How should the propensity score be estimated when some confounders are partially observed?

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Content

- Background
  - Propensity score
  - Missing data

- 3 ways to handle missing data for PS analysis
  - Complete case analysis
  - The missingness pattern approach
  - Multiple imputation

- Simulation study

- Real life example

- Recommendations/conclusion
The problem of confounding

Observational studies are a useful source of information to **establish causal effects** of a treatment/exposure on a health-related outcome.

Because of the lack of randomisation, study groups may be **unbalanced** \( \implies \) Risk of **confounding bias**

Propensity scores (PS) proposed in 1983 to **balance groups** in observational studies.

\[\begin{array}{c}
T: \text{treatment} \\
Y: \text{outcome} \\
X: \text{confounder}
\end{array}\]
The propensity score

The PS is the **individual’s probability of receiving the treatment** rather than the control conditionally to their baseline characteristics

\[ e(x) = P(T = 1 | X = x) \]

The true value of the PS is **unknown** but can be estimated:

\[ \Rightarrow \text{individual predictions from a logistic model} \]

Covariates to be included:

- true confounders
- risk factors
3 assumptions required to estimate unbiased causal effects using the PS:

- Positivity: each patient has a non null probability of receiving the treatment or the control
- SITA (conditional exchangeability): no unmeasured confounders
- SUTVA (consistency):
  - the potential outcome for a patient is not affected by the treatment received by the other patients
  - the treatment has always the same effect on a given patient

Under these assumptions, the PS is a balancing score
PS-based approaches

Stratification

\[ \hat{e}(x) \]

Adjustment

\[ Y = \alpha_0 + \alpha_1 T + \alpha_2 \hat{e}(x) \]

- Treated
- Untreated

Matching

Inverse weighting (IPTW)

\[ w = \frac{1}{\hat{e}(x)} \]

\[ w = \frac{1}{1-\hat{e}(x)} \]
The issue of missing data

If some confounders are partially observed, the PS **cannot be estimated** for individuals without a complete record.

<table>
<thead>
<tr>
<th>T</th>
<th>X_1</th>
<th>X_2</th>
<th>X_3</th>
<th>( \hat{e}(\mathbf{x}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>( x_{11} )</td>
<td>( x_{21} )</td>
<td>( x_{31} )</td>
<td>( \hat{e}_1(\mathbf{x}) )</td>
</tr>
<tr>
<td>0</td>
<td>( x_{12} )</td>
<td>?</td>
<td>( x_{32} )</td>
<td>?</td>
</tr>
<tr>
<td>1</td>
<td>( x_{13} )</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>0</td>
<td>( x_{14} )</td>
<td>( x_{24} )</td>
<td>( x_{34} )</td>
<td>( \hat{e}_4(\mathbf{x}) )</td>
</tr>
<tr>
<td>1</td>
<td>( x_{15} )</td>
<td>( x_{25} )</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>
The PS estimation and analysis strategy depend on the association between the missing value and observed and unobserved variables, the missingness mechanism.

Following Rubin’s taxonomy, missing confounders can be:

- **MCAR** (missing completely at random)
- **MAR** (missing at random)
- **MNAR** (missing not at random)

What can be done?
Focus on 3 approaches (with a binary outcome) for IPTW:

- Complete case analysis
- The missingness pattern approach
- Multiple imputation

For each of them:

- What are the assumptions required?
- What is the best way to implement the method?
A quick check of the literature showed that, among 132 identified papers:

- 46% used complete case analysis
- 5% used the missingness pattern approach
- 36% used multiple imputation

A systematic review would be needed for a better overview of the different methods implemented in practice.
Complete case analysis
Complete case (CC) analysis: analysis on the subgroup of patients with complete records:

- Loss of efficiency because of a loss in sample size
- Risk of bias of the treatment effect estimate

CC analysis leads to an unbiased estimate:

- when data are MCAR
- when missingness does not depend on Y and T in the context of multivariable logistic regression
Background
PS estimation with missing data
Complete cases
Logistic regression
Methods
Results
Summary
The missingness pattern approach
Multiple imputation
Simulation study
Example
Conclusion

Table 1. Bias of Estimates Derived From Complete Records Analysis Logistic Regression Under Different Missingness Assumptions

<table>
<thead>
<tr>
<th>Quantity on Which Missingness Is Dependent</th>
<th>( \beta_0 )</th>
<th>( \beta_x )</th>
<th>( \beta_C )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neither ( Y ) nor ( X ) nor ( C )</td>
<td>Asymptotically unbiased</td>
<td>Asymptotically unbiased</td>
<td>Asymptotically unbiased</td>
</tr>
<tr>
<td>Outcome ( (Y) )</td>
<td>Biased</td>
<td>Asymptotically unbiased</td>
<td>Asymptotically unbiased</td>
</tr>
<tr>
<td>Covariates ( (X, C, or both) )</td>
<td>Asymptotically unbiased</td>
<td>Asymptotically unbiased</td>
<td>Asymptotically unbiased</td>
</tr>
<tr>
<td>Outcome ( (Y) ) and confounders ( (C) )</td>
<td>Biased</td>
<td>Asymptotically unbiased</td>
<td>Biased</td>
</tr>
<tr>
<td>Outcome ( (Y) ), exposure ( (X) ), and possibly confounders ( (C) )</td>
<td>Biased</td>
<td>Biased</td>
<td>Biased</td>
</tr>
</tbody>
</table>


Are these results generalizable to PS analysis?
Simulation study

Setting:
n=10000, binary outcome $Y$, binary treatment $T$, and two binary confounders $C_1$ and $C_2$

$R$ is the complete case indicator ($R=1$ if complete case, 0 otherwise)

Comparison of 3 approaches:
- Multivariable logistic regression to estimate the conditional OR
- Multivariable logistic regression to estimate the marginal OR
- IPTW to estimate the marginal OR
### Bias of log(OR). ORcond=2

<table>
<thead>
<tr>
<th>Variables associated with missingness</th>
<th>Multivariable regression</th>
<th>IPTW</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ORcond</td>
<td>ORmarg</td>
</tr>
<tr>
<td>None</td>
<td>0.001</td>
<td>0.000</td>
</tr>
<tr>
<td>C1,C2</td>
<td>0.002</td>
<td>0.035</td>
</tr>
<tr>
<td>Z</td>
<td>-0.004</td>
<td>0.005</td>
</tr>
<tr>
<td>Y</td>
<td>0.000</td>
<td>0.041</td>
</tr>
<tr>
<td>C1,C2,Z</td>
<td>0.001</td>
<td>0.040</td>
</tr>
<tr>
<td>C1,C2,Y</td>
<td>-0.001</td>
<td>0.130</td>
</tr>
<tr>
<td>Z,Y</td>
<td>-0.838</td>
<td>-0.626</td>
</tr>
<tr>
<td>C1,C2,Z,Y</td>
<td>-0.769</td>
<td>-0.579</td>
</tr>
</tbody>
</table>
## Results (2)

<table>
<thead>
<tr>
<th>Variables associated with missingness</th>
<th>Multivariable regression</th>
<th>IPTW</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>Risk difference</td>
</tr>
<tr>
<td>None</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>C1,C2</td>
<td>0.070</td>
<td>-0.009</td>
</tr>
<tr>
<td>Z</td>
<td>0.016</td>
<td>-0.003</td>
</tr>
<tr>
<td>Y</td>
<td>0.125</td>
<td>-0.036</td>
</tr>
<tr>
<td>C1,C2,Z</td>
<td>0.076</td>
<td>-0.010</td>
</tr>
<tr>
<td>C1,C2,Y</td>
<td>0.227</td>
<td>-0.043</td>
</tr>
<tr>
<td>Z,Y</td>
<td>-0.428</td>
<td>-0.130</td>
</tr>
<tr>
<td>C1,C2,Z,Y</td>
<td>-0.390</td>
<td>-0.122</td>
</tr>
</tbody>
</table>
**CC: a bad idea**

**CC not suitable** for the estimation of marginal effects (both with PS and logistic regression) unless:

- MCAR mechanism
- missingness not associated with both Y and Z AND under H0!!

