

# Standard errors of probabilities, RR and RD estimations using a logistic MSM

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## 1) Introduction

The `ltmleMSM` function from the `ltmle` package estimates parameters of a working Marginal Structural Model (MSM). The MSM is a logistic regression from which OR estimates can be easily calculated using the exponential of the estimated coefficients.

Applying delta method, it is possible to estimate relative risks and risk differences from the same logistic regression MSM.

In order to estimate the marginal interaction effect between two binary exposures  $A_1$  and  $A_2$ , the following MSM is applied:

$$\text{logitm}_\beta(A_1, A_2) = \ln \frac{P(Y_{A_1, A_2} = 1)}{P(Y_{A_1, A_2} = 0)} = \beta_0 + \beta_1 A_1 + \beta_2 A_2 + \beta_3 (A_1 \times A_2)$$

For given values  $A_1 = a_1$  and  $A_2 = a_2$ , we note the predicted probability:

$$m_\beta(a_1, a_2) = \frac{\exp(\beta_0 + \beta_1 a_1 + \beta_2 a_2 + \beta_3 (a_1 \times a_2))}{1 + \exp(\beta_0 + \beta_1 a_1 + \beta_2 a_2 + \beta_3 (a_1 \times a_2))}$$

We also note:

$$e_{a_1, a_2} = \exp(-\beta_0 - \beta_1 a_1 - \beta_2 a_2 - \beta_3 (a_1 \times a_2))$$

so that:

$$m_\beta(a_1, a_2) = \frac{1}{1 + e_{a_1, a_2}}$$

and

$$\begin{aligned} P(Y_{A_1=0, A_2=0} = 1) &= m_\beta(0, 0) = \frac{1}{1 + \exp(-\beta_0)} = \frac{1}{1 + e_{00}} \\ P(Y_{A_1=1, A_2=0} = 1) &= m_\beta(1, 0) = \frac{1}{1 + \exp(-\beta_0 - \beta_1)} = \frac{1}{1 + e_{10}} \\ P(Y_{A_1=0, A_2=1} = 1) &= m_\beta(0, 1) = \frac{1}{1 + \exp(-\beta_0 - \beta_2)} = \frac{1}{1 + e_{01}} \\ P(Y_{A_1=1, A_2=1} = 1) &= m_\beta(1, 1) = \frac{1}{1 + \exp(-\beta_0 - \beta_1 - \beta_2 - \beta_3)} = \frac{1}{1 + e_{11}} \end{aligned}$$

For a given function  $f(\beta)$  of the  $\beta = \{\beta_0, \beta_1, \beta_2, \beta_3\}$  coefficients such as  $m_\beta(a_1, a_2)$ , by Delta method, the variance of  $f(\beta)$  can be calculated by:

$$\text{var}[f(\beta)] = \left( \frac{\partial f(\beta)}{\partial \beta} \right)^T \text{var}(\beta) \left( \frac{\partial f(\beta)}{\partial \beta} \right)$$

where  $var(\beta)$  is a  $4 \times 4$  covariance matrix, that can be estimated using the variance of the influence curve (IC) of the MSM coefficients given in the output values of the `ltmleMSM` function, divided by the sample size:  $var(IC) / n$ .

## 2) Standard errors of point estimates of the probabilities of interest

### 2.1) Standard error of $P(Y_{A_1=0, A_2=0} = 1) = m_\beta(0, 0)$

$$m_\beta(0, 0) = \frac{1}{1 + e_{00}}, \text{ where } e_{00} = \exp(-\beta_0)$$

The partial derivative of  $f(\beta) = m_\beta(0, 0)$  with respect to  $\beta$  is:

$$\left( \frac{\partial m_\beta(0, 0)}{\partial \beta} \right) = \frac{-\left( \frac{\partial e_{00}}{\partial \beta} \right)}{(1 + e_{00})^2}$$

where  $\left( \frac{\partial e_{00}}{\partial \beta_0} \right) = -e_{00}$  and  $\left( \frac{\partial e_{00}}{\partial \beta_1} \right) = \left( \frac{\partial e_{00}}{\partial \beta_2} \right) = \left( \frac{\partial e_{00}}{\partial \beta_3} \right) = 0$ .

