Adjusting for selection bias in case control studies using Bayesian post-stratification

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Outline

- Problem of selection bias
- EMF and childhood Leukaemia data
- Simple example of SB
- Bias breaking model
- Potential sources of data
- Post-stratification method
- Adjustments
- Results
- Discussion

Problem of selection bias

Basic problem

- Selection bias comes about when there is differential selection of cases and controls
- and a variable that is associated to the exposure under investigation is implicated in the selection process
- Case control studies are particularly prone to this problem
- This is because in order to make valid comparisons the populations of cases and controls must come from the same target population
- It is a problem of internal validity
- We tackle the problem using **DAGs, Conditional independence and extra data**

EMF and childhood Leukaemia

Data

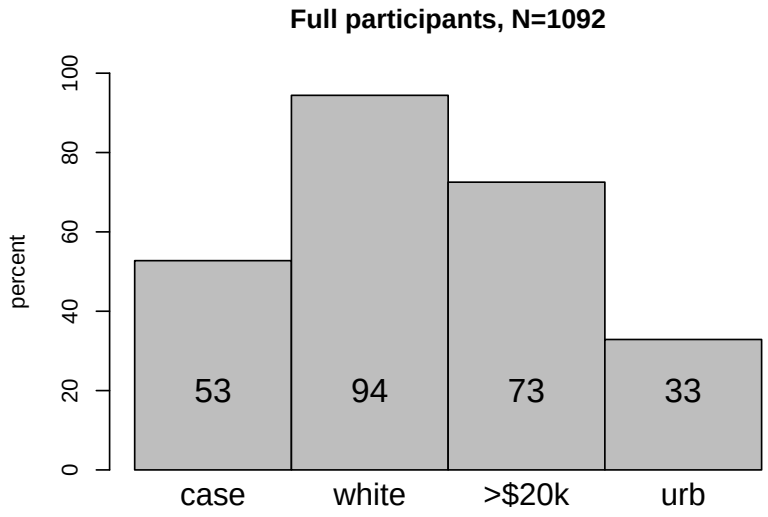
- Case control study to investigate association of Electro-magnetic field exposure (via power lines) and childhood acute lymphoblasitc Leukaemia (ALL) in North Eastern US
- Eligible cases were diagnosed between 1987-1994 and registered at Childhood Cancer Registries
- Controls were contacted via random digit dialling
- No significant effect was found in the study

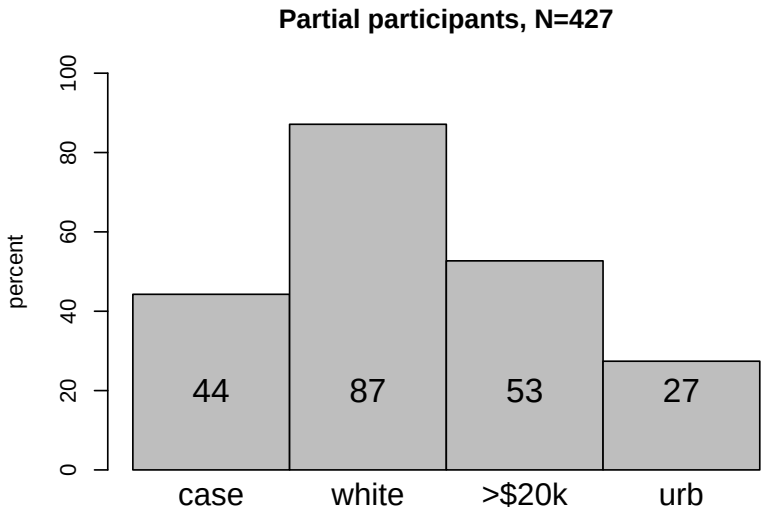
> The odds ratio for ALL was 1.24 (95 percent confidence interval, 0.86 to 1.79) at exposures of 0.200 μT or greater as compared with less than 0.065 μT. (1)

