Flexible models for causal mediation analysis: an introduction to the R package medflex

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Illustrating example

What Triggers Public Opposition to Immigration? Anxiety, Group Cues, and Immigration Threat

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We examine whether and how elite discourse shapes mass opinion and action on immigration policy. One popular but untested suspicion is that reactions to news about the costs of immigration depend upon who the immigrants are. *We confirm this suspicion in a nationally representative experiment: news about the costs of immigration boosts white opposition far more when Latino immigrants, rather than European immigrants, are featured. We find these group cues influence opinion and political action by triggering emotions—in particular, anxiety—not simply by changing beliefs about the severity of the immigration problem. A second experiment replicates these findings but also confirms their sensitivity to the stereotypic consistency of group cues and their context. While these results echo recent insights about the power of anxiety, they also suggest the public is susceptible to error and manipulation when group cues trigger anxiety independently of the actual threat posed by the group.*

American Journal of Political Science, Vol. 52, No. 4, October 2008, Pp. 959–978

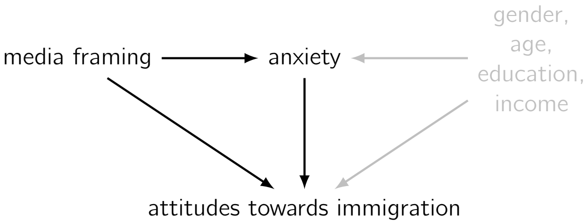
Illustrating example

The web-based platform allows us to deliver stimuli matching those in actual news coverage. The study employed a 2 × 2 design with a control group. We manipulated the ethnic cue by altering the picture and name of an immigrant (white European versus Latino) featured in a mock *New York Times* report about a governors' conference on immigration.[3] We also manipulated the tone of the story, focusing either on the positive consequences of immigration for the nation (e.g., strengthening the economy, increasing tax revenues, enriching American culture) or the negative consequences (e.g., driving down wages, consuming public resources, undermining American values). Tone was also manipulated by portrayal of governors as either glad or concerned about immigration and citizens who had had either positive or negative interactions with immigrants.[4] Every story stated that immigration to the United States is increasing and will continue to do so.[5]

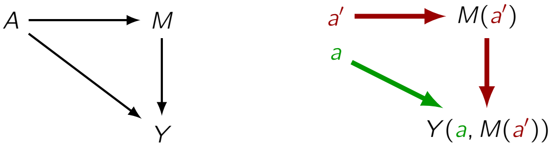
EMOTIONS. "Now, moving on, we would like to know how **you feel** about **increased immigration**. The following questions will ask you how you feel when you think about the high levels of immigration to this country. How [**anxious** (that is, uneasy)/**proud/angry/hopeful/worried/excited**] does it make you feel?" (Very, somewhat, a little, or not at all?)

OPINIONS. *Immigration*: "Do you think the number of immigrants from foreign countries who are permitted to come to the United States to live should be increased a lot, increased a little, left the same as it is now, decreased a little, or decreased a lot?" *English Only*: "Do you favor a law

Causal DAG of a stripped-down example



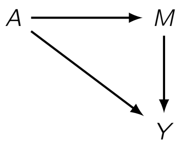
Introducing nested counterfactuals $Y(a, M(a'))$

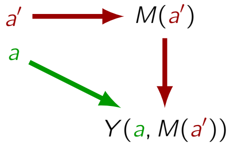


$M(a')$	mediator level that would have been observed had A (possibly contrary to the fact) been set to a'
$Y(a, M(a'))$	outcome that would have been observed had A been set to a and M to $M(a')$

=> conceptualize the intuitive notion of **changing treatment assignment along specific pathways** but not others