$$\begin{aligned} \left( \frac{\partial m_\beta(0, 0)}{\partial \beta_0} \right) &= \frac{-(-e_{00})}{(1 + e_{00})^2} = \frac{1 + e_{00} - 1}{(1 + e_{00})} \times \frac{1}{1 + e_{00}} \\ &= [1 - m_\beta(0, 0)] \times m_\beta(0, 0) \end{aligned}$$

$$\left( \frac{\partial m_\beta(0, 0)}{\partial \beta} \right) = \begin{pmatrix} \left( \frac{\partial m_\beta(0, 0)}{\partial \beta_0} \right) \\ \left( \frac{\partial m_\beta(0, 0)}{\partial \beta_1} \right) \\ \left( \frac{\partial m_\beta(0, 0)}{\partial \beta_2} \right) \\ \left( \frac{\partial m_\beta(0, 0)}{\partial \beta_3} \right) \end{pmatrix} = \begin{pmatrix} [1 - m_\beta(0, 0)] \times m_\beta(0, 0) \\ \frac{-0}{(1+e_{00})^2} \\ \frac{-0}{(1+e_{00})^2} \\ \frac{-0}{(1+e_{00})^2} \end{pmatrix} = \begin{pmatrix} [1 - m_\beta(0, 0)] \times m_\beta(0, 0) \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

The variance of  $m_\beta(0, 0)$  can then be calculated by:

$$var(m_\beta(0, 0)) = \begin{pmatrix} [1 - m_\beta(0, 0)] \times m_\beta(0, 0) \\ 0 \\ 0 \\ 0 \end{pmatrix}^T \times \frac{var(IC)}{n} \times \begin{pmatrix} [1 - m_\beta(0, 0)] \times m_\beta(0, 0) \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

## 2.2) Standard error of $P(Y_{A_1=1, A_2=0} = 1) = m_\beta(1, 0)$

$$m_\beta(1, 0) = \frac{1}{1 + e_{10}}, \text{ where } e_{10} = \exp(-\beta_0 - \beta_1)$$

The partial derivative of  $f(\beta) = m_\beta(1, 0)$  with respect to  $\beta$  is:

$$\left( \frac{\partial m_\beta(1, 0)}{\partial \beta} \right) = \frac{-\left( \frac{\partial e_{10}}{\partial \beta} \right)}{(1 + e_{10})^2}$$

where  $\left( \frac{\partial e_{10}}{\partial \beta_0} \right) = \left( \frac{\partial e_{10}}{\partial \beta_1} \right) = -e_{10}$  and  $\left( \frac{\partial e_{10}}{\partial \beta_2} \right) = \left( \frac{\partial e_{10}}{\partial \beta_3} \right) = 0$ .

$$\begin{aligned} \left( \frac{\partial m_\beta(1, 0)}{\partial \beta_0} \right) &= \left( \frac{\partial m_\beta(1, 0)}{\partial \beta_1} \right) = \frac{-(-e_{10})}{(1 + e_{10})^2} = \frac{1 + e_{10} - 1}{(1 + e_{10})} \times \frac{1}{1 + e_{10}} \\ &= [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \end{aligned}$$

$$\left( \frac{\partial m_\beta(1, 0)}{\partial \beta} \right) = \begin{pmatrix} [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ \frac{-0}{(1+e_{10})^2} \\ \frac{-0}{(1+e_{10})^2} \end{pmatrix} = \begin{pmatrix} [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ 0 \\ 0 \end{pmatrix}$$

The variance of  $m_\beta(1, 0)$  can then be calculated by:

$$\text{var}(m_\beta(1, 0)) = \begin{pmatrix} [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ 0 \\ 0 \end{pmatrix}^T \times \frac{\text{var}(IC)}{n} \times \begin{pmatrix} [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ 0 \\ 0 \end{pmatrix}$$

