Measurement error correction and sensitivity analysis in longitudinal dietary intervention studies using an external validation study

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Outline

1. Lifestyle interventions
2. Measurement error in self-reported diet
3. Motivating example: Sodium intake in the PREMIER Study
4. Methods for measurement error correction
5. Results
6. Conclusions

Lifestyle interventions

- Lifestyle interventions are longitudinal clinical trials designed to improve diet and physical activity behaviors
- A number of trials have shown that healthy changes in diet can reduce morbidity and premature mortality and that effective weight loss interventions can reduce the risk of chronic diseases
- Typically involve coaching, education, self-monitoring, and following a recommended diet
- Interventions often use self-reported measures of diet, and obtaining accurate measurement of diet and its change overtime is a major challenge due to measurement error.

Reasons for measurement error

- In lifestyle interventions, self-reported diet is often obtained using an interviewer-assisted 24-hour recall
- Reasons for measurement error in self-reported diet include:
  - Memory limitations
  - Poor quantification of portion sizes
  - Social desirability

Effect of measurement error

- Most research on measurement error correction concerns those situations where an exposure is measured with error, thus attenuating or distorting the relationship between exposure and outcome.
- Less research on correcting for measurement error when an *outcome* is measured with error—especially a longitudinal outcome

Differential measurement error in longitudinal lifestyle interventions

- The presence of treatment conditions and the longitudinal nature of lifestyle interventions can introduce *differential* measurement error
- Examples:
  - Study may consist of training in self-monitoring and portion size assessment: more accurate report over time
  - Repeated assessment over time may lead to less accurate reporting over time
  - Participants may misreport their diet to appear more compliant with the intervention: compliance bias

Measurement error correction

- Correcting for measurement error requires some source of additional information regarding the association between the variable measured with error and its true value
- The source of this information can come from:
  - An internal validation study (ideal)
  - A external validation study (what we use here)
  - Calibration equations (obtained from an external validation study)
- For self-reported dietary variables, these validation studies are conducted using urinary biomarkers

Urinary biomarkers

- Urinary biomarker: biochemical indicator of dietary intake
- Obtained thorough a 24-hour urine sample
- Currently, only exist for sodium, potassium, nitrogen, and total intake
- Objective, less sensitive to biases seen in self-reported assessments
- High participant burden and rare in intervention studies
- Note: urinary biomarkers are also subject to (classical) measurement error

Motivating Example

- The PREMIER study (Appel et al. 2003) was an RCT designed to determine the effects of multi-component lifestyle interventions on blood pressure
- Participants (n=810) were randomized to three treatment conditions
  1. Advice-only (standard of care)
  2. Established: Instruction and counseling over 6-months to modify diet (including sodium)
  3. Established + DASH: Also taught to follow DASH diet which is rich in fruits, vegetables, and low fat dairy
- For this analyses, we combine the Established and Established + DASH groups
- Participants in these two conditions were counseled to reduce sodium intake to less than 2300 mg/day.