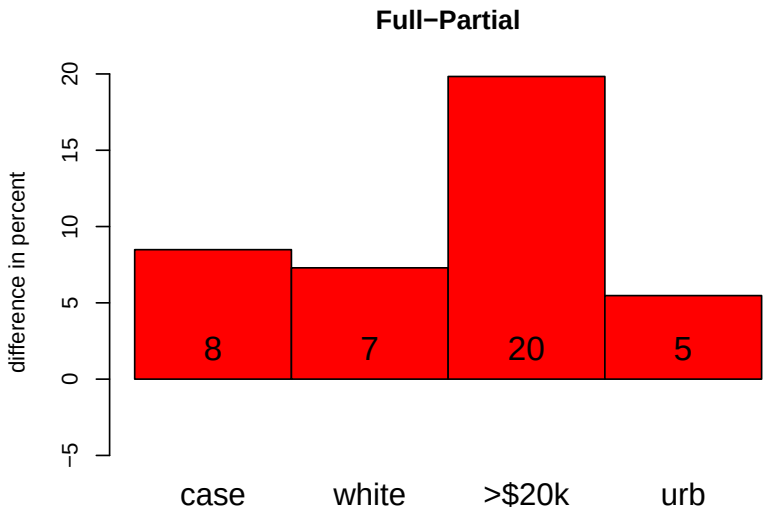
Selection bias?

- Follow-up paper (2) raised issues about potential selection bias
- Partial participants - those who agreed to participate and gave demographic details BUT did not allow indoor measurements of exposure
- were systematically different w.r.t full participants (i.e. those who allowed indoor exposure measurement)
- In particular, they had different proportions of cases, white race, higher income (over $20k) and more urban dwellers
- As expected, all SES indicators

Selection bias?



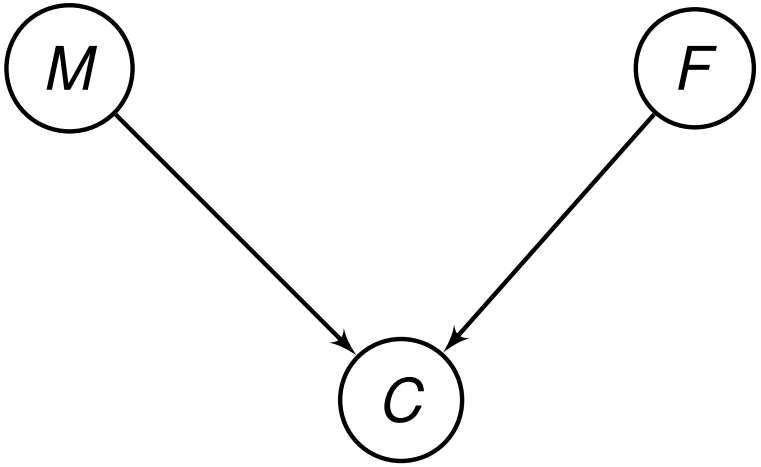




Simple Example - Inheritance

- Male and female are independent $M \perp\!\!\!\perp F$

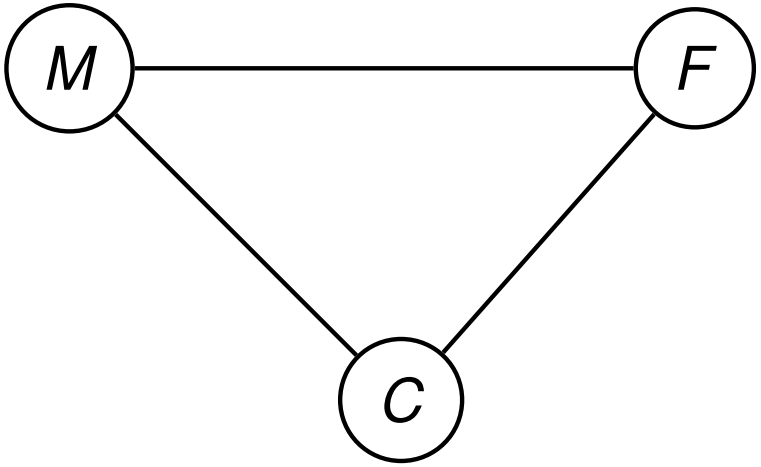
Simple Example - Inheritance



- Male and female are independent $M \perp\!\!\!\perp F$
- Then they meet and have a child

.

