

# Mediation analysis with a binary outcome

August 7, 2023

Denote by  $Y$  an outcome,  $M$  a mediator,  $E$  an exposure, and  $C$  possible confounders (between  $Y$  and  $E$ , or  $Y$  and  $M$ , or  $E$  and  $M$ ).

- $Y(e, m) = Y(e, m, c)$  will be the counterfactual outcome, i.e. the outcome value had the exposure be set to  $e$ , the mediator to  $m$ , and the confounder set to  $c$ .
- $M(e) = M(e, c)$  will be the counterfactual mediator, i.e. the mediator value had the exposure be set to  $e$  and the confounder set to  $c$ .

We define (all at a fixed confounder value  $c$ ):

- the total effect as  $Y(e, M(e)) - Y(e^*, M(e^*))$
- the natural direct effect as  $Y(e, M(e)) - Y(e^*, M(e))$
- the indirect direct effect as  $Y(e^*, M(e)) - Y(e^*, M(e^*))$

## 1 Theory

We consider the following models:

$$\begin{aligned}\text{logit}(\mathbb{P}[Y = 1|E, M, C]) &= \beta_0 + \beta_1 E + \beta_2 M + \beta_3 C \\ \mathbb{E}[M|E, C] &= \alpha_0 + \alpha_1 E + \alpha_3 C\end{aligned}$$

Therefore the counterfactual probability can be expressed as:

$$\begin{aligned}Y(e, M(e^*), c) &= \frac{1}{1 + \exp^{-\beta_0 - \beta_1 e - \beta_2 M(e^*) + \beta_3 c}} \\ &= \frac{1}{1 + \exp^{-(\beta_0 + \beta_2 \alpha_0) - (\beta_1 e + \beta_2 \alpha_1 e^*) + (\beta_3 + \beta_2 \alpha_3) c}} \\ \text{logit}(\mathbb{P}[Y(e, M(e^*), c)]) &= (\beta_0 + \beta_2 \alpha_0) + (\beta_1 e + \beta_2 \alpha_1 e^*) + (\beta_3 + \beta_2 \alpha_3) c\end{aligned}$$

So the odd for the total effect is:

$$OR^{TE} = \frac{\mathbb{P}[Y(e, M(e))] / \mathbb{P}[Y(e, M(e))]}{\mathbb{P}[Y(e^*, M(e^*))] / \mathbb{P}[Y(e^*, M(e^*))]} = \exp((\beta_1 + \beta_2 \alpha_1)(e - e^*))$$

for the natural direct effect:

$$OR^{NDE} = \frac{\mathbb{P}[Y(e, M(e))] / \mathbb{P}[Y(e, M(e^*))]}{\mathbb{P}[Y(e^*, M(e))] / \mathbb{P}[Y(e^*, M(e^*))]} = \exp(\beta_1(e - e^*))$$

for the natural indirect effect:

$$OR^{NIE} = \frac{\mathbb{P}[Y(e^*, M(e))] / \mathbb{P}[Y(e^*, M(e^*))]}{\mathbb{P}[Y(e^*, M(e))] / \mathbb{P}[Y(e^*, M(e^*))]} = \exp(\beta_2\alpha_1(e - e^*))$$

This matches formula in [VanderWeele and Vansteelandt \(2010\)](#)

Note that we can also express the total effect, natural direct effect, and natural indirect effect on the probability scale, e.g.:

$$\begin{aligned} & \mathbb{P}[Y(e, M(e), c) = 1] - \mathbb{P}[Y(e^*, M(e), c) = 1] \\ &= \frac{1}{1 + \exp^{-(\beta_0 + \beta_2\alpha_0) - (\beta_1 e + \beta_2\alpha_1 e) + (\beta_3 + \beta_2\alpha_3)c}} - \frac{1}{1 + \exp^{-(\beta_0 + \beta_2\alpha_0) - (\beta_1 e^* + \beta_2\alpha_1 e) + (\beta_3 + \beta_2\alpha_3)c}} \end{aligned}$$

which will be a function of the confounder value. To get a single estimate we could average it out over the confounder distribution in our population.

## 2 In

```
library(medflex)
data(UPBdata)
head(UPBdata)
sum(is.na(UPBdata))
```

```
      att attbin attcat      negaff initiator gender educ age UPB
1  1.0005617      1      M  0.8404610    myself      F      M  41   1
2 -0.7085889      0      L -1.2574650      both      M      M  42   0
3 -0.7085889      0      L -1.2022564      both      F      H  43   0
4  0.6061423      1      M -0.3741277 ex-partner      M      H  52   1
5  0.2117230      1      M  1.9446325 ex-partner      M      M  32   1
6  2.0523467      1      H -0.8157964 ex-partner      M      H  47   0
[1] 0
```

Manually

```
e.lm <- glm(negaff ~ factor(attbin) + gender + educ + age, data = UPBdata)
e.logit <- glm(UPB ~ attbin + negaff + gender + educ + age, family =
  binomial("logit"), data = UPBdata)
```

```
exp(coef(e.logit)["attbin"])
exp(coef(e.logit)["negaff"]*coef(e.lm)["factor(attbin)1"])
```

## Using Medflex

```
exp(cbind(estimate = coef(neMod1), confint(neMod1))[c("attbin01", "attbin11"), ])
```

```
e.lm <- glm(negafl ~ factor(attbin), data = UPBdata)
e.logit <- glm(UPB ~ attbin + negafl, family = binomial("logit"), data =
  UPBdata)
```

```
attbin
1.541862
negaff
1.430096
```

```
expData <- neWeight(negaiff ~ factor(attbin), family = gaussian, data =
  UPBdata)
neMod1 <- neModel(UPB ~ attbin0 + attbin1, family = binomial("logit"),
  expData = expData)
exp(cbind(estimate = coef(neMod1), confint(neMod1))[c("attbin01", "attbin11"), ])
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attbin01 1.467847 0.9419685 2.253654
attbin11 1.437643 1.2003462 1.711461

```

```

expData <- neImpute(UPB ~ factor(attbin) + negaff + gender + educ + age,
  family = binomial("logit"), data = UPBdata)
neMod1 <- neModel(UPB ~ attbin0 + attbin1 + gender + educ + age, family =
  binomial("logit"), expData = expData, se = "robust")
exp(cbind(estimate = coef(neMod1), confint(neMod1))[c("attbin01", "attbin11"), ])

```

```

      estimate    95% LCL  95% UCL
attbin01 1.494111 0.9833185 2.270238
attbin11 1.405922 1.2006238 1.646326

```

### 3 References

VanderWeele, T. J. and Vansteelandt, S. (2010). Odds ratios for mediation analysis for a dichotomous outcome. *American journal of epidemiology*, 172(12):1339–1348.