Introducing nested counterfactuals $Y(a, M(a'))$





=> provide a framework that allows for **generic effect decomposition** into **natural** direct and indirect effects, irrespective of non-linearities

$$\underbrace{E\{Y(1) - Y(0)\}}_{\text{total effect}} = \underbrace{E\{Y(\mathbf{1}, M(0)) - Y(\mathbf{0}, M(0))\}}_{\text{pure direct effect = NDE(0)}} + \underbrace{E\{Y(1, M(\mathbf{1})) - Y(1, M(\mathbf{0}))\}}_{\text{total indirect effect = NIE(1)}}$$

$$= \underbrace{E\{Y(\mathbf{1}, M(1)) - Y(\mathbf{0}, M(1))\}}_{\text{total direct effect = NDE(1)}} + \underbrace{E\{Y(0, M(\mathbf{1})) - Y(0, M(\mathbf{0}))\}}_{\text{pure indirect effect = NIE(0)}}$$

Parameterization using natural effect models

Extension of marginal structural models for mean nested counterfactuals that allow for decomposition of a causal effect along multiple pathways

Natural effect model, e.g.,

$$E\{Y(a, M(a'))\} = \eta_0 + \eta_1 a + \eta_2 a' + \eta_3 a a'$$

$$\underbrace{E\{Y(1) - Y(0)\}}_{\text{total effect}} = \underbrace{E\{Y(\mathbf{1}, M(0)) - Y(\mathbf{0}, M(0))\}}_{\text{pure direct effect = NDE(0)}} \qquad \eta_1$$

$$+ \underbrace{E\{Y(1, M(\mathbf{1})) - Y(1, M(\mathbf{0}))\}}_{\text{total indirect effect = NIE(1)}} \qquad \eta_2 + \eta_3$$

$$= \underbrace{E\{Y(\mathbf{1}, M(1)) - Y(\mathbf{0}, M(1))\}}_{\text{total direct effect = NDE(1)}} \qquad \eta_1 + \eta_3$$

$$+ \underbrace{E\{Y(0, M(\mathbf{1})) - Y(0, M(\mathbf{0}))\}}_{\text{pure indirect effect = NIE(0)}} \qquad \eta_2$$

Wait, hang on a second...

How can we fit this kind of model when most of the outcomes are missing?

	A	$M(1)$	$M(0)$	$Y(1, M(1))$	$Y(0, M(1))$	$Y(1, M(0))$	$Y(0, M(0))$
1	1	M_1		Y_1			
2	1	M_2		Y_2			
$\vdots$	$\vdots$	$\vdots$		$\vdots$			
	$\vdots$		$\vdots$				$\vdots$
n	0		M_n				Y_n

=> by resorting to established missing data methods

Weighting-based approach

	A	$M(1)$	$M(0)$	$Y(1, M(1))$	$Y(0, M(1))$	$Y(1, M(0))$	$Y(0, M(0))$
1	1	M_1		Y_1		$w_1 Y_1$	
2	1	M_2		Y_2		$w_2 Y_2$	
$\vdots$	$\vdots$	$\vdots$		$\vdots$		$\vdots$	
	$\vdots$		$\vdots$		$\vdots$		$\vdots$
n	0		M_n		$w_n Y_n$		Y_n

Key idea Up- (or down)-weight individuals whose observed mediator level is more (less) typical for the other treatment group

such that, for each treatment group, we can construct a pseudo-population with mediator levels that would have been observed if each subject had been assigned to the other treatment arm. This can be achieved by weighing each observation (in an extended data set) by

$$\frac{\Pr(M = M_i | A = a', C_i)}{\Pr(M = M_i | A = a, C_i)} = \frac{\Pr(M = M_i | A = a', C_i)}{\Pr(M = M_i | A_i, C_i)}.$$

Imputation-based approach

	A	$M(1)$	$M(0)$	$Y(1, M(1))$	$Y(0, M(1))$	$Y(1, M(0))$	$Y(0, M(0))$
1	1	M_1		Y_1	$\hat{Y}_1(0, M_1(1))$		
2	1	M_2		Y_2	$\hat{Y}_2(0, M_2(1))$		
$\vdots$	$\vdots$	$\vdots$		$\vdots$	$\vdots$		
	$\vdots$		$\vdots$			$\vdots$	$\vdots$
n	0		M_n			$\hat{Y}_n(1, M_n(0))$	Y_n