In the literature CC seems to be the **most common approach** for PS analysis...

**What else can be done?**
The missingness pattern approach

Helen Blake’s PhD research
The missingness pattern approach


Definition of a **generalized PS** estimated within each pattern of missingness

<table>
<thead>
<tr>
<th></th>
<th>X2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observed</td>
</tr>
<tr>
<td>X3</td>
<td></td>
</tr>
<tr>
<td>Observed</td>
<td>$\hat{e}(X_1, X_2, X_3)$</td>
</tr>
<tr>
<td>Missing</td>
<td>$\hat{e}(X_1, X_2)$</td>
</tr>
</tbody>
</table>

Relies on an **additional assumption**: an extension of SITA
Let $\mathbf{X}$ the vector of baseline confounders be split in $\mathbf{X} = \{\mathbf{X}_{\text{obs}}, \mathbf{X}_{\text{mis}}\}$ and $\mathbf{R}$ the vector of the missingness indicators for the confounders.

"Classical" SITA assumption: the potential outcomes and the treatment assignment are independent given the measured characteristics (no unmeasured confounders):

$$(Y^0, Y^1) \perp T|\mathbf{X}$$

SITA extension (Mattei):

$$(Y^0, Y^1) \perp T|\mathbf{X}, \mathbf{R}$$

and either

$$\mathbf{X}_{\text{mis}} \perp T|\mathbf{X}_{\text{obs}}, \mathbf{R} \quad \text{or} \quad \mathbf{X}_{\text{mis}} \perp (Y^0, Y^1)|\mathbf{X}_{\text{obs}}, \mathbf{R}$$
For the assumption to hold, $X$ can be a confounder when observed but not when missing.

Assumption required because the generalised PS **balances the observed part** of the covariates only (but not the missing part).
It’s been shown that:

- if the SITA assumption extension does not hold: invalid inferences even under MCAR
- if the SITA assumption extension holds: valid inferences even under some MNAR mechanisms

**Promising approach** that requires further investigation to be applicable in a variety of situations combining MAR and MNAR data.
Summary

The missingness pattern approach:

▶ can lead to **valid inferences** if the SITA assumption extension holds
▶ could be of interest for some **MNAR mechanisms**
▶ is quite straightforward

However:

▶ requires a **large sample size**
▶ difficulties arise with a **lot of patterns**
  ➞ Pooling?
▶ has a **specific applicability** in its present form
  ➞ Combining MPA with other methods?
Multiple imputation
**Aim**: create $M$ complete datasets to estimate the PS for each participant and apply Rubin’s rules to obtain a treatment effect estimate.

**Two key questions:**

- Should the outcome be included in the imputation model?
  - $\Rightarrow$ **PS paradigm $\neq$ Missing data paradigm**

- How to apply Rubin’s rules?
  - $\Rightarrow$ pooled treatment effect or pooled PS?
What should we combine?

\[ \hat{\theta}: \text{treatment effect estimate} \]
In the literature...

Existing studies:

- Mitra & Reiter\(^1\): for PS matching, MIps>MIte but opposite conclusion for IPTW
  \[\Rightarrow\text{Outcome not included} \text{ in the imputation model}\]

- Hill\(^2\): MIte>MIps and outcome in the imputation model
  \[\Rightarrow\text{PS matching} \text{ only}\]

Simulation study but **no theoretical arguments** about the validity of these estimators when data are MAR

Balancing properties

Are the 3 estimated PS balancing scores?
⇒ requirement for valid inferences

For MIte, we showed that within each imputed dataset:
\[ \mathbf{X}_{obs} \perp Z \mid e(\mathbf{X}_{obs}, \mathbf{X}_{m}^{(k)}) \]
\[ \mathbf{X}_{m}^{(k)} \perp Z \mid e(\mathbf{X}_{obs}, \mathbf{X}_{m}^{(k)}). \]