Simple Example - Inheritance

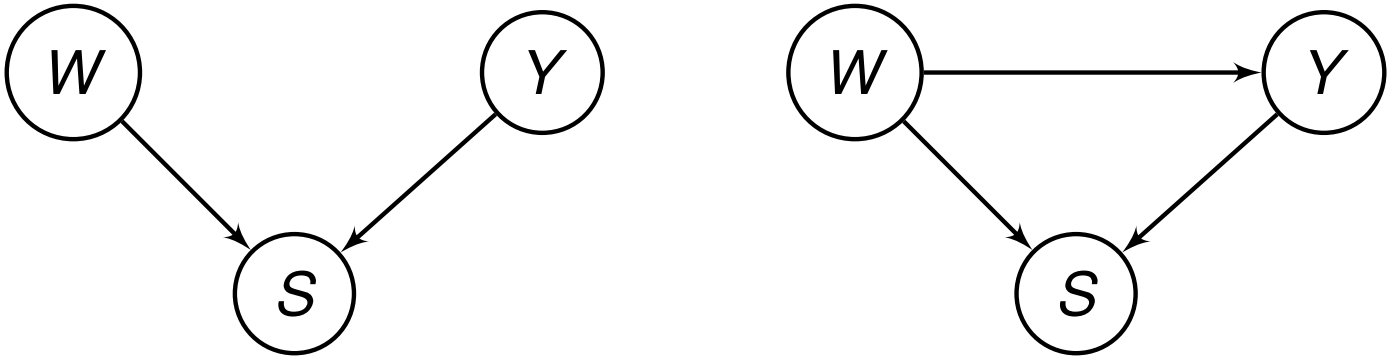


- Male and female are independent $M \perp\!\!\!\perp F$
- Then they meet and have a child
- Now they are dependent through child $M \not\perp\!\!\!\perp F | C$

Selection bias DAG

Basic premise

Selection bias comes about by conditioning on a common child where we don't know distribution of child given parents



- Y is the outcome of interest, W the exposure, S the selection indicator.
- Left: conditioning induces relationship
- Right: conditioning distorts relationship
- Both share <u>v-structure</u>

Problem - we don't know $p(S|Y)$

Odds ratio

True Odds ratio

$$\begin{aligned}\psi &= \frac{p(Y=1|W=1)p(Y=0|W=0)}{p(Y=0|W=1)p(Y=1|W=0)} \\ &= \frac{p(Y=1,W=1)p(Y=0,W=0)}{p(Y=0,W=1)p(Y=1,W=0)} \end{aligned} \tag{1}$$

Observed Odds ratio

$$\psi^o = \frac{p(Y=1,W=1|S=1)p(Y=0,W=0|S=1)}{p(Y=0,W=1|S=1)p(Y=1,W=0|S=1)} \tag{2}$$

Bias Breaking model

- The problem can be addressed if we can find a bias breaking variable B
- s.t. we can **separate** exposure W from selection S

A1 $$W \perp\!\!\!\perp S | (Y, B) \tag{3}$$

- This means we can separate the **exposure-disease process** of interest from the **niusance of the selection process**

A2 Case and control selection are independent

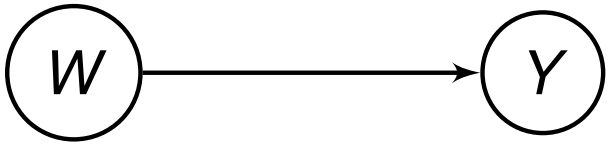
This is usually plausible as case and control recruitment processes are essentially different

An assumption for simplicity:

