Berkson measurement error in epidemiology

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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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<tr>
<th>Name</th>
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<td>Hendriek Boshuizen</td>
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Shaw et al 2018


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

\[ X = X^* + e \]

\( X^* \) is the measurement that has error

\( X \) is the true (unknown) value

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

\( e \) has mean zero

\( e \) is independent of \( X^* \)
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?”
  
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

Each age group prediction equation is a regression of the form: 
\[ \text{REE} = b_0 + b_1 \times \text{Wt} + e, \]
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

<table>
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<tr>
<th>Estimate</th>
<th>Classical</th>
<th>Berkson</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper percentile</td>
<td>Overestimate</td>
<td>Underestimate</td>
</tr>
<tr>
<td>Lower percentile</td>
<td>Underestimate</td>
<td>Overestimate</td>
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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 \( X_{MR} \)
    \[
    X_{MR} = (1 - w) \overline{X^*} + wX^* , \text{ where} \]
    \[
    w = \frac{SD(X)}{SD(X^*)} : \text{note that } w > 1
    \]
    \[
    E(X_{MR}) = E(X) ; \quad var(X_{MR}) = var(X)
    \]

- \( w \) is estimated from **external information**
- Form the distribution using the \( X_{MR} \) values
Example from the OPEN dietary reporting validation study

**Potassium intake (K)**

\[ K_{FFQ} = \text{Food Frequency Questionnaire report of K} \]

The study also included a urinary determination of K

Calibration (prediction) equation:
\[ \ln(K) = 5.895 + 0.271 \times \ln(K_{FFQ}) - 0.193 \times \text{sex} + 0.00035 \times \text{age} \]

This equation for \( \ln(K) \) has Berkson error

\[ \text{Var(predicted } \ln(K)) = 0.0239 \]
\[ \text{Var(prediction residual)} = 0.0682 \]

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

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
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

The impacts of classical and Berkson errors on these estimates are opposite!
Impact on Estimates of Regression Coefficients

Classical Error in X

Berkson Error in X

Classical Error in Y

Berkson Error in Y
<table>
<thead>
<tr>
<th>Variable measured with error</th>
<th>Estimate</th>
<th>Classical</th>
<th>Berkson</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>Regression coefficient</td>
<td>Attenuated</td>
<td>Unbiased</td>
</tr>
<tr>
<td>Y</td>
<td>Regression coefficient</td>
<td>Unbiased</td>
<td>Attenuated</td>
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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:
\[ \ln(K_{\text{den}}) = -0.385 + 0.480 \ln(K_{\text{den}}_{\text{FFQ}}) - 0.029 \times \text{sex} + 0.00602 \times \text{age} \]

This equation for \( \ln(K_{\text{den}}) \) has Berkson error

Var(predicted \( \ln(K_{\text{den}}) \)) = 0.0203

Var(prediction residual) = 0.0696

Inverse regression calibration:
Value of \( Y_{\text{est}} \) to be entered into model of \( Y \) on \( X \):
\[ (\ln(K_{\text{den}}) - 0.124) / 0.226 \]
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

<table>
<thead>
<tr>
<th>Educational level</th>
<th>Using Y = predicted ln(Kden)</th>
<th>Inv. reg. calib.</th>
<th>Unbiased estimate</th>
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<tbody>
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<td>856</td>
<td>996</td>
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<td>933</td>
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<td>Post-grad</td>
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<td>1216</td>
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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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