Grouping vs. non-grouping approaches to correct for measurement error in two-stage designs

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OUTLINE

- Bias in exposure-response relation due to EME

- Bias-correction methods of analysis
  - *grouping* methods
  - *non-grouping* methods

- Two-stage (2S) designs to correct for EME

- Simulation study

Objective: find best bias-correction method of analysis for 2S designs

Exposure-response relationship

Cross-sectional study: effect of carbon black dust on lung function (ie FEV_1)

Assume,

response model: $Y = \alpha + \beta X + \delta$

Y: response, **X**: *true* exposure

Goal: estimation of β

EME in medical research

Mismeasured exposures:

- Systolic blood pressure
- Dietary intakes (ie fat, fiber)
- Environmental & Occupational exposures (ie asbestos, carbon black dust)

Assume an error-prone exposure **W** exists;

$$W = X + \mathbf{error},$$

where error~N(0,σ^2), cov(error,X)=0

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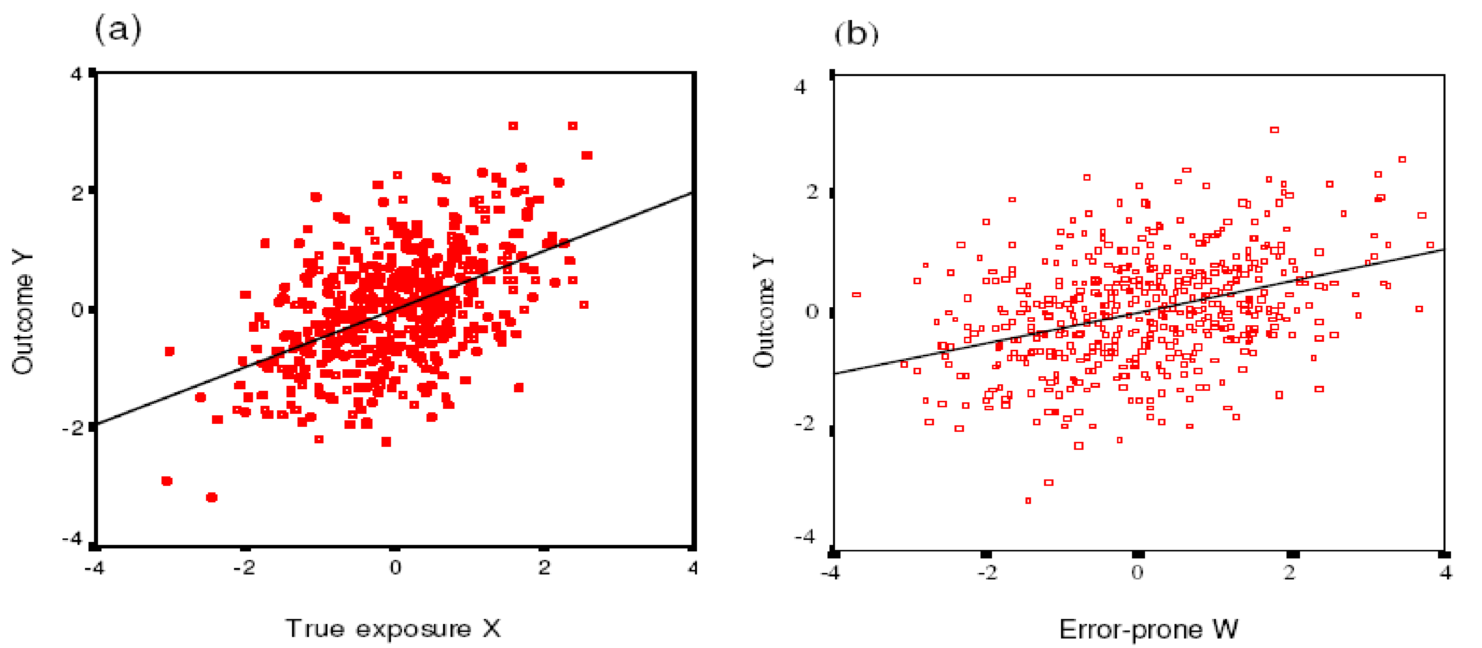
Effect of EME:

In general, the *true* exposure-response relationship will be attenuated



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Biased OLS slope of W-Y relationship (Gustafson 2004):

$$\hat{\beta}_{\text{biased}} = \lambda \cdot \beta,$$

where $$\lambda = \frac{V(X)}{V(X)+V(E)}$$ (V: variance, E: error)

is the *attenuation factor* (*reliability* of exposure W)

☞ Information on reliability λ can be obtained through ie repeated Ws

2S designs to correct for EME

Assume a single W_1 is taken (instead of *true* X) on *n* study subjects and W_2 on $m<n$ subjects

Stage-1: Y, W_1 (*n* subjects)

Stage-2: W_2 ($m<n$ subjects)

Selection of *m* (out of *n*) subjects: random subsampling

☞ Dataset can be viewed as having (MCAR or MAR) missing data

Bias-correction methods of analysis (individual strategies for measuring exposure)

- **Regression calibration approaches**

  - **RCAL** (Carroll *et al*.'s)**:**
    estimate true X, regress Y on $\hat{X}$, adjust SE (ie bootstrap)

  - **RC** (Rosner *et al*.'s)**:**
    regress Y on W_1 (slope estimate $\hat{\beta}_{\text{biased}}$), regress W_2 on W_1 (reliability $\hat{\lambda}$), correct for bias ($\hat{\beta} = \hat{\beta}_{\text{biased}} / \hat{\lambda}$)

- Alternatively:

ICC (Frost *et al*.) / IV (Carroll *et al*.) / SIMEX (Cook *et al*.) approach

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☞ Dataset in a 2S design can be viewed as having (MCAR or MAR) missing data

- **Ignore missingness** and apply a bias-correction method
- **Use missing data methods** ie multiple imputation (MI):

  - impute missing W_2 using Bayesian model applied to complete cases
  - apply a bias-correction method to 'filled in' dataset (Gorfine *et al*.) to estimate true β
  - repeat M times
  - find average β estimate, estimate correct SE (Rubin's rules)

Bias-correction methods of analysis (<u>grouping strategies</u> for measuring exposure)

- **Group mean OLS approach** (*Tielemans et al.*)

Key idea:

- *Prior* to measure exposure, group individuals on the basis of similar exposure characteristics (ie job title, factory)
- W is measured and the group mean, say $\bar{W}$, is assigned to each individual within the group *<u>in place of their individual W</u>*
- Y is regressed on $\bar{W}$ → $\hat{\beta}$

Rationale: The exposure measurements within group could be viewed as repeated measurements of same individual:

$$\lambda = \frac{V(X)}{V(X)+V(E)/l}$$

(*l*: # of exposure measur.)

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In Batistatou & McNamee (2008):

- The group mean $\bar{W}$ can be treated as an IV
- The *group mean OLS/IV approach* does NOT totally remove bias
- The index $k \cdot \varepsilon(\bar{W})$ can be used to choose the grouping scheme that leads to smallest attenuation,

  where

  k: group size, $\varepsilon(\bar{W}) = V(\bar{W})/V(W)$: contrast of exposure

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- **EVROS IV approach** (Batistatou & McNamee):

  - W_2 is replaced by its group mean and treated as an IV for W_1 in an IV analysis

  - The *EVROS IV method* totally removes bias

Simulation methods

Assumptions:

N = 1,000 subjects (1,000 simulations)

X ~ N(5,1), Y = 4.0 **- 0.1***X+*δ*, *δ* ~ N(0, 0.15)

$W_1 = X+E_1$, $W_2 = X+E_2$, reliability λ of W = 0.2, 0.5, 0.8,

Randomly missing data in W_2: 30%, 50%

Aim: Compare **EVROS IV** with **RC**, **RCAL**, **MI-RCAL** approach in 2S designs