S1 Stratify B if it is not discrete

Idea of Separation

The conditional independence **A1** $W \perp\!\!\!\perp S | (Y, B)$ allows us to



1. separate the exposure disease mechanism of inferential interest

Idea of Separation

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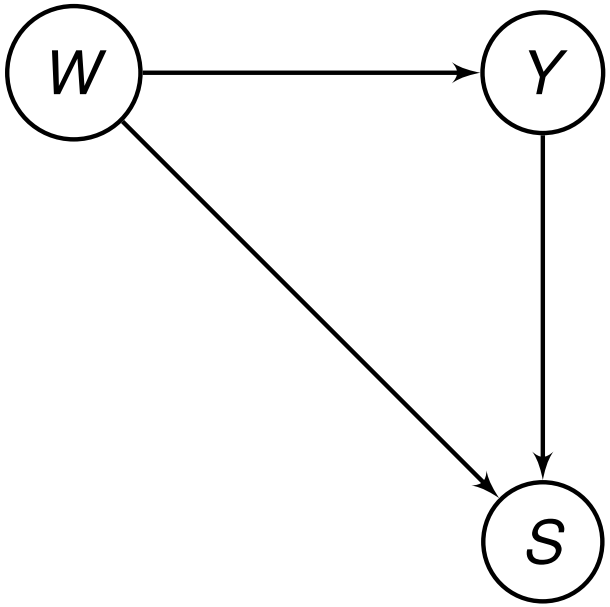

1. separate the exposure disease mechanism of inferential interest
2. from the niusance selection bias mechanism

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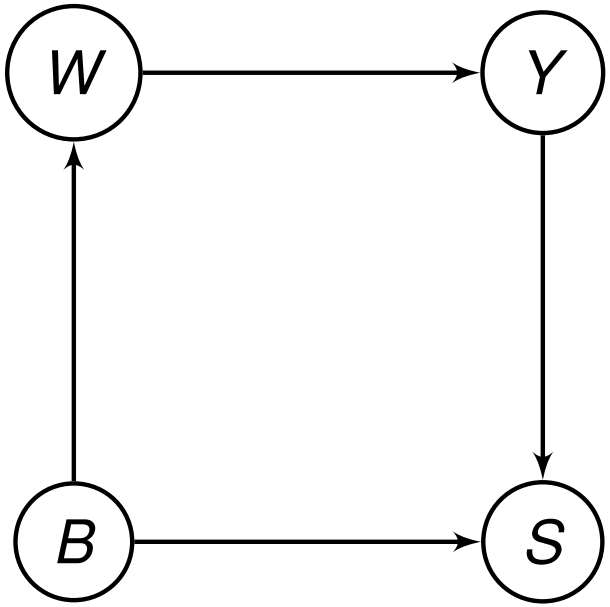

1. separate the exposure disease mechanism of inferential interest
2. from the niusance selection bias mechanism
3. by using B to separate these mechanisms

Bias Breaking model

Now for example for controls we can estimate $p(W = 1|Y = 0)$ as

$$p(W|Y = 0, S = 1, B) = p(W|Y = 0, B)$$
$$\sum_B p(W|Y = 0, B)p(B|Y = 0) = p(W|Y = 0)$$

- Focus is on finding estimates of $p(B|Y)$ as $p(W|Y, B)$ is estimated by stratum specific proportion of exposed cases/controls
- similar argument can be applied to case selection bias

Bias Breakers

Variables

- race - *RAC* (white or other)
- urban status - *URB* (urban or suburban vs other)
- income - *INC* (family income of above $20k or lower)
- So $B = \{RAC, URB, INC\}$

- We assumed that B are potential bias breakers as different distros of B between full and partial participants
- All variables are dichotomized for simplicity
- How to estimate $p(B|Y)$ w/out bias?
- From data "outside" full participant study data

Potential sources of data

Internal

- Pool full and partial participant data from study
- 1519 total, 1092 full participants and 427 partial participants (exclude 13 that have no measurements for one of the 3 BBs)
- Assume this represents target population
- Estimate conditional distribution $p(B|Y = y)$ as we know case/control status
- Estimate marginal distribution $p(B)$ if $p(B|Y = y) \approx p(B)$
- This is often plausible especially for controls

