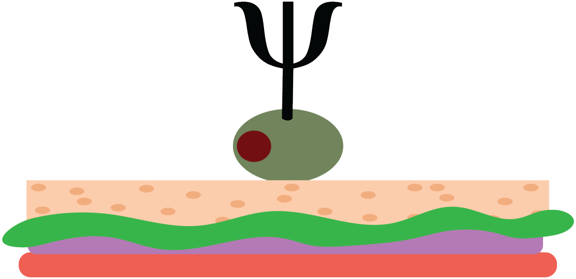
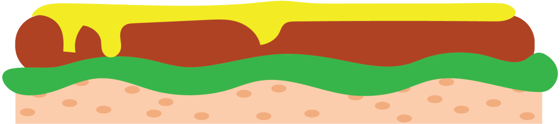


ABC's of M-estimation



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Overview

Section 1: introduction

Break (15min)

Section 2: applied examples

Break (15min)

Section 3: in context

Overview: Section 2 - Applied Examples

1. Logistic regression
2. Standardization
   - Outcome model based standardization
   - Inverse probability weighting
3. Transporting a risk
   - Outcome model based standardization
   - Inverse odds weighting

Each section will include time to work with code

As the goal is to illustrate implementation, we will not dwell on identification assumptions of these examples[1]

[1] Hernan & Robins Causal Inference: What If; Cole et al. *AJE* 2012

Overview: Section 2 - Applied Examples

1. Logistic regression
2. Standardization
   - Outcome model based standardization
   - Inverse probability weighting
3. Transporting a risk
   - Outcome model based standardization
   - Inverse odds weighting

These examples have been published in an IJE Education Corner[2]

[2] Ross et al. M-estimation for common epidemiological measures: introduction and applied examples *IJE*, 2024, 53(2):1-6.

Notation – Reminder

O_i: observed data for unit i

- $O_i = (W_i, X_i, Y_i)$
- $O_i = (S_i, W_i, X_i, S_i \times Y_i)$

$\text{expit}(a) = 1/(1 + \exp(-a))$

Notation – Reminder

Estimating function

$$\psi(O_i; \theta)$$

Estimating equation

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

Logistic regression

Example

Data from the Zambia Preterm Birth Prevention Study (ZAPPS)[3]
$O_i = (W_i, X_i, Y_i)$
W_i, elevated blood pressure
X_i, anemia
Y_i, preterm birth

We want to estimate the parameters of this model

$$\begin{aligned}\text{Pr}(Y_i = 1 | X_i, W_i) &= \text{expit}(\beta_0 + \beta_1 X_i + \beta_2 W_i) \\ &= \text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)\end{aligned}$$

where $\boldsymbol{Z}_i = (1, X_i, W_i)$ and $\boldsymbol{\beta} = (\beta_0, \beta_1, \beta_2)$

[3] Castillo et al. *Gates Open Research* 2019

ZAPPS data

$n = 826$ pregnant people

14.2% delivered preterm

14.3% diagnosed with early-pregnancy anemia

18.9% diagnosed with early-pregnancy elevated blood pressure

Estimating β by MLE

Let $\hat{\boldsymbol{\beta}}_{mle}$ be the estimate of $\boldsymbol{\beta}$ by MLE

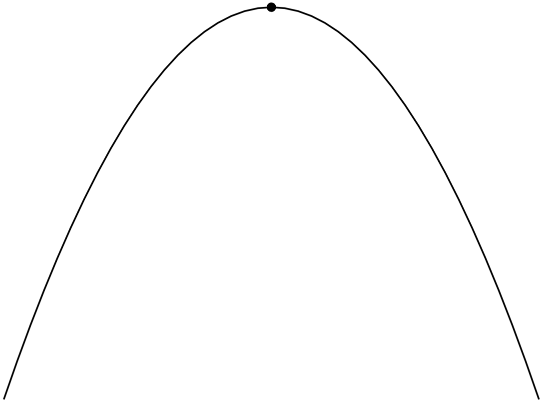
$\hat{\boldsymbol{\beta}}_{mle}$ are the values that maximize the log-likelihood

$$\sum_{i=1}^{n} \ln\Big(L(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{mle})\Big)$$

$$= \sum_{i=1}^{n} \Big\{ Y_i \ln\big(\text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T_{mle})\big) + (1 - Y_i) \ln\big(1 - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T_{mle})\big) \Big\}$$