Creation of 'external' grouping factor:

- Create variable Z = X+error, reliability of Z = 0.5, 0.8
- Order the data
- Divide the data into groups

Number of groups: 2 (group size *k*=500), 20 (*k*=50), 100 (*k*=10)

Simulation results: 30% missing data in W_2

(from 1,000 simulations with true β=-0.1: mean, SD, RMSE of $\hat{\beta}$)

λ	grouping reliability	EVROS IV (*k*=500)	EVROS IV (*k*=50)	EVROS IV (*k*=10)	RC	RCAL	MI-RCAL
0.8	0.8	-0.100 (0.0175) 0.0175	-0.100 (0.0137) 0.0137	-0.100 (0.0138) 0.0138	-0.100 (0.0139) 0.0139	-0.108 (0.0142) 0.0163	-0.099 (0.0128) 0.0128
	0.5	-0.100 (0.0216) 0.0216	-0.100 (0.0171) 0.0171	-0.100 (0.0169) 0.0169			
0.5	0.8	-0.100 (0.0180) 0.0180	-0.100 (0.0143) 0.0143	-0.100 (0.0150) 0.0150	-0.100 (0.0183) 0.0183	-0.122 (0.0201) 0.0298	-0.099 (0.0164) 0.0164
	0.5	-0.100 (0.0223) 0.0223	-0.100 (0.0181) 0.0181	-0.100 (0.0191) 0.0191			
0.2	0.8	-0.101 (0.0199) 0.0199	-0.101 (0.0165) 0.0165	-0.101 (0.0200) 0.0200	-0.103 (0.0362) 0.0363	-0.145 (0.0466) 0.0648	-0.105 (0.0359) 0.0362
	0.5	-0.101 (0.0249) 0.0249	-0.101 (0.0219) 0.0219	-0.101 (0.0285) 0.0285			

Simulation results: 50% missing data in W_2

(from 1,000 simulations with true β=-0.1: mean, SD, RMSE of $\hat{\beta}$)

λ	grouping reliability	EVROS IV (*k*=500)	EVROS IV (*k*=50)	EVROS IV (*k*=10)	RC	RCAL	MI-RCAL
0.8	0.8	-0.100 (0.0175) 0.0175	-0.100 (0.0137) 0.0137	-0.100 (0.0140) 0.0140	-0.100 (0.0140) 0.0140	-0.105 (0.0141) 0.0150	-0.099 (0.0131) 0.0131
	0.5	-0.100 (0.0216) 0.0216	-0.100 (0.0173) 0.0173	-0.100 (0.0178) 0.0178			
0.5	0.8	-0.100 (0.0180) 0.0180	-0.100 (0.0143) 0.0143	-0.100 (0.0157) 0.0157	-0.101 (0.0188) 0.0188	-0.115 (0.0199) 0.0249	-0.100 (0.0175) 0.0175
	0.5	-0.100 (0.0223) 0.0223	-0.100 (0.0184) 0.0184	-0.100 (0.0209) 0.0209			
0.2	0.8	-0.101 (0.0199) 0.0199	-0.101 (0.0169) 0.0169	-0.101 (0.0228) 0.0228	-0.106 (0.0435) 0.0439	-0.135 (0.0644) 0.0733	-0.110 (0.0531) 0.0540
	0.5	-0.101 (0.0249) 0.0249	-0.101 (0.0230) 0.0230	-0.101 (0.0329) 0.0329			

CONCLUSIONS

- RMSE increases as reliability λ of exposure decreases in all methods
- No bias under the *EVROS IV* and *RC* approaches
- *RC* is preferred over *RCAL* in 2S designs:
  - unbiased slope estimates
  - lower RMSEs
- Performance of *RCAL* is improved with use of MIs
- *EVROS IV* outperforms the non-grouping methods, especially for low reliability λ and good/fair good performance of grouping

Grouping strategies for measuring exposure in 2S designs are highly recommended in the presence of severe measurement error

