M-estimation for fusion designs

Paul Zivich

Department of Epidemiology
Causal Inference Research Laboratory
UNC Gillings School of Global Public Health

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pzivich@unc.edu @PausalZ pzivich

[1] Footnotes are reserved asides for possible later discussion or questions

M-estimation

M-estimation[2]

M-estimators are the solution to

$$\frac{1}{n}\sum_{i=1}^{n}\psi(O_i;\hat{\theta}) = 0$$

Estimating function for the mean

$$\frac{1}{n}\sum_{i=1}^{n}Y_i = \mu \qquad \rightarrow \qquad \frac{1}{n}\sum_{i=1}^{n}(Y_i - \mu) = 0$$

[2] For a general introduction see either Chapter 7 of *Essential Statistical Inference* or Stefanski & Boos (2002) *Am Stat*

Stacked functions

Example: inverse probability of missingness weighted mean

- MCAR conditional on W

$$\psi(O_i, \theta) = \begin{bmatrix} \left(R_i - \text{expit}(W_i^T \beta)\right) W_i \\ Y_i R_i \frac{1}{\text{expit}(W_i^T \beta)} - \mu \end{bmatrix}$$

Variance of μ can be estimated via sandwich variance

- Uncertainty of μ depends uncertainty of β

Automation[3,4]

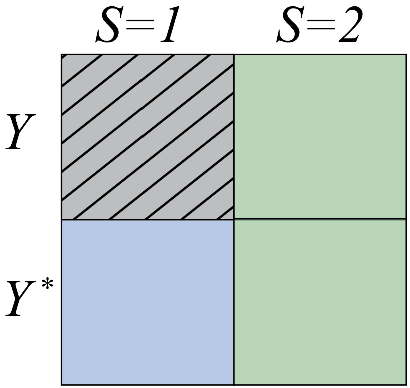
PROC IML;

[3] delicatessen: Zivich et al. (2022) *arXiv*
[4] geex: Saul & Hudgens (2020) *J Stat Softw*

Fusion applications

A1: measurement error[5]

Estimate mean of variable Y for population $S = 1$



[5]Example based on Cole et al. *Am J Epidemiol* in-press

A1: measurement error

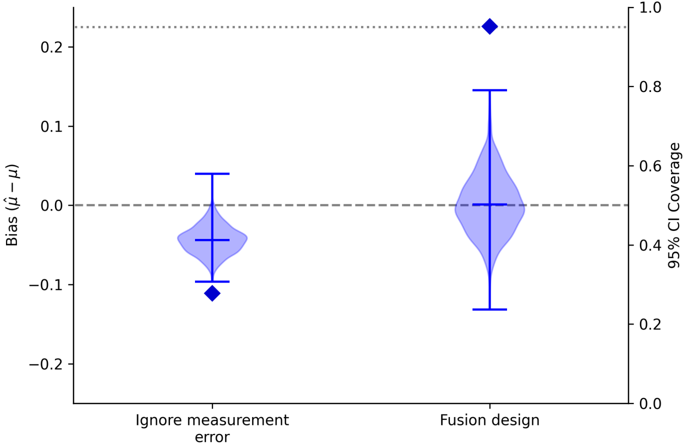
Estimating functions[6]

$$\psi(O_i;\theta) = \begin{bmatrix} I(S_i = 2) Y_i (Y_i^* - \alpha_1) \\ I(S_i = 2)(1 - Y_i)((1 - Y_i^*) - \alpha_0) \\ I(S_i = 1)(Y_i^* - \omega) \\ \mu(\alpha_1 + \alpha_0 - 1) - (\omega + \alpha_0 - 1) \end{bmatrix}$$

where $O_i = (S_i, Y_i, Y_i^*)$ and $\theta = (\alpha_1, \alpha_0, \omega, \mu)$

[6] Measurement correction from Rogan & Gladen (1978) *Am J Epidemiol*

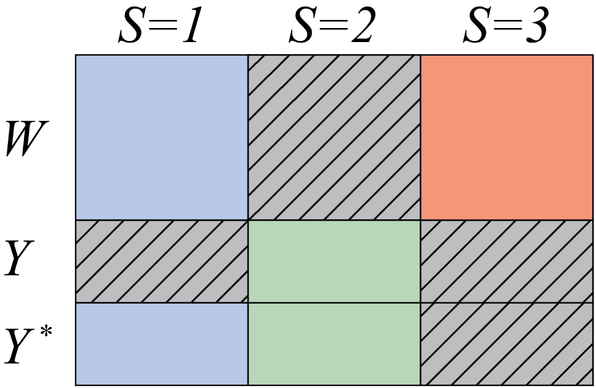
A1: measurement error[7,8]



[7] Details and code available at github.com/pzivich/Presentations
[8] Based on 2000 repetitions with $n_1 = 750$, $n_2 = 200$, and $\mu = 0.37$

