

## Appendix 3. Imputing Potential Outcomes From Simulated Data

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Recall that for the plasmode simulations constructed in the manuscript, treatment assignment was not simulated and was a function of the true underlying covariate associations in the data. However, the outcome variable was simulated and was a function of a known parametric logistic model. Because the “true” outcome model was known, this model could be used to impute the potential outcomes for each individual under alternative treatment conditions. These potential outcomes, in turn, could be used to calculate the value of the true causal parameter of interest (e.g., risk difference).

Here we provide a simple example of imputing potential outcomes from the “true” outcome model to obtain the value of the causal parameter of interest.

For the discussion below, we will use the following notation:

- $Y_1$ : the potential outcome under the exposed condition
- $Y_0$ : the potential outcome under the unexposed condition
- $A$ : a binary exposure
- $Y$ : the observed outcome (corresponds with either  $Y_1$  or  $Y_0$  depending on whether the individual received exposure or remained unexposed).
- $X$ : a set of observed covariates
- $E[Y|A, X]$ : the expected value of  $Y$  given  $A$  and  $X$  (the outcome model)

Suppose our dataset consists of a binary exposure,  $A$ , an outcome,  $Y$ , and three baseline variables,  $X = \{X_1, X_2, X_3\}$ . Further, suppose that the true data generating model for outcome probabilities can be expressed as:

$$\text{logit}(E[Y|A, X_1, X_2, X_3]) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_A A \quad [1]$$

The model expressed in Equation 1 can be used to produce outcome probabilities for each individual under the exposed ( $A = 1$ ) and unexposed ( $A = 0$ ) condition. For example, suppose the beta coefficients in Equation 1 are equal to the following:

$$\begin{aligned}\beta_0 &= 0 \\ \beta_1 &= 0.2 \\ \beta_2 &= 0.1 \\ \beta_3 &= 0.4 \\ \beta_A &= -0.3\end{aligned}$$

The “true” outcome probability for each individual can be computed by simply plugging in their specific covariate values and exposure status into Equation 1. For example, suppose that the first subject in the dataset has  $X_1 = 1$ ,  $X_2 = 1$ ,  $X_3 = 0$ , and  $A = 1$ . Then the predicted outcome probability for subject 1 would be:

$$E[Y|A = 1, X_1 = 1, X_2 = 1, X_3 = 0] = E[Y_1|X_1 = 1, X_2 = 1, X_3 = 0]$$

$$= \text{expit}[0.2(1) + 0.1(1) - 0.3(1)] = 0.5$$

Because subject 1 received exposure, their observed outcome probability is equivalent to their potential outcome probability under the exposed condition as illustrated above. To obtain their counterfactual outcome probability under no exposure, we would simply plug in a value of 0 for exposure status:

$$E[Y_0|X_1 = 1, X_2 = 1, X_3 = 0] = \text{expit}[0.2(1) + 0.1(1)] \approx 0.57$$

Table 1 below shows the counterfactual outcome probabilities for three individuals in a hypothetical dataset, along with their observed outcome probability and baseline covariate values.

Table 1. Counterfactual outcome probabilities for a hypothetical dataset.

Subject	$X_{1i}$	$X_{2i}$	$X_{3i}$	$A$	$E[Y A_i, X_{1i}, X_{2i}, X_{3i}]$	$E[Y_0 X_{1i}, X_{2i}, X_{3i}]$	$E[Y_1 X_{1i}, X_{2i}, X_{3i}]$
1	1	1	0	1	0.5	0.57	0.5
2	1	0	0	0	0.55	0.55	0.48
3	0	1	1	0	0.62	0.62	0.55
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮

The counterfactual outcome probabilities can then be used to generate counterfactual outcomes under exposed and unexposed conditions for each individual. These counterfactual outcomes can then be used to calculate the unbiased or “true” value of the causal parameter of interest. For example, if the parameter of interest is the risk difference, this would be obtained through the expression:

$$\frac{1}{n} \sum_{i=1}^n (Y_{1i} - Y_{0i})$$

Where n is the number of individuals in the dataset. Equivalently, the counterfactual outcome probabilities could be used directly in the calculation of the value for the causal parameter of interest. For example, if the risk difference is again the desired parameter, this would be obtained through the expression:

$$\frac{1}{n} \sum_{i=1}^n (E[Y_1|X_{1i}, X_{2i}, X_{3i}] - E[Y_0|X_{1i}, X_{2i}, X_{3i}])$$

The calculated value for the causal parameter of interest can be considered the “truth” and used as the benchmark when calculating bias and mean squared error in simulations that evaluate the performance of various statistical models.