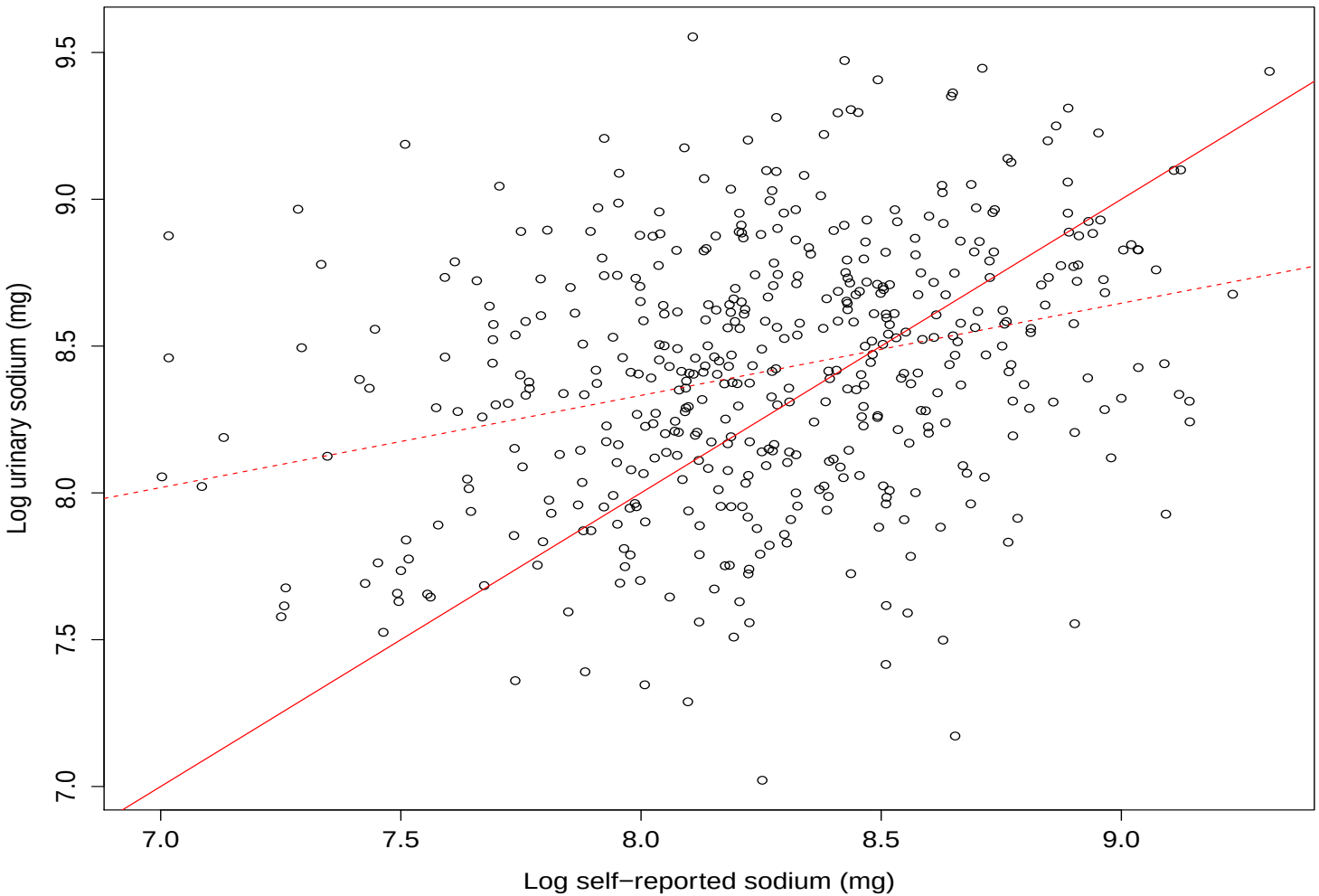
PREMIER dietary assessment

- Diet was measured using 2 unannounced 24-hour recalls on one weekday and one weekend
- Performed at baseline, 6-, and 18-months by telephone
- We focus on *sodium* intake (mg), and the difference in sodium intake between groups at 6-months.
- Following convention, all analyses are based on log-transformed values of sodium

OPEN Study

- The Observing Protein and Energy Nutrition (OPEN; Subar et al. 2003) Study was a validation study designed to assess dietary measurement error in self-reported instruments using unbiased markers of dietary intake
- Participants (n=484) received 1 24-hour recall and collected two 24-hour urine specimens over a 2-week period
- Urinary sodium was divided by 0.81 to reflect that fact that not all dietary sodium appears in urine
- Again we base analyses on log-transformed values

OPEN urinary sodium versus self-reported sodium



Baseline characteristics in PREMIER and OPEN

Variable	Study	
	PREMIER	OPEN
Age	50.0 (8.9)	53.4 (8.3)
BMI	33.1 (5.7)	27.9 (5.3)
Male (%)	38.3%	53.9%
Self-reported sodium	7.96 (0.41)	8.27 (0.42)
Urinary sodium	NA	8.42 (0.44)

Design for measurement error correction in PREMIER

Data Source	Y_0	Z_0	Y_1	Z_1	$\mathbf{X}$	D
PREMIER Intervention Study	■		■		■	■
OPEN External Validation Study	■	■			■	■

Goal

- We want to correct for measurement error in PREMIER sodium intake using information from OPEN
- OPEN contains both self-report and biomarker measures of dietary intake
- OPEN is cross-sectional and observational: does not provide information on changes in measurement error over time or in response to treatment
- Our focus of interest is on changes in sodium intake between treatment and control groups
- Naive analysis would use self-reported sodium intake
- Our goal is difference in *urinary* sodium intake at follow-up between treatment and control conditions.

Definitions of differential measurement error

Non-differential measurement error w.r.t. treatment

- Z_j be the true value of the quantity we wish to measure at time $j, j = 0, \ldots, m$ where baseline is $j = 0$.
- Let Y_j be Z_j measured with error
- Let X be a vector of background covariates measured without error
- D an indicator as to whether a participant has been randomized to the intervention group ($D = 1$) or the control group ($D = 0$)

Definition 1: We define the calibration model as *non-differential with respect to treatment* if

$$f(Z_j \mid Y_j, X, D = 1) = f(Z_j \mid Y_j, X, D = 0), \quad \text{for } j > 0.$$

- Parameters of the calibration model are the same at a given time point in both treatment and control groups and do not change in response to treatment

Non-differential measurement error w.r.t. time

Definition 2: We define the calibration model as *non-differential with respect to time* if

$$f(Z_j \mid Y_j, X, D = d) = f(Z_k \mid Y_k, X, D = d), \quad \text{for all } j \neq k.$$

where j and k are two separate time points.

