 50y, according to educational level

Educational level	Using Y = predicted ln(Kden)	Inv. reg. calib.	Unbiased estimate
High school	1093	856	996
College	1113	933	1095
Post-grad	1159	1110	1216

Summary

- With the increasing use of prediction and calibration equations in medicine, Berkson error will be encountered more and more
- The commonly assumed adage that Berkson error does not cause bias in estimates is wrong.
- Awareness of the effects of Berkson error and methods to adjust for it need more attention

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