A2: transport and measurement error

Estimate mean of variable Y for population $S = 3$



A2: transport and measurement error

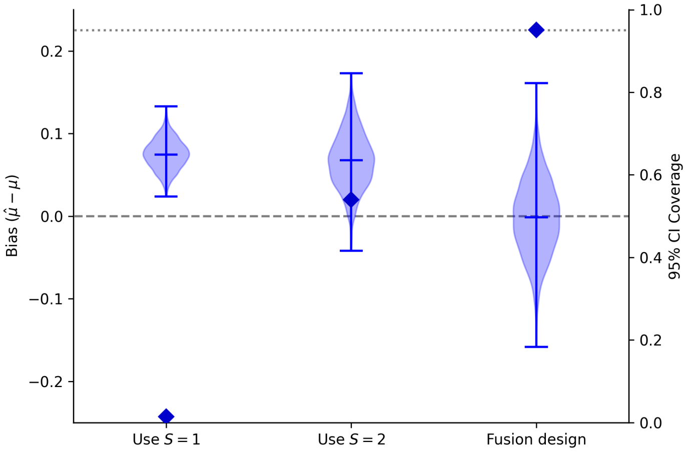
Estimating functions[9,10]

$$\psi(O_i;\theta) = \begin{bmatrix} I(S_i = 2) Y_i (Y_i^* - \alpha_1) \\ I(S_i = 2)(1 - Y_i)((1 - Y_i^*) - \alpha_0) \\ I(S_i \neq 2) \left(I(S_i = 3) - \text{expit}(W_i^T \beta) \right) W_i \\ I(S_i = 1) \frac{1 - \text{expit}(W_i^T \beta)}{\text{expit}(W_i^T \beta)} (Y_i^* - \omega) \\ \mu(\alpha_1 + \alpha_0 - 1) - (\omega + \alpha_0 - 1) \end{bmatrix}$$

where $O_i = (S_i, W_i, Y_i, Y_i^*)$ and $\theta = (\alpha_1, \alpha_0, \beta, \omega, \mu)$

[9] Measurement correction from Rogan & Gladen (1978) *Am J Epidemiol*
[10] Inverse odds weights from Westreich et al. (2017) *Am J Epidemiol*

A2: transport and measurement error[11,12]



[11]Details and code available at github.com/pzivich/Presentations
[12]2000 repetitions with $n_1 = 750$, $n_2 = 200$, $n_3 = 2000$, and $\mu = 0.42$

A3: bridged study design

Triple therapy to mono therapy through dual therapy[13,14]

- Using ACTG 320 and ACTG 175
- Restricting by CD4 between 50-300 cells/mm^3

$$\overbrace{(\text{Triple} - \text{Dual})}^{\text{ACTG 320}} + \overbrace{(\text{Dual} - \text{Mono})}^{\text{ACTG 175}}$$

$$\underbrace{\text{Dual}) + (\text{Dual}}_{\text{Bridge}}$$

[13] Breskin et al. (2021) *Stats in Med*
[14] Zivich et al. (2022) *arXiv*

A3: bridged study design

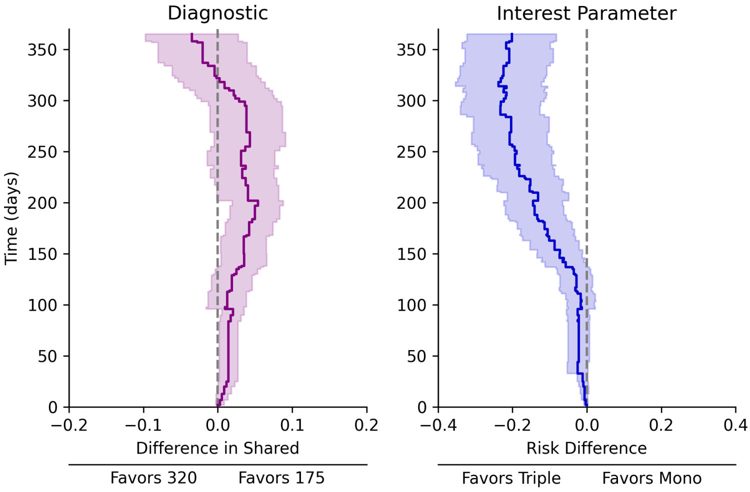
Estimating functions[15]

$$\psi(O_i;\theta) = \begin{bmatrix} \left(I(S_i = 320) - \text{expit}(W_i^T)\right) W_i \\ I(S_i = 175)\left(I(A_i = 1) - \gamma_{0,1}\right) \\ I(S_i = 175)\left(I(A_i = 2) - \gamma_{0,2}\right) \\ I(S_i = 320)\left(I(A_i = 2) - \gamma_{1,2}\right) \\ I(S_i = 320)\left(I(A_i = 3) - \gamma_{1,3}\right) \\ \psi_{AFT}(O_i;\lambda,\alpha) \\ \psi_{RD}(t,a;\mu_t,\beta,\gamma_{a,s},\lambda,\alpha) \end{bmatrix}$$

where $O_i = (S_i, T_i^*, \delta_i, A_i, W_i)$ and $\theta = (\beta, \gamma_{a,s}, \lambda, \alpha, \mu_t)$

[15] Here, I am using a Weibull AFT model

A3: bridged study design



Conclusion

M-estimation provide an adaptable way to develop fusion estimators

- Stack estimating functions together
- Sandwich variance estimator

Limitations of M-estimators

- Reliance on parametric models
- Estimating functions can't depend on i

Supplement

Sandwich variance estimator

$$V_n(O_i;\hat{\theta}) = B_n(O_i;\hat{\theta})^{-1} F_n(O_i;\hat{\theta}) \left(B_n(O_i;\hat{\theta})^{-1} \right)^T$$

where the bread is

$$B_n(O_i;\hat{\theta}) = \frac{1}{n} \sum_{i=1}^{n} -\psi'(O_i;\hat{\theta})$$

and the filling is

$$F_n(O_i;\hat{\theta}) = \frac{1}{n} \sum_{i=1}^{n} \psi(O_i;\hat{\theta}) \psi(O_i;\hat{\theta})^T$$