Key idea $M_i(a') = M_i$ if $A_i = a' \Rightarrow Y_i(a, M_i(a')) = Y_i(a, M_i)$

Then (under sufficient causal assumptions) $Y_i(a, M_i(a'))$ can be imputed by fitted values from any appropriate model for $E(Y_i|A = a, M_i, C_i)$, that is, by the expected outcome one would have observed if subject i had been assigned to treatment $A = a$ instead of $A = a'$, but her mediator level would have remained unaltered.

Fitting natural effect models made easy in R

medflex: an R package that...

=> aids applied researchers to fit natural effect models

=> provides lots of convenience functions to simplify reporting and hypothesis testing

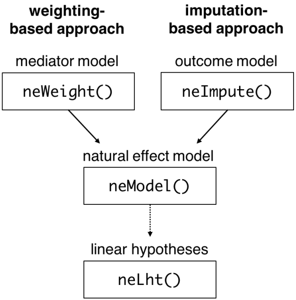


Figure: The medflex workflow

Fitting natural effect models made easy in R

=> medflex 0.6-1 freely available from CRAN:
`https://cran.r-project.org/web/packages/medflex/index.html`

```
install.packages('medflex')
```

=> development release 0.6-2 available from github:
`https://github.com/jmpsteen/medflex`

```
devtools::install_github('jmpsteen/medflex')
```

=> companion paper in Journal of Statistical Software:
`https://www.jstatsoft.org/article/view/v076i11`

Weighting in practice

First 'replicate' the data along unobserved (a, a') combinations (with $A = a$)

	A	a	a'	$M(a')$	$Y(a, M(a'))$
1	1	1	1	M_1	Y_1
2	1	1	1	M_2	Y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
n	0	0	0	M_n	Y_n

Weighting in practice

First 'replicate' the data along unobserved (a, a') combinations (with $A = a$)

	A	a	a'	$M(a')$	$Y(a, M(a'))$
1	1	1	1	M_1	Y_1
1	1	1	**0**	M_1	.
2	1	1	1	M_2	Y_2
2	1	1	**0**	M_2	.
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
n	0	0	0	M_n	Y_n
n	0	0	**1**	M_n	.

Then regress the observed outcomes Y, weighed by

$$\frac{\Pr(M = M_i | A = a', C)}{\Pr(M = M_i | A = a, C)}.$$

Weighting in medflex

`neWeight`:
wrapper of `glm` function that

1. **fits** a model for the mediator density $\Pr(M|A, C)$
2. **replicates** data along unobserved (a, a') combinations (with $A = a$)
3. **calculates** weights $\dfrac{\hat{\Pr}(M|A = a', C)}{\hat{\Pr}(M|A = a, C)}$ for these combinations

```
library(medflex)
weightData <- neWeight(anxiety ~ factor(treat) + ..., data = framing)
head(data.frame(weightData, weights = weights(weightData)))
```

```
##   id treat0 treat1 anxiety immigr   weights
## 1  1      0      0       2      4 1.0000000
## 2  1      0      1       2      4 1.1897101
## 3  2      0      0       3      3 1.0000000
## 4  2      0      1       3      3 0.9799741
## 5  3      0      0       2      3 1.0000000
## 6  3      0      1       2      3 1.1476039
```

Imputing in practice

Again 'replicate' the data along unobserved (a, a') combinations (with $A = a'$)

	A	a	a'	$M(a')$	$Y(a, M(a'))$
1	1	1	1	M_1	Y_1
2	1	1	1	M_2	Y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
n	0	0	0	M_n	Y_n