### 2.3) Standard error of $P(Y_{A_1=0, A_2=1} = 1) = m_\beta(0, 1)$

$$m_\beta(0, 1) = \frac{1}{1 + e_{01}}, \text{ where } e_{01} = \exp(-\beta_0 - \beta_2)$$

The partial derivative of  $f(\beta) = m_\beta(0, 1)$  with respect to  $\beta$  is:

$$\left( \frac{\partial m_\beta(0, 1)}{\partial \beta} \right) = \frac{-\left( \frac{\partial e_{01}}{\partial \beta} \right)}{(1 + e_{01})^2}$$

where  $\left( \frac{\partial e_{01}}{\partial \beta_0} \right) = \left( \frac{\partial e_{01}}{\partial \beta_2} \right) = -e_{01}$  and  $\left( \frac{\partial e_{01}}{\partial \beta_1} \right) = \left( \frac{\partial e_{01}}{\partial \beta_3} \right) = 0$ .

$$\begin{aligned} \left( \frac{\partial m_\beta(0, 1)}{\partial \beta_0} \right) &= \left( \frac{\partial m_\beta(0, 1)}{\partial \beta_2} \right) = \frac{-(-e_{01})}{(1 + e_{01})^2} = \frac{1 + e_{01} - 1}{(1 + e_{01})} \times \frac{1}{1 + e_{01}} \\ &= [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \end{aligned}$$

$$\left( \frac{\partial m_\beta(0, 1)}{\partial \beta} \right) = \begin{pmatrix} [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ \frac{-0}{(1 + e_{01})^2} \\ [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ \frac{-0}{(1 + e_{01})^2} \end{pmatrix} = \begin{pmatrix} [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ 0 \\ [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ 0 \end{pmatrix}$$

The variance of  $m_\beta(0, 1)$  can then be calculated by:

$$\text{var}(m_\beta(0, 1)) = \begin{pmatrix} [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ 0 \\ [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ 0 \end{pmatrix}^T \times \frac{\text{var}(IC)}{n} \times \begin{pmatrix} [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ 0 \\ [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ 0 \end{pmatrix}$$

## 2.4) Standard error of $P(Y_{A_1=1, A_2=1} = 1) = m_\beta(1, 1)$

$$m_\beta(1, 1) = \frac{1}{1 + e_{11}}, \text{ where } e_{11} = \exp(-\beta_0 - \beta_1 - \beta_2 - \beta_3)$$

The partial derivative of  $f(\beta) = m_\beta(1, 1)$  with respect to  $\beta$  is:

$$\left( \frac{\partial m_\beta(1, 1)}{\partial \beta} \right) = \frac{-\left( \frac{\partial e_{11}}{\partial \beta} \right)}{(1 + e_{11})^2}$$

where  $\left( \frac{\partial e_{11}}{\partial \beta_0} \right) = \left( \frac{\partial e_{11}}{\partial \beta_2} \right) = \left( \frac{\partial e_{11}}{\partial \beta_1} \right) = \left( \frac{\partial e_{11}}{\partial \beta_3} \right) = -e_{11}$ .

$$\begin{aligned} \left( \frac{\partial m_\beta(1, 1)}{\partial \beta_0} \right) &= \left( \frac{\partial m_\beta(1, 1)}{\partial \beta_1} \right) = \left( \frac{\partial m_\beta(1, 1)}{\partial \beta_2} \right) = \left( \frac{\partial m_\beta(1, 1)}{\partial \beta_3} \right) = \frac{-(-e_{11})}{(1 + e_{11})^2} = \frac{1 + e_{11} - 1}{(1 + e_{11})} \times \frac{1}{1 + e_{11}} \\ &= [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \end{aligned}$$

$$\left( \frac{\partial m_\beta(1, 1)}{\partial \beta} \right) = \begin{pmatrix} [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \end{pmatrix}$$