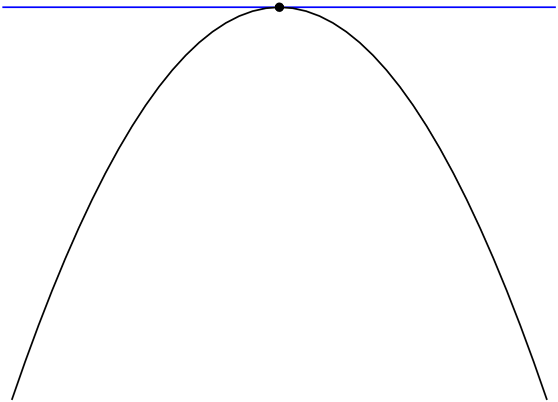
Estimating β by root-finding

Maximum of likelihood is where slope (derivative) is zero ("root")



Estimating β by root-finding

Maximum of likelihood is where slope (derivative) is zero ("root")



Estimating β by root-finding

Our log-likelihood is

$$\ln\big(L(\boldsymbol{O_i}, \boldsymbol{\beta})\big) = Y_i \ln\big(\text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)\big) + (1 - Y_i)\ln\big(1 - \text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)\big)$$

Functions for the slope (derivative[4])

$$\boldsymbol{\psi}(\boldsymbol{O_i}, \boldsymbol{\beta}) = \frac{\partial \ln\big(L(\boldsymbol{O_i}, \boldsymbol{\beta})\big)}{\partial \boldsymbol{\beta}} = \begin{bmatrix} \big(Y_i - \text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)\big)1 \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)\big)X_i \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)\big)W_i \end{bmatrix}$$

[4] first-order partial derivatives, called the "score" functions

Estimating β by root-finding

Let $\hat{\boldsymbol{\beta}}_{me}$ be the estimate of $\boldsymbol{\beta}$ by root finding (M-estimation)

Our estimating equation

$$\sum_{i=1}^{n} \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{me}) = \sum_{i=1}^{n} \begin{bmatrix} Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}_{me}^T) \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}_{me}^T)\big) X_i \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}_{me}^T)\big) W_i \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

Estimating $\hat{\beta}_{me}$: Code

To implement, we need to define the estimating functions

Under Defining estimating equation

- R

```
p <- plogis(beta[1] + beta[2]*dat$anemia + beta[3]*dat$bp)

ef_1 <- (dat$ptb - p)
ef_2 <- (dat$ptb - p)*dat$anemia
ef_3 <- (dat$ptb - p)*dat$bp
```

$\hat{\boldsymbol{\beta}}_{mle}$ and $\hat{\boldsymbol{\beta}}_{me}$ from R

	β_0	β_1	β_2
$\hat{\boldsymbol{\beta}}_{mle}$	-1.89450081814**3**	0.1187353484**2**8	0.3605113262**7**6
$\hat{\boldsymbol{\beta}}_{me}$	-1.89450081814**8**	0.1187353484**3**2	0.3605113262**8**3

Difference is result of algorithm/tolerance

Variance

Let $\boldsymbol{V}(\hat{\boldsymbol{\beta}})$ be the 3×3 covariance matrix of $\hat{\boldsymbol{\beta}}$

$$\boldsymbol{V}(\hat{\boldsymbol{\beta}}) = \begin{bmatrix} \text{var}(\hat{\beta}_0) & \text{cov}(\hat{\beta}_0, \hat{\beta}_1) & \text{cov}(\hat{\beta}_0, \hat{\beta}_2) \\ \text{cov}(\hat{\beta}_0, \hat{\beta}_1) & \text{var}(\hat{\beta}_1) & \text{cov}(\hat{\beta}_1, \hat{\beta}_2) \\ \text{cov}(\hat{\beta}_0, \hat{\beta}_2) & \text{cov}(\hat{\beta}_1, \hat{\beta}_2) & \text{var}(\hat{\beta}_2) \end{bmatrix}$$

The diagonal vector of $\boldsymbol{V}/n$ (i.e., $\text{diag}(\boldsymbol{V}/n)$) are the finite sample variances

For Wald-type confidence intervals, we use $\text{SE}(\hat{\boldsymbol{\beta}}) = \sqrt{\text{diag}(\boldsymbol{V}/n)}$