Potential sources of data

External

- Current Population Survey (CPS)
- The CPS is a monthly survey of about 50,000 households conducted by the Bureau of the Census for the Bureau of Labor Statistics
- Download from US census website `http://www.census.gov/cps/`
- Can access geographic, demographic, health etc. data
- We used the *Basic CPS* from January 1995 for the 9 states in the study as this coincided roughly with the study period
- Variables were coded in the same way/similar as the variables in the study
- From CPS can only estimate $p(B)$ marginal

Recap

- We've assumed that $W \perp\!\!\!\perp S | (Y, B)$
- We've identified a potential $B = \{RAC, INC, URB\}$
- We've got sources of data to estimate $p(B|Y)$ or $p(B)$ w/out selection bias
- Now we need to estimate $p(W|Y, B)$
- combine it with $p(B)$ to estimate $p(W|Y)$
- Use this to estimate marginal OR (as opposed to conditional OR we get from the logistic regression coefficient)

Poststratification Method

Idea

- Take a simple Bayesian logistic regression
- Estimate the parameters using WinBUGS and the full participant study data (i.e. those who have exposure data)
- Then for every possible (not neccesarily observed) combination of the variables (in this case Y and B) estimate the expected logit($p(W|Y,B)$)
- Inverse logit that quantity to get an estimate of $p(W|Y,B)$ for each of these combinations
- From pooled/external data get an empirical distribution for $p(B|Y)$ or $p(B)$
- Multiply this by appropriate $p(W|Y,B)$ and sum over to get an estimate of $p(W|Y)$ which you use to estimate OR
- Follows method in (3)

Bayesian logistic regression model

- To explain We focus on the simple model here
- Variables: w exposure, y case/control status, b single dichotomous variable

Simple

$$\text{logit}(p(w|y,b)) = \alpha + \beta y + \gamma b + \epsilon \tag{4}$$

Why Bayesian?

- We have done this using a simple non-Bayesian logisitc regression (4)
- The advantage with the Bayesian approach is that we do not have to worry about estimating the variance of the estimates in closed form
- As we get a draw of 1000 from the posterior distribution of the ORs the variance "comes out in the wash".

Poststratification method details

Simple Bayesian logistic regression model with only one *B participant data*

W	Y	B
1	0	1
1	1	1
1	1	1
1	1	0
.	.	.
.	.	.
.	.	.
NA	0	0
NA	0	1
.	.	.
.	.	.

Poststratification method details

Simple Bayesian logistic regression model with only one *B*

participant data

W	Y	B
1	0	1
1	1	1
1	1	1
1	1	0
.	.	.
.	.	.
.	.	.
NA	0	0
NA	0	1
.	.	.
.	.	.

pooled internal data

Y	B
0	1
1	1
1	1
1	0
.	.
.	.
.	.
0	0
0	1
.	.
.	.

Poststratification method details

Simple Bayesian logistic regression model with only one *B*

participant data

W	Y	B
1	0	1
1	1	1
1	1	1
1	1	0
.	.	.
.	.	.
.	.	.
NA	0	0
NA	0	1
.	.	.
.	.	.

pooled internal data

Y	B
0	1
1	1
1	1
1	0
.	.
.	.
.	.
0	0
0	1
.	.
.	.

external data

B
0
0
1
1
1
0
1
1
.
.
.

Poststratification method details

- From the full participant data we get estimates $\hat{\alpha}, \hat{\beta}, \hat{\gamma}$
- LW is the vector of possible values of $\text{logit}(p(W = 1 | Y = y, B = b))$, $y, b \in \{0, 1\}$

$$LW = (\hat{\alpha}\ \hat{\beta}\ \hat{\gamma}) \times \begin{pmatrix} 1 & 1 & 1 & 1 \\ 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 1 \end{pmatrix} \tag{5}$$

- The rows of the matrix are 1 for the intercept , Y and B
- There are only 4 possible combinations for 2 binary variables
- So LW is a vector of 4 values

Poststratification method details

- From the full participant data we get estimates $\hat{\alpha}, \hat{\beta}, \hat{\gamma}$
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$$LW = (\hat{\alpha}\ \hat{\beta}\ \hat{\gamma}) \times \begin{pmatrix} 1 & 1 & 1 & 1 \\ 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 1 \end{pmatrix} \tag{6}$$