The variance of  $m_\beta(1, 1)$  can then be calculated by:

$$\text{var}(m_\beta(1, 1)) = \begin{pmatrix} [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \end{pmatrix}^T \times \frac{\text{var}(IC)}{n} \times \begin{pmatrix} [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \end{pmatrix}$$

### 3) Standard errors of risk differences

#### 3.1) Risk difference for the effect of $A_1$ , setting $A_2 = 0$

$$RD_{A_1|A_2=0} = m_\beta(1, 0) - m_\beta(0, 0) = \frac{1}{1 + e_{10}} - \frac{1}{1 + e_{00}}$$

where  $e_{00} = \exp(-\beta_0)$  and  $e_{10} = \exp(-\beta_0 - \beta_1)$ .

The partial derivative of the risk difference  $m_\beta(1, 0) - m_\beta(0, 0)$  with respect to  $\beta$  is:

$$\frac{\partial}{\partial \beta} (m_\beta(1, 0) - m_\beta(0, 0)) = \frac{-\left(\frac{\partial e_{10}}{\partial \beta}\right)}{(1 + e_{10})^2} - \frac{-\left(\frac{\partial e_{00}}{\partial \beta}\right)}{(1 + e_{00})^2}$$

$$\begin{aligned} \frac{\partial}{\partial \beta_0} (m_\beta(1, 0) - m_\beta(0, 0)) &= \frac{-(-e_{10})}{(1 + e_{10})^2} - \frac{-(-e_{00})}{(1 + e_{00})^2} \\ &= [1 - m_\beta(1, 0)] \times m_\beta(1, 0) - [1 - m_\beta(0, 0)] \times m_\beta(0, 0) \end{aligned}$$

$$\frac{\partial}{\partial \beta_1} (m_\beta(1, 0) - m_\beta(0, 0)) = \frac{-(-e_{10})}{(1 + e_{10})^2} - 0 = [1 - m_\beta(1, 0)] \times m_\beta(1, 0)$$

$$\text{and } \frac{\partial}{\partial \beta_2} (m_\beta(1, 0) - m_\beta(0, 0)) = \frac{\partial}{\partial \beta_3} (m_\beta(1, 0) - m_\beta(0, 0)) = 0$$

$$\frac{\partial}{\partial \beta} (m_\beta(1, 0) - m_\beta(0, 0)) = \begin{pmatrix} [1 - m_\beta(1, 0)] \times m_\beta(1, 0) - [1 - m_\beta(0, 0)] \times m_\beta(0, 0) \\ [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ 0 \\ 0 \end{pmatrix} = \Delta$$

The variance of  $RD_{A_1|A_2=0}$  can then be calculated by:

$$\text{var} (RD_{A_1|A_2=0}) = \Delta^T \times \frac{\text{var}(IC)}{n} \times \Delta$$

### 3.2) Risk difference for the effect of $A_1$ , setting $A_2 = 1$

$$RD_{A_1|A_2=1} = m_\beta(1, 1) - m_\beta(0, 1) = \frac{1}{1 + e_{11}} - \frac{1}{1 + e_{01}}$$

where  $e_{11} = \exp(-\beta_0 - \beta_1 - \beta_2 - \beta_3)$  and  $e_{01} = \exp(-\beta_0 - \beta_2)$ .

The partial derivative of the risk difference  $m_\beta(1, 1) - m_\beta(0, 1)$  with respect to  $\beta$  is:

$$\frac{\partial}{\partial \beta} (m_\beta(1, 1) - m_\beta(0, 1)) = \frac{-\left(\frac{\partial e_{11}}{\partial \beta}\right)}{(1 + e_{11})^2} - \frac{-\left(\frac{\partial e_{01}}{\partial \beta}\right)}{(1 + e_{01})^2}$$

$$\begin{aligned} \frac{\partial}{\partial \beta_0} (m_\beta(1, 1) - m_\beta(0, 1)) &= \frac{-(-e_{11})}{(1 + e_{11})^2} - \frac{-(-e_{01})}{(1 + e_{01})^2} \\ &= [1 - m_\beta(1, 1)] \times m_\beta(1, 1) - [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \end{aligned}$$