Estimating $\boldsymbol{V}(\hat{\boldsymbol{\beta}}_{mle})$ by MLE

$$\boldsymbol{V}(\hat{\boldsymbol{\beta}}_{mle}) = \boldsymbol{I}(\hat{\boldsymbol{\beta}}_{mle})^{-1}$$

where $\boldsymbol{I}(\hat{\boldsymbol{\beta}}_{mle})$ is the observed information matrix at $\hat{\boldsymbol{\beta}}_{mle}$

Estimating $\boldsymbol{V}(\hat{\boldsymbol{\beta}}_{mle})$

There are two ways to estimate $\boldsymbol{I}(\hat{\boldsymbol{\beta}}_{mle})$

1. Hessian-based estimator

$$\boldsymbol{I}(\hat{\boldsymbol{\beta}}_{mle}) = \frac{1}{n}\sum_{i=1}^{n}\left[-\boldsymbol{\psi}'(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{mle})\right]$$

where $\boldsymbol{\psi}' = \frac{\partial \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{mle})}{\partial \hat{\boldsymbol{\beta}}_{mle}} = \frac{\partial^2 \ln\left(L(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{mle})\right)}{\partial \hat{\boldsymbol{\beta}}^2_{mle}}$

Estimating $\boldsymbol{V}(\hat{\boldsymbol{\beta}}_{mle})$

There are two ways to estimate $\boldsymbol{I}(\hat{\boldsymbol{\beta}}_{mle})$

2. Residual-based estimator

$$\boldsymbol{I}(\hat{\boldsymbol{\beta}}_{mle}) = \frac{1}{n}\sum_{i=1}^{n}\left[\boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{mle})\boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{mle})^T\right]$$

Estimating $\boldsymbol{V}(\hat{\boldsymbol{\beta}}_{mle})$

There are two ways to estimate $\boldsymbol{I}(\hat{\boldsymbol{\beta}}_{mle})$

1. Hessian-based estimator

$$\boldsymbol{I}(\hat{\boldsymbol{\beta}}_{mle}) = \frac{1}{n} \sum_{i=1}^{n} \left[-\boldsymbol{\psi}'(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{mle}) \right]$$

2. Residual-based estimator

$$\boldsymbol{I}(\hat{\boldsymbol{\beta}}_{mle}) = \frac{1}{n} \sum_{i=1}^{n} \left[\boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{mle}) \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}}_{mle})^T \right]$$

Asymptotically equal when chosen parametric family is correct
Hessian is more efficient and default (`logistic`, `glm`, `GLM`)

Estimating $\boldsymbol{V}(\hat{\boldsymbol{\beta}}_{me})$ by sandwich variance estimator

$$\boldsymbol{V}(\hat{\boldsymbol{\beta}}_{me}) = \boldsymbol{B}(\hat{\boldsymbol{\beta}}_{me})^{-1}\boldsymbol{F}(\hat{\boldsymbol{\beta}}_{me})\left[\boldsymbol{B}(\hat{\boldsymbol{\beta}}_{me})^{-1}\right]^T$$

Recall

- $\boldsymbol{B}(\hat{\boldsymbol{\beta}}) = \frac{1}{n}\sum_i \left[-\boldsymbol{\psi}'(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}})\right]$
  This corresponds to the Hessian-based info matrix estimator
- $\boldsymbol{F}(\hat{\boldsymbol{\beta}}) = \frac{1}{n}\sum_i \left[\boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}})\boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\beta}})^T\right]$
  This corresponds to the residual-based info matrix estimator

Asymptotic equivalence

When chosen parametric family is correct

$$\begin{aligned}
\boldsymbol{V}(\hat{\boldsymbol{\beta}}) &= \boldsymbol{B}(\hat{\boldsymbol{\beta}})^{-1}\boldsymbol{F}(\hat{\boldsymbol{\beta}})\left[\boldsymbol{B}(\hat{\boldsymbol{\beta}})^{-1}\right]^T \\
&\sim \boldsymbol{I}(\hat{\boldsymbol{\beta}})^{-1}\boldsymbol{I}(\hat{\boldsymbol{\beta}})\left[\boldsymbol{I}(\hat{\boldsymbol{\beta}})^{-1}\right]^T \\
&= \boldsymbol{I}(\hat{\boldsymbol{\beta}})^{-1}
\end{aligned}$$

