Marginal structural mean model

- **A marginal structural mean model** is a formula for the dependence of $E(Y_a|M)$ on a and M, e.g.

$$E(Y_a|age) = \beta_0 + \beta_1 a + \beta_2 age + \beta_3 age * a$$

(here M = age).

- Model implies that ATE for a given age is

$$E(Y_1|age) - E(Y_0|age) = \beta_1 + \beta_3 age$$

IPW estimation of β when L has many components: rational

- Weighting each person by

  w = 1/P(A|L)

- creates a pseudo study in which everybody receives A=1 and everybody receives A=0. So, in the pseudo study there is exchangeability and

$$E(Y_a|age) = E(Y|A = a, age)$$

- So, under the MSM model, in the pseudo-study

$$E(Y|A, age) = \beta_0 + \beta_1 A + \beta_2 age + \beta_3 age * A$$

- The last equation is a standard linear regression model.
  - The method of least squares is known to give unbiased estimators of the linear regression parameters.

- So we should estimate β by **weighted** least squares with weights w.

- Since we don't know P(A|L) and we can't estimate it by stratification on L due to L having many components, we must first **estimate P(A|L) under a parametric model**

IPW estimation of β when L has many components: algorithm

- ***STEP 1. Estimate the propensity score under parametric models for P(A|L), e.g.***

$$log\frac{P(A=1|age,hr,\ creat,\ potas)}{P(A=0|age,hr,\ creat,\ potas)} = \alpha 0 + \alpha 1 age + \alpha 2 hr + \alpha 3 creat + \alpha 4 potas$$

  - ***For each treated person compute w=1/fitted value***
  - ***For each untreated person compute w=1/(1-fitted value)***

- ***STEP 2. Run weighted least squares with outcome Y and covariates A and L (according to your MSM model) and weights w.***

- The estimators of the model parameters are your IPW estimators of the parameters of the marginal structural model

Stabilized: IPW estimation of β when L has many components: algorithm

- ***STEP 1. Estimate the propensity score under parametric models for P(A|L), e.g.***

$$\log\frac{P(A=1|age,hr,\ creat,\ potas)}{P(A=0|age,hr,\ creat,\ potas)}=\alpha 0+\ \alpha 1 age+\alpha 2 hr+\alpha 3 creat+\alpha 4 potas$$

- ***Step 2. Estimate the propensity score under parametric models for P(A|M), e.g.***

$$\log\frac{P(A=1|age)}{P(A=0|age)}=\delta 0+\ \delta 1 age$$

- ***Step 3.***
  - ***For each treated person compute***

$$sw=\frac{fitted\ value\ of\ P(A=1|M)}{fitted\ value\ of\ P(A=1|L)}$$

  - ***For each untreated person compute***

$$sw=\frac{fitted\ value\ of\ P(A=0|M)}{fitted\ value\ of\ P(A=0|L)}$$

- ***STEP 4. Run weighted least squares with outcome Y and covariates A and M (according to your MSM model) and weights sw.***
- The estimators of the model parameters are your ***stabilized*** IPW

Validity of IPTW with stabilized weights

- If there is
  1. Unconditional exchangeability, or
  2. Conditional exchangeability given M,
- It holds that

$$E(Y_a \mid M) = E(Y \mid A=a, M)$$

So fitting standard regression models is ok. under (1) or (2)

- Weighting by 1/w = 1/f(A|L) creates a pseudo-population in which (1) holds. ***So plain IPTW ok***
- Weighting by 1/sw = f(A|M)/f(A|L) creates a pseudo-population in which (2) holds. ***So stabilized IPTW ok***

Why stabilized IPTW should reduce variability?

- Variability of plain IPW estimators caused by occasional presence of small weights relative to the rest
- Stabilized IPW makes the distribution of the weights less spread. Idea:

- John has w large. This means that John's estimated P(A=1|L), say $f_1(L)$, is small
- Then it is likely that his estimated p(A=1|M), say $f_2(M)$, is also small
- Since $f_2(M)/f_1(L) \cong$ small/small $\cong$ not so large, then ***John's sw is smaller than John's w***

- Peter has w close to 1. This means that Peter's estimated P(A=1|L), say $f_1(L)$, is close to 1
- Then it is likely that his estimated p(A=1|M), say $f_2(M)$ is also close to 1
- Since $f_2(LM)/f_1(L) \cong 1/1 \cong 1$, then ***John's sw is roughly the same as his w***

Peter and John's w's very different but their sw's are not so different

Inverse weighted probability (IPW) Stabilized- Linear

Use t_ipw.ado

```
t_ipw,outcome(string) treatvar(string) pvars(varlist)
[ovars(varlist)] [pvarstab(varlist)] [stabilized] [binary]
[cvars(varlist) censored] [bootstrap]
```

- `t_ipw, outcome(cardbill) pvars(stent  acutemi ejecfrac  ves1proc p_inter*) treatvar( abcix) /// ovars(ejecfrac ) bootstrap rep(200)`
- `t_ipw, outcome(cardbill) pvars(stent  acutemi ejecfrac  ves1proc p_inter*)  /// treatvar( abcix) ovars(ejecfrac ) pvarstab(ejecfrac )  stabilized  bootstrap rep(200)`

Without Stabilization

beta1*(abcix)*	Boots. sdt Err.	[95% Conf.	Interval(N)]	z
700.199	1025.885	-1322.802	2723.200	0.683

beta2*(ejecfrac)*	Boots. sdt Err.	[95% Conf.	Interval(N)	z
-175.455	52.780	-279.534	-71.375	-3.324

Stabilized

beta1*(abcix)*	Boots. sdt Err.	[95% Conf.	Interval(N)	z
861.719	924.710	-961.769	2685.207	0.932

beta2*(ejecfrac)*	Boots. sdt Err.	[95% Conf.	Interval(N)]	z
-133.303	40.388	-212.946	-53.661	-3.30

MSM model $E(Y_{abcix} \mid ejecfrac) = \beta_0 + \beta_1\ abcix + \beta_2\ ejecfrac$

How do you interpret the parameters β_1 and β_2 ? What assumptions are needed? Do the parameters have the same interpretation in the two analysis?

Regression models for evaluating effect modification when L = M

- If

$$L=M$$

- M = set of effect modifiers
- L = set of variables needed to control confounding bias
- Then, you do not need to weight because already conditionally on M, the treated and untreated are exchangeable.