- Within a treatment condition, the parameters of the calibration model are the same at baseline and post-baseline

Non-differential measurement error w.r.t treatment and time

Definition 3: The calibration model is *nondifferential with respect to treatment and time* if the following holds

$$f(Z_j \mid Y_j, X, D = 1) = f(Z_k \mid Y_k, X, D = 0), \quad \text{for all } j,\ k.$$

Transportability

Definition 4 (Carroll, 2006): Let S denote whether a participant is in the lifestyle intervention ($S = \ell$) or validation study ($S = v$), then under transportability, the following holds:

$$f(Z \mid Y, X, S = \ell) = f(Z \mid Y, X, S = v).$$

- Marginal distribution of Y and Z can differ in the two samples
- Only the *conditional* distributions are assumed to be the same

Methods

Summary of approach

- Fit a model to the observed data
- Make plausible, yet *unverifiable* assumptions in order to identify parameters from those distributions (involving true intake) based on incomplete information
- Impute values of true sodium intake in PREMIER
- Make inferences
- Investigate sensitivity of inferences to unverifiable assumptions regarding differential measurement error

Model

- The joint distribution of $\boldsymbol{Z}$, and $\boldsymbol{Y}$ conditional on X in PREMIER can be written as

$$f(Z_1, Z_0, Y_1, Y_0 \mid X) = f(Z_1 \mid Z_0, Y_1, Y_0, X) \times f(Z_0 \mid Y_1, Y_0, X) f(Y_1, Y_0 \mid X)$$

- We assume this joint distribution is Normal.
- While the focus of our inference is on Z, it is necessary to also model Y due to missingness in Y
- Most of the parameters on the right hand side are not identifiable

Reducing the number of unidentified parameters

- To help identify the conditional distributions above we make the following assumptions:

$$f(Z_1 \mid Z_0, Y_1, Y_0, X) = f(Z_1 \mid Z_0, Y_1, X),$$

and

$$f(Z_0 \mid Y_1, Y_0, X) = f(Z_0 \mid Y_0, X).$$

- That is, the conditional distribution of Z at time t depends only the self-reported measurement at time t and the $t-1$ (if any) true intake.
- Using these assumptions, the factorization reduces to:

$$f(Z_1, Z_0, Y_1, Y_0 \mid X) = f(Z_1 \mid Z_0, Y_1, X) f(Z_0 \mid Y_0, X) f(Y_1, Y_0 \mid X)$$

- Still, only the parameters involved in $f(Y_1, Y_0 \mid X)$ are identified

Design for measurement error correction in PREMIER

Data Source	Y_0	Z_0	Y_1	Z_1	$\mathbf{X}$	D
PREMIER Intervention Study	■		■		■	■
OPEN External Validation Study	■	■			■	■

First unidentified component: $f(Z_0 \mid Y_0, X)$

- The parameters from this model are not identified.
- Assume calibration model from OPEN is *transportable* at baseline:

$$f(Z_0 \mid Y_0, X, \text{Study} = \text{PREMIER}) = f(Z_0 \mid Y_0, X, \text{Study} = \text{OPEN})$$

- So that the calibration parameters are the same in both the trial and the validation study:

Second unidentified component: $f(Z_1 \mid Y_1, Z_0, X)$

- Z_1, Y_1, and Z_0 are never jointly observed
- To identify the parameters of this distribution, we make three assumptions:

$$f(Z_1 \mid Y_1, X) = f(Z_0 \mid Y_0, X) \tag{1}$$
$$corr(Y_1, Z_0 \mid X) \sim Uniform(0, corr(Y_0, Z_0 \mid X)) \tag{2}$$
$$corr(Z_1, Z_0 \mid X) = corr(Y_1, Y_0 \mid X) + \Delta_\rho \tag{3}$$

  where $\Delta_\rho \sim \text{Uniform}(-\delta, \delta)$
- We will do a sensitivity analysis for the first assumption of non-differential measurement error w.r.t time

Design for measurement error correction in PREMIER

Data Source	Y_0	Z_0	Y_1	Z_1	$\mathbf{X}$	D
PREMIER Intervention Study	■		■		■	■
OPEN External Validation Study	■	■			■	■

Sensitivity Analysis

- Under the transportability assumption, the distribution of Z_0 given Y_0 and X is

$$Z_0 \mid Y_0, X \sim N(\beta_{0,Z_0 \cdot Y_0 X} + \beta_{1,Z_0 \cdot Y_0 X} Y_0 + \beta_{2,Z_0 \cdot Y_0 X} X,\ \sigma^2_{Z_0 \cdot Y_0 X})$$

- This is at *baseline*
- Under non-differential measurement error with respect to treatment and time the following holds for both treatment and control groups:

$$\begin{aligned} \boldsymbol{\beta}_{Z_1 \cdot Y_1 X} &= \boldsymbol{\beta}_{Z_0 \cdot Y_0 X} \\ \sigma^2_{Z_1 \cdot Y_1 X} &= \sigma^2_{Z_0 \cdot Y_0 X}. \end{aligned}$$

- We wish to assess the sensitivity our our inferences to the assumption that these relationships hold at follow-up in both treatment and control conditions