Estimating $V(\hat{\beta})$

1. Use the same code for the estimating equation
2. Baking the bread
   - Use software to estimate the Hessian
3. Cooking the filling
   - Use transpose and dot product functions
4. Assembling the sandwich
   - Use inverse function

Standard errors from R

	β_0	β_1	β_2
MLE, Hessian-based	0.01**4**96046	0.077**6**4837	0.056**6**0453
MLE, Residual-based	0.01**5**08328	0.077**6**1366	0.056**7**0628
Sandwich estimator	0.01**4**84043	0.077**7**2035	0.056**5**2969

Time to work with code

Standardization

Data and estimand

Using the same data as the prior example
$O_i = (Y_i, X_i, W_i)$
Y_i, preterm birth
X_i, anemia
W_i, elevated blood pressure

We want to estimate the marginal risk difference and risk ratio of anemia on preterm birth, standardized by elevated blood pressure.

$$E(E(Y|X=1,W)|W) - E(E(Y|X=0,W)|W)$$

$$E(E(Y|X=1,W)|W) / E(E(Y|X=0,W)|W)$$

We will illustrate two standardization approaches

- Outcome model based standardization (i.e., g-computation)
- Inverse probability weighting

Outcome model based standardization

1. Estimate outcome model (from prior example)

$$\Pr(Y_i = 1 | X_i, W_i) = \text{expit}(\beta_0 + \beta_1 X_i + \beta_2 W_i) = \text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)$$

Outcome model based standardization

1. Estimate outcome model (from prior example)

$$\text{Pr}(Y_i = 1 | X_i, W_i) = \text{expit}(\beta_0 + \beta_1 X_i + \beta_2 W_i) = \text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)$$

2. Use $\hat{\boldsymbol{\beta}}$ to predict outcome when $X_i = 1$. Take the mean.

$$\hat{\mu}_1 = \frac{1}{n} \sum_{i=1}^{n} \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 1 + \hat{\beta}_2 W_i)$$

Outcome model based standardization

1. Estimate outcome model (from prior example)

$$\Pr(Y_i = 1 | X_i, W_i) = \text{expit}(\beta_0 + \beta_1 X_i + \beta_2 W_i) = \text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)$$

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$$\hat{\mu}_1 = \frac{1}{n} \sum_{i=1}^{n} \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 1 + \hat{\beta}_2 W_i)$$

3. Use $\hat{\boldsymbol{\beta}}$ to predict outcome when $X_i = 0$. Take the mean.

$$\hat{\mu}_2 = \frac{1}{n} \sum_{i=1}^{n} \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 0 + \hat{\beta}_2 W_i)$$

Outcome model based standardization

1. Estimate outcome model (from prior example)

$$\Pr(Y_i = 1 | X_i, W_i) = \text{expit}(\beta_0 + \beta_1 X_i + \beta_2 W_i) = \text{expit}(\boldsymbol{Z}_i \boldsymbol{\beta}^T)$$

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3. Use $\hat{\boldsymbol{\beta}}$ to predict outcome when $X_i = 0$. Take the mean.

$$\hat{\mu}_2 = \frac{1}{n} \sum_{i=1}^{n} \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 0 + \hat{\beta}_2 W_i)$$

4. Calculate the risk difference $\hat{\delta}_1 = \hat{\mu}_1 - \hat{\mu}_2$ & log risk ratio $\hat{\delta}_2 = \ln(\hat{\mu}_1 / \hat{\mu}_2)$

Outcome model based standardization

Our stacked estimating equation

$$\sum_{i=1}^{n} \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T) \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\big) X_i \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\big) W_i \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 1 + \hat{\beta}_2 W_i) - \hat{\mu}_1 \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 0 + \hat{\beta}_2 W_i) - \hat{\mu}_2 \\ (\hat{\mu}_1 - \hat{\mu}_2) - \hat{\delta}_1 \\ \ln(\hat{\mu}_1 / \hat{\mu}_2) - \hat{\delta}_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

where $\boldsymbol{\theta} = (\boldsymbol{\beta}, \boldsymbol{\mu}, \boldsymbol{\delta})$