Imputing in practice

Again 'replicate' the data along unobserved (a, a') combinations (with $A = a'$)

	A	a	a'	$M(a')$	$Y(a, M(a'))$
1	1	1	1	M_1	Y_1
1	1	**0**	1	M_1	$\hat{Y}_1(\mathbf{0}, M_1(1))$
2	1	1	1	M_2	Y_2
2	1	**0**	1	M_2	$\hat{Y}_2(\mathbf{0}, M_2(1))$
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
n	0	0	0	M_n	Y_n
n	0	**1**	0	M_n	$\hat{Y}_n(\mathbf{1}, M_n(0))$

Then regress imputed counterfactual outcomes $\hat{Y}(a, M(a'))$

Imputing in medflex

`neImpute`:
wrapper of `glm` function that

1. **fits** a model for the outcome mean $E(Y|A, M, C)$
2. **replicates** data along unobserved (a, a') combinations (with $A = a'$)
3. **imputes** counterfactuals by $\hat{E}(Y|A = a, M, C)$ for these combinations

```
impData <- neImpute(immigr ~ factor(treat) + anxiety + ...,
                    data = framing)
head(impData)
```

```
##   id treat0 treat1 anxiety   immigr
## 1  1      0      0       2 3.633748
## 2  1      1      0       2 3.884263
## 3  2      0      0       3 2.853889
## 4  2      1      0       3 3.104404
## 5  3      0      0       2 2.749488
## 6  3      1      0       2 3.000004
```

Fitting natural effect models in medflex

`neModel`:
Both `neWeight` and `neImpute` return an extended data set that readily enables estimation of natural effects by **fitting a natural effect model**, e.g.,

$$E\{Y(a, M(a'))\} = \eta_0 + \eta_1 a + \eta_2 a'$$

either by

=> **weighted** regression of observed outcomes Y

$$E\left[Y \frac{\Pr(M|A=a', C)}{\Pr(M|A=a, C)} \middle| A=a\right]$$

```
neModW <- neModel(immigr ~ treat0 + treat1,
                  expData = weightData, se = "robust")
```

=> regression of **imputed** outcomes $\hat{E}(Y|A=a, M, C)$

$$E\left[E(Y|A=a, M, C)|A=a'\right]$$

```
neModI <- neModel(immigr ~ treat0 + treat1,
                  expData = impData, se = "robust")
```

Connection with the mediation formula

Both weighting- and imputation-based approaches can be considered to lead to alternative formulations of the mediation formula, i.e.

$$
\begin{aligned}
& E\{Y(a, M(a'))|C\} \\
& = \sum_m E(Y|A = a, M = m, C)\mathrm{Pr}(M = m|A = a', C) \\
& = E\left[Y \frac{\mathrm{Pr}(M|A = a', C)}{\mathrm{Pr}(M|A = a, C)}\middle| A = a, C\right] = E\left[E(Y|A = a, M, C)|A = a', C\right]
\end{aligned}
$$

Unlike direct application of the mediation formula, which requires correct specification of both a mediator density model (i) and a model for the outcome mean (ii), the weighting- and imputation-based formulations require only a single correctly specified working model (either (i) or (ii), respectively).

Equivalence under strict linearity

Closed-form expressions for natural direct and indirect effects in terms of parameters of these strictly linear working models

$$E(M|A, C) = \beta_0 + \beta_1 A + \beta_2 C \qquad \text{(i)}$$

$$E(Y|A, M, C) = \theta_0 + \theta_1 A + \theta_2 M + \theta_3 C \qquad \text{(ii)}$$

can be obtained by plugging these working models in the mediation formula

$$\begin{aligned}
E\{Y(a, M(a'))|C\} &= \sum_m E(Y|A = a, M = m, C) \Pr(M = m|A = a', C) \\
&= \sum_m (\theta_0 + \theta_1 a + \theta_2 m + \theta_3 C) \Pr(M = m|A = a', C) \\
&= \theta_0 + \theta_1 a + \theta_2 E(M|A = a', C) + \theta_3 C \\
&= \theta_0 + \theta_1 a + \theta_2(\beta_0 + \beta_1 a' + \beta_2 C) + \theta_3 C \\
&= (\theta_0 + \theta_2\beta_0) + \theta_1 a + \theta_2\beta_1 a' + (\theta_3 + \theta_2\beta_2) C
\end{aligned}$$