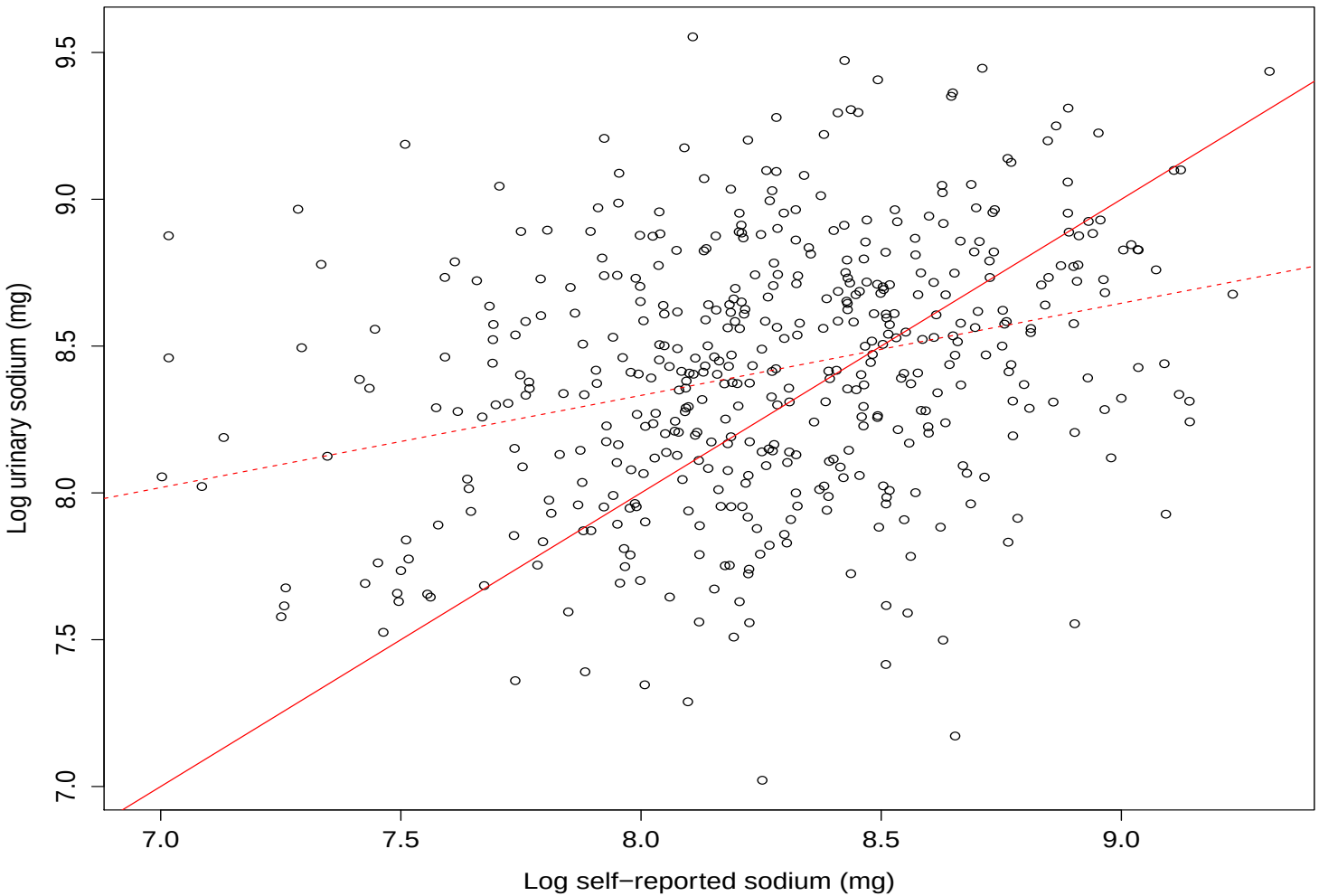
Sensitivity Parameters

- Investigate sensitivity to non-differential measurement error
- Focus on changes in underreporting as compared to baseline in terms of the *intercept* parameter

$$\beta^{(d)}_{0,Z_1 \cdot Y_1 X} = \beta_{0,Z_0 \cdot Y_0 X} + \Delta^{(d)}_{\beta_0}$$

- $\Delta^{(d)}_{\beta_0}$ measures the additional under or over reporting at month 6 ($t = 1$) as compared to baseline
- Can vary by treatment group (d=1) or control group (d=0).
- $\Delta^{(1)}_{\beta_0} = \Delta^{(0)}_{\beta_0}$: Non-differential measurement error with respect to treatment
- $\Delta^{(d)}_{\beta_0} = 0$: Non-differential measurement error with respect to time
- We scale $\Delta^{(d)}_{\beta_0}$ as a percentage of the residual standard deviation $\sigma_{Z_0 \cdot Y_0 X}$

OPEN urinary sodium versus self-reported sodium



Parameter estimation

- Parameter estimation for $f(Y_1, Y_0|X, S = \text{PREMIER})$ and $f(Z_0|Y_0, X, S = \text{OPEN})$ was performed using MCMC
- 100 parameter draws from these posterior distributions
- Noninformative priors for identified parameters
- Uniform priors for unidentified correlations
- Point-mass priors for sensitivity parameters
- Values of $\Delta^1_{\beta_0}$ and $\Delta^0_{\beta_0}$ ranged from minus half a residual standard error to plus half a residual standard error