Outcome model based standardization

Our stacked estimating equation

$$\sum_{i=1}^{n} \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T) \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\big) X_i \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\big) W_i \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 1 + \hat{\beta}_2 W_i) - \hat{\mu}_1 \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 0 + \hat{\beta}_2 W_i) - \hat{\mu}_2 \\ (\hat{\mu}_1 - \hat{\mu}_2) - \hat{\delta}_1 \\ \ln(\hat{\mu}_1 / \hat{\mu}_2) - \hat{\delta}_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

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where $\boldsymbol{\theta} = (\boldsymbol{\beta}, \boldsymbol{\mu}, \boldsymbol{\delta})$

Outcome model based standardization

Our stacked estimating equation

$$\sum_{i=1}^{n} \psi(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T) \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\big) X_i \\ \big(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\big) W_i \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 1 + \hat{\beta}_2 W_i) - \hat{\mu}_1 \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 0 + \hat{\beta}_2 W_i) - \hat{\mu}_2 \\ (\hat{\mu}_1 - \hat{\mu}_2) - \hat{\delta}_1 \\ \ln(\hat{\mu}_1 / \hat{\mu}_2) - \hat{\delta}_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

where $\boldsymbol{\theta} = (\boldsymbol{\beta}, \boldsymbol{\mu}, \boldsymbol{\delta})$

Outcome model based standardization

Our stacked estimating equation

$$\sum_{i=1}^{n} \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T) \\ \left(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\right) X_i \\ \left(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\right) W_i \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 1 + \hat{\beta}_2 W_i) - \hat{\mu}_1 \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 0 + \hat{\beta}_2 W_i) - \hat{\mu}_2 \\ (\hat{\mu}_1 - \hat{\mu}_2) - \hat{\delta}_1 \\ \ln(\hat{\mu}_1 / \hat{\mu}_2) - \hat{\delta}_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

where $\boldsymbol{\theta} = (\boldsymbol{\beta}, \boldsymbol{\mu}, \boldsymbol{\delta})$

Note: we estimate the log risk ratio because 1) it does not have bounds which is better for root-finding and 2) we want to estimate the variance of the log risk ratio for constructing confidence intervals

Outcome model based standardization

Our stacked estimating equation

$$\sum_{i=1}^{n} \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T) \\ \left(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\right) X_i \\ \left(Y_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\right) W_i \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 1 + \hat{\beta}_2 W_i) - \hat{\mu}_1 \\ \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 \times 0 + \hat{\beta}_2 W_i) - \hat{\mu}_2 \\ (\hat{\mu}_1 - \hat{\mu}_2) - \hat{\delta}_1 \\ \ln(\hat{\mu}_1 / \hat{\mu}_2) - \hat{\delta}_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

where $\boldsymbol{\theta} = (\boldsymbol{\beta}, \boldsymbol{\mu}, \boldsymbol{\delta})$

Estimating functions: Code

- R

```
p <- plogis(beta[1] + beta[2]*dat$anemia + beta[3]*dat$bp)
ef_1 <- (dat$ptb - p)
ef_2 <- (dat$ptb - p)*dat$anemia
ef_3 <- (dat$ptb - p)*dat$bp

ef_r1 <- plogis(beta[1] + beta[2]*1 + beta[3]*dat$bp) - mu[1]
ef_r0 <- plogis(beta[1] + beta[2]*0 + beta[3]*dat$bp) - mu[2]

ef_rd <- (mu[1] - mu[2]) - delta[1]
ef_lnrr <- log(mu[1]/mu[2]) - delta[2]
```

Inverse probability weighting

1. Estimate propensity score model

$$\Pr(X_i = 1|W_i) = \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)$$

Inverse probability weighting

1. Estimate propensity score model

$$\text{Pr}(X_i = 1|W_i) = \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)$$

2. Among those with $X_i = 1$, take a mean of the outcome, weighted by the inverse probability of $X_i = 1$,

$$\hat{\mu}_1 = \frac{1}{n} \sum_{i=1}^{n} \left\{ \frac{X_i Y_i}{\text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} \right\}$$

Note: This is the Horvitz-Thompson estimator

Inverse probability weighting

1. Estimate propensity score model

$$\text{Pr}(X_i = 1 | W_i) = \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)$$

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$$\hat{\mu}_1 = \frac{1}{n} \sum_{i=1}^{n} \left\{ \frac{X_i Y_i}{\text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} \right\}$$