For MIps and MIpar:
- the pooled PS is not a function of the covariates
- the true PS is not a function of the estimated PS
⇒ the pooled PS is not a balancing score
Consistency comes from the ability of the PS to balance groups:
**MIps and MIpar are not consistent** estimators

MIte: Seaman and White: the consistent estimator for an infinite number of imputations

In practice: how well these 3 estimators perform?
Different ways to apply Rubin’s rules after MI of the partially observed covariates for IPTW

\[ \text{MIte only is a consistent estimator of the treatment effect (MAR mechanism)} \]

Simulation results found in the literature are not clear so need to empirically assess these methods:

- variance estimation?
- outcome in the imputation model?
- strength of the bias for MIps and MIpar
Simulation study
Simulation plan

Observational study:
- estimation of the effect of a binary treatment $T$ on a binary outcome $Y$ (RR), $n=5000$
- 3 confounders (2 with 30% of data missing)

Multiple imputation:
- Chained equations (FCS)
- $M=10$
- Imputation model: $X_1, X_2, X_3, T, Y$

Y: binary outcome
T: treatment
R: missingness indicator
Xobs: observed confounders
Xmiss: missing confounders
Analysis strategies

IPTW estimator:

- Estimation of the weighted marginal proportions $\hat{P}_0$ and $\hat{P}_1$ and $RR = \frac{\hat{P}_1}{\hat{P}_0}$
- Use of Williamson et al.\(^1\) variance estimator for IPTW (two-step estimator)

Compared approaches:

- Complete case: exclusion of participants with partial data
- Missingness pattern: 4 different PS models
  - MIte: the M IPTW estimates of the treatment effect are pooled according to Rubin’s rules
  - MIps: 1 IPTW estimate obtained from the average PS
  - MIpar: 1 IPTW estimate obtained from the PS of the average covariates

Results: bias

RR=1, outcome predictor of missingness

**Similar results** with:

- RR=2
- missingness not associated with Y

- The **outcome must be included** in the imputation model
- **Pooling the treatment effects** ($M_{lte}$) performs best
Balancing properties

Standardized differences (in%) between groups: \[ SD = \frac{100 \times |\bar{X}_1 - \bar{X}_0|}{\sqrt{s^2_0 + s^2_1}} \]

<table>
<thead>
<tr>
<th>Method</th>
<th>(X_1) (partially observed)</th>
<th>(X_2) (fully observed)</th>
<th>(X_3) (partially observed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude (without IPTW)</td>
<td>81.3</td>
<td>74.7</td>
<td>51.7</td>
</tr>
<tr>
<td>Full data (IPTW)</td>
<td>4.6</td>
<td>4.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Mlte</td>
<td>4.5</td>
<td>4.5</td>
<td>2.4</td>
</tr>
<tr>
<td>MIps (full dataset)</td>
<td>15.9</td>
<td>5.5</td>
<td>10.7</td>
</tr>
<tr>
<td>MIps (observed part)</td>
<td>7.6</td>
<td>5.5</td>
<td>4.9</td>
</tr>
<tr>
<td>MIpar (full dataset)</td>
<td>14.7</td>
<td>4.8</td>
<td>9.7</td>
</tr>
<tr>
<td>MIpar (observed part)</td>
<td>7.7</td>
<td>4.8</td>
<td>5.4</td>
</tr>
</tbody>
</table>

PS obtained from MP, MIps and MIpar do not balance the missing part of the covariates.
Real life example
Example

**Data:** THIN database (records from GP in the UK)

**Population:** focus on patients with a pneumonia episode, n=9073 (Douglas et al.)

**Intervention:** statins vs no statins

**Outcome:** death within 6 months

**Confounders:** 21 variables (demographic, medical history, treatments)

**Missing data:** body mass index (19.2%), smoking status (6.2%) and alcohol consumption (18.5%)
Example: PS distribution (CC)