Imputation and analyses

- Imputed values of Z_0 and Z_1 in PREMIER were generated from from $f(Z_0 \mid Y_0, X)$ and $f(Z_1 \mid Y_1, Z_0, X)$
- 200 imputations were generated for each missing value
- For each imputed data set we estimated the the difference in change in sodium intake between the two intervention conditions at follow-up

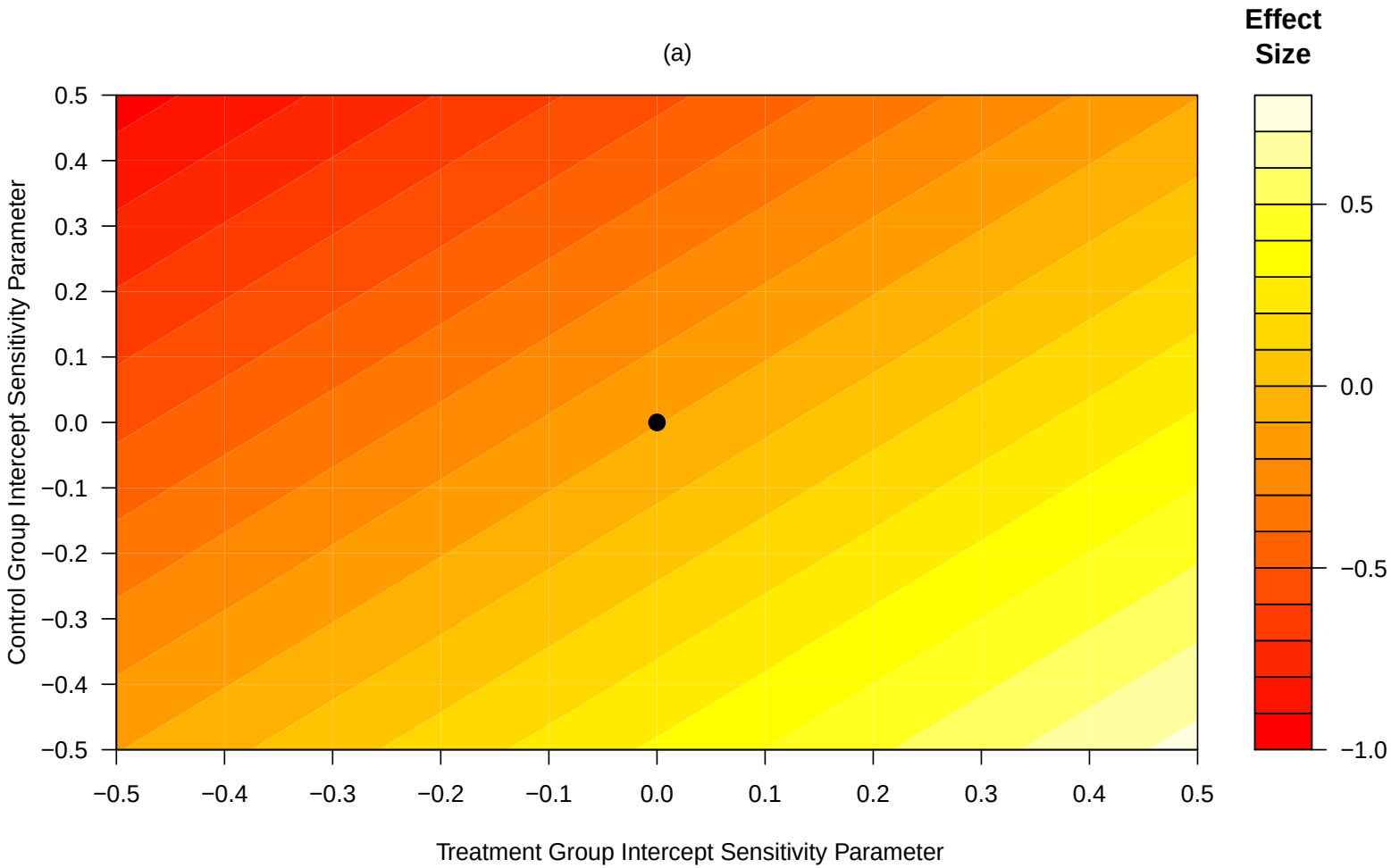
$$\psi = \{E(Z_1|D=1) - E(Z_0|D=1)\} - \{E(Z_1|D=0) - E(Z_0|D=0)\}$$

- When $\psi < 0$, reduction in sodium intake is greater in the treatment group than the control group
- We scale by the pooled standard deviation in order to calculate an effect size.