- The rows of the matrix are 1 for the intercept , Y and B
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Poststratification method details

- From the full participant data we get estimates $\hat{\alpha}, \hat{\beta}, \hat{\gamma}$
- LW is the vector of possible values of $\text{logit}(p(W = 1 | Y = y, B = b))$, $y, b \in \{0, 1\}$

$$LW = (\hat{\alpha}\ \hat{\beta}\ \hat{\gamma}) \times \begin{pmatrix} 1 & 1 & 1 & 1 \\ 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 1 \end{pmatrix} \tag{7}$$

- The rows of the matrix are 1 for the intercept, Y and B
- There are only 4 possible combinations for 2 binary variables
- So LW is a vector of 4 values

Poststratification method details

- From the pooled internal data we get the vectors
- $ICA = (\hat{p}_{01}, \hat{p}_{11})$
- $ICN = (\hat{p}_{00}, \hat{p}_{10})$
- where $\hat{p}_{by} = \hat{p}(B = b | Y = y)$ the internal conditional empirical distribution estimates
- From the external data we get the vector
- $EM = (\hat{p}_0, \hat{p}_1)$
- where $\hat{p}_b = \hat{p}(B = b)$ the external marginal empirical distribution estimate

$$\hat{p}(W = 1 | Y = 1)_{ICA} = LW(2,4) \times ICA \quad (8)$$
$$\hat{p}(W = 1 | Y = 0)_{ICN} = LW(1,3) \times ICN \quad (9)$$
$$\hat{p}(W = 1 | Y = 1)_{EM} = LW(2,4) \times EM \quad (10)$$
$$\hat{p}(W = 1 | Y = 0)_{EM} = LW(1,3) \times EM \quad (11)$$

Poststratification method details

- Finally, we combine (6) and (7)

$$OR_{IC} = \frac{\hat{p}(W=1|Y=1)_{ICA} \times [1-\hat{p}(W=1|Y=0)_{ICN}]}{\hat{p}(W=1|Y=0)_{ICN} \times [1-\hat{p}(W=1|Y=1)_{ICA}]} \quad (12)$$

- And we combine (8) and (9)

$$OR_{EM} = \frac{\hat{p}(W=1|Y=1)_{EM} \times [1-\hat{p}(W=1|Y=0)_{EM}]}{\hat{p}(W=1|Y=0)_{EM} \times [1-\hat{p}(W=1|Y=1)_{EM}]} \quad (13)$$