$$\frac{\partial}{\partial \beta_1} (m_\beta(1, 1) - m_\beta(0, 1)) = \frac{-(-e_{11})}{(1 + e_{11})^2} - 0 = [1 - m_\beta(1, 1)] \times m_\beta(1, 1)$$

$$\begin{aligned} \frac{\partial}{\partial \beta_2} (m_\beta(1, 1) - m_\beta(0, 1)) &= \frac{-(-e_{11})}{(1 + e_{11})^2} - \frac{-(-e_{01})}{(1 + e_{01})^2} \\ &= [1 - m_\beta(1, 1)] \times m_\beta(1, 1) - [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \end{aligned}$$

$$\frac{\partial}{\partial \beta_3} (m_\beta(1, 1) - m_\beta(0, 1)) = \frac{-(-e_{11})}{(1 + e_{11})^2} - 0 = [1 - m_\beta(1, 1)] \times m_\beta(1, 1)$$

$$\frac{\partial}{\partial \beta} (m_\beta(1, 1) - m_\beta(0, 1)) = \begin{pmatrix} [1 - m_\beta(1, 1)] \times m_\beta(1, 1) - [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) - [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \end{pmatrix} = \Delta$$

The variance of  $RD_{A_1|A_2=1}$  can then be calculated by:

$$var(RD_{A_1|A_2=0}) = \Delta^T \times \frac{var(IC)}{n} \times \Delta$$

### 3.3) Risk difference for the effect of $A_2$ , setting $A_1 = 0$

$$RD_{A_2|A_1=0} = m_\beta(0, 1) - m_\beta(0, 0) = \frac{1}{1 + e_{01}} - \frac{1}{1 + e_{00}}$$

where  $e_{01} = \exp(-\beta_0 - \beta_2)$  and  $e_{00} = \exp(-\beta_0)$ .

The partial derivative of the risk difference  $m_\beta(0, 1) - m_\beta(0, 0)$  with respect to  $\beta$  is:

$$\frac{\partial}{\partial \beta} (m_\beta(0, 1) - m_\beta(0, 0)) = \frac{-\left(\frac{\partial e_{01}}{\partial \beta}\right)}{(1 + e_{01})^2} - \frac{-\left(\frac{\partial e_{00}}{\partial \beta}\right)}{(1 + e_{00})^2}$$

$$\begin{aligned} \frac{\partial}{\partial \beta_0} (m_\beta(0, 1) - m_\beta(0, 0)) &= \frac{-(-e_{01})}{(1 + e_{01})^2} - \frac{-(-e_{00})}{(1 + e_{00})^2} \\ &= [1 - m_\beta(0, 1)] \times m_\beta(0, 1) - [1 - m_\beta(0, 0)] \times m_\beta(0, 0) \end{aligned}$$

$$\frac{\partial}{\partial \beta_1} (m_\beta(0, 1) - m_\beta(0, 0)) = 0$$

$$\begin{aligned} \frac{\partial}{\partial \beta_2} (m_\beta(0, 1) - m_\beta(0, 0)) &= \frac{-(-e_{01})}{(1 + e_{01})^2} - 0 \\ &= [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \end{aligned}$$

$$\frac{\partial}{\partial \beta_3} (m_\beta(0, 1) - m_\beta(0, 0)) = 0$$

$$\frac{\partial}{\partial \beta} (m_\beta(0, 1) - m_\beta(0, 0)) = \begin{pmatrix} [1 - m_\beta(0, 1)] \times m_\beta(0, 1) - [1 - m_\beta(0, 0)] \times m_\beta(0, 0) \\ 0 \\ [1 - m_\beta(0, 1)] \times m_\beta(0, 1) \\ 0 \end{pmatrix} = \Delta$$