Results

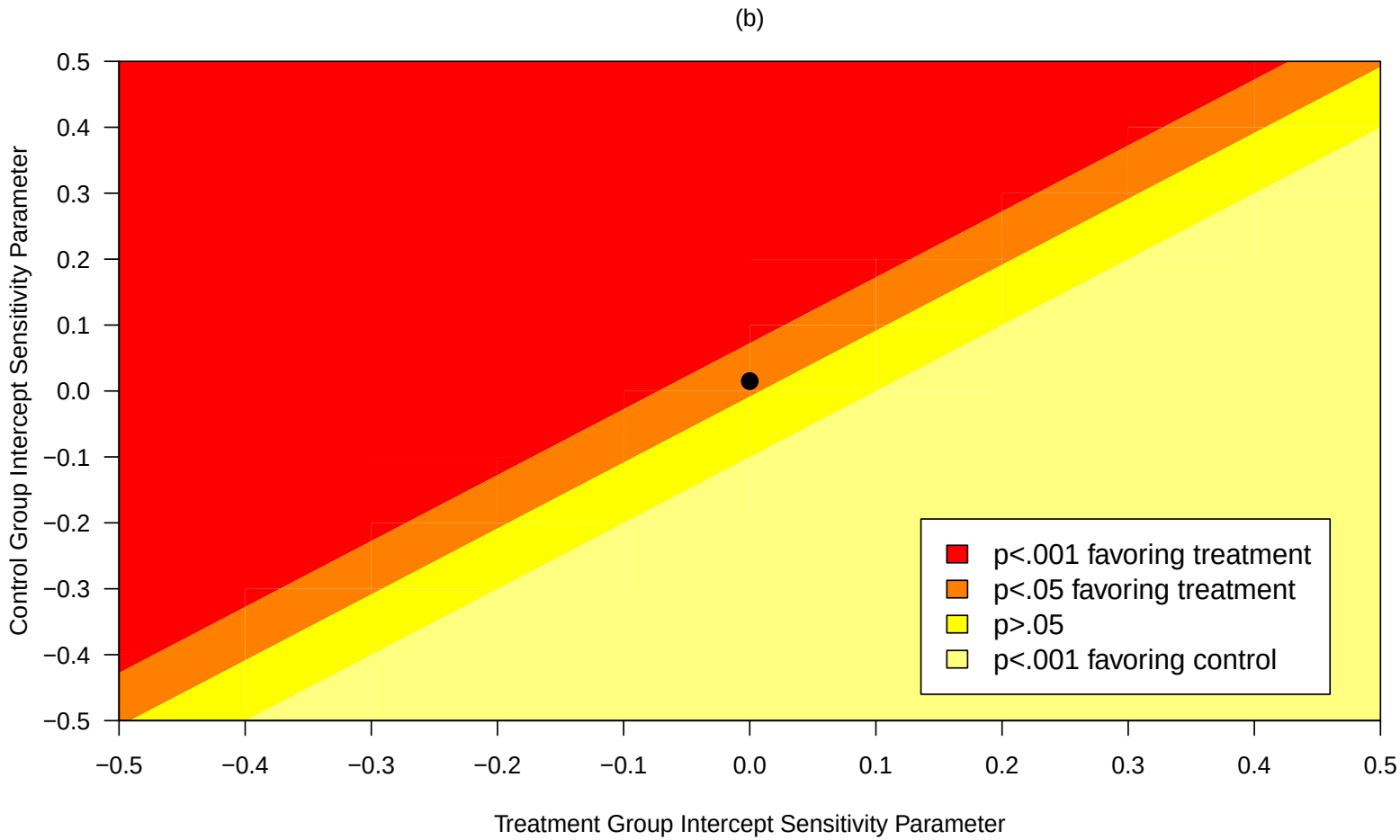
Contour plot of effect sizes by $\Delta^{(1)}_{\beta_0}$ and $\Delta^{(0)}_{\beta_0}$

- Effect size based on self-report: -0.49
- Effect size assuming no differential measurement error w.r.t treatment and time: -0.11



Contour plot of p-values by $\Delta^{(1)}_{\beta_0}$ and $\Delta^{(0)}_{\beta_0}$

- p-value based on self-report: p$<$.001
- p-value assuming no differential measurement error w.r.t treatment and time: $p = .006$



Conclusion

- We have described a framework for measurement error correction using external validation studies
- In PREMIER, corrected treatment effects were small
- Inferences were sensitive to mild assumptions regarding nature of measurement error
- Sensitivity analyses provided inferences within the range of naive analyses
- If the goal is to produce a single analyses that incorporates uncertainty regarding non-differential measurement error, could draw sensitivity parameters from prior distributions, rather than using point mass priors as done here

Reference

Siddique J, Daniels MJ, Carroll RJ, Raghunathan TE, Stuart EA, Freedman LS. Measurement error correction and sensitivity analysis in longitudinal dietary intervention studies using an external validation study. *Biometrics.* In press.