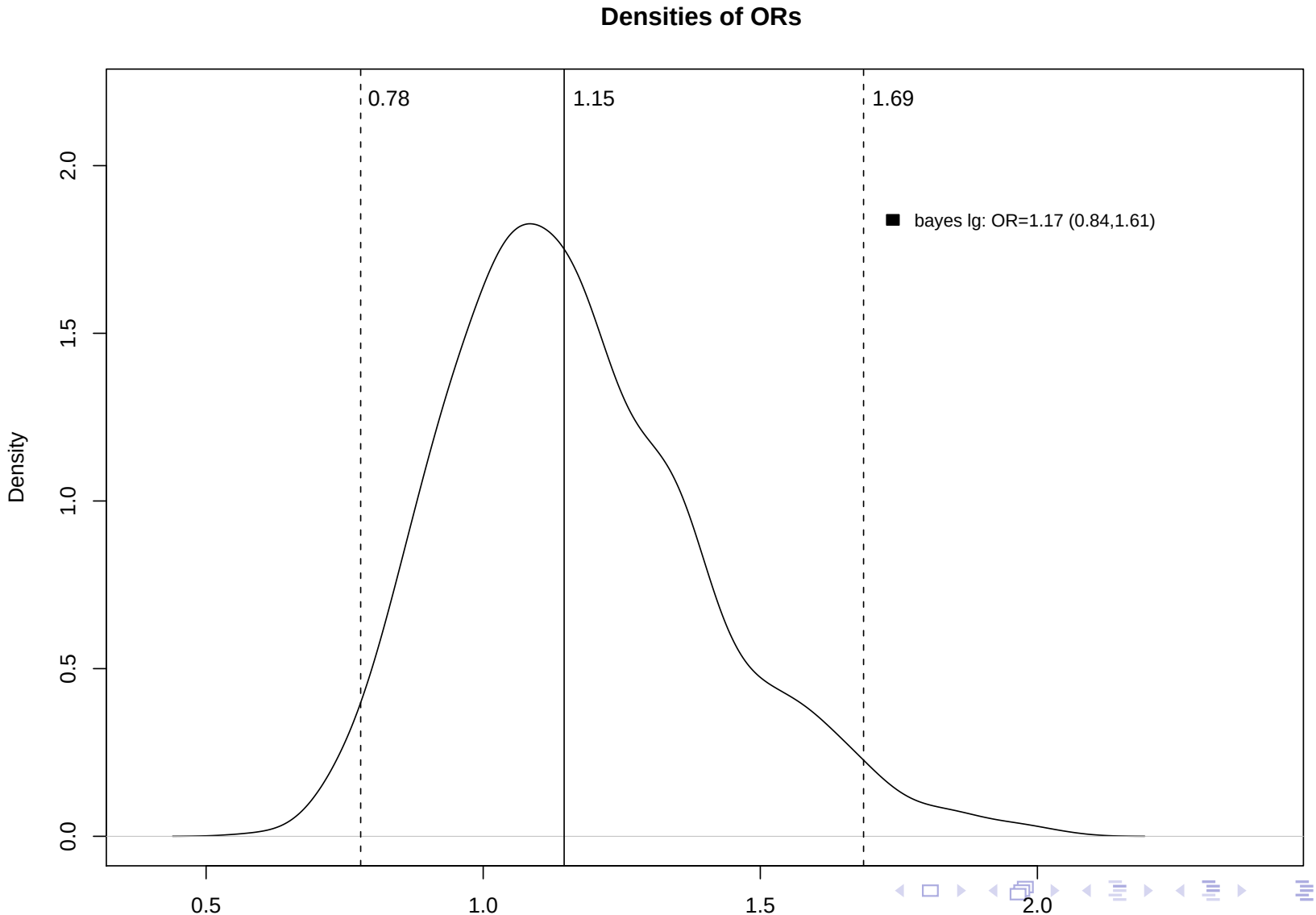
- Note that when we are using the marginal adjustment, we use the same distribution to adjust both cases and controls
- We look at whether this should be done in the discussion
- We can also pool the internal data to get marginal estimates for $p(B)$ - this we term *IM* estimates

Analysis

- We estimated the parameters using WinBUGs
- We ran 20000 iterations and kept the last 1000
- Convergence was good
- We ran a number of different models including interaction terms but results were similar
- We also ran hierarchical models using the state information but results were similar
- We show density plots for the 1000 estimates of the ORs for one chain