- Statin users
- Non statin users

Density vs. PS distribution
### Example: balance

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Missing (%)</th>
<th>Statin users n=599</th>
<th>Missing (%)</th>
<th>Non statin users n=6559</th>
<th>Crude</th>
<th>CC*</th>
<th>MP</th>
<th>MIte</th>
<th>MIps</th>
<th>MLpar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [mean (sd)]</td>
<td>66.9 (10.7)</td>
<td>68.8 (10.9)</td>
<td>27.0</td>
<td>3.8</td>
<td>2.0</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
</tr>
<tr>
<td>Male</td>
<td>322 (53.8)</td>
<td>3173 (48.4)</td>
<td>10.8</td>
<td>2.0</td>
<td>2.2</td>
<td>2.1</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>BMI [mean (sd)]</td>
<td>43 (7.2)</td>
<td>27.6 (5.9)</td>
<td>1444 (22.0)</td>
<td>25.8 (5.9)</td>
<td>31.9</td>
<td>7.8</td>
<td>9.0</td>
<td>9.0</td>
<td>11.4</td>
<td>11.4</td>
</tr>
<tr>
<td>Drinkers</td>
<td>67 (11.2)</td>
<td>98 (18.4)</td>
<td>1334 (20.3)</td>
<td>814 (15.6)</td>
<td>7.6</td>
<td>2.1</td>
<td>0.3</td>
<td>2.3</td>
<td>2.9</td>
<td>3.0</td>
</tr>
<tr>
<td>Smokers</td>
<td>7 (1.2)</td>
<td>256 (43.2)</td>
<td>505 (7.7)</td>
<td>2728 (45.1)</td>
<td>3.7</td>
<td>1.7</td>
<td>1.5</td>
<td>2.5</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetics</td>
<td>243 (40.6)</td>
<td>715 (10.9)</td>
<td>72.1</td>
<td>5.0</td>
<td>7.1</td>
<td>7.2</td>
<td>7.1</td>
<td>7.1</td>
<td>7.1</td>
<td>7.1</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>141 (23.5)</td>
<td>651 (9.9)</td>
<td>37.1</td>
<td>11.4</td>
<td>13.6</td>
<td>13.6</td>
<td>13.6</td>
<td>13.6</td>
<td>13.6</td>
<td>13.6</td>
</tr>
<tr>
<td>Circulatory disease</td>
<td>426 (71.1)</td>
<td>3471 (52.9)</td>
<td>38.2</td>
<td>13.6</td>
<td>16.6</td>
<td>16.7</td>
<td>16.6</td>
<td>16.6</td>
<td>16.6</td>
<td>16.6</td>
</tr>
<tr>
<td>Heart failure</td>
<td>51 (8.5)</td>
<td>426 (6.5)</td>
<td>7.7</td>
<td>11.6</td>
<td>6.2</td>
<td>12.8</td>
<td>12.8</td>
<td>12.8</td>
<td>12.8</td>
<td>12.8</td>
</tr>
<tr>
<td>Cancer</td>
<td>37 (6.2)</td>
<td>607 (9.2)</td>
<td>11.5</td>
<td>2.1</td>
<td>0.4</td>
<td>0.0</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Dementia</td>
<td>6 (1.0)</td>
<td>190 (2.9)</td>
<td>13.7</td>
<td>7.3</td>
<td>13.0</td>
<td>11.6</td>
<td>11.6</td>
<td>11.6</td>
<td>11.6</td>
<td>11.6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>330 (56.1)</td>
<td>1163 (17.8)</td>
<td>52.1</td>
<td>13.3</td>
<td>21.5</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>205 (34.2)</td>
<td>182 (2.8)</td>
<td>88.5</td>
<td>11.1</td>
<td>4.1</td>
<td>1.9</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
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<tr>
<td>Treatments</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressant</td>
<td>108 (18.0)</td>
<td>995 (15.2)</td>
<td>7.7</td>
<td>1.7</td>
<td>5.9</td>
<td>0.3</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>11 (1.8)</td>
<td>340 (5.2)</td>
<td>18.3</td>
<td>0.5</td>
<td>11.3</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
<td>37 (6.2)</td>
<td>277 (4.2)</td>
<td>8.8</td>
<td>0.9</td>
<td>0.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Steroid</td>
<td>93 (15.5)</td>
<td>1090 (16.6)</td>
<td>3.0</td>
<td>1.0</td>
<td>2.2</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>272 (45.4)</td>
<td>1165 (17.8)</td>
<td>62.3</td>
<td>12.6</td>
<td>27.5</td>
<td>18.0</td>
<td>17.8</td>
<td>17.9</td>
<td>17.9</td>
<td>17.9</td>
</tr>
<tr>
<td>Diuretics</td>
<td>319 (53.3)</td>
<td>2416 (36.8)</td>
<td>33.4</td>
<td>14.3</td>
<td>19.8</td>
<td>15.8</td>
<td>15.9</td>
<td>15.9</td>
<td>15.9</td>
<td>15.9</td>
</tr>
<tr>
<td>Betablocker</td>
<td>193 (32.2)</td>
<td>1061 (16.2)</td>
<td>38.1</td>
<td>11.4</td>
<td>7.2</td>
<td>13.8</td>
<td>13.8</td>
<td>13.8</td>
<td>13.8</td>
<td>13.8</td>
</tr>
<tr>
<td>Nitrate</td>
<td>74 (12.4)</td>
<td>334 (5.1)</td>
<td>25.9</td>
<td>17.3</td>
<td>14.8</td>
<td>17.5</td>
<td>17.6</td>
<td>17.6</td>
<td>17.6</td>
<td>17.6</td>
</tr>
</tbody>
</table>