3. Among those with $X_i = 0$, take a mean of the outcome, weighted by the inverse probability of $X_i = 0$,

$$\hat{\mu}_2 = \frac{1}{n} \sum_{i=1}^{n} \left\{ \frac{(1 - X_i) Y_i}{1 - \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} \right\}$$

Inverse probability weighting

1. Estimate propensity score model

$$\Pr(X_i = 1|W_i) = \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)$$

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4. Calculate the risk difference $\hat{\delta}_1 = \hat{\mu}_1 - \hat{\mu}_2$ & log risk ratio $\hat{\delta}_2 = \ln(\hat{\mu}_1 / \hat{\mu}_2)$

Inverse probability weighting

Our stacked estimating equation

$$\sum_{i=1}^{n} \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} X_i - \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i) \\ \left(X_i - \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)\right) W_i \\ \frac{X_i Y_i}{\text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} - \hat{\mu}_1 \\ \frac{(1-X_i) Y_i}{1-\text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} - \hat{\mu}_2 \\ (\hat{\mu}_1 - \hat{\mu}_2) - \hat{\delta}_1 \\ \ln(\hat{\mu}_1 / \hat{\mu}_2) - \hat{\delta}_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

where $\boldsymbol{\theta} = (\boldsymbol{\alpha}, \boldsymbol{\mu}, \boldsymbol{\delta})$

Inverse probability weighting

Our stacked estimating equation

$$\sum_{i=1}^{n} \psi(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} X_i - \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i) \\ (X_i - \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i))\, W_i \\ \frac{X_i Y_i}{\text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} - \hat{\mu}_1 \\ \frac{(1-X_i) Y_i}{1-\text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} - \hat{\mu}_2 \\ (\hat{\mu}_1 - \hat{\mu}_2) - \hat{\delta}_1 \\ \ln(\hat{\mu}_1 / \hat{\mu}_2) - \hat{\delta}_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

where $\boldsymbol{\theta} = (\boldsymbol{\alpha}, \boldsymbol{\mu}, \boldsymbol{\delta})$

Inverse probability weighting

Our stacked estimating equation

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where $\boldsymbol{\theta} = (\boldsymbol{\alpha}, \boldsymbol{\mu}, \boldsymbol{\delta})$

Estimating functions: Code

- R

```
pscore <- plogis(alpha[1] + alpha[2]*bp)
ef_1 <- (anemia - pscore)
ef_2 <- (anemia - pscore)*bp

wt <- anemia/pscore + (1-anemia)/(1-pscore)
ef_r1 <- anemia*wt*ptb - mu[1]
ef_r0 <- (1 - anemia)*wt*ptb - mu[2]

ef_rd <- (mu[1] - mu[2]) - delta[1]
ef_lnrr <- log(mu[1]/mu[2]) - delta[2]
```

Aside: IPW GEE trick for conservative SE/intervals

The propensity score parameters are excluded from the stack of estimating functions, i.e. treats $\boldsymbol{\alpha}$ parameters as known

$$
\sum_{i=1}^{n} \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} \cancel{X_i - \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} \\ \cancel{\left(X_i - \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)\right) W_i} \\ \frac{X_i Y_i}{\text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} - \hat{\mu}_1 \\ \frac{(1 - X_i) Y_i}{1 - \text{expit}(\hat{\alpha}_0 + \hat{\alpha}_1 W_i)} - \hat{\mu}_2 \\ (\hat{\mu}_1 - \hat{\mu}_2) - \hat{\delta}_1 \\ \ln(\hat{\mu}_1 / \hat{\mu}_2) - \hat{\delta}_2 \end{bmatrix}
$$

Then use sandwich variance estimator[5]

[5] Robins et al. Marginal Structural Models and Causal Inference in Epidemiology *Epidemiology* 2000.

Time to work with code

Transporting a risk

Data and estimand

Using the same data as the prior examples (ZAPPS) PLUS external target sample (simulated)

$O_i = (S_i, X_i, W_i, S_i \times Y_i)$
S_i, sample indicator: $S_i = 1$ for ZAPPS, $S_i = 0$ for external target
X_i, anemia
W_i, elevated blood pressure
Y_i, preterm birth, which is only observed when $S_i = 1$

We want to estimate the risk of preterm birth in the external target sample, i.e., $\Pr(Y = 1|S = 0)$.