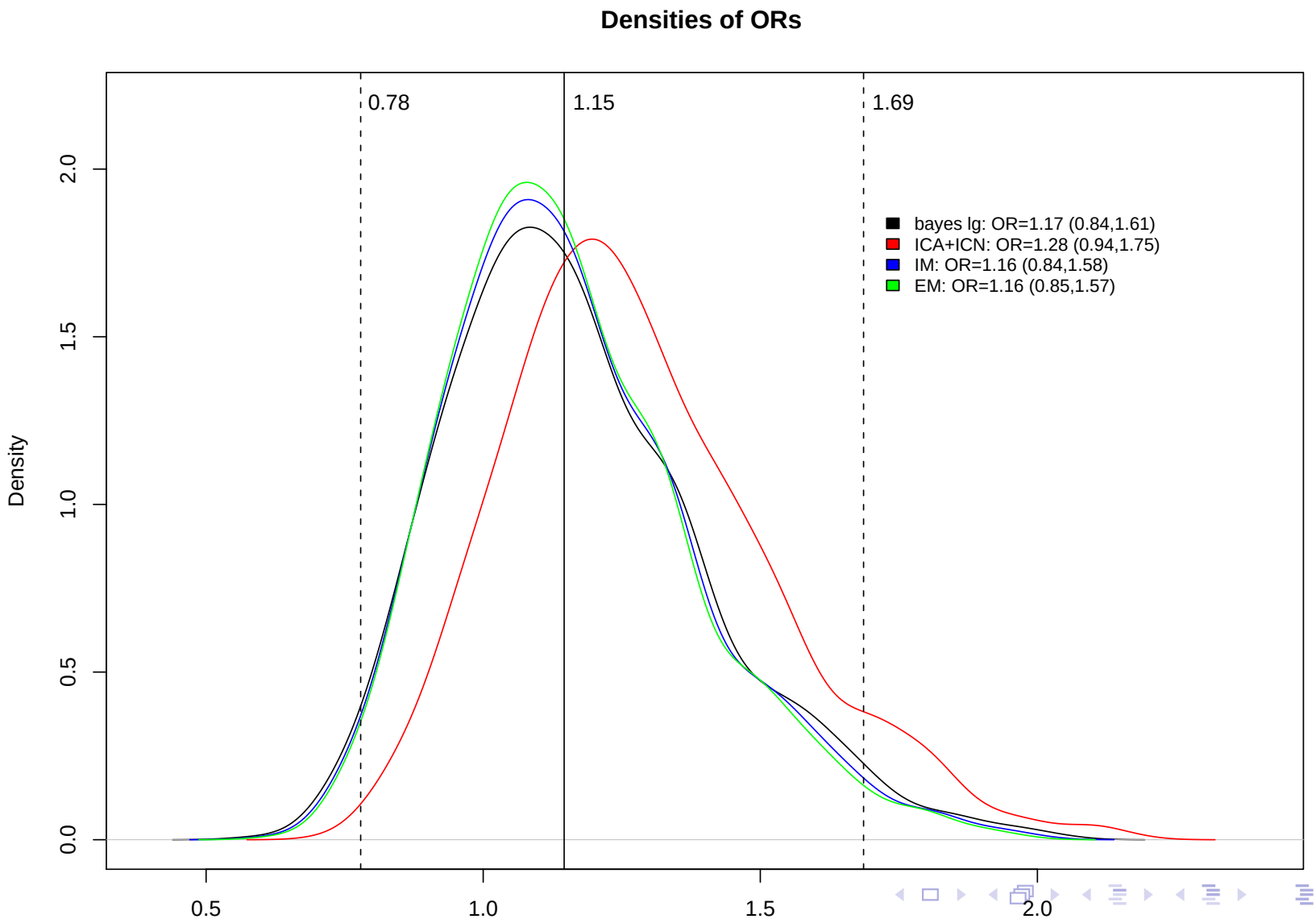
Results for Simple model with $B = \{RAC, INC, URB\}$

We began by looking at the Bayesian regression coefficient OR



Results for Simple model with $B = \{RAC, INC, URB\}$

Then we included the both case/control adjusted estimates



Discussion

No selection bias?

- Generally there appears to be little reason to suspect selection bias
- The point estimates are close
- the variances are similar
- In fact, the although the partial participants are atypical w.r.t some characteristics, it would appear that they are too few to sway the results

Discussion

- We estimate the marginal OR as opposed to the conditional OR in the logistic regression
- We used Empirical distributions for the weights.
- For the external data it probably does not make sense to model the weights as there are over 50,000 data points
- For the pooled internal data however, there might be some scope for modelling, especially when the number of partial participants is low
- In particular, we can impose constraints on the weights if we believe that the OR point estimate must be above 1 etc.

Further work

- Develop a simulation study based on EMF data with selection bias and see what happens with adjustments
- Replace $p(W|Y = y)$ with the 2x2 table estimate and see what happens is we assume there is no selection bias in either cases or controls
- Is it possible to come up with bounds to determine just how bad selection bias has to be in order to significantly change results?
- Develop a model for the weights using Bayesian contingency table methods and use this to constrain the OR
- More generally, relate to other weighting procedures such as inverse probability weighting, and imputation

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