The variance of  $RD_{A_2|A_1=0}$  can then be calculated by:

$$var(RD_{A_2|A_1=0}) = \Delta^T \times \frac{var(IC)}{n} \times \Delta$$



### 3.4) Risk difference for the effect of $A_2$ , setting $A_1 = 1$

$$RD_{A_2|A_1=1} = m_\beta(1, 1) - m_\beta(1, 0) = \frac{1}{1 + e_{11}} - \frac{1}{1 + e_{10}}$$

where  $e_{11} = \exp(-\beta_0 - \beta_1 - \beta_2 - \beta_3)$  and  $e_{10} = \exp(-\beta_0 - \beta_1)$ .

The partial derivative of the risk difference  $m_\beta(1, 1) - m_\beta(1, 0)$  with respect to  $\beta$  is:

$$\frac{\partial}{\partial \beta} (m_\beta(1, 1) - m_\beta(1, 0)) = \frac{-\left(\frac{\partial e_{11}}{\partial \beta}\right)}{(1 + e_{11})^2} - \frac{-\left(\frac{\partial e_{10}}{\partial \beta}\right)}{(1 + e_{10})^2}$$

$$\begin{aligned} \frac{\partial}{\partial \beta_0} (m_\beta(1, 1) - m_\beta(1, 0)) &= \frac{-(-e_{11})}{(1 + e_{11})^2} - \frac{-(-e_{10})}{(1 + e_{10})^2} \\ &= [1 - m_\beta(1, 1)] \times m_\beta(1, 1) - [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \end{aligned}$$

$$\begin{aligned} \frac{\partial}{\partial \beta_1} (m_\beta(1, 1) - m_\beta(1, 0)) &= \frac{-(-e_{11})}{(1 + e_{11})^2} - \frac{-(-e_{10})}{(1 + e_{10})^2} \\ &= [1 - m_\beta(1, 1)] \times m_\beta(1, 1) - [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \end{aligned}$$

$$\begin{aligned} \frac{\partial}{\partial \beta_2} (m_\beta(1, 1) - m_\beta(1, 0)) &= \frac{-(-e_{11})}{(1 + e_{11})^2} - 0 \\ &= [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \end{aligned}$$

$$\begin{aligned} \frac{\partial}{\partial \beta_3} (m_\beta(1, 1) - m_\beta(1, 0)) &= \frac{-(-e_{11})}{(1 + e_{11})^2} - 0 \\ &= [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \end{aligned}$$

$$\frac{\partial}{\partial \beta} (m_\beta(1, 1) - m_\beta(1, 0)) = \begin{pmatrix} [1 - m_\beta(1, 1)] \times m_\beta(1, 1) - [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) - [1 - m_\beta(1, 0)] \times m_\beta(1, 0) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \\ [1 - m_\beta(1, 1)] \times m_\beta(1, 1) \end{pmatrix} = \Delta$$

The variance of  $RD_{A_2|A_1=1}$  can then be calculated by:

$$\text{var} (RD_{A_2|A_1=1}) = \Delta^T \times \frac{\text{var}(IC)}{n} \times \Delta$$

## 4) Standard errors of relative risks

### 4.1) Relative risk for the effect of $A_1$ , setting $A_2 = 0$

Applying a log transformation of the relative risk,

$$\log RR_{A_1|A_2=0} = \log \frac{m_\beta(1,0)}{m_\beta(0,0)} = \log m_\beta(1,0) - \log m_\beta(0,0)$$

and the variance of  $\log RR$  is:

$$var(\log RR) = \left( \frac{\partial \log RR}{\partial \beta} \right)^T \times var(\beta) \times \left( \frac{\partial \log RR}{\partial \beta} \right)$$

With  $p = \frac{1}{1+e}$ , we have:  $(\log p)' = \frac{p'}{p} = \frac{-e'}{(1+e)^2} \times (1+e) = \frac{-e'}{1+e}$

where  $e_{00} = \exp(-\beta_0)$  and  $e_{10} = \exp(-\beta_0 - \beta_1)$ .