Data and estimand

We will illustrate two (standardization) approaches

- Outcome model based standardization
- Inverse odds weighting

For simplicity, we assume early-pregnancy anemia and blood pressure are sufficient to identify this transported risk

Outcome model based standardization

1. Estimate outcome model **in the ZAPPS data** (as in prior examples)

$$\begin{aligned}\Pr(Y_i = 1 | X_i, W_i, S_i = 1) &= \text{expit}(\hat{\beta}_0 + \hat{\beta}_1 X_i + \hat{\beta}_2 W_i) \\ &= \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)\end{aligned}$$

2. Use $\hat{\boldsymbol{\beta}}$ to predict outcome **in the external target**. Take the mean.

$$\hat{\mu} = \frac{1}{\sum_{i=1}^{n}(1 - S_i)} \sum_{i=1}^{n} (1 - S_i) \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\beta}}^T)$$

Outcome model based standardization

Our estimating equation

$$\sum_{i=1}^{n} \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} S_i\big(Y_i - \text{expit}(\boldsymbol{Z}_i\hat{\boldsymbol{\beta}}^T)\big) \\ S_i\big(Y_i - \text{expit}(\boldsymbol{Z}_i\hat{\boldsymbol{\beta}}^T)\big)X_i \\ S_i\big(Y_i - \text{expit}(\boldsymbol{Z}_i\hat{\boldsymbol{\beta}}^T)\big)W_i \\ (1 - S_i)\big(\text{expit}(\boldsymbol{Z}_i\hat{\boldsymbol{\beta}}^T) - \hat{\mu}\big) \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

where $\boldsymbol{\theta} = (\boldsymbol{\beta}, \mu)$

Estimating functions: Code

- R

```
p <- plogis(beta[1] + beta[2]*anemia + beta[3]*bp)

ef_1 <- S*(ptb - p)
ef_2 <- S*(ptb - p)*anemia
ef_3 <- S*(ptb - p)*bp

ef_r <- (1-S)*(p - mu[1])
```

Inverse odds weighting

1. Estimate selection model

$$\begin{aligned}\text{Pr}(S_i = 1 | X_i, W_i) &= \text{expit}(\hat{\gamma}_0 + \hat{\gamma}_1 X_i + \hat{\gamma}_2 W_i) \\ &= \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\gamma}}^T)\end{aligned}$$

2. Among those with $S_i = 1$, take the weighted mean of the outcome, weighted by the inverse odds of $S_i = 1$

$$\hat{\mu} = \frac{1}{\sum_{i=1}^{n} S_i \pi_S(Z; \hat{\gamma})} \sum_{i=1}^{n} S_i Y_i \pi_S(Z; \hat{\gamma})$$

where $\pi_S(Z; \hat{\gamma}) = \frac{1 - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\gamma}}^T)}{\text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\gamma}}^T)}$

Note: This is a Hajek estimator. We used a Horvitz-Thompson estimator in the previous section

Inverse odds weighting

Our stacked estimating equation

$$\sum_{i=1}^{n} \boldsymbol{\psi}(\boldsymbol{O_i}, \hat{\boldsymbol{\theta}}) = \sum_{i=1}^{n} \begin{bmatrix} S_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\gamma}}^T) \\ \big(S_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\gamma}}^T\big) X_i \\ \big(S_i - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\gamma}}^T\big) W_i \\ S_i \pi_S(Z; \hat{\gamma})(Y_i - \mu) \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

where $\boldsymbol{\theta} = (\boldsymbol{\gamma}, \mu)$ and $\pi_S(Z; \hat{\gamma}) = \frac{1 - \text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\gamma}}^T)}{\text{expit}(\boldsymbol{Z}_i \hat{\boldsymbol{\gamma}}^T)}$

Estimating functions: Code

- R

```
p <- plogis(gamma[1] + gamma[2]*anemia + gamma[3]*bp)
ef_1 <- (S - p)
ef_2 <- (S - p)*anemia
ef_3 <- (S - p)*bp

oddswt <- (1-p)/p
ef_r <- S*oddswt*(ptb - mu[1])
```

Time to work with code

Overview

Section 1: introduction

Break (15min)

Section 2: applied examples

Break (15min)

Section 3: in context