For CC analysis, n=5168 (503 statin users and 4665 non users).

CC: complete case; MP: missingness pattern; MIte: treatment effects combined after multiple imputation; MIps: propensity scores combined after multiple imputation; MLpar: propensity score parameters combined after multiple imputation.
Example: results

<table>
<thead>
<tr>
<th>Method</th>
<th>RR</th>
<th>95% CI(RR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude</td>
<td>0.587</td>
<td>[0.497;0.684]</td>
</tr>
<tr>
<td>CC</td>
<td>0.702</td>
<td>[0.534;0.924]</td>
</tr>
<tr>
<td>MP</td>
<td>0.708</td>
<td>[0.555;0.904]</td>
</tr>
<tr>
<td>MIte</td>
<td>0.654</td>
<td>[0.513;0.835]</td>
</tr>
<tr>
<td>MIps</td>
<td>0.653</td>
<td>[0.512;0.834]</td>
</tr>
<tr>
<td>MIpar</td>
<td>0.654</td>
<td>[0.513;0.834]</td>
</tr>
</tbody>
</table>

CC: complete case; MP: missingness pattern; MIte: treatment effects combined after multiple imputation; MIps: propensity scores combined after multiple imputation; MIpar: propensity score parameters combined after multiple imputation; RR: relative risk

The 3 partially observed covariates are **not strong confounders**

MP: Need to **pool some patterns** because of small sample and SITA assumption extension unlikely to be valid

Similar results for MI when increasing artificially the missingness rate
Recommendations

Complete case analysis: **bad idea**, unless MCAR mechanism

Multiple imputation:
- good statistical properties under a MAR mechanism
- the treatment effects should be pooled rather than the PSs
- the outcome must be included in the imputation model

The missingness pattern approach:
- good statistical properties if missing values are not confounders
- promising technique for MNAR mechanisms
Future work

Multiple imputation:
- to study the issue of **compatibility** between the substantive, PS and imputation models
- to study how to assess **covariate balance** after MI

The missingness pattern approach:
- to **combine MPA with MI** when both MAR and MNAR mechanisms
- to study how to **pool patterns** when small sample size
- to develop a **variance estimator**
Thank you!