Equivalence under strict linearity

$$E\{Y(a, M(a'))|C\} = (\theta_0 + \theta_2\beta_0) + \theta_1 a + \theta_2\beta_1 a' + (\theta_3 + \theta_2\beta_2)C$$

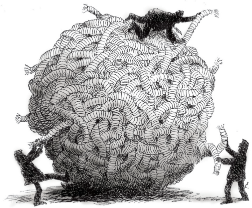
This corresponds with a natural effect model specification

$$E\{Y(a, M(a'))|C\} = \delta_0 + \delta_1 a + \delta_2 a' + \delta_3 C,$$

where $\delta_1 = \theta_1$ and $\delta_2 = \theta_2\beta_1$. Note that under strict linearity, we obtain the well-known LSEM plug-in estimators for the direct and indirect effect (i.e. product-of-coefficients)

However, linearity rarely applies in practice...

Beyond linear settings...



As soon as non-linearities enter the picture things get much more complex as (even simple) working models (i) and (ii) don't usually combine into a simple natural effect model; or at least, it's difficult to specify (i) and (ii) in such a way that they combine into a natural effect model with a simple structure.

A toy example

Suppose that we allow treatment and mediator to interact in their effect on the outcome (in order to allow for mediated interaction), i.e. we specify working model (ii) as

$$E(Y|A, M, C) = \theta_0 + \theta_1 A + \theta_2 M + \theta_3 AM + \theta_4 C.$$

Combined with (i), this yields

$$\begin{aligned}
E\{Y(a, M(a'))|C\} &= \sum_m (\theta_0 + \theta_1 a + (\theta_2 + \theta_3 a)m + \theta_4 C)\Pr(M = m|A = a', C) \\
&= \theta_0 + \theta_1 a + (\theta_2 + \theta_3 a)E(M|A = a', C) + \theta_4 C \\
&= \theta_0 + \theta_1 a + (\theta_2 + \theta_3 a)(\beta_0 + \beta_1 a' + \beta_2 C) + \theta_4 C \\
&= (\theta_0 + \theta_2\beta_0) + (\theta_1 + \theta_3\beta_0)a + \theta_2\beta_1 a' + (\theta_3\beta_1)aa' \\
&\qquad + (\theta_4 + \theta_2\beta_2)C + (\theta_3\beta_2)aC,
\end{aligned}$$

which involves effect modification by C, even though such modification was never postulated in (i) nor (ii). It turns out difficult to come up with combinations of working models (i) and (ii) that do not result in effect expressions that vary across levels of C while still allowing for treatment-mediator interaction.

The appeal of natural effect modeling

It may therefore be more attractive to prioritize parameterization of the natural effects of interest and, if necessary, refine the corresponding natural effect model until it yields a good model fit.

=> **alleviates modeling demands** (as only (i) or (ii) needs to be (correctly) specified) and may thus reduce risk of modeling bias

=> no more need to derive closed-form expressions for each specific combination of (i) or (ii)

=> may offer an **alternative to computer-intensive Monte Carlo integration** (such as implemented in the mediation R package), which has been suggested to deal with intractable effect expressions (whenever sandwich variance estimator is available for inference)

=> offers an **elegant framework for hypothesis testing**, i.e. hypotheses of interest can be captured by (a linear combination of) targeted model parameters

=> imposing **parsimonious model structures** may be helpful in more complex settings, especially for extensions to multiple (causally ordered) mediators