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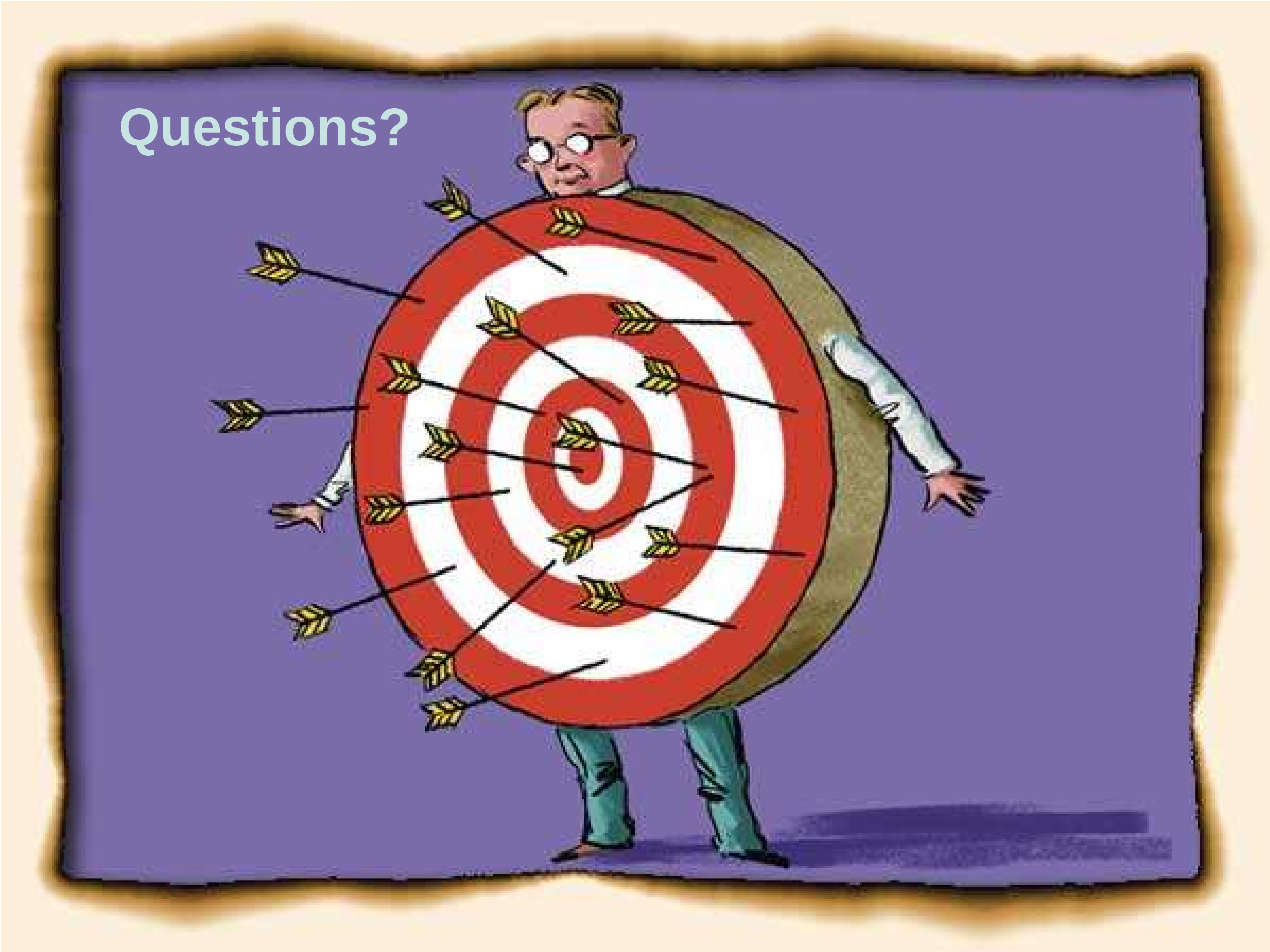
Questions?

Thank you!