Thank you

Sensitivity Analysis, cont'd

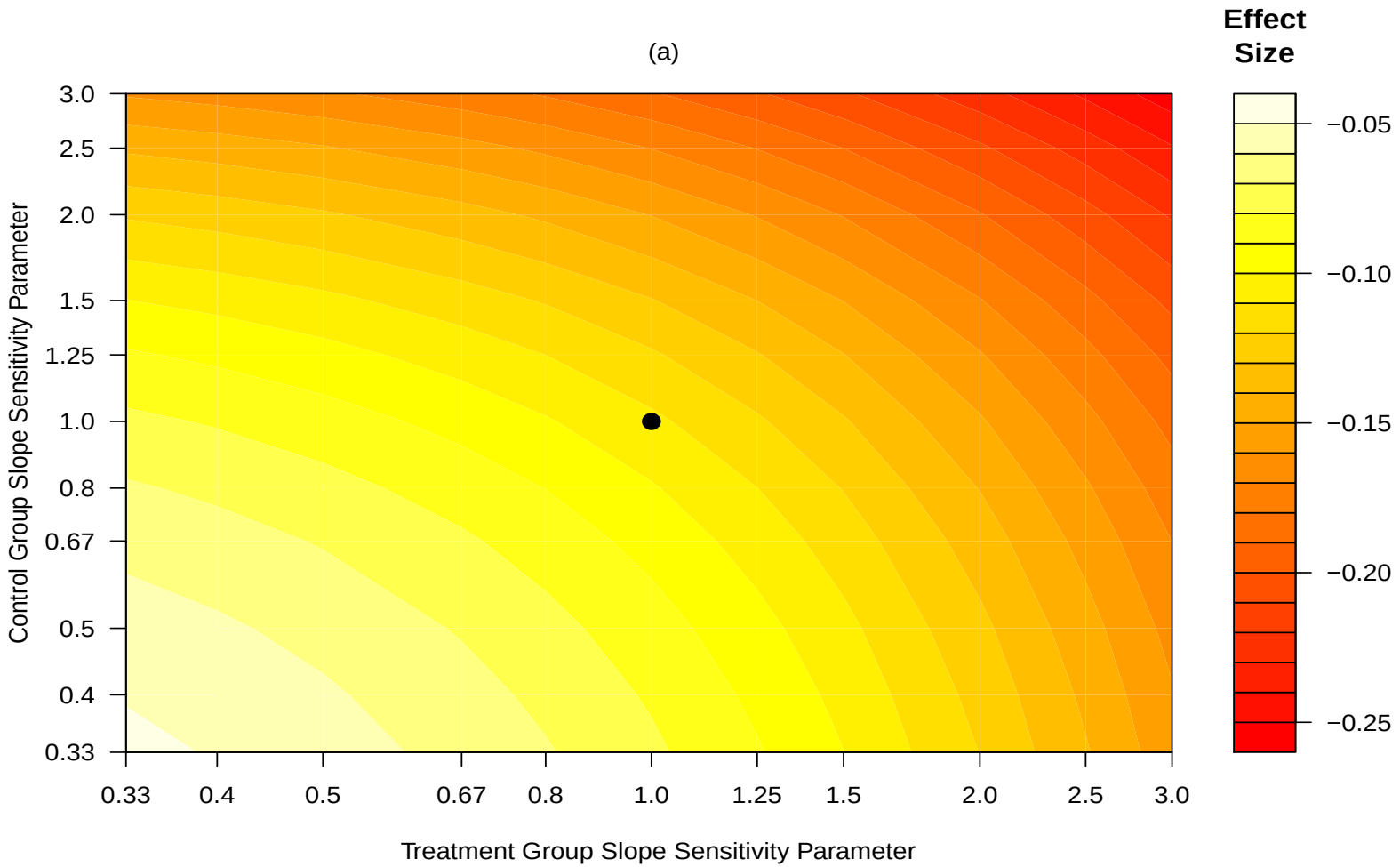
- The second sensitivity parameter focuses on the *slope* of the measurement error model at follow-up
- We center the regression line around the target value of intake: 2300mg/day
- Then multiply the baseline slope by the sensitivity parameter $\Delta^{d}_{\beta_1}$ so that we have:

$$\beta^{(d)}_{0,Z_1 \cdot Y_1} = \beta_{0,Z_0 \cdot Y_0} + (1 - \Delta^{(d)}_{\beta_1}) \times \beta_{1,Z_0 \cdot Y_0} \times \log(2300)$$
$$\beta^{(d)}_{1,Z_1 \cdot Y_1} = \Delta^{(d)}_{\beta_1} \times \beta_{1,Z_0 \cdot Y_0}.$$

- When $\Delta^{(d)}_{\beta_1} > 1$, participants whose fail to meet the target value self-report less—for a given level of true intake—than they did at baseline by an amount that increases the further they deviate from the target value
- Participants who did achieve the target value self-report more than they did at baseline

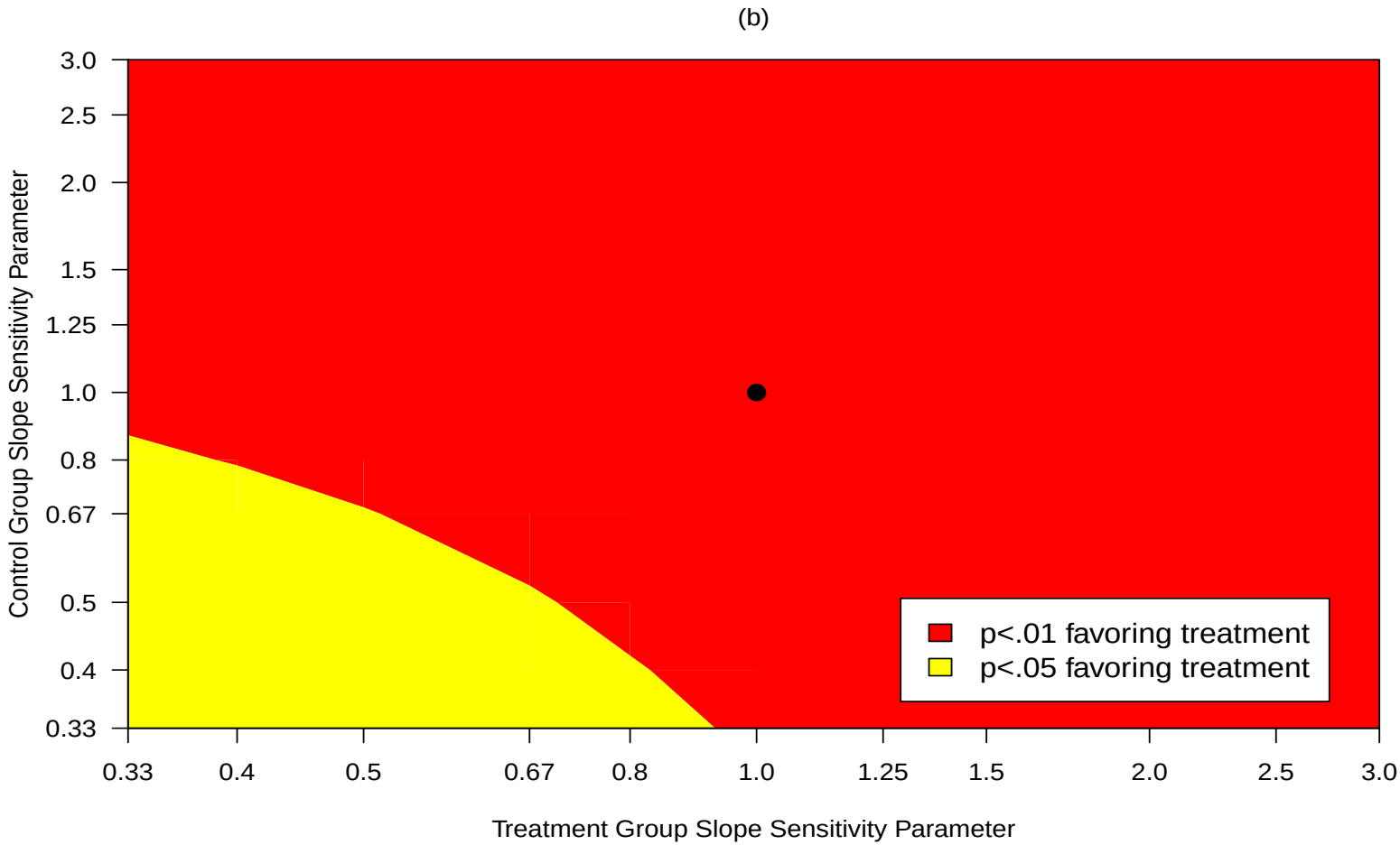
Contour plot of effect sizes by $\Delta^1_{\beta_1}$ and $\Delta^0_{\beta_1}$

- Effect size based on self-report: -0.49
- Effect size assuming no differential measurement error w.r.t treatment and time: -0.11



Contour plot of p-values by $\Delta^1_{\beta_1}$ and $\Delta^0_{\beta_1}$

- p-value based on self-report: p$<$.001
- p-value assuming no differential measurement error w.r.t treatment and time: $p < .006$



A model for: $f(Z_0 \mid Y_0, X)$

- Reminder, urinary sodium is typically considered unbiased but is still subject to (classical) measurement error
- Idea (Willet, 2013): use the replicate measures of urinary sodium to partition out the within-subject variance, i.e. the measurement error
- Let W_{ij} be the jth urinary biomarker measurement for participant i, $j = 1, 2$
- Using OPEN, we fit the following random effects model to decompose between- and within-subject variance

$$W_{ij} = \beta_{0,Z_0 \cdot Y_0 X} + \beta_{1,Z_0 \cdot Y_0 X} Y_{0i} + \beta_{2,Z_0 \cdot Y_0 X} X_i + b_{0i} + \varepsilon_{ij}$$

  where $b_{0i} \sim N(0, \sigma^2_{Z_0 \cdot Y_0 X})$ and $\varepsilon_{ij} \sim N(0, \sigma^2_w)$.
- Then distribution $f(Z_0 \mid Y_0, X)$ in OPEN is

$$Z_0 \mid Y_0, X \quad \sim \quad N(\beta_{0,Z_0 \cdot Y_0 X} + \beta_{1,Z_0 \cdot Y_0 X} Y_0 + \beta_{2,Z_0 \cdot Y_0 X} X,\ \sigma^2_{Z_0 \cdot Y_0 X})$$

Future work

- Measurement error correction with nonignorably missing self-reported data
- Incorporating more than one validation study
- Measurement error correction when there is no recovery biomarker